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Epidemiology of operation-related medical errors in inpatients in Japan: the JET study

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P1

Cerebral autoregulation testing in a porcine model of intravenously administrated *E. coli* induced fulminant sepsis

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Critical Care 2015, **19(Suppl 1):**P1 (doi: 10.1186/cc14081)

Introduction To assess cerebral hemodynamics in an experimental sepsis model.
Methods Nineteen juvenile female Hungahib pigs were subjected into control group ($n = 9$) or septic group ($n = 10$). Under general anesthesia in animals of the sepsis group, *Escherichia coli* culture (2.5×10^5/ml; strain: ATCC 25922) was intravenously administrated in a continuously increasing manner as follows: 2 ml in the first 30 minutes, then 4 ml in 30 minutes and afterwards 16 ml/hour for 2 hours (so a total of 9.5×10^6 *E. coli* within 3 hours). In the control group the anesthesia was maintained for 8 hours, infusion was administered as a similar volume of isotonic saline solution and no other intervention was made. Hemodynamic monitoring of all animals was performed by PiCCo monitoring system. The middle cerebral artery of the pigs was insonated through the transorbital window and cerebral blood flow velocity (MCAV) and pulsatility index was registered.
Results In the septic group, as expected, all animals developed fulminant sepsis and died within 3 to 7 hours two animals in 3 to 4 hours, and three in 6 to 7 hours). In the septic animals the heart rate rose and mean arterial pressure dropped, their ratio increased significantly compared with both the base values (at the 6th hour: $P < 0.001$) and the control group ($P = 0.004$). The control animals showed stable condition over the 8-hour anesthesia. MCAV significantly decreased during the development of sepsis (from 23.6 ± 6.6 cm/s to 16.0 ± 3.9 cm/s, $P < 0.01$) and pulsatility indices increased (from 0.68 ± 0.22 to 1.37 ± 0.58, $P < 0.01$), indicating vasoconstriction of the resistance vessels. A significant relationship was fund between percent change of the MAP and the pulsatility index in septic animals ($R^2 = 0.32$) referring to maintained cerebral autoregulation.
Conclusion Cerebral autoregulation is preserved in the pig model of experimentally induced fulminant sepsis.

P2

New real-time bowel sound analysis may predict disease severity in septic patients

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Critical Care 2015, **19(Suppl 1):**P2 (doi: 10.1186/cc14082)

Introduction Healthy bowel function is an important factor when judging the advisability of early enteral nutrition in critically ill patients, but long-term observation and objective evaluation of gastrointestinal motility are difficult. We developed a non-invasive monitoring system capable of quantifying and visualizing gastrointestinal motility in real time. In the study gastrointestinal motility was performed in patients with severe sepsis using this developed bowel sound analysis system, and the correlation between bowel sounds and changes over time in blood concentrations of IL-6, which is associated with sepsis severity, was evaluated.
Methods The study was a prospective, observational pilot study conducted in our hospital. Consecutive adult patients with severe sepsis, on a mechanical ventilator with an IL-6 blood concentration ≥100 pg/ml in the acute phase, defined as being up to the 28th day of illness in the ICU, were entered in this study between June 2011 and December 2012. Subjects were divided into those who were treated with steroids (steroid treatment group) and those who were not (no-steroids group) during the target period, because steroids strongly affect IL-6 blood levels.
Results The subjects were five adult patients in the acute phase of severe sepsis on a mechanical ventilator. Gastrointestinal motility was measured for a total of 62,399 minutes: 31,544 minutes in three subjects in the no-steroids group and 30,855 minutes in two subjects in the steroid treatment group. In the no-steroids group, the bowel sound counts were negatively correlated with IL-6 blood concentration ($r = -0.76$, $P < 0.01$), suggesting that gastrointestinal motility was suppressed as IL-6 blood concentration increased. However, in the steroid treatment group, gastrointestinal motility showed no correlation with IL-6 blood concentration ($r = -0.25$, $P = 0.27$). The IL-6 blood concentration appears to have decreased with steroid treatment irrespective of changes in the state of sepsis, whereas bowel sound counts with the monitoring system reflected the changes in the state of sepsis, resulting in no correlation.
Conclusion The new real-time bowel sound analysis system provides a useful method of continuously, quantitatively, and non-invasively evaluating gastrointestinal motility in severe patients. Furthermore, this analysis may predict disease severity in septic patients.

P3

Usefulness of sepsis screening tools and education in recognising the burden of sepsis on hospital wards

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Critical Care 2015, **19(Suppl 1):**P3 (doi: 10.1186/cc14083)

Introduction Sepsis is defined as the presence of infection with systemic signs of infection, and severe sepsis as sepsis plus sepsis-induced organ dysfunction or tissue hypoperfusion [1]. Since the Surviving Sepsis Campaign (SSC) in 2002, the Health Service Ombudsman for England published recommendations for improving recognition and treatment of sepsis [2], the Royal College of Physicians issued a toolkit for the management of sepsis in the acute medical unit [3], and NHS England released a patient safety alert to support prompt recognition and treatment of sepsis [4]. In 2012 our Trust introduced a sepsis screening

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tool and electronic order set (EPR alert) alongside an education programme to improve delivery of the SSC bundle. Previous audits showed only 43% full bundle compliance in those that were alerted, and this raised concerns regarding the burden of unalerted sepsis. We sought to estimate the number of unalerted sepsis episodes to assess the efficacy of our screening tool and improve early recognition.

Methods All referrals to our critical care response team with a diagnosis of sepsis over a 3-month period (September to November 2014) were investigated to determine how many had an EPR sepsis alert comprising a prompt for blood cultures, serum lactate measurement, fluid challenge if hypotensive, and antibiotics within 1 hour.

Results Only 25/174 (14%) patients with a diagnosis of sepsis had an EPR sepsis alert. There was no significant difference between acute and nonacute ward areas in their likelihood of using the screening tool or alert, in contrast to previous audits of the alerted population which showed that acute areas such as A&E and medical acute admission wards had higher utilisation and bundle completion rates.

Conclusion Despite these interventions, most patients still do not receive the full recommended treatment bundle. These findings have prompted a point prevalence audit at ward level, which will examine all patients' notes for the preceding 24 hours to ascertain if sepsis is truly unrecognised or whether it is simply that our current tool is not a helpful adjunct to care. With national guidelines expected within the year, we will redesign and re-launch our screening tools and education programme to improve awareness and management of this common medical emergency.

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P4

Continuous versus intermittent temperature measurement in the detection of fever in critically ill patients

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Critical Care 2015, **19(Suppl 1):**P4 (doi: 10.1186/cc14084)

Introduction An elevated body temperature is one of the four criteria in diagnosing systemic inflammatory response syndrome (SIRS), and is often used at the bedside to trigger diagnostic investigations for infection. Standard intermittent temperature measurement may, however, delay the detection of an elevated temperature or miss this altogether. The aim of the study is to compare intermittent non-invasive versus continuous invasive body temperature measurement as a tool to detect an elevated body temperature.

Methods This was a secondary analysis of a prospective study in 25 critically ill patients comparing different measurement techniques. Temperature was measured intermittently with an axillary digital thermometer every 4 hours, and a urinary bladder thermistor catheter was used for continuous temperature measurement; the latter was considered the reference method. Fever (core temperature ≥38.3°C) episodes occurring within 60 minutes after each other were classified as one episode. We compared the fever detection rate of both methods and calculated the difference in timing between both techniques.

Results Twenty-nine episodes of fever were detected in 10 patients (seven male) with a median APACHE II score of 10 (IQR 3 to 24) and a median SOFA score of 10 (IQR 8 to 11). Median duration of a fever episode was 1 hour 24 minutes (IQR 47 minutes to 2 hours 59 minutes) and median maximum temperature was 38.4°C (IQR 38.3 to 38.7). Median axillary temperature was 0.7°C (IQR 0.3 to 0.9) lower than core temperature. Using intermittent, non-invasive measurement, 27 out of 29 fever episodes (93.1%) remained undetected.

Conclusion Intermittent, non-invasive temperature measurement failed to detect most of the fever episodes as measured by a bladder thermistor catheter and should not be used to screen for elevated body temperature in critically ill patients.

P5

Audit of strategies to improve sepsis management in emergency departments

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Critical Care 2015, **19(Suppl 1):**P5 (doi: 10.1186/cc14085)

Introduction Severe sepsis results in ~36,800 UK deaths each year [1]. Prior studies demonstrate the benefit of early recognition and treatment of sepsis in reducing mortality [2]. The Sepsis Six [1] bundle aims to optimise the first hour of sepsis management. We assessed the proportion of emergency department (ED) patients with severe sepsis receiving the Sepsis Six bundle and whether this was improved by a combination of staff education and use of Sepsis Six management stickers in patient notes.

Methods A closed loop audit was completed in the ED at Ipswich Hospital, UK. Each cycle was 14 days with interventions made in a 4-week period between the two cycles. The interventions consisted of: Sepsis Six management stickers and posters placed in the ED; two training sessions for all ED nurses on sepsis recognition and management; a teaching session for all middle-grade doctors; and a trolley in the ED with equipment required for the Sepsis Six. The notes of all patients with lactate ≥2 mmol/l were retrospectively reviewed. Those with ≥2 systemic inflammatory response syndrome criteria and a documented suspicion of infection were deemed to have severe sepsis. The times at which these patients had each of the Sepsis Six completed were recorded, as were the final diagnosis and 7/28 day mortality.

Results In Cycle 1, 31/106 patients met the criteria for severe sepsis, compared with 36/120 in Cycle 2. The delivery of the Sepsis Six interventions was highly variable. In Cycle 1 lactate levels and i.v. access had the highest 60-minute completion rates (90.3%, 83.9% respectively). Blood cultures and i.v. fluid resuscitation were completed for 61.3% and 64.5% of patients within 60 minutes. Only 38.7% of septic patients were given i.v. antibiotics within 60 minutes. In total, 58.9% of patients received antibiotics in accordance with trust guidelines. High flow oxygen, catheters and fluid balance charts had the lowest 60-minute completion rates (35.5%, 6.5%, 6.5% respectively). In Cycle 2, post intervention, there was no significant change in the percentage of patients receiving the Sepsis Six bundle.

Conclusion The low rates of Sepsis Six completion require improvement to meet the targets set out by the College of Emergency Medicine. Our results suggest that simple interventions are ineffective in increasing Sepsis Six completion and thus lend support to the case for integrated interventions such as electronic recording and alert systems.

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P6

Systemic symptoms as markers for severity in sepsis

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Critical Care 2015, **19(Suppl 1):**P6 (doi: 10.1186/cc14086)

Introduction The objective of this study was to evaluate six general symptoms as markers for severe sepsis in patients with suspected bacterial infections. Severe sepsis is a common cause of death and morbidity. Early detection and treatment is critical for outcome. Clinical presentation varies widely and no single test is able to discriminate severe sepsis from uncomplicated infections or non-infectious emergencies. Apart from local symptoms of infection, the systemic inflammatory reaction itself may give rise to general symptoms such as muscle weakness and vomiting.

Methods We present an observational, consecutive study. Data from ambulance and hospital medical records were analyzed. The survey included 290 patients (mean age: 70.6 years; median age: 74 years; male: 47%) who were admitted to a 550-bed secondary care hospital, receiving intravenous antibiotics for suspected community-acquired infections. General symptoms (fever/shivering, dyspnea, muscle

weakness, gastrointestinal symptoms, localized pain, altered mental status) that were part of the reason the patient sought medical care were registered. Additionally, age, sex, vital signs, C-reactive protein, and blood cultures were registered. Patients that within 48 hours from admission fulfilled any criteria for severe sepsis were compared with patients that did not. Odds ratios for severe sepsis were computed using univariable as well as multivariable logistic regression, controlling for age and gender as confounders.

Results Severe sepsis criteria were fulfilled in 31% (n = 91) of the patients. These were older (median age: 79 years vs. 71 years) and experienced more symptoms (mean: 2.2, SD 0.9 vs. mean: 1.4, SD 0.7) than patients without severe sepsis, while there was no difference in C-reactive protein levels (OR per 50 mg/l: 1.07, 95% CI: 0.96 to 1.20). Among individual symptoms, altered mental status (OR: 4.4, 95% CI: 2.2 to 9.0), dyspnea (OR: 3.5, 95% CI: 2.1 to 5.9), and muscle weakness (OR: 2.2, 95% CI: 1.0 to 4.4) were significantly related to severe sepsis. Adjusting for age and sex, altered mental status (adj. OR: 4.1, 95% CI: 2.0 to 8.4) and dyspnea (adj. OR: 3.1, 05% CI: 1.8 to 5.3) remained significant.

Conclusion General symptoms, especially altered mental status and dyspnea, appear to be more common in severe sepsis than in milder infections. These symptoms might be utilized as a diagnostic aid for severe sepsis in the clinical setting, complementing vital signs and laboratory tests.

P8

Clinical scores and blood biomarkers for prediction of bacteremia in emergency department patients: Bacteremia Assessment in Clinical Triage (BACT) study

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Critical Care 2015, **19(Suppl 1):**P8 (doi: 10.1186/cc14088)

Introduction Collection of blood cultures is routinely performed in patients with suspicion of infection in the emergency department (ED) despite a low yield of positive culture results. To increase sensitivity, different clinical prediction rules and blood biomarkers have been put forward. Herein, we validated the performance of different promising clinical prediction rules alone and in combination with novel blood biomarkers to predict blood culture positivity.

Methods This is an observational cohort study including consecutive medical patients with suspected infection and collection of ED admission blood cultures. Five clinical prediction rules were calculated and admission concentrations of procalcitonin (PCT), C-reactive protein, neutrophil–lymphocyte count ratio (NLCR), lymphocyte count, white blood cell count, and red blood cell distribution width were measured. True blood culture positivity was assessed by two independent physicians. We used logistic regression models with area under the curve (AUC) to establish associations between clinical prediction rules and blood culture positivity.

Results Of 1,083 included patients, 106 (9.8%) cultures were positive. Of the clinical prediction rules, the Shapiro rule performed best (AUC 0.733) followed by the Metersky rule (AUC 0.609). The best biomarkers were PCT (AUC 0.796), NLCR (0.692) and lymphocyte count (AUC 0.671). Combination of the Shapiro rule and PCT showed the best combination result (AUC of combined model 0.822). Limiting blood cultures to either the Shapiro rule ≥4 points or PCT >0.11 µg/l would reduce negative sampling by 25.6% while still identifying 100% of positive cultures. Using a Shapiro rule ≥3 points or PCT >0.25 µg/l limit would reduce negative sampling by 42.1% while still identifying 96.2% of positive cultures.

Conclusion Combination of clinical parameters combined in the Shapiro rule together with admission levels of PCT allows reduction of unnecessary blood cultures with minimal false negative rates.

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P9

Assessment of specific risk scores for patients admitted to the ICU for severe community-acquired pneumonia

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Critical Care 2015, **19(Suppl 1):**P9 (doi: 10.1186/cc14089)

Introduction The aim of the study is to evaluate the calibration and discrimination of two specific risk scores for community-acquired pneumonia (CAP) in patients with this illness who required ICU admission.

Methods A retrospective descriptive study of patients with severe CAP admitted to the ICU between January 2008 and September 2013. We analyzed clinical and epidemiological variables and APACHE II, SAPS III, CURB-65 and Pneumonia Severity Index (PSI) that were recorded in the first 24 hours. We used the Student t test to compare means and the chi-square test for univariate analysis. The standardized mortality ratio (SMR) and Hosmer–Lemershow test were calculated to analyze the calibration and ROC curve analysis for discrimination of different scores.

Results We analyzed 111 patients aged 57.5 ± 17.7 years, with 63.1% (70) males. The APACHE II score at admission was 19.8 ± 17.7 and SAPS III was 60.6 ± 16.7. ICU mortality was 29.7% (33). There was association between the four scores and mortality. The SMR for APACHE II was 0.87 and 0.85 for the SAPS III. Figure 1 shows the ROC curve for the four scores, the best observed discrimination obtained was for SAPS III score (AuC 0.79) and the worst was obtained for CURB-65 score (AuC 0.7). The Hosmer–Lemeshow test showed acceptable calibration for the four predictive systems (P > 0.05).

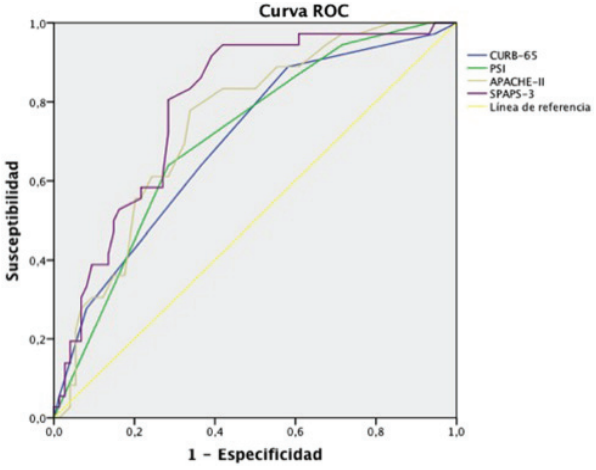


Figure 1 (abstract P9).

Conclusion The four analyzed scores presented good calibration, but discrimination seems better in SAPS III. Given the difficulty of calculating PSI, and its low discrimination (similar to CURB-65), we prefer to use the CURB-65 score in routine clinical practice.

P10

Predisposing factors for deep sternal wound infection after cardiac surgery

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Critical Care 2015, **19(Suppl 1):**P10 (doi: 10.1186/cc14090)

Introduction The aim of our study was to investigate perioperative risk factors associated with deep sternal wound infections in complicated cardiac surgery.

Methods A total of 1,017 patients underwent cardiac surgery in a 2-year period. We investigate the correlation between deep sternal

wound infection with the following 14 preoperative characteristics and perioperative parameters: age >75, female gender, diabetes mellitus (DM), insulin dependence, body mass index (BMI) >30, current smokers, COPD, cardiopulmonary bypass time (CBP) >120 minutes, use of steroids, emergency operation, prolonged mechanical ventilation (>48 hours), reintubation, transfusion with more than 3 units of red blood cells, and the postoperative use of non-invasive ventilation (NIV). The chi-square test was used for statistical analysis.

Results A total of 35 patients (3.44%) were complicated by deep sternal wound infections. No statistical correlation was found with age >75, gender, DM, BMI >30, steroids, emergent operation, prolonged ventilation, CBP time >120 minutes, reintubation and NIV. Factors with statistical significant correlation are presented in Table 1.

Table 1 (abstract P10)

	Sternal infection	*P* value
Insulin	9/85	0.001
Current smoker	4/272	0.037
COPD	11/197	<0.001
Transfusion >3	19/302	0.001

Conclusion Postoperative deep sternal wound infections have statistical significant correlation with the following parameters: transfusion with >3 red blood cell units, history of COPD, insulin dependence and when the patient is a current smoker. Also there is a tendency for correlation with CBP time >120 minutes ($P = 0.056$).

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P11

Risk factors for bacteremia in adult febrile patients in emergency settings

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Critical Care 2015, **19(Suppl 1):**P11 (doi: 10.1186/cc14091)

Introduction Blood culture is a critical procedure for detecting potentially life-threatening bloodstream infections (BSI). At the same time, early diagnosis and appropriate treatment of BSI are the key factors in order to improve prognosis. The purpose of the current analysis was to identify risk factors for bacteremia in adult febrile patients in emergency settings.

Methods We conducted a retrospective case–control study within a population of adult patients visiting the emergency department at a community hospital (St Luke's International Hospital, Tokyo, Japan) and who underwent two sets of blood culture testing between 2003 and 2012. Among a total of 13,582 patients, 1,322 (10%) were detected as bacteremia. We included in this study 179 randomly selected patients from the bacteremia group and 321 randomly selected patients from the negative blood culture group to serve as the comparison group. Multivariate logistic regression was used to evaluate the relationship between clinical characteristics factors and bacteremia.

Results In a multivariate logistic regression model, a statistically significant independent effect was found for body temperature (BT) >38°C (OR = 2.58, 95% CI, 1.76 to 3.79, P <0.001), systolic blood pressure (SBP) <100 mmHg (OR = 1.72, 95% CI, 1.11 to 2.65, $P = 0.01$), CRP >10 mg/dl (OR = 3.03, 95% CI, 2.05 to 4.49, P <0.001) and $PaCO_2$ <32 mmHg (OR = 2.3, 95% CI, 1.57 to 3.37, P <0.001). Receiver operating characteristic curve analysis revealed an area under the curve value of 0.725 for differentiating patients with bacteremia from negative culture.

Conclusion BT >38°C, SBP <100 mmHg, CRP >10 mg/dl and $PaCO_2$ <32 mmHg are independently associated with bacteremia. These factors might be useful to know whether or not adult febrile patients have bacteremia.

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P12

Pre-exposure to mechanical ventilation and endotoxin influence bacterial growth and immune response during experimental ventilator-associated pneumonia

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Critical Care 2015, **19(Suppl 1):**P12 (doi: 10.1186/cc14092)

Introduction Overproduction of nitric oxide (NO) is correlated with adverse outcomes in sepsis. NO is additionally a central part of the innate immune system defense against pathogens causing ventilator-associated pneumonia (VAP), which can complicate the clinical course during mechanical ventilation (MV). We hypothesized that pre-exposure to MV and systemic inflammation from endotoxin each would influence bacterial growth in lung tissue, based on an altered immune response in experimental pneumonia. We used a porcine *Pseudomonas aeruginosa* VAP model with ventilatory and inflammatory pre-exposures before inoculation to evaluate bacterial growth, development of lung damage, total NO production and inflammatory cytokine response.

Methods Three groups of mechanically ventilated pigs were subjected to experimental VAP for 6 hours with intrapulmonary 1×10^{11} CFU *P. aeruginosa* at baseline. Two groups were pre-exposed to MV for 24 hours before bacterial inoculation: MV + Etx ($n = 6$, received endotoxin 0.063 μg × kg^{-1} × $hour^{-1}$) and MV ($n = 6$, received saline in equivalent volume). One group, Un ($n = 8$), started the experiment unexposed to both MV and endotoxin, directly from the initiation of VAP. Postmortem lung tissue samples rendered bacterial cultures. NO production was measured with urinary nitrate levels over 6 hours of VAP.

Results The animals pre-exposed to endotoxin (MV + Etx) displayed higher bacterial growth (CFU × g^{-1}) (P <0.05), lower PaO_2/FiO_2 (P <0.05) and lower nitrate levels (P <0.01) than the unexposed animals (Un). Plasma TNFα levels were higher in Un than in both pre-exposed groups MV + Etx and MV (P <0.01). There were no significant differences between the two pre-exposed groups.

Conclusion Mechanical ventilation for 24 hours with concomitant endotoxin exposure enhances bacterial growth and lung damage during *P. aeruginosa* VAP, compared with inoculation without any pre-exposure to MV or endotoxin. The greater bacterial clearance in the unexposed animals was associated with higher NO production and higher levels of pro-inflammatory cytokines.

P13

Percutaneous drainage for patients with cervical necrotizing fasciitis with novel CT classification based on extension of fluid collection along the deep cervical space

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Critical Care 2015, **19(Suppl 1):**P13 (doi: 10.1186/cc14093)

Introduction Cervical necrotizing fasciitis (CNF) is a rapidly evolving and life-threatening condition. Therefore, it is important for physicians to evaluate the severity of illness and to predict clinical outcome exactly in the early phase. We focused on extension of acute fluid collection along the deep cervical space by CT findings. The purpose of this study was to produce the CT grade and to analyze whether our CT grade is related to the clinical features and the responses to treatment of CNF.

Methods Between June 2004 and December 2012, 42 patients diagnosed and treated for CNF in two institutions were included in

this study. Cervical spaces were subdivided into three components according to the concept of interfascial planes. The extension of acute fluid collection in cervical spaces was classified into three grades: Grade I, fluid collection confined to one component; Grade II, fluid collection spreading into two or three components; and Grade III, fluid collection spreading into four components or mediastinum. We analyzed association with CT grades and severity of illness (SOFA score, APACHE II score, CRP). All patients underwent percutaneous catheter drainage either ultrasonography guided or CT guided. We compared treatment outcome of CNF with CT grades.
Results According to elevation of CT grades, severity of illness was significantly associated with high score (APACHE II: 10.5 to 4.0, 12.8 to 4.2, 16 to 4.2, SOFA: 2.6 to 1.5, 2.9 to 1.9, 6.8 to 3.7, CRP: 17.8 to 10.6, 22.4 to 10.1, 33.3 to 11.9) and also duration of mechanical ventilation and length of hospital stay were longer (duration of mechanical ventilation: 10.9 to 6.6, 11.5 to 6.7, 15.8 to 7.2, length of hospital stay: 23.4 to 10.6, 27.9 to 21.4, 48.7 to 36.2).
Conclusion Novel classification of CNF based on CT findings showing the extension of fluid collection is a useful indicator of the disease severity and predicting clinical outcome. These findings may influence the strategy for the success of percutaneous catheter drainage.

P14

ICU mortality rates in patients with sepsis compared with patients without sepsis

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Critical Care 2015, **19(Suppl 1):**P14 (doi: 10.1186/cc14094)

Introduction The aim of the study was to evaluate the difference in mortality rates between those admitted to the ICU with and without sepsis, and to assess the proportion of patients who had sepsis. Septic patients are one of the key groups of patients admitted to ICUs around the world. Septic patients have an extremely poor prognosis with published mortality rates ranging from 20.7% (severe sepsis) to 45.7% (septic shock) [1]. With septic patients making up roughly 21% of patients admitted to ICUs, it is important to assess whether these rates of mortality hold true to a district general ICU and to assess the extent of the difference in prognosis between patients with and without sepsis [2].
Methods We performed a retrospective case note review, looking at a sample of 5,954 patients 18 years or older who were admitted to East Surrey Hospital (ESH) ICU, which has an elective admissions rate of 3%, between 1 January 2005 and 31 October 2014. The total number of patients with sepsis was 941 compared with 5,013 without sepsis. We looked at mortality rates, APACHE II scores and length of stay on the unit.
Results From the beginning of 2005 to the end of October 2014, mortality rates in septic patients were 44.6% compared with 26.2% in nonseptic patients. Fisher's two-tailed test showed a significant difference (P <0.0001) between the mortality in septic and nonseptic patients. There was a significant difference (Mann–Whitney) between APACHE II scores, with median scores of 18 and 13 in septic and nonseptic patients respectively. Septic patients had longer lengths of stay, with the mean and median 8.73 and 3.89 days respectively, compared with 4.90 and 2.5 in nonseptic patients. Septic patients made up 15.8% of all patients admitted to the ICU.
Conclusion Patients with sepsis admitted to ESH ICU made up a significant minority of patients admitted to the ICU. Septic patients had a 70% relative higher mortality rate compared with nonseptic patients. The mortality rate of 44.6% fits with previously quoted mortality rates in septic shock. Patients with sepsis had a significantly higher predicted mortality, recorded by their APACHE II score, which was statistically significant. This also meant they needed longer ICU care, with the average length of stay almost doubled.
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P15

ICU mortality rates in patients with sepsis before and after the Surviving Sepsis Campaign

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Introduction The aim of this study was to evaluate the effect of the Surviving Sepsis Campaigns on mortality rates, before and after the second surviving sepsis publication, and to assess whether patients with sepsis being admitted to the ICU had a lower APACHE II score on admission. Patients with sepsis, who require ICU care, have an extremely poor prognosis. It has been shown that the mortality rates range from 20.7% (severe sepsis) to 45.7% (septic shock) [1]. The surviving sepsis campaign was initiated in 2002. The first, second and third publications were published in 2004, 2008 and 2012 respectively [2].
Methods A retrospective case note review was performed, looking at a sample of 5,954 patients who were 18 years or older who had been admitted to East Surrey Hospital (ESH) ICU between 1 January 2005 and 31 October 2014. The total number of patients with sepsis was 941. We compared results before and after the second publication of the surviving sepsis campaign, looking at mortality rates, age of patients, admission length prior to ICU transfer, APACHE II score and the length of stay on the ICU.
Results From the beginning of 2005 to the end of 2008, the mortality rates for septic patients was 51.9% compared with 41.3% from the beginning of 2009 to end of October 2014. Fisher's two-tailed test showed a significant difference (P = 0.003) between the mortality before and after the second publication. The median ages before and after 2009 were 63.9 and 64.8 years. The time in hospital before admission to the ICU was greater before 2009 (6.15 days) compared with after 2009 (5.53 days). There was no significant difference (Mann–Whitney test) between the APACHE II scores, with the mean and median score the same at 17.6 and 18 for both groups. The mean length of stay was 1 day longer after 2009 (8.07 days compared with 9.07 days).
Conclusion Patients with sepsis admitted to ESH ICU had a 20% relative decrease in mortality after the second publication of surviving sepsis guidelines. The original aim of the campaign was to reduce mortality from sepsis by 25% in 5 years [3]. This decrease was not due to a significant difference between the sets of patients. The decreased time to admittance to ICU may be due to improved recognition of the need for ICU care. Overall the surviving sepsis campaign has had a significantly beneficial effect on mortality rates in patients with sepsis.
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P16

Independent risk factors for long-term mortality in patients with severe infection

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Critical Care 2015, **19(Suppl 1):**P16 (doi: 10.1186/cc14096)

Introduction The purpose of this study was to examine long-term mortality, 5 years after severe infection, and to identify independent risk factors associated with it.
Methods A prospective cohort study developed at a tertiary care university-affiliated 600-bed hospital including all patients with severe infection admitted into intensive care, medical, surgical, haematology and nephrology wards, over a 1-year period (2008/2009). The outcome of interest was mortality 5 years following hospitalisation and its association with specific risk factors was studied through logistic regression.
Results There were 1,013 patients included in the study. Hospital mortality rate was 14% (n = 137) and 5-year mortality was 37% (n = 379). Factors independently associated with 5-year mortality were (adjusted odds ratio (95% confidence interval)): age = 1.04 per year (1.03 to 1.05), cancer = 8.00 (3.06 to 20.88), chronic hepatic disease = 3.06 (1.06 to 8.87), chronic respiratory disease = 2.21 (1.06 to 4.62), haematologic

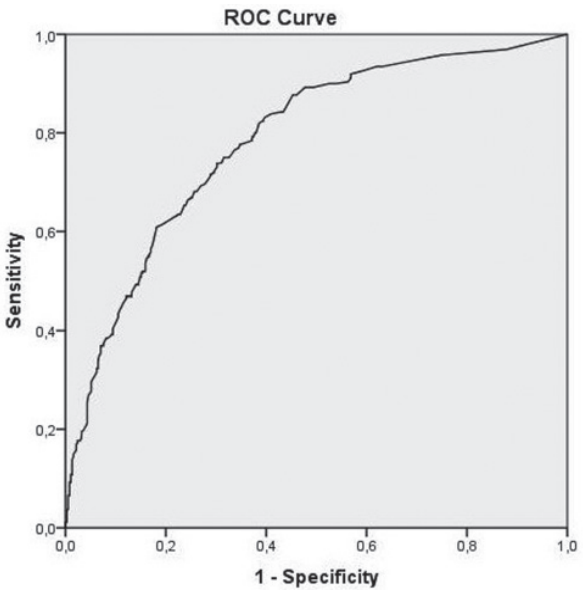


Figure 1 (abstract P16).

disease = 3.40 (1.64 to 7.04), Karnovsky Index <70 = 2.56 (1.63 to 3.71), infection by an ESKAPE pathogen = 1.65 (1.02 to 2.66) and severity of infection (reference is infection without SIRS): sepsis = 1.14 (0.7 to 1.83), severe sepsis = 1.18 (0.73 to 1.93), septic shock = 3.69 (1.78 to 7.65). The final model had a very good discrimination for long-term mortality with an area under the ROC curve of 0.78 (Figure 1).

Conclusion The authors identified several factors that were significantly associated with increased long-term mortality in patients with severe infection. This information will help clinicians in the discussion of individual prognosis and clinical decision-making.

P17

Direct intensive care costs of severe sepsis and septic shock patients in Thailand

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Critical Care 2015, **19(Suppl 1):**P17 (doi: 10.1186/cc14097)

Introduction Costs of severe sepsis care from middle-income countries are lacking. This study investigated direct ICU costs and factors that could affect the financial outcomes.

Methods A prospective cohort study was conducted in the medical ICU of a tertiary referral university teaching hospital in Thailand over a 4-year period.

Results A total of 897 patients, with 683 (76.1%) having septic shock. Overall ICU mortality was 38.3%. The median (interquartile range) ICU length of stay (LOS) was 4 (2 to 9) days. Community, nosocomial and ICU-acquired infection were documented in 574, 282 and 41 patients, respectively. The median ICU costs were €2,067.2 (986.3 to 4.084.6) per patient and €456.6 (315.3 to 721.8) per day. The ICU costs accounted for 64.7% of the hospital costs. In 2008 to 2011, the ICU costs significantly decreased by 40% from €2,695.7 to €1,617, whereas the daily ICU costs decreased only 3.3% from €463.9 to €448.7 (Figure 1). The average ICU costs of patient with nosocomial and ICU-acquired infection were significantly higher than patients with community-acquired infection. By multivariate logistic regression analysis, age, nosocomial or ICU infection, admission from emergency department, number of organ failures, ICU LOS, and fluid balance in the first 72 hours were independently associated with total ICU costs.

Conclusion The ICU costs of severe sepsis management significantly declined in Thailand. However, the ICU costs were a financial burden accounting for two-thirds of the hospital costs. It is essential for intensivists to contribute a high standard of care within a restricted budget. The cost-effectiveness analysis should be evaluated in sepsis care cases.

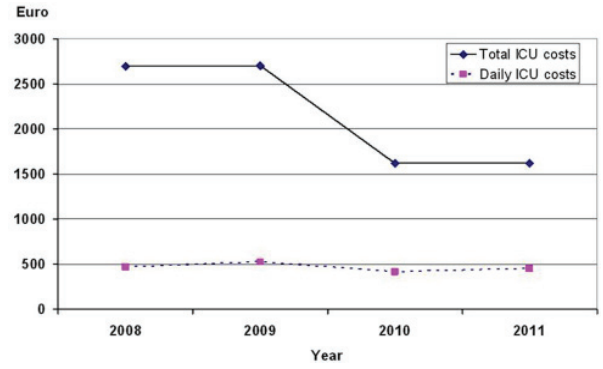


Figure 1 (abstract P17). Median ICU costs per patients and ICU cost per day according to study years.

P18

Long-term health-related quality of life in survivors of sepsis: an epidemiological study

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Introduction Survivors of sepsis report persistent problems that can last years after hospital discharge. The main aim of this study was to investigate long-term health-related quality of life in survivors of SIRS and sepsis compared with Welsh normative data, controlling for age, length of stay and pre-existing conditions. The second aim was to investigate any differences in long-term health-related quality of life specifically with the patients categorised into three groups: SIRS, uncomplicated sepsis, and severe sepsis/septic shock.

Methods A prospective study design was used in order to investigate all sepsis patients either presenting to the emergency department or admitted to the ICU of a regional trauma centre. A total of 106 patients were recruited and all patients were considered eligible as per the SIRS and sepsis criteria [1]. The Sepsis-related Organ Failure Assessment score was determined over the first 24 hours to assess organ function. Patients were assigned to groups as follows: sterile SIRS; uncomplicated sepsis; severe sepsis or septic shock as per the criteria. Assignment into groups was blinded and performed by an intensive care specialist independent of the study. Baseline demographics, clinical characteristics and outcomes were collected and surviving patients were sent a SF-12v2 survey at between 6 months and 2 years post hospital discharge.

Results A total of 106 patients were included in the study. A mortality rate of 34% was recorded, leading to a final response rate of 72% by the end of the data collection period. Quality of life was significantly reduced in all patients when compared with local normative data (all P <0.0001). Reductions in the physical components of health-related quality of life were more pronounced in severe sepsis/septic shock patients when compared with uncomplicated sepsis and SIRS patients.

Conclusion This is the first observational study to specifically focus on the different groups of SIRS and sepsis patients to assess long-term quality of life. Local population norms were used for comparison, rather than wide geographical norms that fail to reflect the intricacies of a country's population. Significant reductions in quality of life were found in severe sepsis/septic shock patients compared with in uncomplicated sepsis and SIRS patients, when controlling for age, pre-existing conditions, hospital and ICU length of stay.

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P19

Analysis of the mortality rate in patients admitted to the ICU for severe community-acquired pneumonia

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Introduction The aim of the study was to analyze the factors associated with hospital mortality in patients with severe community-acquired pneumonia (CAP) who required ICU admission.
Methods An observational, retrospective study of patients with severe CAP admitted to the ICU between January 2008 and September 2013. We analyzed clinical, epidemiological and outcome variables. Quantitative variables were expressed as the mean and standard deviation. Qualitative variables are expressed as the percentage and absolute value. We applied the Mann–Whitney and Fisher's exact test, as needed, with an alpha error of 5%.
Results We analyzed 111 patients, 57.5 ± 17.7 years old, with 63.1% (70) males and APACHE II score on admission of 19.8 ± 17.7. ICU mortality was 29.7% (33) and in-hospital mortality was 32.4% (36). Ten percent of patients met criteria for medical care-associated pneumonia (HCAP); there were no significant differences in mortality between HCAP and CAP (P = 0.075). Patients chronically taking immunosuppressive therapy had a significantly higher mortality compared with the rest of the patients (47.8% vs. 28.4%, P = 0.07). The mortality rate was also higher in patients in whom NIV fail in the first 24 hours (42.9% vs. 17.6% with P = 0.09). Patients who required intubation and mechanical ventilation in the first 24 hours had a higher mortality rate (47.2% vs. 19%, P = 0.002). Regarding the etiology of pneumonia, in 11 patients the viral origin of infection was confirmed (10 patients had H1N1 pneumonia and one patient CMV pneumonia), with a mortality rate significantly lower than in patients with bacterial pneumonia (3.6% vs. 35.3%, P = 0.06). The use of the right antibiotic therapy at admission was associated with mortality (P = 0.0001).
Conclusion Patients admitted to the ICU with severe CAP and immunosuppressive therapy have higher mortality, with no differences between HCAP and CAP. The delay in intubation as well as bacterial and inappropriate antibiotic treatment are factors that increase mortality.

P20

Evaluation of the cost of severe sepsis and septic shock in a private ICU in Brazil

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Introduction Sepsis is a high-prevalence disease in ICUs, associated with high mortality and high costs, mainly in developing countries. The aim of this study is to demonstrate the ICU costs, in a private hospital, in patients admitted with severe sepsis and septic shock.
Methods A retrospective, observational, single-center study of patients admitted from November 2013 to March 2014 with severe sepsis and septic shock. The records data were taken from the Software Epimed, MV System, and IBM SPSS Statistics 21. The classification was based on the Surviving Sepsis Campaign 2012. We included all 50 beds of an adult ICU, clinical and surgical. All patients older than 18 years with severe sepsis and septic shock were included. We evaluated the costs of patients during their ICU stay, and its relation to clinical presentation (severe sepsis and septic shock), antibiotic start time, permanence of ICU stay, and mortality. Only the first episode per patient was recorded.
Results From November 2013 to March 2014 were included 82 patients with criteria for severe sepsis and septic shock. The mean age of patients was 62.5 ± 21.8 years, divided equally between the genres. The overall mortality rate was 34.15%. The SAPS 3 was 56.43, with death probability set to Latin America 38.83%. Patients with severe sepsis had a mortality of 23.2% and those with septic shock had a mortality rate of 58%. The average total cost during ICU admission per patient was US$17,834 and the average daily cost was US$1,641. The daily cost in patients with severe sepsis and septic shock was US$1,263 and US$2,465 (P = 0.002), respectively, and in survivors and nonsurvivors was US$1,189 and US$2,512 (P = 0.001). The length of stay of patients in the ICU was 11.09 days, being 11.3 days in patients with severe sepsis and 10.7 days in patients with septic shock (P = 0.785). The beginning of the antibiotics in nonsurvivors was 73.7 minutes and in survivors was 64.7 minutes (P = 0.757), with the earliest onset in patients with septic shock than in patients with severe sepsis (38.5 vs. 81.5 minutes, P = 0.141).
Conclusion Severe sepsis and septic shock are conditions that consume large amounts of resources. Nonsurvivors had higher average spending than survivors. Patients admitted with septic shock had higher mortality than patients with severe sepsis with high mortality in relation to the prognostic indices adopted. The beginning of the antibiotics was longer in the nonsurvivors. We should adopt measures aimed at recognizing and earlier treatment of sepsis. If we improve our treatment, especially in septic shock, we will prevent deaths and decrement costs.

P21

Global burden of sepsis: a systematic review

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Introduction Sepsis is a global healthcare challenge. However, comprehensive information on sepsis morbidity and mortality across the world is scarce. We aimed to estimate the global burden of sepsis and to identify knowledge gaps based on available evidence from observational epidemiological studies.
Methods We searched 15 international and national citation databases for population-level estimates on incidence rates of sepsis or severe sepsis per 100,000 person-years and case fatality rates in adult populations using consensus criteria and published in the last 40 years. No language or publication restrictions were applied. Studies were stratified into four subgroups (setting: hospital or ICU for sepsis and severe sepsis) and meta-analyzed using metaprop of the R 3.0.2 package. Heterogeneity of the underlying effects across studies was expressed by the estimated τ, the square root of the between-study variance.
Results The search yielded 1,553 reports from 1979 to 2013, of which 37 met our criteria and 33 provided data for meta-analysis. The included studies were from 15 high-income countries in North America, Europe, Asia, and Australia. For these countries, the population incidence rate was 256 (95% CI, 182 to 360, τ = 0.43) hospital-treated sepsis cases and 151 (95% CI, 94 to 242, τ = 0.98) hospital-treated severe sepsis cases per 100,000 person-years, with large between-study heterogeneity. Restricted to the last decade, the incidence rate was 427 (95% CI, 281 to 648, τ = 0.24) sepsis cases and 331 (95% CI, 207 to 530, τ = 0.59) severe sepsis cases per 100,000 person-years. Hospital mortality was 15% for sepsis and 25% for severe sepsis during this period of time. There were no population-level sepsis incidence estimates from lower income countries. A tentative extrapolation from high-income-country data suggests global estimates of 30.7 million sepsis and 23.8 million severe sepsis cases, with potentially six million deaths each year.
Conclusion Our analyses underline the urgent need to implement global strategies to monitor sepsis morbidity and mortality – especially in low-income and middle-income countries. For further epidemiological studies, more consistent and standardized methodological approaches are needed to reduce between-study heterogeneity. In particular, further research on sepsis coding using administrative data seems necessary to derive sensitive and specific sepsis case identifications.

P22

Disparities in acute sepsis care: a systematic review

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Introduction Disparities in the incidence and outcomes of sepsis have been documented in observational studies but little is known about

how these occur and how we might prevent them. Our objective is to identify disparities by race, language, gender, socioeconomic status, insurance status and geography in acute sepsis care in emergency department (ED) or ICU settings in the published literature.

Methods We performed a systematic review of disparities in sepsis care. The search strategy and inclusion and exclusion criteria were defined *a priori*. A medical librarian searched the entire MEDLINE (PubMed), EMBASE and Cinahl databases prior to 2013. One author reviewed all abstracts and a second author reviewed 10% of all abstracts for agreement. Both reviewers independently reviewed each included article using an explicit study review tool. We included studies that met the following inclusion criteria: ED or ICU setting; disparities due to race, language, gender, socioeconomic status, insurance status or geography; process of care measures (antibiotics, lactate, i.v. fluid resuscitation, central line placement, vasopressor use) or outcome measures (mortality, length of stay, complications, costs). We excluded studies involving organ-specific infectious conditions, pediatric populations, case reports, and review articles.

Results We identified 778 abstracts; yielding 31 for inclusion ($k = 0.95$), 26 of 31 studies were excluded due to quality issues. Five articles met our inclusion criteria. Only one of the studies [1] contained data on process of care measures, showing that central venous monitoring was less likely to occur in older patients. Three studies [2-4] showed that Black patients had a higher incidence of sepsis, a higher hospitalization rate, and higher mortality rate. Plurad and colleagues [5] reported that Asian patients had increased incidence of post-traumatic sepsis. Overall, Black patients with sepsis were younger, had lower socioeconomic status and were more likely to be cared for in urban settings compared with their cohorts.

Conclusion We found little published data addressing whether disparities due to race, language, gender, socioeconomic status, insurance status or geography exist in the acute care of sepsis. As sepsis is a leading cause of in-hospital mortality, future research should determine whether such disparities exist. Specifically, prospective studies of the process of care in sepsis management may further elucidate additional factors that may contribute to these disparities.

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P23

Sublingual leukocyte activation in patients with severe sepsis or septic shock

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Critical Care 2015, **19(Suppl 1):**P23 (doi: 10.1186/cc14103)

Introduction The objective of this study was to compare the number of rolling and adhered leukocytes in patients with severe sepsis/septic shock with non-infected controls. Microcirculatory flow alterations and endothelial cell dysfunction are elements of sepsis pathophysiology. Traditionally, microcirculatory emphasis has been on red blood cell vessel perfusion. However, assessment of interactions between white blood cells and endothelial cells may be another early diagnostic modality.

Methods We included adult (age >18 years) ED patients presenting with severe sepsis/septic shock (sepsis with elevated lactate (>4 mmol/l)) or hypotension) from the prospective clinical ProCESS trial. We studied a subset of patients with microcirculatory videos obtained along with non-infected control patients. Using a sidestream dark-field videomicroscope, we obtained image sequences from the sublingual mucosa and used video stabilization and frame averaging techniques to visualize slowly-moving leukocytes. We quantified the number of rolling and adhered leukocytes present per 1 mm × 1 mm visual field in a standardized 3-second clip. Furthermore, we extracted the total length of vessels candidate for counting of rolling/adhered leukocytes (vessels with an adequate focus). We report sample means with standard deviation and compare them with Student's *t* test.

Results We included a total of 64 patients with severe sepsis/septic shock and 32 non-infected controls. The mean number of adhered leukocytes per field in the sepsis group was 2.1 (SD 2.3) compared with 0.4 (SD 0.8) in the non-infected group ($P < 0.001$). This corresponded to a mean number of adhered leukocytes per unit vessel length of 0.16/mm (SD 0.22) and 0.03/mm (SD 0.06) for sepsis and non-infected groups, respectively ($P < 0.001$). For the rolling leukocytes, we observed a mean number of 27.8 (SD 19.4) in the sepsis group and 12.0 (SD 8.7) in the non-infected group ($P < 0.001$) per field. This corresponded to a mean number of rolling leukocytes per unit vessel length of 2.00/mm (SD 1.67) and 0.75/mm (SD 0.55), respectively ($P < 0.001$).

Conclusion Our results show a higher number of rolling and adhered leukocytes in patients with severe sepsis/septic shock when compared with non-infected controls. This also applies when taking the total vessel length in the field of view into consideration. This may hold potential as a useful tool in sepsis assessment.

P24

Time course of redox potential and antioxidant capacity in patients undergoing cardiac surgery

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Critical Care 2015, **19(Suppl 1):**P24 (doi: 10.1186/cc14104)

Introduction Cardiac surgery regularly provokes inflammation and oxidative stress which contribute to the development of organ failure and mortality of patients. While the assessment of single markers does not reflect a comprehensive investigation of redox status, the measurement of oxidation–reduction potential (ORP) provides a reliable measure to assess the balance between total prooxidant and antioxidant balance in the blood. The aim of the present study was to investigate the overall redox potential in patients undergoing cardiac surgery.

Methods This is a prospective observational study in patients scheduled for elective cardiac surgery. Serum samples were drawn prior to surgery, after connection to cardiopulmonary bypass (ischemia), after opening of cross-clamp (reperfusion) and after termination of surgery. The redox status of patients was measured using the bedside point of care RedoxSYS Diagnostic System™ (Luoxis, USA). Simultaneously the antioxidant capacity in serum samples were calculated in all perioperatively obtained serum samples.

Results All patients' sera ($n = 17$) demonstrated a significant increase of ORP upon start of myocardial ischemia (141.0 ± 4.8 mV vs. 157.9 ± 4.9 mV; $P = 0.002$) and compared with reperfusion (141.0 ± 4.8 mV vs. 158.6 ± 4.9mV; $P < 0.001$, Figure 1A). In parallel, the antioxidant capacity significantly decreased during surgery (0.505 ± 0.190 µC vs. 0.384 ± 0.120 µC; $P = 0.022$) corresponding to the increase of oxidative stress (Figure 1B).

Conclusion This preliminary study is the first to highlight the time course of overall redox potential and antioxidant capacity in cardiac surgery patients. Further studies are underway to evaluate the clinical significance on outcome in cardiac surgery patients.

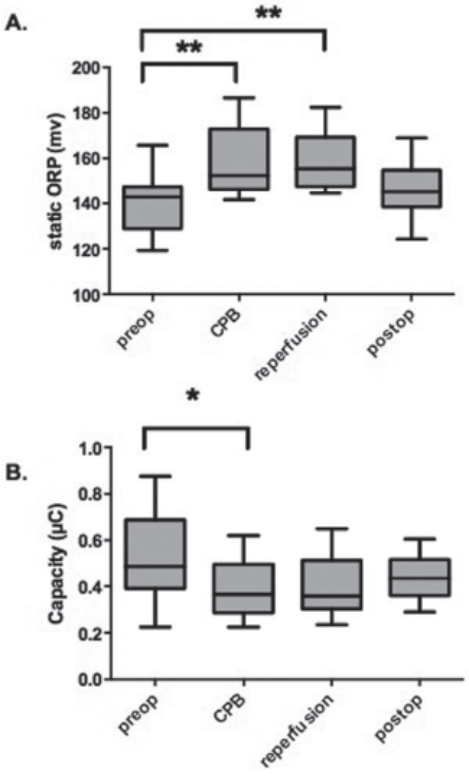


Figure 1 (abstract P24). (A), **(B)** Perioperative time course of oxidative stress and antioxidant capacity.

P25

Fatty acid composition of erythrocytes in multiple organ dysfunction syndrome

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Critical Care 2015, **19(Suppl 1):**P25 (doi: 10.1186/cc14105)

Introduction Change in fatty acid composition of erythrocytes and blood plasma in cases of various pathological conditions is evidence of lipid metabolism disorder and can indicate the reasons for and the degree of these disorders [1]. The aim of this study was to assess the FA composition of plasma and erythrocytes in patients with multiple organ dysfunction syndrome (MODS).
Methods The objects of study were 19 people with MODS (37.6 ± 8.3 years) of various etiologies. The blood of 17 healthy volunteers aged 38.4 ± 3.3 years served as control. The FA analysis was conducted using capillary gas–liquid chromatography. Quantitative evaluation of individual FA content was made as a mass percentage of their total ($C_{14:0}$ to $C_{22:6}$). Statistical analysis was performed using the Mann–Whitney *U* test (P <0.05).
Results Our data indicate that changes in blood plasma FA composition in patients with MODS are mainly caused by activation of lipolysis in fat depots and are accompanied by an increase of monounsaturated fatty acids, a decrease in saturated stearic acid and polyunsaturated fatty acids in the ratio. In conditions of increased level of monounsaturated palmitoleic ($C_{16:1}$) and oleic ($C_{18:1}$) FA in blood plasma (2.53 ± 0.40% vs. 1.55 ± 0.29%, P <0.001 and 25.18 ± 2.15% vs. 16.55 ± 1.17%, P <0.001, respectively), only the level of palmitoleic ($C_{16:1}$) acid is increased in erythrocytes (0.56 ± 0.12% vs. 0.16 ± 0.12%, P <0.001). Despite the high content of oleic ($C_{18:1}$) acid in blood plasma in case of MODS, in erythrocytes its relative level is not changed as compared with the control group. The disorder of lipid composition constancy in erythrocyte membranes is also manifested by change in the content of saturated palmitic ($C_{16:0}$) and polyunsaturated linoleic ($C_{18:2}$) fatty acids. In the test group of patients, as compared with the control group there was an elevated level (27.12 ± 0.78% vs. 25.80 ±0.77%, P <0.05) of saturated palmitic ($C_{16:0}$) acid combined with the reduced (11.46 ± 0.52% vs. 13.95 ± 1.09%, P <0.001) level of linoleic ($C_{18:2}$) acid.
Conclusion The changes revealed in fatty acid composition of erythrocytes may indicate systemic modifications of cell membranes in MODS.

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P26

Lower platelet mitochondrial function in severe septic patients than in controls

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Introduction The oxidative phosphorylation system (OXPHOS) in septic patients has been scarcely analyzed in studies of small sample size and the results are apparently inconsistent. Previously, including 96 severe septic patients, we found that nonsurviving severe septic patients showed lower platelet respiratory complex IV (CIV) activity than surviving patients at the moment of severe sepsis diagnosis and during the first week of sepsis diagnosis. However, we did not examine this enzyme activity in normal individuals. Thus, the objective of this study was to compare the CIV activity between severe septic patients and healthy control individuals in a larger series of patients (including 198 severe septic patients).
Methods This was a prospective, multicenter, observational study in six Spanish ICUs. We obtained blood samples from 198 severe septic patients at days 1, 4 and 8 of the severe sepsis diagnosis and from 96 sex-matched and age-matched healthy control individuals and determined platelet CIV activity/protein quantity. The endpoint of the study was 30-day mortality.
Results We found that severe septic patients showed lower CIV activity/protein quantity than controls at day 1 (P <0.001), day 4 (P <0.001) and day 8 (P <0.001) of severe sepsis diagnosis. Survivor severe septic patients (n = 130) showed lower CIV activity/protein quantity than controls at day 1 (P <0.001), day 4 (P <0.001) and day 8 (P <0.001) of severe sepsis diagnosis. In addition, nonsurvivor severe septic patients (n = 68) showed lower CIV activity/protein quantity than controls at day 1 (P <0.001), day 4 (P <0.001) and day 8 (P <0.001) of severe sepsis diagnosis. Besides, nonsurvivor severe septic patients showed lower CIV activity/protein quantity than survivor ones at day 1 (P <0.001), day 4 (P <0.001) and day 8 (P <0.001) of severe sepsis diagnosis.
Conclusion The major finding of our work, that represents the largest series of severe septic patients with data on OXPHOS function, was that survivor and nonsurvivor severe septic patients showed lower platelet CIV activity than healthy controls during the first week of severe sepsis diagnosis.

P27

Influence of genetic variants in the susceptibility and outcome of influenza virus infection

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Introduction The role of genetic variability in the susceptibility and outcome of influenza virus infection (IVI) remains largely unknown. We

have previously demonstrated that variants at SFTPA2 influence the severity of H1N1pdm infection. We have now studied genetic variants at different genes, some of them previously associated with infections by influenza and/or other viruses. The purpose of this study was to analyze the role of genetic variants in the susceptibility and outcome of IVI.

Methods In total, 136 white Spanish patients developed IVI (80.3% of them by H1N1pdm virus). The general population group consisted of 1,466 unrelated healthy volunteers. Patients and controls were analyzed for different polymorphisms at 13 genes (FCGR2A, FCGR3A, FCGR3B, IL1RN, IL6, LTA, TIRAP, TLR1, TLR2, TLR3, TLR4, CCR5, IGHG2).

IVI was detected in nasopharyngeal swabs using real-time PCR. The Hardy–Weinberg equilibrium was analyzed by Haploview v. 4.2. The comparisons of genotypes distribution based on susceptibility and severity were performed using the chi-squared test or Fisher's exact test when needed. The relationship between severity in hospitalized patients and genotypes was evaluated by binary logistic regression models.

Results No associations were found between the different genetic variants and susceptibility or severity of IVI. Variants at LTA, FCGR2A, IGHG2, TLR3 and CCR5, previously associated with severity of IVI were not replicated in our study.

Conclusion Our study does not suggest that polymorphisms at LTA, FCGR2A, IGHG2, TLR3 and CCR5 genes are associated with susceptibility or severity of IVI.

P28

Phenotypic factors associated with outcome in 977 intensive care patients with faecal peritonitis: analysis of trends in the GenOSept cohort

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Introduction Patients admitted to intensive care following surgery for faecal peritonitis present particular challenges in terms of clinical management and risk assessment that require close collaboration between surgical and intensive care teams [1]. We aimed at establishing whether dynamic assessment of trends in selected variables may be associated with outcomes, and therefore inform medical decision-making.

Methods We analysed trends in all 35 variables available for the first week of ICU stay in 977 patients from 102 centres across 17 countries. The primary study outcome was 6-month mortality. Secondary outcomes were ICU, hospital and 28-day mortality. For each trend, Cox proportional hazards (PH) regression analyses, adjusted for age and gender, were performed for each endpoint. Trends found to be significant in these analyses, after Bonferroni correction for multiple testing, were entered into a multivariate Cox PH model, to determine independent associations with mortality.

Results The trends over the first 7 days of ICU stay (primary analysis) retained as independently associated with 6-month outcome were worsening thrombocytopaenia (mortality HR = 1.02, 95% CI = 1.01 to 1.03, P <0.001) and changes in renal function (total daily urine output HR = 1.02, 95% CI = 1.01 to 1.03, P <0.001; renal SOFA subscore HR = 0.87, 95% CI = 0.75 to 0.99, P = 0.047), highest recorded level of bilirubin (HR = 0.99, 95% CI = 0.99 to 0.99, P = 0.02) and GCS SOFA subscore (HR = 0.81, 95% CI = 0.68 to 0.98, P = 0.028). Changes in renal function (total daily urine output and renal component of the SOFA score), GCS component of the SOFA score, total SOFA and worsening thrombocytopaenia were also independently associated with secondary outcomes. Dynamic trends over the first 7 days of ICU stay in all other measured laboratory variables, physiological parameters or radiological findings failed to be retained as independently associated with outcome on multivariate analyses. Furthermore, changes in respiratory support, renal replacement therapy and inotropic and/or vasopressor requirements appeared not to be independently associated with any of the primary or secondary outcomes. Secondary *post hoc* analyses on trends over the first 3 and 5 days corroborated these findings.

Conclusion Only deterioration in renal function, thrombocytopaenia and hyperbilirubinaemia over the first 7 days of ICU stay were consistently associated with mortality at all endpoints.

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P29

Elevated basal levels of circulating activated platelets predict ICU-acquired sepsis and mortality: a prospective study

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Introduction Platelets are now considered to be immune and inflammatory agents as well as key cells in coagulation, and as such have been implicated in the pathophysiology of sepsis [1]. Thrombocytopenia is associated with sepsis severity and poor prognosis, and hyperactivated platelets probably contribute to microvascular thrombosis and organ failure. In the present study, we evaluated platelet activation markers as potential predictive markers of sepsis and of mortality among four commonly encountered populations of patients admitted to ICUs.

Methods Ninety-nine non-infected ICU patients were prospectively screened at day 1 (T1) and day 3 (T2) of admission after elective cardiac surgery, trauma, acute neurologic dysfunction or prolonged ventilation (>48 hours). A third sample was drawn when infection was diagnosed (Tx). We evaluated platelet activation by measuring the expression of P-selectin (CD62P) and fibrinogen binding on the cell surface before and after stimulation with major platelet agonists (ADP, collagen, and TRAP) through flow cytometry. Clinical scores were obtained at admission.

Results Patients who developed sepsis (n = 18) presented with significantly higher platelet fibrinogen binding at T1 compared with patients who did not get infected (basal: P = 0.0014, upon stimulation: P <0.0035). At T1, ROC AUC for association of basal fibrinogen binding with the occurrence of sepsis was 0.79 (95% CI: 0.68 to 0.89). Elevated basal CD62P expression level was associated with increased 90-day mortality (P = 0.042, ROC AUC = 0.78 (0.64 to 0.88)). Kaplan–Meier survival curves illustrated that mortality was significantly higher after stratification based on T1 basal CD62P level (cutoff MFI >31.56, HR = 13.6, $P = 8.23 \times 10^{-6}$). Multivariate logistic regression analysis using clinical scores (SOFA, APACHE II, SAPS II, SAPS III) indicated that addition of CD62P level or of bound fibrinogen level significantly improved prediction of mortality (odds ratio 1.078, P = 0.003) and sepsis (odds ratio 1.033, P = 0.0012), respectively.

Conclusion Predisposition to severe infection in selected critically ill medico-surgical adults can be identified on day 1 of admission based on circulating basally activated platelets. Levels of activated platelets may add incremental prognostic information to clinical scoring.

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P30

Antiplatelet therapy does not influence outcome or host response biomarkers during sepsis: a propensity-matched analysis

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Introduction Sepsis is a life-threatening condition, during which triggering of inflammatory and coagulation cascades, together with endothelial damage, invariably leads to activation of platelets. Although platelets are essential components of primary hemostasis, uncontrolled platelet activation during sepsis may contribute to organ failure. The aim of this study was to investigate whether chronic antiplatelet therapy impacts on the presentation and outcome of, and the host response to, sepsis.

Methods We performed a prospective observational study in patients admitted with sepsis to the mixed ICUs of two hospitals in the Netherlands between January 2011 and July 2013. Cox proportional hazards regression was used to estimate the effect of antiplatelet therapy on mortality. To account for indication bias, a propensity score was constructed, and used to match antiplatelet therapy users to nonusers. Plasma biomarker levels, providing insight into hallmark host responses to sepsis, including activation of endothelial cells and the cytokine network, were determined during the first 4 days after ICU admission.
Results Of 1,070 sepsis patients, 297 (27.8%) were on antiplatelet therapy, including acetylsalicylic acid, clopidogrel and dipyridamole, prior to ICU admission. Antiplatelet users and nonusers differed significantly with regard to several baseline characteristics, such as age, gender and cardiovascular disease. Antiplatelet therapy was not related to sepsis severity at presentation, the primary source of infection, causative pathogens, the development of organ failure or shock during ICU stay, or mortality up to 90 days after admission, in either the unmatched or propensity-matched analyses. Antiplatelet therapy did also not modify plasma concentrations of biomarkers.
Conclusion Pre-existing antiplatelet therapy does not influence clinical disease severity at presentation, nor the host response or outcome following sepsis.
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P31

Perioperative programmed death-1 expression on CD4$^+$ T cells predicts the incidence of postoperative infectious complications following gastrointestinal surgery

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Introduction Programmed death-1 (PD-1) has been reported to be an immunoinhibitory receptor expressed by chronically stimulated T cells after T-cell activation. The present study was designed to evaluate the relationship between perioperative PD-1 expression on CD4$^+$ T cells and the incidence of postoperative infectious complications in patients undergoing gastroenterological surgery.
Methods This was a prospective observational study. The subjects of this study included 101 patients with gastroenterological disease who underwent elective abdominal surgery via laparotomy at the National Defense Medical College Hospital. Blood samples were taken on the preoperative day (Pre) and the first postoperative day (POD1). We calculated CD4$^+$ T-cell count and PD-1 expression on CD4$^+$ T cells by flow cytometer. The occurrence of postoperative infectious complications was defined according to a combination of clinical findings and the results of laboratory and other tests. The postoperative infectious complications in this study included incisional surgical site infections (SSIs), organ/space SSIs, enterocolitis, urinary tract infections, and pneumonia. Incisional and organ/space SSIs were diagnosed according to the definitions stated in the guidelines issued by the Center for Disease Control and Prevention.
Results Postoperative infectious complications occurred in 30 of the 101 patients. CD4$^+$ T-cell count was significantly lower in the patients who developed postoperative infectious complications at POD1 compared with those from the patients who did not. In addition, PD-1 expression on CD4$^+$ T cells was significantly higher at Pre or POD1 in patients who developed postoperative infectious complications. Those results were similar for the incidence of organ/space surgical site infection. Preoperative PD-1 expression on CD4$^+$ T cells tended to be higher in males than in females. We found there was a significant negative correlation between preoperative PD-1 expression on CD4$^+$ T cells and CD4$^+$ T-cell count.
Conclusion Perioperative CD4$^+$ T-cell count or PD-1 expression on CD4$^+$ T cells could be an early predictive marker for the development of postoperative infectious complications.

P32

Mitochondrial dysfunction and ischemia in critical illness: an adipose tissue microdialysis study in 203 ICU patients

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Introduction Ischemia and mitochondrial dysfunction have been implicated in critical illness. The potential of MD to diagnose and separate ischemia and mitochondrial dysfunction in ICU patients remains currently unknown.
Methods A retrospective, observational study of 203 mechanically ventilated patients studied over a 6-year period with MD including medical, surgical and trauma patients. Sepsis stages: SIRS (n = 24), severe sepsis (n = 46) and septic shock (n = 133). Median age 67 years (range: 17 to 92 years). Mortality was 53%. All subjects had a MD catheter placed in femoral adipose tissue upon admission to the ICU. Interstitial fluid samples were collected six times per day, for 3 consecutive days, and were analyzed for glucose, lactate, pyruvate, and glycerol levels. The lactate to pyruvate (LP) ratio was calculated. Blood lactate was measured. Ischemia was defined as LP ratio >30 and pyruvate level <70 mmol, while mitochondrial dysfunction was defined as LP ratio >30 and pyruvate >70 mmol.
Results Analysis during the course of the 3-day period revealed three distinct patterns: no ischemia/mitochondrial dysfunction (n = 150 or 74%), ischemia (n = 27 or 13%) and mitochondrial dysfunction (n = 26 or 13%). On day 1, median blood lactate was higher in mitochondrial dysfunction (2.2 mmol/l) compared with both ischemia (1.3 mmol/l) and with no ischemia/mitochondrial dysfunction (1.3 mmol/l) (P = 0.004). Again on day 1, median interstitial fluid lactate was higher in mitochondrial dysfunction (8.4 mmol/l), in comparison with ischemia (1.4 mmol/l) and with the group without ischemia/mitochondrial dysfunction (2.5 mmol/l) (P <0.001). Similar results were obtained with interstitial fluid glycerol levels (P = 0.009). Median LP ratio was higher in ischemia (LP = 36), and mitochondrial dysfunction (LP = 33) compared with those without ischemia/mitochondrial dysfunction (LP = 17) (P <0.001). Median interstitial fluid glucose was lower in ischemia (2 mmol/l) compared with both mitochondrial dysfunction (4 mmol/l) and with no ischemia/mitochondrial dysfunction (5 mmol/l) (P <0.001). ICU mortality was 77% in mitochondrial dysfunction, 52% in ischemia and 49% in the group without ischemia/mitochondrial dysfunction (P = 0.033).
Conclusion Bedside subcutaneous adipose tissue MD is possible to diagnose and separate ischemia and mitochondrial dysfunction in general ICU patients. These two conditions are not so common; however, mitochondrial dysfunction seems to be associated with higher mortality rates.

P33

Pyruvate dehydrogenase levels are low in sepsis

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Introduction Pyruvate dehydrogenase (PDH) is a key component of aerobic metabolism. Multiple rodent studies have shown that PDH levels are low in sepsis. This leads to a shift to anaerobic metabolism, resulting in increased lactic acid. Alteration in PDH levels during sepsis, however, has never been studied in humans. The aim of this study was to identify whether PDH levels (activity and quantity) were altered in humans in sepsis.
Methods We conducted a case–control study at a single urban tertiary care center. We compared PDH levels between sepsis and healthy control subjects by measuring PDH levels in peripheral blood mononuclear cells via a novel assay. We measured PDH levels in control subjects at baseline and in sepsis subjects at 0, 24, 48 and 72 hours.
Results There were 39 sepsis (age 67 ± 14 years, M ± SD) and 19 control (age 50 ± 12 years) subjects of similar gender (56% and 63% female, respectively) and race (79% and 68% Caucasian, respectively). PDH levels in the sepsis group were significantly lower than the control

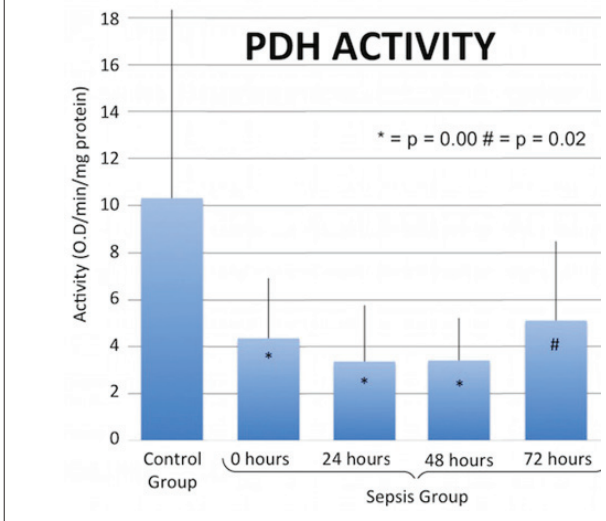


Figure 1 (abstract P33).

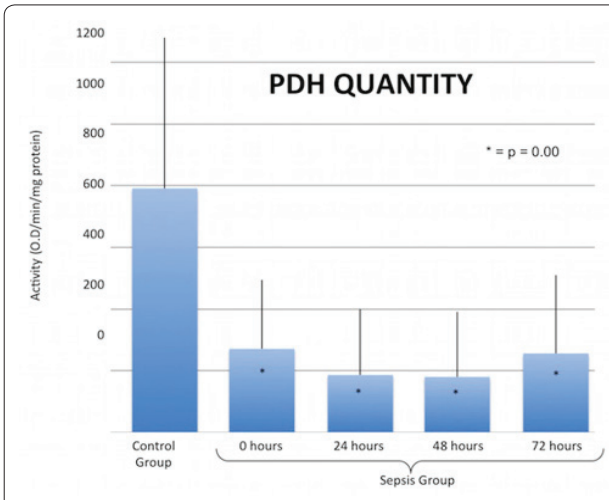


Figure 2 (abstract P33).

group at all time points (Figures 1 and 2). After controlling for age, gender, race, and assay plate via multivariable linear regression, the effect of treatment group remained significant. We were unable to control for comorbid illness, which was exclusively concentrated in the sepsis group.

Conclusion PDH levels are significantly lowered in humans during sepsis when compared with healthy controls, even when controlling for age, race and gender. Further research is needed to determine whether this finding persists after adjustment for comorbid disease, and whether lower PDH levels are associated with clinical outcomes.

P34

Serial change of C1 inhibitor in patients with sepsis: a preliminary report

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Introduction C1 inhibitor (C1INH), belonging to the superfamily of serine protease inhibitors, regulates not only complement system, but also the plasma kallikrein–kinin system, fibrinolytic system and coagulation system. The biologic activities of C1INH can be divided into the regulation of vascular permeability and anti-inflammatory functions. In recent years, hereditary angioedema (HAE), caused by an inherited deficiency of C1INH, has been focused. During HAE attacks, vascular permeability was markedly increased, which leads to angioedema. In sepsis, significant endothelial hyperpermeability is similarly observed systemically, but the role of C1INH has not been clarified in the pathogenesis. The serial change of C1INH in patients with sepsis is not clear. The objective of this study was to clarify the serial change in C1INH in patients with sepsis and evaluate the impact of C1INH on their clinical course.

Methods We serially examined C1INH activity values (normal range 70 to 130%) and quantitative values (normal range 160 to 330 μg/ml) in patients with sepsis during the period between December 2012 and February 2013. We also analyzed their clinical course: prognosis, volume of infusion, body weight, urine volume, catecholamine administration, and steroid administration.

Results The serial change of C1INH was evaluated in five patients with sepsis (three male and two female; four survivors and one nonsurvivor; mean age, 68 ± 11 years). In the nonsurvivor, C1INH activity on admission value was 97.2% (normal range), and quantitative value was 133.1 μg/ml (below normal). In the patient with severe sepsis requiring fluid resuscitation, catecholamine and steroid administration to maintain hemodynamics, C1INH activity value on admission was 94.4% (normal range), and quantitative value was 126.7 μg/ml (below normal range). His general condition was improved on day 6, and C1INH activity value and quantitative value increased (139.9%; above normal range, 250.1 μg/ml; normal range). In the other three patients with sepsis not requiring steroid administration, C1INH activity value on admission was 130.6 ± 8.7% (above normal range), and quantitative value was 215 ± 26.5 μg/ml (normal range).

Conclusion In the nonsurvivor or the severe patient with sepsis requiring steroid administration, the enhancement of C1INH activity was not observed, and the C1INH quantitative values were low. Further evaluation of the serial change of C1INH and the validity of C1INH replacement therapy in patients with septic shock may lead to a new strategy for management in sepsis.

P35

Expression of apolipoproteins L in neutrophils during sepsis

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Introduction Sepsis is characterized by a strong systemic inflammatory reaction. The pathogenesis is driven by alterations in the immune system and is associated with high neutrophil counts related to a specific delay in apoptosis [1]. The apolipoproteins L (ApoLs) family comprises six members in humans (ApoL1 to ApoL6). In light of their deregulated expression in several pathologies, they are likely to be important molecular players of programmed cell death [2]. We analyzed ApoL expression in cohorts of septic and nonseptic ICU patients and healthy volunteers in order to test whether ApoLs could be involved in the neutrophil apoptotic program.

Methods By means of magnetic cell sorting, peripheral neutrophils were purified from 20 healthy volunteers and 40 ICU patients with (n = 20) or without sepsis (n = 20). ApoL expression was analyzed at the mRNA and protein levels by real-time PCR and western blot analysis respectively. Apoptosis of purified neutrophils was assessed using flow cytometry following 4 and 24 hours of *in vitro* incubation. We monitored the expression of C-reactive protein (CRP), an inflammatory marker, and its correlation with ApoL expression in PMNs was studied by linear regression analysis.

Results Our results showed a significant downregulation in mRNA expression of ApoL1 (P <0.0001), ApoL2 (P = 0.0009), ApoL3 (P <0.0001)

and ApoL6 ($P = 0.0003$) in purified PMNs from ICU patients as compared with the healthy individuals. This downregulation was also validated at the protein level for ApoL1 and ApoL2, whereas ApoL 6 was upregulated in septic patients. We could not detect ApoL3 protein in any of the cohorts. This was accompanied by a significant delay in PMN apoptosis in septic patients as compared with healthy volunteers ($P < 0.05$) at 4 and 24 hours. We also showed a strong negative correlation in the three mixed groups between CRP and ApoL1 ($R = -0.607$), ApoL2 ($R = -0.651$), ApoL3 ($R = -0.578$) and ApoL6 ($R = -0.506$).

Conclusion The altered apoptotic fate of neutrophils in sepsis was correlated with the modification of the expression profile of ApoLs, a family of proteins thought to be involved in the apoptotic process. The role of these proteins in the sepsis-associated phenotype of neutrophils remains to be further elucidated.

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P36

Ex vivo and *in vivo* generation of neutrophil extracellular traps by neutrophils from septic patients

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Introduction The primary aim of this study was to determine the differences in *ex vivo* generation of neutrophil extracellular traps (NETs) by neutrophils from septic and nonseptic patients. We further sought to examine plasma levels of cell-free DNA (cf-DNA) and histones to assess *in vivo* NET formation.

Methods We isolated neutrophils from consecutive patients with sepsis ($n = 17$) and without sepsis ($n = 18$) admitted to the ICU. Neutrophils were activated by incubation with phorbol myristate acetate to induce release of NETs and NET formation was assessed by measuring the extracellular DNA level. Immunolabeling and fluorescence imaging were also performed. Extracellular killing of bacteria by NETs was studied by co-culture of *Escherichia coli* and neutrophils in the presence of the phagocytosis inhibitor cytochalasin D. To assess *in vivo* NET formation, plasma levels of cf-DNA and histones were measured.

Results The condition of the nonseptic patients was significantly less severe than that of the septic patients. The SOFA score of septic patients and the nonseptic patients was 6 (3 to 18) and 2.5 (1 to 8), respectively (median (IQR), $P = 0.02$). The overall mortality rate was 29%. After stimulation with PMA, neutrophils isolated from septic patients released 4.08 ± 1.02% of their total DNA, whereas neutrophils from nonseptic patients released 29.06 ± 2.94% ($P < 0.0001$). Immunofluorescent staining of released DNA, elastase, and myeloperoxidase also revealed similar results. Neutrophils from nonseptic patients showed effective extracellular killing of *E. coli* through NETs, whereas neutrophils from septic patients did not ($P < 0.001$). Plasma levels of cf-DNA and histones were higher in septic patients than in nonseptic patients ($P < 0.001$).

Conclusion The increase of the immature PMN count and immature/total PMN ratio confirmed recruitment of immature neutrophils from the bone marrow into the circulation. The *ex vivo* generation of NETs is downregulated in neutrophils isolated from patients with sepsis. However, it is unclear whether *in vivo* NET formation is also impaired during sepsis, so further investigation is necessary.

P37

Specific patterns of T-cell cytokines as an early marker of outcome in septic patients

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Introduction The inflammatory response of sepsis is developed in two phases, an inflammatory phase (SIRS) and a phase more variable in frequency and intensity (CARS): this balance has an important effect on morbidity and mortality. Lymphopenia affects particularly T cells, and correlates inversely with outcome. The aim of the study was to identify phenotypic and functional early markers of T cells and NK cells related to prognosis in the septic patient population.

Methods We collected peripheral blood mononuclear cells from 47 patients with severe sepsis or septic shock at ICU admission (T0) and from 50 healthy controls. On these subjects we evaluated frequency and absolute numbers of $CD4^+$ and $CD8^+$ T cells and of NK and B lymphocytes, the rates of regulatory $CD4^+CD25^+Foxp3^+$ T cells (Tregs), the cytotoxic potential of $CD4^+$, $CD8^+$ T cells and of NK cells by evaluation of perforin (PER) and granzyme (GRA) expression and production of effector cytokines (namely IL-2, IL-17, IL-4, TNFα, IFNγ) by $CD4^+$, $CD8^+$ T cells and NK cells upon polyclonal stimulation. The markers were compared in patients with different outcome.

Results Septic patients, compared with healthy donors, were characterized by global lymphopenia; we found increased frequencies of $CD4^+$ T cells producing IL-2 ($P = 0.0000000003$), increased percentage of CD8 T cells producing IFNγ ($P = 0.03$), and reduced proportion of $CD4^+$ T cells ($P = 0.00007$) and NK cells ($P = 0.002$) producing IFNγ. We also noticed an increased frequency of $CD8^+$ T cells expressing PER ($P = 0.00000025$) and GRA ($P = 0.01$); moreover, the proportion of NK cells expressing GRA was also significantly increased ($P = 0.000019$). To establish the prognostic value of these biological markers, we compared the cytokine expression by lymphocytes in septic patients that survived with those that died (D). We found that $CD4^+$ and $CD8^+$ TNFα-producing T cells were significantly increased in D ($P = 0.01$ and $P = 0.0001$ respectively); similarly the percentage of $CD8^+$ T cells producing IFNγ was more elevated in D ($P = 0.006$). The same was observed for IL-17 production by $CD4^+$ T cells ($P = 0.03$) in D. On the contrary we observed a tendency to the reduction of circulating $CD4^+CD25^+$foxp3 (Tregs) in D ($P = 0.08$).

Conclusion Septic patients are characterized by a peculiar immunophenotype which includes global lymphopenia and a specific pattern of cytokines. Some of the evaluated markers seem to individuate those with worse outcome; in particular, this group showed an inflammatory phenotype with a higher expression of IFNγ, TNFα, IL-17 and a tendency to a reduction of Tregs.

P38

Reduced responsiveness of blood leukocytes to lipopolysaccharide does not predict nosocomial infections in critically ill patients

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Introduction Critically ill patients show signs of immune suppression, which is considered to increase vulnerability to nosocomial infections. Whole blood stimulation is a frequently used functional test for immune suppression. We here aimed to assess the association between whole blood leukocyte responsiveness to lipopolysaccharide (LPS) and the subsequent occurrence of nosocomial infections in critically ill patients admitted to the ICU.

Methods All consecutive critically ill patients admitted to the ICU between April 2012 and June 2013 with two or more systemic inflammatory response syndrome criteria and an expected length of ICU stay of more than 24 hours were enrolled. Age-matched and gender-matched healthy individuals were included as controls. Blood was drawn the first morning after ICU admission and stimulated *ex vivo* with 100 ng/ml ultrapure LPS for 3 hours. Tumor necrosis factor (TNF)α, interleukin (IL)-1β and IL-6 were measured in supernatants.

Results Seventy-three critically ill patients were included, 10 of whom developed an ICU-acquired infection. Compared with healthy subjects, whole blood leukocytes of patients were less responsive to *ex vivo* stimulation with LPS, as reflected by strongly reduced TNFα, IL-1β and IL-6 levels in culture supernatants. However, results were not different between patients who did and those who did not develop an ICU-acquired infection (Figure 1).

Conclusion The extent of reduced LPS responsiveness of blood leukocytes in critically ill patients on the first day after ICU admission does not relate to the subsequent development of ICU-acquired infections.

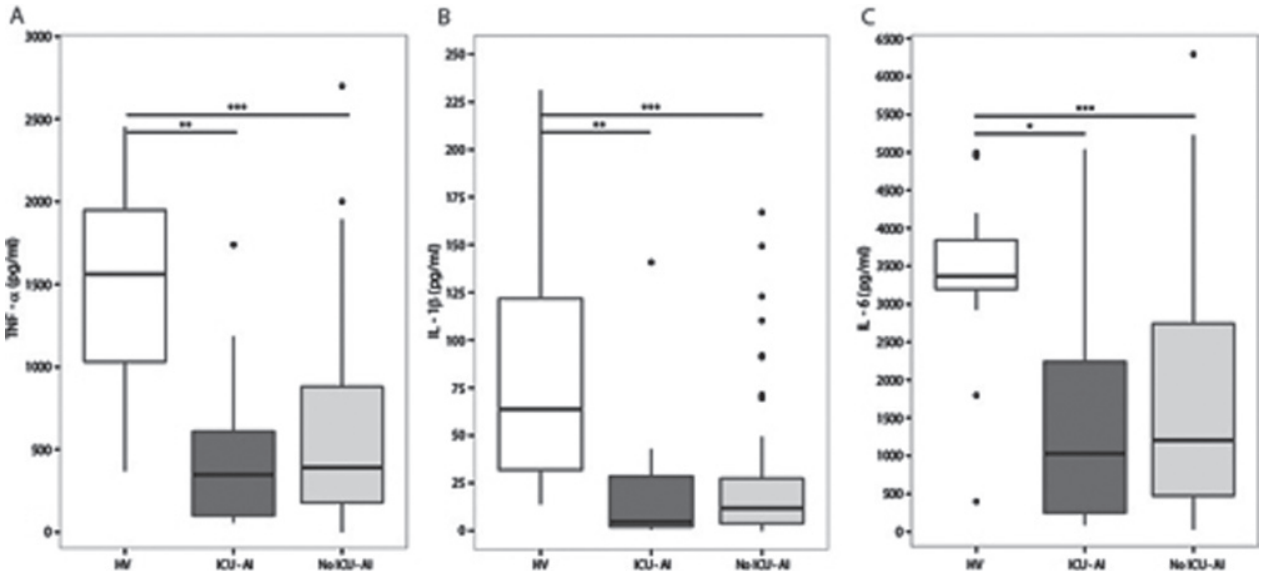


Figure 1 (abstract P38). Similarly reduced responsiveness of whole blood leukocytes to lipopolysaccharide.

P39

Cell-culture model to study endothelial activation in sepsis

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Introduction The endothelium is a complex organ influenced by circulating mediators, adjacent cells, physico-chemical factors, and shear stress. During systemic inflammation and sepsis, excessive and sustained activation of the endothelium result in the loss of its anti-coagulant and anti-adhesive characteristics as well as in a loss of endothelial barrier function. We set up a cell-culture model to study endothelial activation induced by lipopolysaccharide (LPS) or by plasma from septic patients and studied the effect of adsorbent-based mediator modulation on endothelial activation.
Methods Human whole blood was stimulated with LPS (100 ng/ml) from *Escherichia coli* for 4 hours. The stimulated blood or plasma from septic patients was treated *in vitro* with 10 vol% polystyrene–divinylbenzene (PS-DVB)-based polymers (CG161, mean pore size 16 nm; CG300, mean pore size 30 nm) or left untreated. After adsorption, the plasma was separated and diluted with cell culture medium. The resulting conditioned medium was used to stimulate human umbilical vein endothelial cells (HUVEC) for 16 hours. HUVEC activation was assessed by the release of interleukin (IL)-1β, IL-6, IL-8, IL-10, and tumor necrosis factor (TNF)α, plasminogen activator inhibitor-1 (PAI-1), as well as the expression of intercellular adhesion molecule (ICAM)-1 and E-selectin. HUVEC were cultured at a shear stress of 5 dyne/cm^2 using the Ibidi perfusion system. Adhesion of monocytic THP-1 cells to HUVEC was studied after 4 hours of HUVEC stimulation with conditioned media. THP-1 cells were perfused over HUVEC at 1 dyne/cm^2 for 15 minutes, and adhering THP-1 were quantified over time.
Results The adsorbents CG161 and CG300 substantially decreased levels of TNFα, IL-1β, IL-6, IL-8 and IL-10 in LPS-stimulated blood. TNFα, a key stimulus for HUVEC, was reduced to 12% and 8% of the initial concentration by CG161 and CG300, respectively. Stimulation of HUVEC with the adsorbent-treated plasma resulted in significantly diminished release of IL-6, IL-8, PAI-1 and decreased ICAM-1 and E-selectin expression, indicating reduced HUVEC activation. THP-1 adhesion was substantially decreased when HUVEC were stimulated with CG300-treated plasma as compared with untreated controls.
Conclusion The flow model allows to study the effect of cytokine modulation on endothelial activation and to assess the interaction of activated endothelial cells with blood cells. Modulation of inflammatory mediators with porous polystyrene-based polymers attenuates endothelial activation and reduces monocyte adhesion.

P40

Alarming levels of heat shock proteins 72 and 90α in critically ill children

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Introduction Extracellular heat shock proteins (HSP) act as inducers of interleukins (IL) and stimulants for immune cells during systemic inflammatory response syndrome (SIRS). Little is known about the alarming roles of extracellular HSP72 and HSP90α in the acute phase [1] of sepsis (S) or severe sepsis (SS). We determined serum HSP90α, HSP72 and neutrophil CD64 expression, IL-6, IL-8, IL-10, and TNFα in children with S or SS compared with SIRS (brain injury) or healthy children (H).
Methods Critically ill children with S (n = 16), SS (n = 15) or SIRS (n = 18) and H (n = 21) were enrolled in the study. ELISA was used to evaluate HSPs, chemiluminescence to measure ILs, and flow cytometry to evaluate nCD64 expression (IRB approved).
Results Patients in both septic groups had elevated HSP90α (P <0.0001), HSP72 (P <0.05), IL-6 (P <0.0001), IL-8 (P <0.02) and IL-10 (P <0.05) levels compared with H, whereas SS had increased HSP72, IL6 and TNFα compared with SIRS (P <0.05). SIRS patients presented increased HSP90α, IL-6 and IL-8 compared with H (P <0.05). Both HSPs were dramatically increased among nonsurvivors. In a logistic regression model, only HSP90α was independently associated with mortality (P <0.0001). HSP90α related positively (P <0.001) to nCD64, IL-8, IL-10, CRP, PRISM, PELOD, TISS, and LOS and negatively to HDL (P <0.001) and LDL (P <0.02). HSP72 also related negatively to HDL (P <0.001).
Conclusion Extracellular HSP72 and HSP90α are alarmingly elevated in critically ill children, especially in severe sepsis. HSP90α levels are independently associated with mortality, related to CD64, IL-8, IL-10, severity of illness, and outcome. Both HSPs are inversely related to the low LDL/low HDL septic metabolic pattern [2].
Acknowledgements This research has been co-financed by the European Union (European Social Fund) and Greek national funds through the Operational Program 'Education and Lifelong Learning' of the National Strategic Reference Framework Research Funding Program: THALES. Investing in knowledge society through the European Social Fund.

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P41

Early heat shock protein 72 and 90α intracellular and extracellular responses in patients with severe sepsis or systemic inflammatory response syndrome

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Introduction Heat shock proteins (HSPs) have intracellular cytoprotective actions, while they act extracellularly as inducers of cytokines and stimulants for immune cells during stress. Their induction constitutes a highly conserved cellular defense mechanism against all kinds of stress. Our objective was to determine the intracellular as well as extracellular levels of HSP72 and HSP90α in patients with severe sepsis (SS) or systemic inflammatory response syndrome (SIRS) admitted to a general ICU, compared with those of healthy individuals; to correlate their expression with severity of illness.
Methods Eighty-two consecutively admitted patients in the ICU (35 SIRS, 47 SS) as well as 35 healthy controls (H) were finally enrolled in the study. Patients' demographic characteristics, laboratory examinations and Acute Physiology and Chronic Health Evaluation (APACHE II) score were recorded on admission. HSP levels were determined intracellularly using four-color flow cytometry. Mean fluorescence intensity (MFI) values for each HSP were measured and analyzed. Extracellular levels of HSPs were determined via ELISA.
Results HSP expression differed significantly between groups (Kruskal–Wallis), both intracellularly (HSP72 lower in SS, P <0.001), and extracellularly (higher levels of HSP90α (P <0.001) and HSP72 (P = 0.003) in SS). HSP72 and HSP90α intracellular expression was inversely correlated to severity of illness, as expressed by APACHE II score (Spearman's, P = 0.003 and P = 0.025 respectively). Intracellular HSP72 was correlated to mortality when confounding factors were excluded from the analysis (logistic regression, P = 0.05). Extracellular HSP90α levels correlated with prolonged PT (P = 0.021) and INR (P = 0.008). Finally, in the SIRS group, intracellular levels of HSP90α were higher in nonsurvivors (P <0.001).
Conclusion SS is characterized by high levels of extracellular HSPs. Intracellular HSP72 is highly expressed during the acute phase of stress in SIRS, while being downregulated in SS. HSP72 and HSP90α intracellular expression and extracellular level variations correlate with severity of illness and mortality.
Acknowledgements This research was co-financed by the European Union (European Social Fund) and Greek national funds through the Operational Program 'Education and Lifelong Learning' of the National Strategic Reference Framework Research Funding Program: THALES.

P42

Heat shock proteins 70/90 and associations with immunosuppression along with sepsis: preliminary data

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Introduction CD14/HLADR is an index of immune suppression. Heat shock proteins (hsp) regulate cell response to oxidative stress. We evaluated the relationship of CD14/HLADR and hsp70/90 in patients with SIRS and severe sepsis versus healthy volunteers.
Methods We evaluated 31 patients with SIRS or severe sepsis against a group of sex-matched healthy volunteers. Demographic data were obtained for all patients. APACHE score was calculated upon admission. Blood samples were collected upon diagnosis of SIRS or severe sepsis. To evaluate the %HLA-DR expression on monocytes, the fresh whole blood was stained with anti-CD14-FITC, anti-HLA-DR-PE and CD45-PC5 while staining with anti-CD33-PE, anti-CD45-PC7, anti-hsp70-FITC and anti-hsp90-PE allowed evaluation of the MFI expression of hsps on $CD33^+$ monocytes. Cells were then analyzed using flow cytometry. ANOVA with *post hoc* tests was used to compare CD14/HLADR cell counts and hsp70 and hsp90 levels among the three groups.
Results Nineteen controls, six SIRS patients and 25 severe sepsis patients were studied. The percent expression of HLADR on $CD14^+$ monocytes was significantly different between the three groups showing progressive decrease from controls (mean 90.5 ± 3.8%) to SIRS (mean 61.2 ± 5.9%) to severe sepsis (mean 39.2 ± 5.5%) patients (controls vs. severe sepsis, P <0.001; controls vs. SIRS, P = 0.006; SIRS vs. severe sepsis, P = 0.03). hsp70 and hsp90 MFI were significantly different between controls (mean 49.5 ± 4.9 and 33.5 ± 3.4 respectively), SIRS (mean 69.9 ± 16.5 and 46.5 ± 5.7 respectively) and severe sepsis patients (mean 33.3 ± 4.5 and 21.7 ± 2.7 respectively) (P <0.05 for all comparisons). Notably, the hsp level rose from controls to SIRS and fell from SIRS to severe sepsis patients. APACHE score increased significantly (P = 0.023) in septic patients compared with SIRS.
Conclusion There were a significant difference in CD14/HLADR, a marker of immune paralysis, between controls and patients with SIRS or severe sepsis. hsp70 and hsp90 showed an initial stimulation followed by exhaustion as sepsis progressed.
Acknowledgements This research was co-financed by the European Union (European Social Fund) and Greek national funds through the Operational Program 'Education and Lifelong Learning' of the National Strategic Reference Framework Research Funding Program: THALES. This abstract is part of the study 'Heat Shock Proteins and Glutamine Alterations Related to Hormonal, Immunological, Inflammatory and Molecular Response to Sepsis: A Combined Clinical and Experimental Study'.

P43

Prospective immune profiling in critically ill adults: before, during and after severe sepsis and septic shock

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Introduction Rethinking the host's defense mechanisms during severe infection has led to the use of flow cytometry (FCM) and to the current concept of sepsis-induced immunosuppression. However, organ dysfunctions that develop in the period preceding severe sepsis as a consequence of surgery, trauma or burn might also trigger immune reprogramming predisposing to overwhelming infection. Our aim was to look for correlation of specific phenotypes among four commonly encountered populations of patients and the later occurrence of severe sepsis and septic shock.
Methods In total, 114 non-infected patients were prospectively screened via FCM on days 1 (T1) and 3 (T2) of elective cardiac surgery, trauma, acute neurologic dysfunction and prolonged ventilation (>48 hours). A third sample was drawn when infection was diagnosed (Tx) and 7 days later (Tx + 7). Exclusion criteria included use of immunosuppressive agent(s). The broad panel of cell-specific antibodies focused on B, T lymphocytes (Tregs, Th17, NKT), NK cells, monocytes and neutrophils. Plasmatic levels of IL-2/IL-6/IL-7/TNFα/IFNγ were also determined.
Results Ninety-nine patients were included in the final analysis. Eighteen patients developed severe sepsis or septic shock. They presented with significantly higher levels of intermediate ($CD14^{++}/16^+$) and $CD62L^-$ monocytes and lower IL-2 levels at T1 compared with patients who did not get septic. ROC AUC for association of these parameters with the occurrence of sepsis were 0.78 (95% CI: 0.63 to 0.91), 0.72 (0.62 to 0.82) and 0.73 (0.65 to 0.82), respectively. High counts of these monocytic cells were also associated with increased 90-day mortality (P <0.01, ROC AUC = 0.87 (0.77 to 0.95), 0.79 (0.66 to 0.9)). Kaplan–Meier survival curves showed significantly higher mortality after stratification based on these cell counts at T1 ($CD14^{++}CD16^+$: cutoff >236.8 cells/μl, HR = 23.6 ($P = 1.24 \times 10^{-5}$); $CD62L^-$: cutoff >95.4 cells/μl, HR = 6.67 ($P = 7.6 \times 10^{-4}$)). Multivariate logistic regression analysis using

clinical scores indicated that addition of IL-2 levels at T1 significantly improved prediction of sepsis (OR = 0.834, $P = 0.02$).
Conclusion Predisposition to sepsis in selected critically ill medico-surgical adults can be identified on day 1 of admission based on high counts of circulating intermediate and $CD62L^-$ monocytes and low levels of IL-2 (the latter provide incremental prognostic information). High counts of these specific monocytes correlate with higher 90-day mortality.

P44

Macrophage phenotype in sepsis immunosuppression

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Introduction Sepsis is followed by profound, yet poorly characterized, innate immune system suppression. While low monocyte HLA-DR expression is observed in septic patients, its clinical significance has not been established [1]. *In vitro*, repeated LPS stimulation induces a tolerant or M2 macrophage phenotype, characterized by decreased cytokine production [2], which could contribute to sepsis immunosuppression. The present study examines macrophage phenotype in a mouse model and in patients with sepsis immunosuppression.
Methods Sepsis was induced in C57Bl6 mice by cecal ligation and puncture (CLP) followed by intratracheal instillation of *Pseudomonas aeruginosa*. Bronchoalveolar lavage fluid (BALF), cells and serum, collected 12 hours after lung infection, were analyzed for bacterial load, cytokine levels and the classical M1 marker, iNOS. Peripheral blood monocytes isolated from septic adult patients admitted to the ICU on the 1st and 7th day after admission were analyzed by flow cytometry for the expression of HLA-DR and CD86 (co-stimulatory molecule and M1 marker), and for the M2 markers, CD163 and CD206. Additional blood samples from patients and healthy volunteers were exposed *ex vivo* to LPS prior to isolation and analysis of monocyte markers.
Results CLP-induced sepsis resulted in immunosuppression in mice, indicated by higher BALF bacterial load after infection in CLP than in sham-operated mice, and more severe injury on histology. Serum cytokines TNF and MIP2 were greater in CLP than in sham-operated mice. Although recruitment of $CD11c^+$ alveolar macrophages post infection was threefold greater in CLP than in sham-operated mice, those macrophages expressed 40% lower levels of iNOS. Evidence of sepsis immunosuppression was present in most patients on the 7th day after ICU admission. Low expression of CD86 and/or HLA-DR was observed in 71% of patients, and increased expression of M2 markers in 15% of patients. Upon LPS stimulation the normal decrease in M2 markers was absent in all patients on day 1, and partially restored in 50% of patients on day 7.
Conclusion Sepsis is associated with decreased monocyte expression of M1 markers and increased expression of M2 markers in septic mice and critically ill patients. Therefore, in addition to decreased HLA-DR expression, M2 macrophage polarization appears to be a component of sepsis-induced monocyte dysfunction, and should be considered for immune monitoring and targeted intervention.
Acknowledgement Supported by GSRT research grant Excellence-4620.
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P45

Expression of mRNA levels of HLA-DRA in relation to monocyte HLA-DR: a longitudinal sepsis study

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Critical Care 2015, **19(Suppl 1):**P45 (doi: 10.1186/cc14125)

Introduction Decreased monocyte surface HLA-DR (mHLA-DR) measured by flow cytometry (FCM) is an independent marker of immunosuppression in sepsis. In a previous report we demonstrated that septic patients display a strong correlation between mHLA-DR and mRNA-levels of HLA-DRA in whole blood [1]. mRNA-based HLA-DR monitoring by PCR would improve the clinical usage and facilitate conduction of multicentre studies. The primary focus in this study was to evaluate the correlation between mHLA-DR and HLA-DRA at different time points during sepsis. In addition, we assessed the dynamic expression of both mHLA-DR and HLA-DRA, in relation to sepsis severity.
Methods Study patients ($n = 54$) were included at day 1 to 2 after hospital admission if blood cultures turned positive. Repeated sampling at days 1 to 2, 3, 7, 14 and 28 was performed. mHLA-DR was monitored by FCM and HLA-DRA by quantitative RT-PCR. Mixed models for longitudinal data were used after logarithmic transformation to calculate the interactional effects of time and severity on HLA-DR expression.

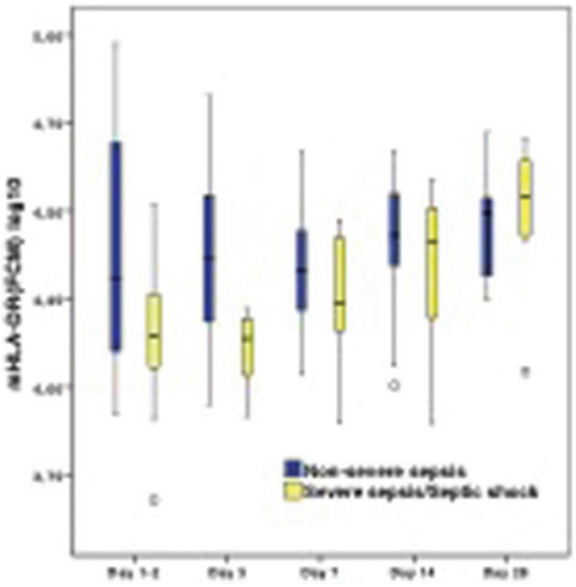


Figure 1 (abstract P45). Box plots of mHLA-DR, measured by flow cytometry.

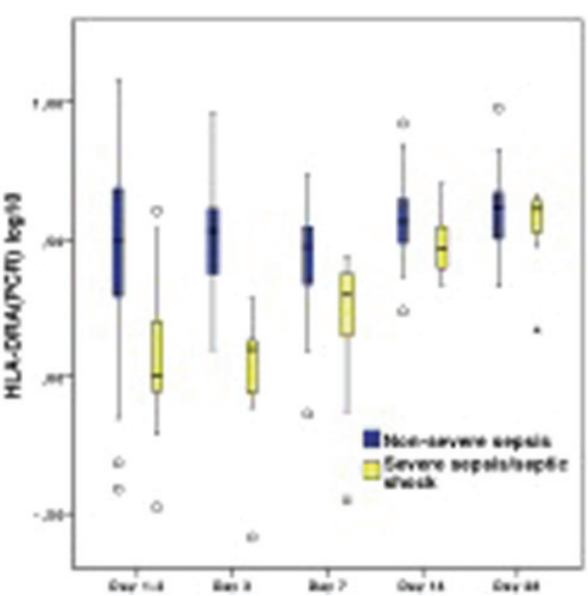


Figure 2 (abstract P45). Box plots of HLA-DRA, measured by qRT-PCR.

Results Correlation between mHLA-DR(FCM) and HLA-DRA(PCR) at day 1 to 2 ($R = 0.78$) and day 14 ($R = 0.27$). Both HLA-DR markers increased linearly on a log scale over time. The linear association was significantly different between the severe ($n = 16$) and nonsevere septic patients ($n = 38$) when measuring either mHLA-DR(FCM) or HLA-DRA(PCR). By pairwise comparison of means between the two severity groups, at every time point, the differences between groups were shown to be significant at days 1 to 2 and 3 when monitoring mHLA-DR(FCM) and at days 1 to 2, 3 and 7 for HLA-DRA(PCR) (Figures 1 and 2).
Conclusion The correlation between flow cytometry and PCR-based HLA-DR monitoring is stronger in the early phase of sepsis. However, the linear associations over time, in relation to sepsis severity, display similar results for both HLA-DR markers. HLA-DRA(PCR) as a biomarker could be an alternative approach in monitoring immune status in sepsis but needs to be evaluated in relation to clinically relevant immunosuppression.
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P46

HLA-DR monocyte antigen expression as predictors of outcome in patients with community-acquired infections presenting with fever

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Introduction The aim of the present study was to evaluate the prognostic value of HLA-DR antigen expression in monocytes, in patients with community-acquired infections presenting with fever, as possible markers for the patients' final outcome.
Methods A total of 81 patients (males = 46; females = 35) presenting with fever >38°C to the emergency room (ER) of the Department of Internal Medicine of the Patras University Hospital were enrolled in the study during a period of 12 months. Sera for monocyte HLA-DR expression were obtained from the patients on admission (day 1) and on days 3, 7 or discharge/death. Results were expressed as percentages of HLA-DR-positive monocytes, calculated by the coexpression of CD14 and HLA-DR antigens in the total $CD14^+$ population. Additionally, the patients were evaluated using the Simplified Acute Physiology Score (SAPS-II), the Sequential Organ Failure Assessment (SOFA) and the Mortality in Emergency Department Sepsis (MEDS) score on the same days while all the indicated clinical, laboratory and imaging procedures as required for fever's differential diagnosis were followed. A questionnaire regarding demographic characteristics, comorbidities, medications used and patients' survival was also completed. All statistical analyses were performed using SPSS v.21.
Results Lower mean HLA-DR monocyte antigen expression percentages were significantly correlated to lower Glasgow Scale scores on all days of measurement. HLA-DR expression was significantly negatively correlated to MEDS, SOFA and SAPS-II scores whereas patients who developed sepsis, severe sepsis, septic shock and MODS had significantly lower HLA-DR values compared with the ones who did not. HLA-DR expression on day 1 was lower in patients who would develop SIRS and/or sepsis on days 3 and 7 ($P < 0.01$). Additionally, HLA-DR expression was significantly decreased in nonsurvivors ($n = 33$) compared with survivors ($n = 48$), whereas lower HLA-DR expression was correlated to longest duration of hospital stay at all time points ($P < 0.01$).
Conclusion Monocyte HLA-DR appears to be an early indicator for survival and infection progression and therefore it can be used as a predictive marker for the final outcome of patients presenting in ER departments with fever.

P47

Eosinopenia as a marker of sepsis and mortality in critically ill patients

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Introduction The idea of using the eosinophil count (EC) as a diagnostic marker for clarifying the nature of systemic inflammatory response syndrome (SIRS) belongs to K Abidi, who showed that EC could be used as a diagnostic criterion of sepsis. There are no published data to define the role of dynamic control of EC in the process of intensive therapy as a prognostic marker and indicator of severity condition in critically ill patients. The aim was to determine the informative value of EC in the development of SIRS as a biomarker of sepsis and indicator of the severity condition and prognosis of outcome in the pathological process.
Methods A total of 143 patients were enrolled in this study who were admitted to the ICU and had SIRS. All patients were divided into a septic group – patients with community-acquired pneumonia, complicated by sepsis – and two SIRS groups of noninfectious genesis – patients who had an acute cerebrovascular accident (CVA) and an acute myocardial infarction (AMI). The absolute EC was measured at admission and in the dynamics on days 3 to 5 of stay.
Results The median EC was 75 cells/mm^3 in septic patients on admission, which was significantly lower than in patients with CVA (120 cells/mm^3) and AMI (130 cells/mm^3). Comparison of EC in septic patients between survivors and those who died showed significant differences (Table 1). Receiver operating characteristic (ROC) analysis determined a value less than 80 cells/mm^3 as the optimal diagnostic cutoff value with a high level of confidence in the comparison of septic and noninfectious groups. Area under the ROC curves was 0.94, sensitivity of 80.8%, specificity of 95.6%, $P < 0.0001$. There was a significant increase of EC in survivors, while the EC did not change significantly among those who died in the dynamics. ROC analysis determined the cutoff values of EC, which indicated a high risk of an adverse outcome in septic patients (Table 2).

Table 1 (abstract P47). Dynamics of eosinophil count depending on outcome in groups

	EC (cells/mm^3) at admission			EC (cells/mm^3) on the 3rd to 5th days		
Group	**Survivors**	**Died**	***P* value**	**Survivors**	**Died**	***P* value**
Sepsis	100	50	0.006	240	70	0.0004
CVA	120	115	0.74	150	90	0.001
AMI	145	120	0.60	195	120	0.017

Table 2 (abstract P47). Informational value of eosinophil count in assessment of disease outcome

Day/group	AUC	Cutoff (EC, cells/mm^3)	Sensitivity (%)	Specificity (%)	*P* value
At admission					
Sepsis	0.83	≤220	100	61.5	0.0001
CVA	0.53	≤150	78.3	37.5	0.743
AMI	0.56	≤190	85.7	35.7	0.6136
On the 3rd to 5th days					
Sepsis	0.91	≤120	92.3	69.2	<0.0001
CVA	0.81	≤140	91.3	68.8	<0.0001
AMI	0.75	≤90	92.9	46.7	0.0052

Conclusion EC may be an additional diagnostic marker which characterizes the nature of SIRS. Eosinopenia associated with prognosis of outcome in critical conditions.

P48

Prevalence and clinical significance of early endotoxin activity in septic shock patients

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Introduction The endotoxin activity (EA) assay is a useful test to risk stratify critically ill patients and assess for Gram-negative (GN) infection. However, the prevalence and significance of early high levels of EA in patients with septic shock (SS) has yet to be elucidated.

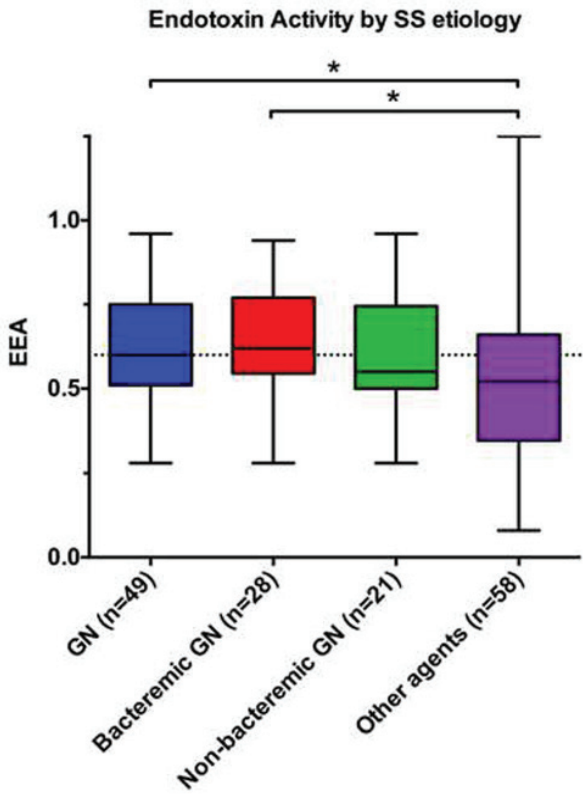


Figure 1 (abstract P48).

Methods We designed a prospective observational study including adult patients with clinically diagnosed SS. EA was measured on arterial blood by a chemiluminescent assay within the first 24 hours from SS diagnosis. The finding of an EA value ≥0.6 was used as the cutoff for test positivity, as described elsewhere. In addition, laboratory, microbiological and clinical data were collected at inclusion. In-hospital follow-up was also conducted.
Results A total of 107 consecutive patients were included. The overall median EA was 0.56 (0.44 to 0.71), with 46/107 (43%) patients testing positive for elevated EA (≥0.6). GN species were identified in microbial cultures as the infective etiology in 49/107 (46%) patients, of which 28 (57%) developed bacteremia. GN infections were associated with higher levels of EA compared with other microbial causatives (0.61 (0.52 to 0.77) vs. 0.52 (0.38 to 0.64), $P = 0.021$). Patients with EA ≥0.6 showed significantly higher lactate levels (2 (1 to 3) vs. 3.8 (1.7 to 6.4), $P = 0.01$), Sequential Organ Failure Assessment (9 (6 to 12) vs. 10 (8 to 14), $P = 0.04$) and inotropic score (20 (5 to 50) vs. 50 (16 to 100), $P = 0.003$) at inclusion. See Figure 1.
Conclusion Elevated EA is a common finding in SS patients. In patients developing SS from a GN infection, higher levels of endotoxin activity could be measured within 24 hours. Furthermore, in our study, EA ≥0.6 identified a subgroup of subjects at greater risk for worse clinical outcomes. We therefore propose use of the EA assay for the early identification and risk stratification of SS patients.

P49

Usefulness of endotoxin activity assay for early diagnosis of sepsis

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Introduction The purpose of this study was to evaluate the diagnostic and prognostic value of the endotoxin activity assay (EAA) of sepsis in patients with systemic inflammatory response syndrome (SIRS) and organ failure in ICU setting.
Methods In total, 76 patients with SIRS and organ failure or who were suspected of sepsis during critical care were included. According to the levels of EAA, all patients were classified into three groups (group L, EAA <0.4; group M, EAA ≥0.4 or EAA <0.6; group H, EAA ≥0.6). In order to evaluate the severity of illness, the Acute Physiology and Chronic Health Evaluation II (APACHE II) score, Sequential Organ Failure Assessment (SOFA) score and catecholamine (CA) index were recorded. Blood samples were obtained to measure EAA levels, inflammatory markers (procalcitonin, C-reactive protein and white blood cells), serum lactate level as an indicator of tissue hypoxia, and for blood culture. All patients were followed up for 6 months. APACHE II score, SOFA score, CA index, inflammatory markers, serum lactate levels and blood culture results were examined for diagnosis of sepsis, severe sepsis, septic shock and for prognosis of 30-day mortality. Each value was also compared with EAA levels.
Results Patient age was 69 ± 9.9 years (male: $n = 48$, female: $n = 25$). The total number of samples was 106 (group L/group M/group H: 35/35/36). Twenty-seven specimens were obtained from nonseptic patients and 83 specimens were obtained from septic patients. APACHE II score was highly correlated with SOFA score ($P < 0.05$). In group H, the APACHE II score was significantly higher (22.2 ± 0.8) than that in group M (18.4 ± 0.87) ($P = 0.01$). The SOFA score in group H was significantly higher (9.9 ± 0.5) than that in group M (7.5 ± 0.6) and group L (7.9 ± 0.6) ($P = 0.006$). EAA levels were significantly increased in septic patients (septic patients: 0.56 ±0.03, nonseptic patients: 0.42 ±0.05) ($P = 0.011$) and in the positive blood culture group (positive group: 0.66 ± 0.05, negative group: 0.48 ± 0.03) ($P = 0.006$). There was no relationship between EAA levels and other inflammation markers or 30-day mortality.
Conclusion In patients with suspected sepsis and positive blood culture, EAA levels were significantly increased and had strong correlation with severity of disease. This result suggests that EAA indicates the state of sepsis regardless of the possibility of infection in patients with SIRS with organ failure.

P50

Biomarkers in sepsis: a systematic review

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Introduction Sepsis is a common reason for admission to ICUs throughout the world. During the past two decades, the incidence of sepsis in the USA has tripled and is now the 10th leading cause of death. As sepsis continues to impact negatively on critically ill patients, it is clear that early diagnosis and effective management could improve patient morbidity and mortality. Numerous studies have attempted to examine biomarkers and their ability to diagnose and prognosticate septic patients. Despite multiple efforts, currently there are no reliable markers that can effectively improve our clinical effectiveness in diagnosing and managing septic patients. The purpose of our systematic review was to evaluate the diagnostic and prognostic value of various biomarkers used in septic patients.
Methods A systematic search of the literature was performed with MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials databases using terminology selected for biomarkers (through to and including November 2013). All articles involving neonates and not in English were excluded. Inclusion was agreed on by two independent reviewers of abstracts or full text. Assessment was based on the biomarker's ability to diagnose septic patients and its ability to predict mortality.
Results Of 5,257 articles identified, all abstracts were screened, and 750 full-text articles were selected for review. These included primarily randomized controlled trials, cohort studies and postmortem studies. Of 49 biomarkers examined, 72% of the studies examined procalcitonin. Comparing the serum of septic patients with that of controls, most biomarkers were elevated in septic patients, even though only a few had high sensitivity (>85%) and high specificity (>80%). It was often

difficult to compare study group with control group as the control group patients were usually not healthy controls.
Conclusion Overall the heterogeneity of studies, small sample size and the lack of true healthy controls influenced the ability to use the biomarker for prognostication of a septic patient. Furthermore, the lack of healthy control raises the question of redefining selection criteria in order to better study septic patients.

P51

C-reactive protein and hemogram parameters for the nonsepsis SIRS and sepsis: what do they mean?

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Introduction The aim of this study was to investigate the laboratory parameters as an indicator of sepsis. Sepsis is one of the most common reasons of mortality and morbidity in the ICU [1]. Thus, it is important to distinguish sepsis from nonsepsis SIRS. CRP and hemogram parameters may be fast, easy and affordable alternatives in distinguishing sepsis from nonsepsis SIRS. Eosinophil count (EoC), lymphocyte count (LymC) and neutrophil–lymphocyte count ratio (NLCR) are used as sepsis indicators [1,2].
Methods A total of 2,777 patients admitted to the ICU of two centers between 2006 and 2013 were evaluated retrospectively. The patients were diagnosed as SIRS(–), nonsepsis SIRS or sepsis at ICU admission by the consensus of two doctors in accordance with 1992 sepsis guidelines [3]. The patients who were under 18 years old, readmitted, immunosuppressive, SIRS(–) and whose laboratory values and outcomes were unknown were excluded. In total, 1,302 patients were divided into two groups as the nonsepsis SIRS group and the sepsis group. The patient's age, gender, diagnoses (medical, elective and urgent surgery), APACHE II, SOFA, CRP, WBC, neutrophil count (NeuC), LymC, NLCR, EoC, platelet, mean platelet volume, length of ICU stay and mortality were recorded by a third doctor. In the fully adjusted model, WBC, CRP, LymC, NeuC, NLCR and EoC were entered into the model.
Results A total of 1,302 patients were categorized as nonsepsis SIRS (816, 62.7%) and sepsis (486, 37.3%). In the sepsis group, age, APACHE II, SOFA, mortality, length of ICU stay, CRP, NLCR and EoC were higher; LymC was lower than in the nonsepsis SIRS group (P <0.001 for each). Likelihood of sepsis (reference to nonsepsis SIRS) increased 2.62 (2.05 to 3.34), 2.02 (1.42 to 2.88) and 1.88 (1.36 to 2.60) times (OR (95% CI)) by the values of CRP >4.4 mg/dl, LmyC <500/mm^3 and NLCR >15.7 respectively in mutually adjusted multivariate logistic regression (P <0.001 for each).
Conclusion CRP, LymC and NLCR may distinguish sepsis from nonsepsis SIRS. Thus, CRP and hemogram parameters may contribute to early diagnosis of sepsis.
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P52

Serum cholinesterase activity as an early indicator of systemic inflammation

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Introduction Early diagnosis of systemic inflammation, a generalised response to noxious stimuli, is fundamentally important for effective and goal-directed therapy. Various inflammation biomarkers have been used in clinical and experimental practice. However, a definitive diagnostic tool for an early detection of systemic inflammation remains to be identified. Acetylcholine (Ach) has been shown to play an important role in the inflammatory response. Serum cholinesterase (butyrylcholinesterase (BChE)) is the major Ach hydrolyzing enzyme in plasma. The role of this enzyme during inflammation has not yet been fully understood. Here, we describe a correlation between the BChE activity and the early systemic inflammatory response upon traumatic injury.
Methods We measured BChE activity in patients with traumatic injury admitted to the emergency room using a point-of-care-test (POCT) system. In addition, we measured levels of routine inflammation biomarkers during the initial treatment period. We used the Injury Severity Score to assess the trauma severity. Data were statistically analyzed using the Friedman test. Correlation analysis was performed using Spearman's rank correlation test. P <0.05 was considered statistically significant.
Results Reduced BChE activity correlated with trauma severity and the resulting systemic inflammation. Compared with serum levels of routinely measured inflammatory biomarkers, changes in the BChE activity were detected significantly earlier, suggesting that the BChE activity might serve as an early indicator of systemic inflammation.
Conclusion Our results suggest that BChE activity, measured using a POCT system, might play an important role in the early diagnosis of trauma-induced systemic inflammation.

P53

Association between apoptosis and mortality in severe septic patients

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Introduction The apoptotic process, in which cells are actively eliminated by a programmed pathway, is increased in sepsis. Extrinsic and intrinsic apoptotic death cell pathways activate caspase-3, which leads to cell apoptosis. Cytokeratin 18 (CK-18), a protein present in most epithelial and parenchymal cells, is cleaved by the action of caspases and released into the blood as caspase-cleaved CK (CCCK)-18 during apoptotic death. The novel objectives of this study were to determine whether there are associations between serum caspase-3 levels, serum CK-18 levels and mortality in septic patients.
Methods A prospective, multicenter, observational study in six Spanish ICUs, including 216 patients with severe sepsis. We collected blood samples at the severe sepsis diagnosis moment to determine serum levels of caspase-3 (to assess the main executor of apoptosis) and CCCK-18 (to assess the apoptosis level). The endpoint was 30-day mortality.
Results We found that nonsurvivor (n = 76) in comparison with survivor (n = 140) septic patients showed higher serum levels of caspase-3 (0.41 ng/ml (0.14 to 0.52) vs. 0.11 ng/ml (0.10 to 0.25); P <0.001) and CCCK-18 (448 (310 to 723) vs. 319 (236 to 445); P <0.001). Multiple logistic regression showed that serum caspase-3 levels >0.25 ng/ml were associated with mortality at 30 days (odds ratio = 6.51; 95% confidence interval = 3.32 to 12.77; P <0.001), controlling for SOFA score and age. Kaplan–Meier survival analysis showed a higher risk of death in septic patients with serum caspase-3 levels >0.25 ng/ml than in patients with lower levels (hazard ratio = 3.80; 95% CI = 2.35 to 6.15; P <0.001). We found a positive association between serum levels of caspase-3 and CCCK-18 (ρ = 0.32; P <0.001).
Conclusion The novel findings of our study were that there is an association between serum caspase-3 levels, serum CK-18 levels and mortality in septic patients. There has been reported decreased apoptosis and increased survival in septic rats with the administration of caspase inhibitors; thus, it may be interesting to explore those agents in septic patients.
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P54

Sphingosine-1-phosphate is a new biomarker for severity in human sepsis

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Introduction During sepsis a leading symptom is capillary leakage caused by endothelial damage, followed by multiorgan dysfunction. Sphingosine-1-phosphate (S1P) is a bioactive lipid with multiple functions. Cellular reactions depend on the S1P concentration in the blood and its binding to five specific G-protein coupled receptors. S1P-regulated functions include: control of endothelial permeability; lymphocyte migration across microvessels depending on an S1P gradient; and control of vascular tone [1]. This clinical study will address the question of whether S1P blood concentrations are associated with sepsis severity.
Methods Following ethical approval we enrolled patients fulfilling the ACCP/SCCM sepsis criteria into three groups (Group A: sepsis; Group B: severe sepsis; Group C: septic shock). A group of 20 healthy donors served as controls. Serum blood samples, laboratory data and clinical parameters are presented for day 1. The primary outcome variable was serum S1P concentration (µg/l) quantified by mass spectrometry (Agilent®). The SOFA score was used to describe disease severity.
Results We included 87 patients (32 Group A, 25 Group B, 30 Group C). The serum concentration of S1P (mean ± SD) in the control group was 484.6 ± 152.6 µg/l and significantly higher compared with Group A 239.4 ± 61.3 µg/l, Group B 248.6 ± 93.7 µg/l and Group C 141.6 ± 46.3 µg/l. We observed a negative correlation between S1P and SOFA score (Pearson $r = -0.45$, $P < 0.001$, $R^2 = 0.2$). The median SOFA score in our cohort was 6. We divided the cohort into two groups: SOFA score <6; and SOFA score >6. We tested the sensitivity and specificity of S1P to indicate disease severity by ROC analysis. In our cohort the area under the curve (AUC) for S1P was 0.77 (CI 0.670 to 0.870) and therefore higher when compared with common markers of inflammation (PCT, IL-6, CRP with AUC of 0.68 (0.560 to 0.796), 0.68 (0.554 to 0.786) and 0.67 (0.571 to 0.794), resp.).
Conclusion Our findings suggest that S1P is a novel marker for severity of sepsis with severe sepsis and septic shock being associated with low levels of S1P. Moreover, blood concentrations of S1P might play a key role in sepsis pathophysiology.
Acknowledgements MSW and AN are equal contributors.
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P55

Diagnostic accuracy and clinical relevance of an inflammatory biomarker panel in early sepsis in adult critical care patients

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Introduction Low awareness, late recognition and delayed treatment of sepsis are still common. CD64 is a marker of the innate immune response upregulated in sepsis. The primary goal of this prospective, double-blind study was to compare the diagnostic accuracy of neutrophil CD64 and other cellular markers, along with C-reactive protein (CRP) and procalcitonin (PCT) levels, in early sepsis.
Methods Adult ICU patients, between 2012 and 2014 were eligible. The eight-color flow cytometric biomarker panel included CD64, CD163, HLA DR, CD15 and others. Diagnostic test results were compared with infection as the reference standard and sepsis as the target condition, using receiver operating characteristic curve analyses. Multivariable logistic regression was used to assess the relationship of sets of markers with the probability of sepsis, adjusting for other patient characteristics.
Results A total of 219 patients were enrolled, 120 with sepsis, 99 served as controls. APACHE IV (median 70 vs. 57), SOFA (8 vs. 7), ICU (2 vs. 1) and hospital length of stay (6 vs. 4) were higher in the sepsis group. Mortality was not different. After adjustment for APACHE IV, CRP and PCT, CD64 molecules/neutrophil measure remained a significant predictor of sepsis (OR = 1.852 for one-unit increase on the log scale, 95% CI = 1.083 to 3.168, $P = 0.02$, AUC = 0.90). See Table 1.

Table 1 (abstract P55). Area under the curve (AUC) for individual biomarkers

Measure	*N*	AUC	Cutoff for sepsis	Sensitivity (%)	Specificity (%)
C-reactive protein (mg/l)	208	0.86	43	76.9	76.9
CD64 molecules/neutrophil	196	0.83	1,040.5	76.4	76.7
Procalcitonin (ng/ml)	216	0.82	0.74	73.1	73.2
%CD64$^+$ neutrophils	196	0.81	49.96	74.5	74.4

Conclusion Neutrophil CD64 expression is an accurate predictor of early sepsis.

P56

Validation of B·R·A·H·M·S PCT direct, a new sensitive point-of-care testing device for rapid quantification of procalcitonin in emergency department patients: a prospective multinational trial

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Introduction Procalcitonin (PCT) is increasingly the standard in the emergency department (ED) for the diagnostic and prognostic workup of patients with suspected infections. Recently, B·R·A·H·M·S PCT direct, a new high-sensitive point-of-care test, has been developed for fast PCT measurement on capillary or venous blood samples with a measuring range of 0.1 to 10.0 µg/l.
Methods This is a prospective, comparative international study conducted in three European EDs. Consecutive patients with suspicion of bacterial infection were included. Duplicate determination of PCT was performed on two distinct B·R·A·H·M·S PCT direct test devices on capillary (fingertip) and venous whole blood (EDTA), and compared with the reference method (B·R·A·H·M·S PCT sensitive Kryptor or Elecsys B·R·A·H·M·S PCT, respectively). The diagnostic accuracy was evaluated by correlation and concordance analyses.
Results A total of 303 patients were included over a 6-month period (60.4% male, median age 65.2 years). The correlation between capillary or venous whole blood and the reference method was excellent: $r^2 = 0.96$ and 0.97, sensitivity 88.1% and 93.0%, specificity 96.5% and 96.8%, concordance 93% and 95% respectively at a 0.25 µg/l threshold. No significant bias was observed (–0.04 and –0.02 for capillary and venous whole blood) although there were 6.8% and 5.1% outliers, respectively. B·R·A·H·M·S PCT direct had a shorter time to result as compared with the reference method (25 vs. 147 minutes, difference 122 minutes, 95% CI = 110 to 134 minutes, $P < 0.0001$).
Conclusion This study found a high diagnostic accuracy and a faster time to result of the PCT direct in the ED setting. The B·R·A·H·M·S PCT direct may allow a more widespread use of PCT tests in outpatient clinics and smaller institutions.

P57

Serum procalcitonin level correlates with endotoxin activity in patients with septic shock

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Introduction Endotoxin, a key component on the outer membrane of Gram-negative bacteria, is considered to be the most important toxin

involved in the development of septic shock, and procalcitonin (PCT) serum concentration has been strongly associated with the severity of sepsis. The effect of elevated endotoxin activity (EA) on PCT serum level, organ function and mortality of patients with septic shock was evaluated on the day of admission to the ICU.
Methods ICU patients with diagnosis of septic shock were consecutively added to the study group within the first 24 hours. Serum PCT level and whole blood EA was immediately measured in all patients on admission (n = 157). Endotoxemia was defined as EA >0.4 EAU.
Results Endotoxemia was present in 61% of patients (group 1, n = 95, age 66 (57 to 75)), and in 39% of patients EA was low (group 2, n = 62, age 63 (55 to 76)). Median EA was 0.57 EAU (0.46 to 0.67) in group 1 and 0.27 EAU (0.17 to 0.36) in group 2 (P <0.001). The PCT level was six times higher in group 1 than in group 2 (19.6 ng/ml vs. 3.1 ng/ml, P <0.001) and was correlated with EA (P <0.001, R = 0.5). Median APACHE II score was 23 points (16 to 29) in group 1 and 19 (16 to 25) in group 2; but observed difference was not significant. The severity of clinical status estimated by SOFA score was similar in both groups (10 (7 to 13) in group 1 and 11 (8 to 12) in group 2; NS). Forty-six percent of patients in group 1 and 27% in group 2 required renal replacement therapy (P = 0.01). ICU mortality of patients was 41%. The mortality rate was higher in group 1, compared with group 2, and Kaplan–Meier survival analysis of time to death showed statistical significance between the two groups (P = 0.001, log-rank test). A Gram-negative pathogen as the primary source of infection was identified in 64% of patients in group 1 and in 44% in group 2 (P = 0.004); bacteremia was detected in 26% of cases in group 1 and in 12% in group 2 (P = 0.02).
Conclusion Septic shock with endotoxemia was associated with biochemical and clinical consequences including a higher PCT level, higher frequency of bacteremia, kidney failure, and death.

P58

Procalcitonin as prognostic marker in severe sepsis of abdominal origin

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Introduction We evaluated the utility of procalcitonin (PCT) as a marker of outcome in severe sepsis of abdominal origin (SSAO). SSAO is one of the most prevalent pathologies in surgical ICUs (sICUs). Mortality from 19 to 70% has been reported. Biomarkers are basic tools for diagnosis, follow-up and outcome of sepsis. One of the most studied in last decades has been PCT. Its levels and kinetics could be useful to evaluate the outcome of septic patients.
Methods We studied all patients admitted to a sICU with SSAO, from 2007 to 2008. Data collected were: PCT levels on days 1, 3 and 7, gender, age, APACHE II on admission, positivity of surgical cultures, microorganisms isolated and sepsis origin (community or nosocomial).
Results Sixty-nine patients were included. Mortality was 23%. Median age was 64.94 years. Median APACHE II was 16.43 points. At day 1, PCT levels were higher in survivors (S) than in exitus (E) (S: 29.22 ng/ml vs. E: 14.93 ng/ml, P <0.05). PCT levels were influenced by gender (males: 27.74 ng/ml vs. females: 15.04 ng/ml, P <0.05), positive cultures (positive: 25.25 ng/ml vs. negative: 13.49 ng/ml, P <0.05) and isolation of Gram-negative microorganisms (Gram-negative: 27.53 ng/ml vs. Gram-positive: 14.77 ng/ml, P <0.05). Patients with community-acquired sepsis had higher levels of PCT on admission (37.53 ng/ml vs. 13.29 ng/ml, P <0.02). None of these factors had an influence on mortality. On day 3 PCT levels where higher in S (S: 20.65 ng/ml vs. E: 16.23 ng/ml, P <0.05). On day 7 PCT levels were higher in E (S: 3.54 ng/ml vs. E: 12.88 ng/ml, P <0.05). PCT kinetics was different depending on outcome. E patients presented persistently higher levels, whereas PCT in S decreased over time (P <0.05). PCT on day 7 best identified outcome (AUC ROC 0.768). PCT ≥3.5 ng/ml predicted mortality (sensitivity 55%, specificity 73%).
Conclusion PCT on day 7 and PCT kinetics can be useful to predict outcome in SSAO. PCT is higher in community-acquired sepsis, when surgical cultures are positive, in Gram-negative isolations and in males.

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P59

Procalcitonin or lactate clearance, or both, for risk assessment in patients with sepsis? Results from a prospective US ICU patient cohort

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Introduction Blood lactate level is a routinely used biomarker for management of patients in septic conditions in the ICU. There is a lack of clinical research data comparing lactate with novel sepsis biomarkers, such as procalcitonin, in regard to the diagnostic and prognostic potential. Herein, we investigated the diagnostic and prognostic value of initial lactate and procalcitonin levels and their kinetics within the ICU stay for prediction of positive blood cultures and fatal outcome in a well characterized cohort of sepsis patients in a US critical care setting.
Methods This is a retrospective, observational cohort study of adult patients with confirmed severe sepsis or septic shock and with at least one procalcitonin and lactate measurement on admission to the ICU of Morton Plant Hospital (Clearwater, FL, USA). Logistic regression models were calculated to assess the association of biomarkers with blood culture positivity and fatal ICU outcome with area under the curve (AUC) as a measure of discrimination.
Results The in-hospital mortality rate of the 1,075 included patients (age 68 years) was 23.8% (95% CI = 21.2 to 26.3%) and 18.4% of patients had positive cultures. In regard to the diagnostic value for bacteremic disease, initial procalcitonin had a higher discriminatory value (AUC 0.71) compared with initial lactate levels (AUC 0.52). In regard to prognosis, initial lactate level was the better mortality predictor (AUC 0.69) compared with procalcitonin (AUC 0.55), although both initial levels were significantly lower compared with APACHE III (P >0.05 for both comparisons). When looking at biomarker kinetics, procalcitonin decrease was more strongly associated with fatal outcome compared with initial levels alone (AUC 0.66), but still lower compared with lactate kinetics (AUC 0.73).
Conclusion Both biomarkers, procalcitonin and lactate provide diagnostic and prognostic information in ICU patients with sepsis, particularly when looking at biomarker kinetics. An evidence-based protocol incorporating both markers may further improve management of septic patients.

P60

Diagnostic value of procalcitonin and IL-6 for sepsis of older patients and other patients in the emergency department

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Introduction Emergency physicians are able to identify severely ill older patients with SIRS in the emergency department (ED). A previous study showed that elevated procalcitonin (PCT) and IL-6 level is a known marker of sepsis and predicts bacteremia and mortality. We assessed the diagnostic value of PCT and IL-6 in older patients and other patients with SIRS and sepsis in the ED.
Methods This retrospective cohort study was conducted from January 2013 to December 2013. We enrolled 122 patients with SIRS, 55 were classified as the older age group (>65 years of age). Measurement of serum PCT, IL-6, and white blood cell count was performed on initial admission to the ED. We analyzed these markers in older patients and other patients groups with sepsis.
Results Of the 55 patients in the older group 33 (60%) patients had sepsis, and 40 (59.7%) patients of the other group had sepsis. PCT and IL-6 levels were significantly higher in other patients with sepsis (P <0.001, P <0.001). But PCT and IL-6 levels were not higher in old age

patients with sepsis ($P = 0.400$, $P = 0.169$). The area under the receiver operating characteristic curve (AUC) for diagnosis of sepsis according to PCT and IL-6 was 0.823, and 0.772 for the other patients group. The diagnostic sensitivity, specificity, positive predictive value, and negative predictive value of PCT for sepsis in other patients group were 79.5%, 81.5%, 86.1%, and 73.3% respectively, with a PCT cutoff value of 0.18 ng/ml. The diagnostic sensitivity, specificity, positive predictive value, and negative predictive value of IL-6 for sepsis in other patients group were 67.5%, 81.5%, 84.4%, and 62.9% respectively, with a IL-6 cutoff value of 74.43 pg/ml.

Conclusion PCT and IL-6 is useful predictive markers for diagnosing sepsis in adult patients (<65 years of age) with SIRS in the ED. But these markers are not useful for identification of sepsis in older patients.

P61

Procalcitonin levels in patients undergoing left ventricular assist device implantation

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Introduction Procalcitonin (PCT) is used for diagnosis of a bacterial infection. Several works described nonspecific elevation of PCT after cardiac surgery with cardiopulmonary bypass (CPB) caused by systemic inflammatory response syndrome (SIRS) with various cutoff values for the presence of the infection (0.47 to 2.47 µg/l). However, in patients undergoing left ventricular assist device (LVAD), implantation data about PCT dynamics are lacking.

Methods PCT levels in 25 patients indicated for LVAD were prospectively assessed before surgery and during the postoperative period (days 1, 2, 14 and 30). Values were compared according to the presence of infectious complications (IC) and non-infectious complications such as acute renal failure (ARF) defined as injury by RIFLE criteria or necessity of right ventricular assist device (RVAD). Data were also analyzed using combined endpoints A (ARF, RVAD) and B (IC, ARF, RVAD). Values are presented as median with interquartile range (in µg/l).

Results PCT levels were low before surgery (0.16, 0.10 to 0.35), increased significantly within the first (5.72, 2.18 to 9.75; P <0.001) and second (5.94, 2.54 to 11.99; P <0.001) day after operation and decreased on the 14th (0.27, 0.11 to 0.74) and 30th (0.10, 0.06 to 0.19) day. There was no significant difference in PCT values between patients with or without IC as well as with or without RVAD. ARF increased PCT level significantly only 14 days after LVAD implantation (0.68, 0.37 to 1.65 vs. 0.15, 0.11 to 0.34; $P = 0.015$). Subjects with endpoint A had significantly higher PCT values on the second (19.53, 5.66 to 63.12 vs. 3.95, 2.33 to 8.85; $P = 0.033$), 14th (0.55, 0.31 to 1.44 vs. 0.15, 0. to 0.34; $P = 0.020$) and 30th (0.19, 0.11 to 0.29 vs. 0.08, 0.05 to 0.13; $P = 0.016$) day after operation. Patients with endpoint B had significantly elevated PCT levels 2 (11.99, 3.23 to 24.16 vs. 3.95, 2.54 to 7.39; $P = 0.027$) and 14 (0.55, 0.28 to 0.90 vs. 0.13, 0.09 to 0.23; $P = 0.005$) days after surgery.

Conclusion PCT levels in patients undergoing LVAD implantation rise significantly in the first 2 days after surgery. Interestingly, this elevation is much higher than after routine cardiac surgery with CPB. Recent works suggest that PCT concentrations are affected by SIRS caused by contact with a nonphysiological surface. In the case of LVAD this immunological stimulation is long lasting and even more potent with additional RVAD or ARF treated with renal replacement therapy. In accordance with this hypothesis, our data show that the ability of PCT to detect infectious complication in LVAD patients is limited and its concentrations more probably correlate with postoperative complications in general.

P62

Changes in procalcitonin and presepsin before and after immunoglobulin administration in septic patients

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Introduction The potentially envisaged actions of intravenous immunoglobulin (IVIg) on severe infectious disease include: virus or toxin neutralizing action; opsonic effect; complement bacteriolytic activity; and enhancement of sensitivity to antibiotics. In the case of severe infectious disease, antibiotics are often supplemented with administration of IVIg.

Methods The changes in sepsis markers (procalcitonin, presepsin, interleukin-6, C-reactive protein) followed by IVIg administration were investigated in severe sepsis or septic shock patients. The subjects were 410 patients admitted to an ICU with a diagnosis of severe sepsis or septic shock and from whom informed consent had been obtained for the present study. IVIg was administered intravenously for 3 days (5.0 g/day) and measurements were undertaken before administration (day 1), on the day after completion of administration (day 4), and on day 7. The items measured were procalcitonin, presepsin, IL-6, and CRP. The effect of IVIg administration on these markers was then studied. The IVIg studied was polyethylene glycol-treated human immunoglobulin injection fluid (2.5 g, 50 ml, one vial).

Results The patient APACHE II score were 24.9 ± 8.2, the SOFA score 9.1 ± 3.7, and the survival rate after 28 days 83.4%. The values before IVIg administration were: procalcitonin 36.0 ± 463.3 (median 110) ng/ml, presepsin 4,548 ± 4,250 (median 3,337) pg/ml, CRP 15.6 ± 9.6 (median 14.7) mg/dl, and IL-6 13,860 ± 47,299 (median 630) pg/ml. All values were thus elevated. On the days after the completion of IVIg administration and on day 7, the level of almost all mediators (procalcitonin, presepsin, CRP, IL-6) decreased significantly. In patients with suspected severe sepsis and septic shock, presepsin reveals valuable diagnostic capacity to differentiate sepsis severity compared with procalcitonin, IL-6, CRP, and WBC. Additionally, presepsin and IL-6 reveal prognostic value with respect to 30 days and 6 months all-cause mortality throughout the first week of ICU treatment [1].

Conclusion The results of the present study found significant decreases of procalcitonin, presepsin and IL-6 resulting from 3 days of immunoglobulin administration, but evidence is still limited and this needs to be confirmed in larger studies.

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P63

Diagnostic and prognostic performance of PATHFAST Presepsin in patients with SIRS and early sepsis

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Introduction Presepsin (sCD14-ST) serves as a mediator of the response to infectious agents. First evidence suggested that presepsin may be utilized as a sepsis marker.

Methods Presepsin was determined at presentation (T0), after 8, 24 and 72 hours in 123 individuals admitted with signs of SIRS and/or infection. Primary endpoint was death within 30 days. Presepsin was determined using the POC assay PATHFAST Presepsin (Mitsubishi Chemical, Japan).

Results Mean presepsin concentrations of the patient group at presentation and of the control group were 1,945 and 130 pg/ml, respectively (P <0.0001). Baseline presepsin differed highly significant between patients with SIRS, sepsis, severe sepsis and septic shock.

Table 1 (abstract P63). Presepsin levels during the course of the disease in survivors and nonsurvivors

	PSEP, median (IQR) (pg/ml)			
	T0	T8 hours	T24 hours	T72 hours
Survivors	590 (345 to 1,396)	622 (367 to 1,912)	574 (336 to 1,610)	533 (324 to 1,246)
Nonsurvivors	1,763 (705 to 6,616)	1,859 (1,001 to 5,744)	1,731 (809 to 4,586)	2,056 (811 to 5,540)
P value	0.0046	0.0005	0.0003	0.0013

Twenty-four patients died during 30 days. The 30-day mortality was 19.5% in total, ranging from 10 to 32% between the first and the fourth quartile of presepsin concentration. Nonsurvivors showed high presepsin values with increasing tendency during the course of the disease while in surviving patients this tendency was decreasing. See Table 1.

Conclusion Presepsin demonstrated a strong relationship with disease severity and outcome. Presepsin provided reliable discrimination between SIRS and sepsis as well as prognosis and early prediction of 30-day mortality already at admission. Presepsin showed close association with the course of the disease.

P64

Examination of the diagnostic accuracy of sepsis using procalcitonin, presepsin and CD64 for patients with or without acute kidney injury

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Introduction At the moment, we have few reports about the diagnostic accuracy of procalcitonin (PCT), presepsin (P-SEP) and CD64 as a diagnostic marker of sepsis for patients with acute kidney injury (AKI). This study aimed to clarify which is a more useful diagnostic biomarker for sepsis using PCT, P-SEP and CD64 with or without AKI in ICU patients.

Methods This study was a single-center observational retrospective study. Blood samples were collected from 334 patients admitted to our ICU between April 2013 and March 2014. Then, we classified the patients with or without AKI. In this study, we adopted RIFLE criteria for AKI diagnosis. After that, the patients in each group were classified into the sepsis group and the nonsepsis group. We measured PCT, P-SEP and CD64 levels at the time of ICU admission and subsequently investigated the diagnostic accuracy of these biomarkers for detecting sepsis.

Results In this study we met 225 patients with non-AKI and 109 patients with AKI. We conducted ROC analysis for diagnosing sepsis. In non-AKI patients, the AUC of PCT, P-SEP and CD64 were 0.904 (95% CI: 0.824 to 0.950), 0.892 (95% CI: 0.794 to 0.947) and 0.917 (95% CI: 0.842 to 0.958), respectively. In AKI patients, the AUC were 0.933 (95% CI: 0.859 to 0.970), 0.755 (95% CI: 0.642 to 0.840) and 0.905 (95% CI: 0.803 to 0.957), respectively.

Conclusion CD64 and PCT were a useful biomarker for detecting sepsis for ICU patients with AKI.

P65

Prognostic value of procalcitonin in respiratory tract infections across clinical settings

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Introduction Whether the inflammatory biomarker procalcitonin (PCT) provides prognostic information across clinical settings and different acute respiratory tract infections (ARI) is poorly understood. Herein, we investigated the prognostic value of admission PCT levels to predict adverse clinical outcome in a large ARI population.

Methods We analyzed data from 14 trials and 4,211 ARI patients to study associations of admission PCT levels and setting specific treatment failure and mortality alone at 30 days. We used multivariable hierarchical logistic regression and conducted sensitivity analyses stratified by clinical settings and ARI diagnoses to assess the results' consistency.

Results Overall, 864 patients (20.5%) experienced treatment failure and 252 (6.0%) died. The ability of PCT to differentiate patients with and without treatment failure was highest in the emergency department setting (treatment failure; area under the curve (AUC): 0.64 (95% confidence interval (CI): 0.61, 0.67), adjusted odds ratio (OR): 1.85 (95% CI: 1.61, 2.12), P <0.001 – mortality; AUC: 0.67 (95% CI: 0.63, 0.71), adjusted OR: 1.82 (95% CI: 1.45, 2.29), P <0.001). In lower respiratory tract infections, PCT was a good predictor of identifying patients at risk for mortality (AUC: 0.71 (95% CI: 0.68, 0.74), adjusted OR: 2.13 (95% CI: 1.82, 2.49), P <0.001). In primary care and ICU patients no significant associations of initial PCT levels and outcome were found. See Figure 1.

Conclusion Admission PCT levels are associated with setting specific treatment failure and provide most prognostic information in ARI in the emergency department setting.

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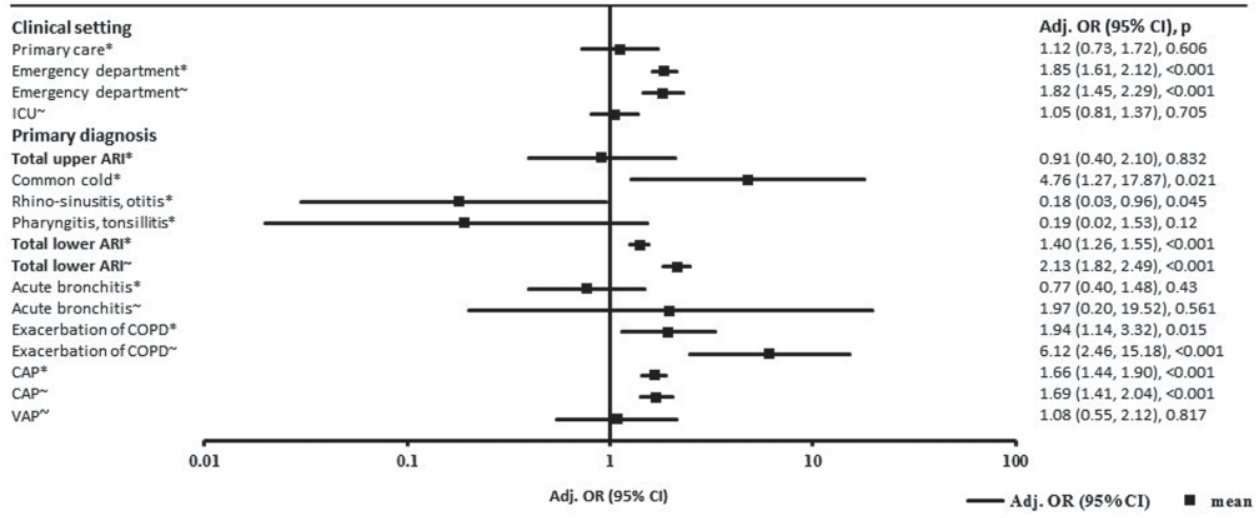


Figure 1 (abstract P65). Multivariate regression analysis for estimation of predictive value of PCT levels on admission stratified by adverse events and mortality in different settings and diagnoses. *Treatment failure, ~mortality. ARI, acute respiratory tract infection; ECOPD, exacerbated chronic obstructive pulmonary disease; CAP, community-acquired pneumonia; VAP, ventilator-associated pneumonia; Adj., adjusted; OR, odds ratio; CI, confidence interval.

P66

Neutrophil to lymphocyte count ratio performs better than procalcitonin as a biomarker for bacteremia and severe sepsis in the emergency department

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Introduction The objective of this study was to evaluate the neutrophil to lymphocyte count ratio (NLCR) versus procalcitonin (PCT) in diagnosing bacteremia in the emergency department (ED). The NLCR is a biomarker that appears early in the course of the acute inflammatory response and reaches maximum levels within 4 hours after onset. An elevated NLCR has been shown to correlate to bacteremia at a cutoff level of >10 [1]. It is rapidly analyzed on a full blood cell count at low cost. The lowest recommended cutoff level for PCT is <0.5 ng/ml.
Methods We randomly chose 425 patients from a 9-month epidemiologic study on the incidence of community-onset severe sepsis and septic shock in western Sweden 2011 to 2012. In total, 207 had severe sepsis and 218 had sepsis, mean age 71.2 versus 64.2 years; males 51%. Sampling was made on arrival in the ED. The NLCR was analyzed immediately, PCT later on plasma frozen at –80°C. A total of 122/425 patients had bacteremia, 72 (35%) in the severe sepsis group versus 50 (23%) in the sepsis group. Most common findings were *Escherichia coli* (n = 33), *Staphylococcus aureus* (n = 24), streptococcal spp. (n = 33) and other enterobacteriacae spp. (n = 17).
Results The NLCR shows significantly higher sensitivity than PCT at recommended cutoff levels for bacteremia. Interestingly, this is true even for all 207 patients with severe sepsis, irrespective of bacteremia or not. Sensitivity figures with 95% confidence interval: bacteremia (n = 122): NLCR 80% (0.73 to 0.87) versus PCT 66% (0.58 to 0.75), P = 0.01; severe sepsis with bacteremia (n = 72): NLCR 85% (0.77 to 0.93) versus PCT 70% (0.59 to 0.81), P = 0.03; and severe sepsis but no bacteremia (n = 135): NLCR 71% (0.65 to 0.77) versus PCT 61% (0.54 to 0.68), P = 0.03.
Conclusion The NLCR can be used in the ED as a biomarker for bacteremia as well as severe sepsis and seems to perform as well as or even better than PCT in this setting. Rapid response, low cost and no need for extra sampling make it useful as a screening tool.
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P67

Prognosis value of biomarkers in severe sepsis and septic shock

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Introduction The purpose of the study was to assess the prognosis value of pro-adrenomedullin (pADM), C-reactive protein (CRP) and procalcitonin (PCT), lactate (LT), albumin (ALB), cholesterol (CHOL), white blood cell (WBC) and severity score in patients with severe sepsis or septic shock.
Methods A prospective, observational study in adult patients with severe sepsis or septic shock in a polyvalent ICU. Demographics, severity scores (APACHE II and SOFA) and all of the biomarkers were studied within 24 hours from septic shock onset. Descriptive and comparative statistical analysis was performed using the statistical software packages SPSS v.15 and MedCalc® 9.2.1.0.
Results We analyzed 246 consecutive episodes of severe sepsis (38%) or septic shock (62%). The 28-day mortality was 36.2%. The profile of dead patients had a significantly higher average age (65 (IQR: 75.5 to 57.5) vs. 63 (47 to 72); P <0.06), APACHE II (27 (22 to 30) vs. 23 (18 to 27); P <0.001) and SOFA (11 (9 to 12.75) vs. 9 (7 to 10); P <0.001). CRP (168.4 (106 to 285) vs. 165.4 (87.8 to 275) mg/dl; P = NS), PCT (6.5 (0.94 to 23.8) vs. 5.8 (0.97 to 19.59) ng/ml; P = NS) and WBC 14.7 (9.5 to 21.4) vs. 12.9 (5.5 to 17.5); P = NS) were increased in those who died, but CHOL (102 (75 to 134) vs. 108 (86 to 141) mg/dl; P = NS) had lower values. These differences were significant in pADM (2.46 (1.21 to 4.89) vs. 1.68 (0.94 to 3.32) nmol/l; P = 0.012), LT (2.6 (1.6 to 3.94) vs. 1.6 (1.2 to 2.43) mmol/l; P <0.001) and ALB (2 (1.55 to 2.38) vs. 2.22 (1.96 to 2.7) g/dl; P = 0.001).
Conclusion The protein pADM, LT and ALB showed good prognosis accuracy when measured on admission of septic patients to the ICU.

P68

Differential diagnosis of bacterial from candidal bloodstream infections in ICU patients: the role of procalcitonin

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Introduction Early differentiation of bacterial from candidal bloodstream infections (BSIs) in the presence of sepsis or septic shock is crucial because of the need for appropriate treatment initiation. Clinical data, although limited, suggest a role for procalcitonin (PCT) [1-3]. The aim of this study was to investigate a possible association between the etiology of BSIs and the serum PCT levels.
Methods ICU patients with clinical and laboratory signs of sepsis or septic shock, with documented BSIs and with both serum PCT and CRP measurements on the day of the positive blood sample (±1 day), were included. Illness severity was assessed by SOFA score on both admission and BSI day. Demographic, clinical, and laboratory data including PCT and CRP levels, as well as the white blood cell (WBC) count on the day of the BSI were recorded. PCT was measured by an electrochemiluminescence analyzer and CRP by the tholosimetric method (Roche, Switzerland).
Results A total of 64 ICU patients (mean age 58 ± 18 years, 39 males) with BSIs were included. SOFA sore was 9 ± 4 on ICU admission and 8 ± 4 on the day of BSI. In 30 of these patients *Candida* spp. were isolated in blood culture (candidemia group) whereas the remaining 34 had a bacterial etiology of BSI (bacteremia group). Serum PCT concentrations remained within normal ranges in most patients with candidemia whereas a wide range was observed in patients with bacteremia. Mean values of PCT and CRP levels were higher in the bacterial than in the candidemia BSI group: 18.5 ± 33.2 versus 0.73 ± 1.40 ng/ml, P <0.001 and 17.7 ± 10.3 versus 8.9 ± 8.0 mg/dl, P = 0.001, respectively. There was a significant difference in WBC count between the two groups: 19,460 ± 10.174 versus 11,000 ± 5,440, P <0.001 for the bacteremia and candidemia BSI group, respectively. A ROC curve analysis of the predictive ability of PCT showed an AUC of 0.79 (P <0.001). When a cutoff point of 0.40 ng/ml was selected using Youden's J statistic, a low value of PCT had in our sample a negative predictive value of 0.76 and a likelihood ratio (negative) of 0.30.
Conclusion A low serum PCT value could be considered as a diagnostic marker in distinguishing between BSIs of candidal or bacterial origin in ICU patients with varying severity of sepsis.
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P69

Performance of the beta-glucan test and a dynamic prediction rule to identify patients in the ICU at high risk to develop candidemia

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Introduction Early initiation of antifungal therapy (AFT) improves the outcome in candidemic patients, but empiric AFT is not considered the standard of care.
Methods We used a scoring system based on the presence of a central venous catheter and receipt of antibiotics, plus at least two of the

following: dialysis, surgery, pancreatitis, and receipt of corticosteroids, other immunosuppressive agents or parenteral nutrition. Different from the original description of the score which considered only the first 7 days of ICU stay, we selected patients who fulfilled these criteria at any time during the ICU stay. Once a patient fulfilled these criteria, AFT (anidulafungin 200 mg followed by 100 mg daily) was initiated provided that the patients also presented with any of the following: fever, hypothermia, hypotension, leukocytosis, acidosis or elevated C-reactive protein. Blood cultures (days 1 to 2) and baseline serum BDG (days 1 to 3) were performed. Patients with candidemia were treated for ≥14 days, those without candidemia but ≥1 positive BDG (≥80 pg/ml) received AFT for ≥10 days, and patients with negative blood cultures and negative BDG discontinued anidulafungin.

Results A total of 2,148 patients were screened, and 85 (4%) fulfilled entry criteria. The incidence of candidemia in these 85 patients was 8.2%, compared with 0.5% in the remaining 2,063 patients (relative risk 16.9%, 95% confidence interval (CI) = 6.63 to 43.55). Baseline BDG was positive in 74 patients (87%), with a median number of positive tests of 3 (range 1 to 3) and a median value of 523 pg/ml (range 83 to 6,860). All seven patients with candidemia had positive baseline BDG (median value 523 pg/ml, range 203 to 3,660). The best cutoff of baseline BDG for the diagnosis of candidemia was 522 pg/ml (area under the ROC curve 0.883, 95% CI = 0.769 to 0.997), with sensitivity and specificity of 86% and 88%, respectively. The cutoff value of 80 pg/ml had sensitivity and specificity of 73% and 27%, respectively.

Conclusion This dynamic prediction rule was able to differentiate a group of ICU patients at high risk to develop candidemia, with a relative risk of 16.9. BDG is frequently positive in ICU patients. A cutoff value of 522 pg/ml was able to discriminate between candidemic and noncandidemic patients. A revision of the cutoff value for BDG in the ICU is needed.

P70

Low serum iron as a risk factor for ICU-acquired bacteremia: study of a large cohort database

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Introduction Bloodstream infections in the ICU are a major trigger of morbidity and mortality. Several risk factors for bacteremia have been previously identified, such as presence of a central venous catheter or invasive ventilation [1,2]. Iron is a key element for bacteria growth, and its metabolism is extensively altered by inflammation. We aim to determine whether iron deficiency is a risk or protective factor for bacteremia in the ICU.

Methods We performed a retrospective analysis of patients included in the MIMIC-II database, an ICU database that collected data from patients admitted to the medical, surgical, coronary and cardiac surgery ICU of Boston's Beth Israel Deaconess Medical Center during a period of 7 years. We performed logistic regression models to assess the association between iron and bloodstream infection.

Results We included 3,980 patients, 2,988 with low serum iron (<60 ng/ml) and 992 with normal/high serum iron (≥60 ng/ml). During their first stay in the ICU, 351 (8.82%) patients developed bloodstream infections. Low serum iron was associated with increased odds of bloodstream infection (OR: 1.37; 95% CI: 1.04 to 1.80). After adjusting for age, gender, Simplified Acute Physiology Score, presence of central venous catheter, ICU type, transfusions performed before iron measured, neoplastic disease, diabetes mellitus, hepatic disease, congestive heart failure and ferritin levels, low levels of iron were still associated with an increased odds of bacteremia (OR: 1.41; 95% CI: 1.03 to 1.9). In contrast, low serum iron was associated with a decreased risk of death in the hospital (adj OR: 0.73, CI: 0.57 to 0.95).

Conclusion Low serum iron increases the risk of bloodstream infection in the ICU, and should be considered as a risk factor to stratify patients' risk of bacteremia during ICU stay.

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P71

Estimating the duration of a central venous catheter at time of insertion

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Introduction The aim of this study was to investigate whether clinicians can estimate, at the time of insertion, the length of time a central venous catheter (CVC) will remain in place, and to identify clinical variables which may predict CVC duration. CVC-related bloodstream infection is a known complication among critically ill patients. As infection rates may increase with duration of catheterization, more expensive antimicrobial-coated catheters may be used in patients with anticipated long duration of CVC use.

Methods We conducted a single-center, prospective study from January 2012 to November 2012. Clinicians prospectively estimated the anticipated duration of CVC at the time of line placement in an electronic procedure note. We collected demographics, past medical history, type of ICU, vital signs, laboratory values, SOFA score, mechanical ventilation and use of vasopressors at the time of placement. Continuous variables were compared with the Wilcoxon rank-sum test and categorical variables with the Fisher's exact test. Pearson's correlation coefficient was used to assess the correlation between estimated CVC time and actual time. Duration of CVC use was dichotomized into long (≥7 days) or short (<7 days), based on previous literature, and sensitivity and specificity for predicting long duration was calculated. We performed a logistic regression analysis to identify variables associated with long CVC duration and calculated the area under the ROC curve (AUC).

Results We enrolled 150 patients; median age was 65 (IQR: 52 to 74), 63 (42%) were female and mortality was 22%. Median time from CVC placement to removal was 5 (IQR: 3 to 8) days. The correlation between estimated CVC time and actual time was low ($r = 0.36$, $P < 0.001$). Forty-eight (32%) patients had a long CVC duration. Clinician estimate had 46% sensitivity and 76% specificity for predicting long duration of CVC. Of 30 variables tested, only temperature at the time of insertion was significantly associated with long duration (OR: 1.30, 95% CI: 1.04 to 1.63, $P = 0.02$). The AUC for this model was 0.59 (95% CI: 0.49 to 0.69).

Conclusion Our results suggest a low correlation between clinician prediction at time of insertion and actual duration of CVC. We did not find any good predictors of long duration of CVC. Given our relatively low sample size, we may have been underpowered. It may not be feasible to identify patients at the time of insertion who may benefit from antimicrobial-coated catheters.

P72

Preventing catheter-related infections in ICUs: comparing catheter care techniques

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Introduction Catheter-related bloodstream infections (CRBSI) are common and an important cause of morbidity and mortality in critical patients. Optimum approaches for preventing infections are presented in guidelines. This study aims to evaluate efficacy of different care techniques and education, to define risk factors for decreasing ratio of CRBSIs and to analyze effects on morbidity and mortality.

Methods After ethics committee approval, patients admitted to the ICU, older than 18 years, who were thought to have a central venous catheter (CVC) for more than 48 hours, and whose first catheter was inserted in the ICU were included in the study. Staff were educated before the study and periodically during the study. Catheter care and insertion were applied according to the guidelines. The study was planned as three sequences. In the first group, catheter care was made with a sterile gauze pad. In the second and third groups, catheter care was made with chlorhexidine gluconate impregnated dressing. Also in the third group, a silver-coated needleless connector was inserted into the tip of venous catheters.
Results Totally 105 patients were included in the study and every group included 35 patients. There was no difference between groups when evaluating reasons for catheter insertion. There was no statistically significant difference according to emergent or elective catheterization, trying times, or catheter insertion side (P >0.05). CRBSI was determined in two patients in group 1, in one patient in group 2, and in no patient in group 3. In group 1 it was observed on the 4th and 11th days. In group 2 it was observed on the 18th day after catheterization. Before the study, a statistically significant decrease was determined in CRBSI ratios before and after education (16.4/1,000, 12.9/1,000 catheter-days (P <0.001)). According to Group 1 a statistically meaningful decrease was assigned in CRBSI ratios in Groups 2 and 3 (4.84/1,000, 2.22/1,000, 0/1,000 catheter-days) (P <0.001, P <0.001, P <0.001).
Conclusion Continued education is important in preventing CRBSIs. Maximum precautions must be taken. Usage of antiseptic solutions with clorhexidine and chlorhexidine gluconate impregnated dressing decreased insertion side infections and usage of silver-coated needleless connectors reduced microorganism entry through the catheter lumen and provided a severe decrease in infection ratio.
Reference

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P73

Comparison of three cutaneous antiseptic solutions for the prevention of catheter colonization in an ICU for adult patients: a multicenter prospective randomized controlled trial

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Introduction The current CDC guideline for the prevention of intravascular catheter-related infections recommends skin preparation with a greater than 0.5% chlorhexidine with alcohol solution before central venous catheter (CVC) or peripheral arterial catheter (AC) placement. However, few studies investigated the superiority of 1% alcoholic chlorhexidine gluconate (1% CHG) over either 0.5% alcoholic chlorhexidine gluconate (0.5% CHG) or 10% aqueous povidone iodine (10% PVI) for the prevention of catheter colonization. The aim of this study is to compare the effectiveness of three skin antiseptic solutions for the prevention of intravascular catheter colonization.
Methods This multicenter prospective randomized controlled trial was conducted in 15 Japanese ICUs from December 2012 to March 2014. Patients over 18 years of age undergoing CVC and AC placement in the ICU are randomized to have one of three skin antiseptic preparations before catheter insertion. After removal of the catheter, the distal tip is cultured using semiquantitative or quantitative techniques. The incidence of catheter colonization and catheter-related bloodstream infection (CRBSI) is compared between the three groups.
Results A total of 997 catheters were placed, including 339 catheters using 1% CHG, 329 using 0.5% CHG, and 329 using 10% PVI. The median duration of catheter indwelling in the entire population was 3.7 days with an interquartile range of 2.0 to 6.7 days, with no significant difference between the groups (P = 0.36). Thirteen catheters (5.1%) in the 10% PVI group were positive for catheter-tip colonization, whereas six catheters (2.2%) in the 1% CHG group and five catheters (1.9%) in the 0.5% CHG group were positive (P = 0.07). The probability of catheter colonization was significantly higher in the 10% PVI group than each CHG groups (P = 0.028, log-rank test). The incidence of catheter colonization and CRBSI is compared between the three groups.
Conclusion In this randomized controlled trial comparing the effectiveness of three cutaneous antiseptic solutions for the prevention of catheter colonization, either 0.5% or 1.0% CHG was superior to 10% PVI.

P74

Catheter-associated bloodstream infections in an ICU of a university hospital in Wroclaw, Poland: an international nosocomial infection control consortium's findings

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Introduction Catheter-associated bloodstream infections are serious but potentially possible to reduce complication of treatment in the ICU. The aim of the study was to evaluate the frequency and etiology of central line-associated bloodstream infections (CLA-BSI) in ICU patients according to the International Nosocomial Infection Control Consortium (INICC) project.
Methods A prospective, observational study was conducted in the 20-bed ICU of the University Hospital in Wroclaw from January 2011 to November 2014. CLA-BSI were diagnosed and evaluated according to protocols standardized by the INICC. The density of CLA-BSI/1,000 central line-days, the incidence index/100 admissions to the hospital, the central line utilization ratio (CL-UR) as well as the microbiological profile of CLA-BSI were evaluated. The results were compared with our earlier published data and with the findings of international reports.
Results Among 1,746 ICU patients, CLA-BSI were diagnosed in 69 cases. The incidence index was 3.88/100 admissions to the ICU. CLA-BSI were diagnosed in 18% of the overall number (381) of device-associated healthcare-associated infections. Central line was used in 91.41 ± 4.4% patients during 19,819 patient-days and 18,155 central line-days. The median density of CLA-BSI/1,000 central line-days was 3.88/3.77/3.36 and 0.0 accordingly in years 2011/2012/2013 and 2014 (from January to November). The main pathogens of CLA-BSI were CN staphylococci (22%), *Staphylococcus aureus* (21%), and Enterobacteriaceae (29%). In this study, the density of CLA-BSI was about 50% lower (2.75 (2.0 to 6.06)) than in our previous study and in the INICC's report (2014), but higher than in the CDC's NHSN (2012) report.
Conclusion The implementation of the infection control program and preventive interventions for patients with central venous catheters improved the safety and quality of healthcare in the ICU by reducing CLA-BSI rate.
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P75

Removal of an implanted central venous catheter from neutropenic patients admitted to the ICU due to sepsis from any source

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Introduction Long experience in the treatment of neutropenic patients admitted to the ICU has taught us the importance of removing the permanent central venous catheter when infection is suspected, because of the great mortality associated. The problem usually comes when the origin of sepsis is not clear and we assume that mortality is

not easy to avoid. It is important to know what happens to neutropenic patients admitted to the ICU because of sepsis from any source, in whom catheter infection cannot be excluded.
Methods A retrospective, cohort, descriptive study was carried out between January 2013 and November 2014. Epidemiology data were collected from all neutropenic patients admitted to the ICU who came from hemato-oncology services and had an implanted central venous catheter. Microbiology results and data related to the catheter removal were described.
Results A total of 15 patients were included, mean age was 53 years old and 66% were male. The implanted catheter was removed in 80% of patients. Platelet transfusion was needed in 100% of patients before catheter removal and no complication was observed during catheter removal or in the insertion of a new one. In 53% of patients, catheter infection was confirmed *a posteriori*.
Conclusion Removal of an implanted central venous catheter from neutropenic patients admitted to the ICU due to sepsis from any source can be beneficial for this kind of patient as it was found that in more than 50% of patients catheter infection was confirmed *a posteriori*.

P76

Effect of insertion route on risk of central line-associated bloodstream infection in critically ill patients

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Introduction Femoral, jugular or subclavian central venous catheterization (CVC) is routinely performed during the care of the critically ill. These invasive procedures contribute to additional morbidity, mortality, and costs derived from the interactions between traumatic, infectious and other complications. The aim of this study is to determine whether the subclavian, jugular or femoral central venous access (CVA) routes have an effect on the incidence of CLABSI in critically ill patients and to compare between these routes regarding major complications and ICU mortality.
Methods A retrospective observational study in a medical and surgical ICU in a tertiary care hospital on adult patients admitted from January 2010 to December 2013. The study enrolled 845 patients divided into 283 internal jugular CVC (IJC), 270 subclavian CVC (SCC) and 287 femoral CVC (FC) in which the catheters were inserted in the ICU by experienced physicians with at least 50 previously successful trials of central line insertion, using CVC bundle checklist. ICU length of stay, incidence of complications, APACHE II score adjusted severity and mortality were calculated for each group.
Results Patient and catheter characteristics including the duration of catheterization were similar in all groups. The rate of CLABSI in the IJC, SCC and FC groups was 5.8 versus 7.2 versus 3.45 per 1,000 catheter-days respectively with $P = 0.35$. ICU mortality was 134 (47%) cases of the IJC group, 108 (39%) cases of the SCC group and 113 (39%) cases of the FC group. There was no significant difference between the three groups of CVC in the incidence of CLABSI rate in the critically ill patients, and a slight increase in ICU mortality in the IJC group compared with the other two groups. Pneumothorax occurred in six (2.2%) cases of SCC and 11 (3.8%) cases of IJC with no significant difference between the two groups as the *P* value was 0.3.
Conclusion Site of insertion of CVC does not appear to affect the rate of CLABSI among critically ill patients. Pneumothorax was recorded in SCC and IJC groups with no statistical preference to either group.

P77

Role of neutrophil extracellular traps against soft tissue infections

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Introduction Neutrophils work as the frontline of defense against infections and neutrophil extracellular traps (NETs) are one of the immune systems to suppress dissemination of infection by the netted chromatin decorated with antibacterial molecules. It was reported that NETs play an important role in various kinds of infections such as pneumonia. However, there is no report on NETs in patients of soft tissue infections. In this study, we evaluated NET production in pus and clarified the role of NETs as a host defense in patients of soft tissue infections.
Methods This study was conducted in the ICU of the Trauma and Acute Critical Care Center at Osaka University Hospital. We collected pus from the patients of soft tissue infections at the time when drainage or debridement was performed and when clinical improvement was observed. The smears of pus specimens were examined by immunohistochemistry to visualize the major NET components: DNA, neutrophil elastase, and histone H1. Concurrently, the patients' clinical data and laboratory data of blood were recorded to analyze the relationship with NET production.
Results A total of five patients were included in this study and drainage of abscess or debridement of infection site was performed in all of the cases. Four patients of them were diagnosed as necrotizing soft tissue infections by *Clostridium* spp. ($n = 1$) and *Bacteroides* spp. ($n = 3$) and the other was diagnosed as cervical abscess by *Streptococcus* spp. In all cases, no NETs but neutrophils were identified in the first pus: however, NETs appeared in the later smears as the patients' condition was getting better.
Conclusion These results suggested that NETs also worked as an immune system against soft tissue infections. Drainage or debridement of infection focus might promote NET production.

P78

Use of nanotechnology-based surface antiseptic solutions in the ICU

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Introduction In our study, we aimed to compare the application of benzalkonium chloride (BC) – a nanotechnology-based product – for 24-hour periods and didecyl dimethyl ammonium chloride (DDAC) for 12-hour periods regarding efficiency in application of surface antiseptics in the ICU.
Methods Two different areas with eight beds at both sides of a common corridor in the ICU were named as areas A and B. BC was applied in area A with 24-hour periods and DDCA was applied in area B with 12-hour periods for surface cleaning. Samples were taken from a total of 20 different surfaces including nurse-station desks, phones, keyboards, beds, bedside monitors and ventilators by the same infection control nurse every 24 hours from area A and every 12 hours from area B for 7 days. Swab samples were cultured on 5% sheep bloody agar and McConkey agar in the laboratory. Then the cultured mediums were incubated at 35 to 37°C in an aerobic environment for 18 to 24 hours. NCSS (Number Cruncher Statistical System) 2007 and PASS 2008 Statistical Software (UT, USA) programs were used for the statistical analysis.
Results There were no statistical differences between two groups (Table 1).

Table 1 (abstract P78). Isolated pathogen ratio percentage

	A (BC)	B (DDCA)	*P* value
First day	25	20	1.000
Second day	5	15	0.605
Third day	30	20	0.715
Fourth day	65	50	0.527
Fifth day	45	60	0.527
Sixth day	25	25	1.000
Seventh day	60	45	0.527

Conclusion The effect of a good surface disinfectant should begin immediately and it should have a long-lasting disinfecting effect on the surface. DDAC is an efficient disinfectant used in medicine and the food industry to protect the surfaces. However, it may cause severe skin itching. BC, which is a nanotechnology-based product, leaves its active metabolites on the surface; it is applied by constituting a spongy layer. Since the efficiency of BC lasts for 24 hours and it is applied to perform cleaning with 24-hour intervals, we think that it is preferable with regards to workforce gain and cost.

P79

Reduction of deep surgical site infections in cardiac surgery by introducing a multimodal infection control program

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Introduction Deep surgical site infections (DSSI) are a major complication after cardiac surgery with a high mortality rate and reported incidences between 0.5 and 5%. Implementing a comprehensive infection control program (ICP) reduces this incidence [1]. The incidence in our hospital varied from 3.1 to 3.8%, which was considered too high. We evaluated the impact of introducing a multimodal ICP on the incidence of DSSI.
Methods We noticed a too high incidence of DSSI after cardiac surgery during an observational 3-year period (Figure 1). In February 2013 we introduced a bundle of interdisciplinary infection control measures. Medical and nursing staff of all involved departments took part in developing and implementing these guidelines. Besides emphasizing the importance of existing guidelines (antiseptic shower, hair removal by clipper, strict hand hygiene, prophylactic antibiotics, limiting OR traffic, tight glycemic control (80 to 110 mg/dl), and so on), new strategies were introduced. The most important new strategies were nasal decolonization with mupirocin twice daily 48 hours perioperatively, preoperative antiseptic skin preparation twice (chlorhexidine gluconate 0.5%), applying topical skin adhesive to the sternal wound postoperatively and in the case of CABG procedures maintaining a strict barrier between the vein harvesting procedure and the chest procedure.
Results We observed a significant reduction in DSSI rates in cardiac surgery following implementation of a multimodal ICP from 3.1% in 2010 down to 0.23% in November 2014 (Figure 1).



Figure 1 (abstract P79). Incidence of DSSI.

Conclusion Implementing a multimodal ICP significantly reduced the incidence of DSSI in our hospital but it remains difficult to identify which interventions were most effective.
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P80

Effect of chlorhexidine and urinary catheter infection prevention in a Brazilian coronary ICU

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Introduction Urinary catheter insertion is a common procedure in ICUs and can be an important cause of infection in the hospital environment [1,2]. We aimed to analyze the effect of chlorhexidine on long-term urinary catheter insertion and urinary tract infection (UTI) during a 5-year period in patients admitted to a coronary ICU.
Methods Analysis of patients admitted to a coronary ICU of a medium-sized hospital in Brazil from January 2010 to May 2014. The institutional protocol of periprocedural antisepsis was changed from iodine-based antiseptic to chlorhexidine in 2012. The UTI diagnosis was based on urine culture (>10^5 colony-forming units per ml of urine) associated with at least one clinical/laboratory abnormality (fever >38°C, urination urgency, increased urinary frequency, dysuria, or suprapubic or lumbar pain). The UTI rate represents the urinary tract infections associated with long-term urinary catheter (patient with UTI associated with long-term urinary catheter divided by patients with long-term urinary catheter × 1,000).
Results The urinary tract infection rates were 4.8 (year 2010: patients·day^{-1} (*n*: 2,511), long-term urinary catheter·day^{-1} (*n*: 1,455), device usage rate (958%)), 4.4 (year 2011: patients·day^{-1} (*n*: 2,529), long-term urinary catheter·day^{-1} (*n*: 1,140), device usage rate (45%)), 0.0 (year 2012: patients·day^{-1} (*n*: 2,660), long-term urinary catheter·day^{-1} (*n*: 783), device usage rate (29%)), 0.0 (year 2013: patients·day^{-1} (*n*: 2,573), long-term urinary catheter·day^{-1} (*n*: 960), device usage rate (37%)), and 0.0 (year 2014: patients·day^{-1} (*n*: 1,070), long-term urinary catheter·day^{-1} (*n*: 444), device usage rate (42%)).
Conclusion The use of chlorhexidine in the periprocedural antisepsis of urinary catheterization contributed to the decrease of urinary tract infections associated with long-term urinary catheter in patients admitted to the coronary ICU.
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P81

Effect of daily bathing with chlorhexidine on hospital-acquired bloodstream infection in critically ill patients: a meta-analysis of randomized controlled trials

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Introduction Whole-body skin decolonization with chlorhexidine in critically ill patients reduces multidrug-resistant bacterial colonization, and catheter-related bloodstream infection (BSI). We performed a meta-analysis of randomized controlled trials to determine whether daily bathing with chlorhexidine decreased hospital-acquired BSIs in critically ill patients.
Methods We searched the MEDLINE, EMBASE, and Cochrane Central Register of Controlled Trials databases to identify randomized controlled trials that compared daily bathing with chlorhexidine and a control (daily bathing with soap and water or nonantimicrobial washcloths, or implementation of MRSA screening and isolation) in critically ill patients. The primary outcome was hospital-acquired BSIs. Secondary outcomes were adverse effects of chlorhexidine and the incidence of identified pathogens.
Results This meta-analysis included four studies. The overall incidence of hospital-acquired BSIs was significantly lower in the chlorhexidine group compared with the control 0.80 (95% CI, 0.71 to 0.90; P <0.001; I^2 = 29.4%). Gram-positive (RR = 0.59, 95% CI, 0.44 to 0.79, P = 0.000; I^2 = 46.0%) and MRSA-induced (pooled RR = 0.64; 95% CI, 0.47 to 0.88, P = 0.006; I^2 = 0.0%) bacteremias were significantly less common in the chlorhexidine group. Chlorhexidine did not affect Gram-negative bacteremia or fungemia. The overall incidence of adverse events, such as skin rashes, was similar in both groups.

Conclusion Daily bathing with chlorhexidine was associated with a reduction in the rates of hospital-acquired BSI without significant complications in critically ill patients. It also decreased the incidence of Gram-positive hospital-acquired BSIs, especially MRSA.

P82

Improving hand hygiene compliance leads to improved health outcome: an analysis

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Introduction Hand hygiene is the single most effective but least practiced action in breaking the chain of transmission of microbes. Studies have shown a correlation between the compliance of hand hygiene and its impact on the health outcome.
Methods A quasi-experimental study was done in three level III ICUs of a tertiary care hospital in Kolkata (January to April 2014). Data were collected on existing hand hygiene compliance rate, ventilator-associated pneumonia (VAP) rate, catheter-related bloodstream infection (CRBSI) rate, catheter-related urinary tract infection (CAUTI) rate, standardized mortality ratio (SMR) and average ICU length of stay in the abovementioned units. Root cause analysis was done and interventions were developed to improve hand hygiene compliance and was implemented (July to October 2014). Comparison was done between preintervention and postintervention periods.
Results In the preintervention period (January to April 2014) the hand hygiene compliance among the caregivers was found to be 40%, VAP rate (8.77), CRBSI rate (3.42), CAUTI rate (5.27), SMR (1.14) and average ICU length of stay was 6 days ± 5.85 SD (median 4.5). Interventions were developed and implemented as follows: education and awareness – road shows; positive reinforcement; secret watch nurse; e-ICU – electronic surveillance; ring the bell once every hour – baseline hand hygiene; visual reminders; availability of alcohol-based hand rub, soap and water and sinks; random hand swabs; and compliance audits. In the postintervention period (July to October 2014) data showed a significant improvement in the hand hygiene compliance (75%). Further analysis showed an association with decrease in the incidence of VAP rate (4.71), CAUTI rate (3.51), CRBSI rate (2.65), SMR (1.05) and average ICU LOS 5.05 days ± 4.03 SD (median 4).
Conclusion Improved hand hygiene compliance can be attributed to decreased incidence of VAP, CRBSI, CAUTI, SMR and average ICU LOS. This does definitely impact the overall clinical outcome. However, continued surveillance of hand hygiene compliance and regular audits is of utmost importance to make the change sustainable.

P83

Effects of infection control bundle to prevent nosocomial infection in the ICU

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Introduction Multidrug-resistant organism (MDRO) infections in critically ill patients are often life-threatening. To prevent nosocomial infections of MDRO, we made an infection control bundle in our ICU in 2013. In this study we evaluated the effect of our infection control bundle to prevent nosocomial MDRO transmission and infection.
Methods Our infection control bundle consists of preemptive contact precaution to all care, active surveillance culture and isolation of patients with MDRO. This bundle was applied to all patients admitted to our ICU since 2013. The study period to evaluate the effects of the bundle was from April 2012 to March 2014, and we divided it into two periods; first period (before introduction of the bundle) and second period (after introduction of the bundle). We compared the incidence of nosocomial transmission and infection of MDRO between the two periods. MDRO was defined as bacteria that were resistant to more than three kinds of antibiotics. Nosocomial transmission was defined when MDRO was detected later than 48 hours after admission. Nosocomial infection was diagnosed according to the National Nosocomial Infection Surveillance Manual.
Results Admission to the ICU comprised 363 patients in the first period and 380 patients in the second period. The incidence of transmission was decreased from 48 (13.2%) to 21 (5.5%) in methicillin-resistant *Staphylococcus aureus* (MRSA), from 16 (4.4%) to zero (0%) in multidrug-resistant *Acinetobacter baumannii*. The incidence of nosocomial infection by MDRO was also decreased from 23 (6.3%) to 17 (4.5%) in pneumonia, from five (1.4%) to two (0.3%) in urinary tract infection, and from 12 (3.3%) to one (0.3%) in surgical site infection. The incidence of antibiotic use for MDRO infection was decreased from 41 (11.3%) to 24 (6.3%) in anti-MRSA antibiotics, and from 19 (5.2%) to eight (2.1%) in carbapenems.
Conclusion Introduction of infection control bundle in the ICU reduced the incidence of nosocomial MDRO transmission and infection, which resulted in the reduction of anti-MRSA antibiotics and carbapenems use in critically ill patients.

P84

Clinical validation of an electronic hand hygiene surveillance system

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Introduction Good hand hygiene (HH) is critical to infection control in the ICU. Electronic HH surveillance systems are purported to improve HH practices. Such a system was recently trialed in our ICU. The system is based on radiofrequency transponders in three locations: bracelets worn by ICU personnel; on all HH product dispensers; and above each patient's bed. By correlating input from these three sources the system detects whether HH was performed before and after each patient contact. In the event that HH is not performed, the bracelet alerts the user (by vibration) in real time. This study represents a clinical validation of the system.
Methods ICU staff (nurses and physicians) were followed by a trained observer over 60-minute periods. Each movement and contact during the period was documented. HH opportunities were determined according to WHO criteria and actual HH performance recorded. Observer and electronic data were compared for number of opportunities, HH performance and compliance. A satisfaction questionnaire was distributed to all users. Paired Student's *t* test was used for comparison of the observer and electronic data.
Results Observations were made over 56 time periods that included 836 HH opportunities and 485 occasions when HH was performed. The observer recorded 10.9 ± 7.6 HH opportunities/hour compared with 6.8 ± 6.9 for the electronic system (P <0.001). HH performance occurred on 8.7 ± 3.9 occasions/hour versus 6.0 ± 3.1 occasions/hour as recorded by the electronic system (P <0.001). Overall HH compliance was 62.5 ± 17.7% versus 57.5 ± 21.0% respectively (P = 0.523). On comparison of specific observation periods, there was poor correlation between compliance as recorded by the observer and electronic system (r = 0.03, P = 0.915). Satisfaction questionnaires were completed by 41 personnel. Satisfaction with the system was low or very low for 21/41 (61%). System inaccuracy (either bracelet alerts without cause, or lack of bracelet alerts when HH was required) was the most common reason for dissatisfaction (31/41, 76%), followed by physical discomfort from the bracelet (18/41, 44%).
Conclusion The electronic HH system consistently underestimated both HH opportunities and HH performance. The main reason for dissatisfaction with the system was inaccuracy of bracelet alerts. These data suggest that for an electronic system to be accepted by ICU staff, it has to be highly accurate and comfortable for the user.

P85

Evaluation of the microbial tightness of closed system transfer devices by simulating airborne and touch contamination

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Introduction The use of intravascular catheter devices is often associated with serious bloodstream infections due to microbial contaminations. To minimize risk of such infections NIOSH recommends

the use of closed system transfer devices (CSTDs). To evaluate the microbial tightness of CSTDs we developed two methods which simulate the bioburden in ambient air of operating rooms and ICUs.
Methods The methods simulate airborne and touch contamination. We tested the microbial tightness of the integrated Safeflow® valve of a Mini-Spike® which is used for drug admixture. The airborne contamination was done in an exposure chamber in which a nebulizer distributed defined *B. subtilis* spore aerosols [1]. A Mini-Spike® was inserted into a vial of 0.9% sodium chloride solution (NaCl). A nebulizer with a suspension of 4.8×10^5 CFU spores of *B. subtilis* per ml was used to generate an aerosol for 1 minute. The volume of *B. subtilis* suspension nebulized per minute was 0.278 ml. This corresponds to 1.34×10^3 aerosolized spores in the exposure chamber, which has a volume of 0.24 m^3 (5.6×10^3 CFU per m^3 air). The used concentration was 100 times higher than the microbial burden found in hospitals [2]. After nebulization the valve was disinfected and NaCl was withdrawn into a syringe at certain time intervals. The NaCl was incubated on tryptic soy agar at 37°C for 48 hours. Results were documented as CFU. For touch contamination, a Mini-Spike® was attached to a vial of NaCl. The valve of the Mini-Spike® was contaminated with 10^5 CFU *Staphylococcus aureus*. The subsequent procedure was done as described above.
Results Out of nine tested valves, none showed transmission of *B. subtilis* spores after airborne contamination. Three out of nine tested valves were contaminated with *S. aureus* after touch contamination.
Conclusion Our study shows that both methods are suitable for evaluating the microbial tightness of CSTDs.
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P86

A survey of UK acute clinicians' knowledge of personal protective requirements for infectious diseases and chemical, biological, and radiological warfare agents

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Introduction We conducted a survey to assess clinicians' knowledge of personal protective equipment (PPE) requirements for infectious diseases and biochemical warfare agents. A safe level of PPE is essential when treating patients with highly infectious diseases or those contaminated with hazardous substances. The recent Ebola virus disease (EVD) outbreak in West Africa has highlighted that, although uncommon, contagious diseases with high mortality rates can be a threat to healthcare systems at local, national, and international levels [1]. Chemical, biological, radiological or nuclear (CBRN) contamination presents similar risks.
Methods A validated, hand-delivered, multiple-choice questionnaire [2] was used to assess intensive care, emergency medicine, and anesthetics specialist registrars' knowledge of respiratory and skin protection needed during a resuscitation scenario with advanced life support. Participants selected the PPE required for the biological hazards: EVD, severe acute respiratory syndrome (SARS), inhalational anthrax, plague and smallpox; and the biochemical hazards: sarin, hydrogen cyanide, phosgene and mustard gas (dichlordiethyl sulfide). Responses were compared with UK national recommendations and a previous survey in 2009 [2].
Results Ninety-eight clinicians (anesthetics $n = 51$, emergency medicine $n = 21$, intensive care medicine $n = 26$) completed surveys. The best knowledge (76% correct) was for SARS, with less knowledge for anthrax, plague, EVD, and smallpox (60%). We found limited knowledge for chemical warfare agents (20 to 30%). Sixty to 80% of all incorrect responses were over-rated. There was no difference in knowledge compared with previous published results [2].
Conclusion Despite national and regional training since previous surveys [2], the results indicate that further training on PPE is required for clinicians treating patients exposed to infectious diseases and CBRN agents, ideally in a simulation setting. Further research into whether the required levels of PPE are readily available to clinicians would be pertinent.
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P87

Tuberculosis in the ICU: a retrospective cohort study

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Introduction To describe the characteristics of the patients with tuberculosis (TB) requiring intensive care and to identify the factors associated with in-hospital mortality in an ICU in Portugal.
Methods A retrospective cohort study between January 2007 and July 2014 of all patients with TB admitted to the ICU of the Infectious Diseases Department of Centro Hospitalar de São João. Comorbid diagnoses, clinical features, radiological and laboratory investigations and outcomes were reviewed. The primary outcome was the in-hospital mortality. A univariate analysis was performed to identify risk factors for death.
Results During the study period, 40 patients with TB were admitted to the ICU; 75% male and median age of 52 years (IQR 37.5 to 62.8). Overall, 22 (55%) patients died in the hospital, of whom 16 (40%) died in the ICU. Comorbid illness was identified in 32 (80%) patients, with HIV infection being the most common, present in 15 (37.5%) patients. The main reason for ICU admission was respiratory failure (70%), followed by sepsis/septic shock (22.5%). Twenty-eight (70%) patients had isolated pulmonary disease, four (10%) had isolated extrapulmonary disease and eight (20%) had association of pulmonary and extrapulmonary disease. Mycobacterial cultures were positive in 31 (77.5%) patients; three patients presented monoresistant strains. Twenty-nine (72.5%) patients required mechanical ventilation and 21 (52.5%) required vasopressor infusion in the ICU; two patients were treated with ECMO. Thirty-four (85%) patients received antituberculosis therapy. The median length of stay was 11.5 (IQR 3.25 to 28.5) days in the ICU and 40.5 (IQR 21.0 to 62.8) days in the hospital. The presence of at least one comorbidity, smoking, age, sepsis/septic shock on admission, high SAPS II and APACHE II score, positive direct examination and PCR in respiratory samples, the need for mechanical ventilation or vasopressor infusion were significantly associated with mortality ($P < 0.05$). There was no association between mortality and HIV status, site of TB disease, concomitant acute disease or development of hospital infections.
Conclusion In this cohort we found a high mortality rate in the TB patients requiring intensive care. The risk factors for mortality due to severe TB are mainly related to the severity of organ failure, patient characteristics and burden of disease and not to HIV status or site of TB disease.

P88

Cutaneous mucormycosis in the ICU

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Introduction Mucormycosis is a devastating disease most commonly seen in immunosuppressed individuals. It has the propensity to disseminate in humans and cause rhinocerebral, pulmonary, gastrointestinal, and cutaneous infections. This study focuses on cutaneous mucormycosis, incidence, epidemiologic characteristics and mortality in intensive care medicine.

Methods We present a descriptive study in an ICU between the years 2001 and 2013 on the incidence of patients with cutaneous mucormycosis. Sociodemographics, comorbidities and laboratory data were recorded. Clinical data were collected to calculate the APACHE score. The main outcome was to analyze the epidemiological characteristics of patients with cutaneous mucormycosis and mortality.
Results Seven patients were identified with cutaneous mucormycosis between the years 2001 and 2013. The mean age of patients was 52 ± 4, with an APACHE score of 19 ± 9, and 57% died. All patients were admitted for trauma-related injury suffering blast, abrasive injuries or burns. Mortality among patients with signs of sepsis was 100%, and only in one of them was empirically antifungal therapy started; in the others antibiotic treatment was directed. Among patients without signs of sepsis, the survivor was treated with amputation where mucoral infection was isolated. Procalcitonin rose in all patients with signs of sepsis.
Conclusion Cutaneous mucormycosis is less common than other clinical forms, most frequently seen in inmunocompetent patients but potentially lethal if treatment is not rapid. Patients at risk are those with disruption of the normal protective cutaneous barrier. In these patients, if signs are of sepsis it is very important to suspect the possibility of infection by Mucor and initiate empiric antifungal treatment with surgery to avoid high mortality. Surprisingly, in our series, determination of procalcitonin showed high levels in spite of not having value in fungal infection.

P89

Low-pathogenicity mycoplasma species induce immunoparesis and are highly prevalent amongst patients with ventilator-associated pneumonia

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Introduction Ventilator-associated pneumonia (VAP) remains a significant problem within ICUs. There is a growing recognition of the impact of critical-illness-induced immunoparesis on the pathogenesis of VAP, but the mechanisms of this immunoparesis remain incompletely understood. We hypothesised that, because of limitations in their routine detection, *Mycoplasmataceae* are more prevalent amongst patients with VAP than previously recognised, and that these organisms potentially impair immune cell function.
Methods Two cohorts [1,2], totalling 159 patients, were recruited from 12 UK ICUs; all patients had suspected VAP and underwent bronchoscopy and bronchoalveolar lavage. VAP was defined as growth of organisms at $>10^4$ CFU/ml on conventional culture. Thirty-six healthy donors underwent lavage for comparison. Samples were tested for *Mycoplasmataceae* (*Mycoplasma* and *Ureaplasma* spp.) by PCR, and positive samples underwent sequencing for speciation. Additionally, healthy donor monocytes and macrophages (MDM) were exposed to *Mycoplasma salivarium* and their ability to respond to lipopolysaccharide and undertake phagocytosis was assessed.
Results *Mycoplasmataceae* were found in 48% of patients with VAP, compared with 14% of patients without VAP (P <0.0001). Patients with sterile lavage had a similar prevalence to healthy donor lavage (10 vs. 8%, P = 0.54). The commonest organism identified was *M. salivarium*. Human blood monocytes and MDM incubated with *M. salivarium* displayed impaired cytokine responses to lipopolysaccharide and MDM demonstrated impaired phagocytosis.
Conclusion This study demonstrates a high prevalence of *Mycoplasmataceae* amongst patients with VAP, with a markedly lower prevalence amongst patients with suspected VAP in whom subsequent cultures refuted the diagnosis. The commonest organism found, *M. salivarium*, is able to profoundly impair the functions of key immune cells and thus suggests that *Mycoplasmataceae* may contribute to VAP pathogenesis.
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P90

Comparative analysis of microflora and antibiotic resistance in patients with sepsis in 1999 and 2013

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Introduction Changes in infection agents and their sensitivity to antibiotics are the main cause of severity of surgical infections. In spite of development and introduction of new drugs and methods of treatment, the number of patients with sepsis increases, so the problem in diagnosing and treatment is still far from resolution.
Methods A comparative retrospective analysis of 52 histories of patients with sepsis, which were treated in the Department of Surgical Infections in 1999 and 2013.
Results The number of patients with sepsis in 2013 was raised 2.7 times, in comparison with 1999. Mortality decreased from 79% in 1999 to 55% in 2013. In most cases sepsis was accompanied with immunosuppressive disorders, such as diabetes, oncology, alcohol and drug addiction, and HIV infection. We analyzed crops of discharge from the wound and blood cultures in 52 patients with sepsis. Crops of wound were taken during the initial surgical intervention, then every 3 to 7 days, as well as the surgical interventions being repeated. Blood cultures were performed in the presence or suspected diagnosis of sepsis, in accordance with the classification Bone criteria. In comparison of spectrum of infection agents, *Staphylococcus aureus* is still leading (1999 – 36.6% of isolates, 2013 – 25%), and the percentage of MRSA was 0% in 1999 and 37.5% in 2013. The frequency of Gram-negative flora has increased: *E. coli* (8.5%/20%), *P. aeruginosa* (8.5%/12%), *Klebsiella pneumoniae* (0%/16%) and *Acinetobacter* spp. (0%/16%). Speaking about the resistance of microorganisms, there is still a high percentage of sensitivity to aminoglycoside antibiotics (79.4%/75%), glycopeptides (77.2%/71%), carbapenems (88.4%/78%) and also to the combination therapy (71.8%/62.4%), but also a reduction in sensitivity to the group of beta-lactam antibiotics (58.2%/32.5%) and fluoroquinolones (64.6%/36.4%).
Conclusion The number of patients with sepsis has increased; the mortality of sepsis has decreased. The frequency of *S. aureus* isolation is still high, MRSA is the same. The frequency of Gram-negative flora isolation has increased, especially *K. pneumoniae* and *Acinetobacter* spp. The resistance of microorganisms to beta-lactams and fluoroquinolones is rising but the sensitivity to aminoglycosides, glycopeptides, and carbapenems is still maintained.

P91

Infectious events and prescription of antimicrobials in the coronary ICU

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Introduction The effectiveness of initially used antimicrobials represents an important factor in infectious events in coronary intensive care units (CICU) [1]. This study aimed to analyze the prevalence of infectious events and the prescribed antimicrobial in CICU.
Methods We analyzed the data of 2,005 patients admitted to the CICU for 3 years. The infectious events were based on general characteristics, main sites and outbreaks of infectious events in addition to the main microorganisms and pathogens. The prescription of antimicrobials was analyzed based on the isolated or associated use of antimicrobials. We also analyzed the adequacy of initial empirical antimicrobial according to the microbiological evidence. The general characteristics of events – that is, time, evidence of infection, infections by multidrug-resistant pathogens – are also presented.
Results The prevalence of infection was 4% (n = 81). Ventilator-associated pneumonia was 35% (n = 28), whereas urinary and primary bloodstream associated with catheters was 14% (n = 11) and 9% (n = 7), respectively. There was 82% (n = 66) evidence of microbiological infection. The main pathogens and microorganisms found were

Gram-positive bacteria (*n* = 24, 30%; *Staphylococcus aureus* (*n* = 16, 20%), *Enterococcus faecalis* (*n* = 4, 5%), *Staphylococcus epidermidis* (*n* = 3, 4%)), Gram-negative (*n* = 43, 53%; klebsiella sp. (*n* = 13, 16%), *Pseudomonas aeruginosa* (*n* = 7, 9%), *Escherichia coli* (*n* = 7, 9%)) and fungi (*n* = 5, 6%; candida sp. (*n* = 2, 3%), *Candida albicans* (*n* = 1, 1%), *Candida dubliniensis* (*n* = 1, 1%)). The commonly prescribed antimicrobials were piperacillin/tazobactam (*n* = 32, 40%), vancomycin (*n* = 30, 37%), polymyxin B (*n* = 23, 28%), cefepime (*n* = 16, 20%), meropenem (*n* = 12, 15%), cefuroxime (*n* = 8, 10%), ciprofloxacin (*n* = 6, 7%), tigecycline (*n* = 6, 7%), ampicillin (*n* = 5, 6%), clindamycin (*n* = 4, 5%), chloramphenicol (*n* = 4, 5%), oxacillin (*n* = 4, 5%) and others (*n* = 32, 28%). There was 75% (*n* = 46) infection during hospitalization in the unit. Approximately 32% of infections were caused by multidrug-resistant pathogens, although there was efficiency of 81% in the proper use of initial antimicrobials.
Conclusion We conclude that infection is prevalent even in CICU, and that the microbiological profile is quite diverse, as well as the antibiotics. This allows us to better understand the profile of this kind of unit.
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P92

Analysis of Gram-negative rod bacteremia in the surgical and medical ICU

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Introduction The aim was to analyze the Gram-negative bacteremia profile and the predisposing factors for length of stay in the surgical and medical ICU and outcome.
Methods Retrospective data analysis of patients during 4 years treated in a surgical and medical ICU with positive blood culture for Gram-negative rod.
Results Gram-negative rod monobacteremia (*n* = 160) cultures revealed: *Escherichia coli* (*n* = 52, 32.5%), *Acinetobacter* spp. (*n* = 47, 29.4%), *Klebsiella* spp. (*n* = 22, 13.7%), *Enterobacter* spp. (*n* = 20, 12.5%), *Proteus* spp. (*n* = 11, 6.9%), anaerobes (*n* = 3, 1.9%) and other Gram-negative rods, including *Stenotrophomonas maltophilia*, *Haemophilus influenzae*, *Neisseria meningitidis*, *Achromobacter* spp. and *Actinobacillus limirensi* (*n* = 5, 3.1%). Both *E. coli* and *Acinetobacter* spp. were responsible for the vast majority of Gram-negative rod monobacteremia (*n* = 99, 61.8%, *P* = 0.0128). Also most often (*n* = 50, 72.5%, *P* = 0.049) primary bacteremia was caused by *E. coli* and *Acinetobacter* spp. Separate group's multidrug resistance was found: *E. coli* in 12 (23.1%) cases, *Acinetobacter* spp. in 45 (95.7%, *P* = 0.02), *Klebsiella* spp. in nine (40.9%), *Enterobacter* spp. in 11 (55.0%), *Proteus* spp. in six (54.6%) cases. The vast majority of patients with multidrug-resistant bacteremia were aged over 65 years (*n* = 64, 77.1%, *P* = 0.042), stayed in the ICU less than 14 days (*n* = 70, 84.3%, *P* = 0.039), and had lethal outcome (*n* = 74, 89.2%, *P* = 0.03). Patients who stayed in the ICU less than 14 days presented with primary Gram-negative rod bacteremia (*n* = 67, 57.7%, *P* = 0.03), need for mechanical ventilation (*n* = 90, 77.6%, *P* = 0.043) and lethal outcome (*n* = 112, 96.6%, *P* = 0.01). Lethal outcome was confirmed in patients with primary Gram-negative rod bacteremia (*n* = 55, 79.7%, *P* = 0.03), MDR strain (*n* = 74, 89.2%, *P* = 0.03), presence of shock (*n* = 120, 75.0%, *P* <0.001), mechanical ventilation (*n* = 133, 74.3%, *P* <0.001), cancer chemotherapy (*n* = 18, 90.0%, *P* = 0.03), and chronic obstructive pulmonary disease (*n* = 13, 100%, *P* = 0.03).
Conclusion *E. coli* and *Acinetobacter* spp. – the most often pathogens of Gram-negative rod bacteremia – were mostly multidrug resistant. Multidrug-resistant bacteremia was related to age, length of stay less than 14 days, and lethal outcome. Predisposing factors for shorter length of stay: primary bacteremia, mechanical ventilation, lethal outcome, and for lethal outcome: primary bacteremia, multidrug resistance, presence of shock, mechanical ventilation, cancer chemotherapy, chronic obstructive pulmonary disease.

P93

Is carriage of multidrug-resistant organisms a risk factor for nosocomial infections in an infectious diseases ICU?

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Introduction The objective was to evaluate whether asymptomatic carriage of methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE) and extended-spectrum beta-lactamase producing Gram-negative bacilli (ESBL-GN) on admittance to the ICU of the University Hospital of Infectious Diseases Cluj-Napoca, Romania is a risk factor for infection due to these multidrug-resistant organisms (MDRO) during hospitalization.
Methods A prospective study during a 6-month period (June to November 2014), including all adult patients admitted to our ICU. All patients were screened on admittance for nasal MRSA, intestinal VRE and ESBL-GN carriage. Patients admitted with any localization of infections due to these organisms were excluded. Patients were monitored for developing nosocomial infections due to MDRO during hospitalization. We evaluated previous colonization as a risk factor for future infections. We used bioMerieux selective chromogenic media for MDRO for screening and Vitek2Compact for identification. Statistical analysis was performed with chi-square test and univariate analysis.
Results From 119 screened adult patients, 65 women (54.6%), average age 67 years, we had at screening on admittance into the ICU: 14 positive MRSA (11.8%), 63 positive ESBL-GN (52.9% – 41 strains of *Escherichia coli*, 26 strains of *Klebsiella* sp., 11 strains of *Proteus mirabilis* and one strain of *Enterobacter cloacae*) and 35 positive VRE (29.4% – 33 strains of *Enterococcus faecium* and two strains of *Enterococcus faecalis*) without concomitant infection with these MDRO. The average duration of ICU stay was 7.32 days. During hospitalization, 14 patients (11.8%) developed nosocomial infections due to MDRO. Colonization with MDRO preceded nosocomial infections in: one of four patients with MRSA-positive blood cultures (*P* = 0.96), seven of eight patients with ESBL-GN infections (*P* = 0.10) and three of four patients with VRE urinary tract infections (*P* = 0.14). Although not statistically significant, owing to the low number, most patients who developed infections with ESBL-GN had previous intestinal colonization.
Conclusion The carriage of MDRO in ICU-admitted patients is important, especially for ESBL-GN. The incidence of nosocomial infections with MDRO in the ICU is high. ESBL-GN intestinal colonization could be a risk factor for nosocomial infections but further studies are needed to confirm this.

P94

Patient epidemiology in a level II hospital ICU and how main nosocomial infections affect morbidity and mortality

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Introduction We describe the type of patient and the main nosocomial infections in a level II hospital ICU unit, 18 beds (12 polyvalent-general, six coronary).
Methods We used the ENVIN-HELICS database and made statistical calculations for all patients admitted to the ICU between 1 October 2012 and 30 September 2013 using SPSS v.15.
Results Patients admitted (1,126): 65.1% were male; mean age 61.72 (SD ±15.8), CI (60.7 to 62.7); mean APACHE II 12.6 (SD ±8.42), CI (12.12 to 13.11); and a mean time stay of 4.84 days (SD ±6.26). In total, 68.9% were provided from the community. A total of 44.1% were coronary, 2.84% trauma and 53.02% medical–surgical patients. A total of 29.8% had antibiotic therapy in the ICU, 20% had it before incoming. In total, 18.38% were treated with artificial airway (MV, tracheostomy). In total, 54.09% used a urinary catheter and 38.8% needed a central venous catheter. Fifteen percent of patients had some kind of surgery before

admission; 4.8% required the extrarenal depuration technique. In total, 497 patients (44.1%) were coronary, 49.5% male, mean age 66.18 (SD ±12.6), CI (64.88 to 67.48); mean APACHE II 9.74 (SD ± 6.1), CI (9.1 to 10.3); and a mean time stay of 3.62 days (SD ±4.7), CI (3.1 to 4.1). Mortality in this group was 3.7%. In 61.9% of cases the diagnosis of admission was AMI, 16% arrhythmia and 11.6% unstable angina. Of patients, 629 were polyvalent (55.8%), 53.85% male, mean age 58.05 (SD ±17.2), CI (56.7 to 59.4); mean APACHE II 14.6 (SD ±9.1), CI (13.8 to 15.3); and a mean time stay of 4.64 days (SD ±7.7), CI (4 to 5.25). Mortality was 11.6%. In 33.2% the cause of income was digestive, 23.2% acute or chronic exacerbated respiratory failure, 12.4% severe sepsis/septic shock and 10.1% postoperative cardiovascular surgery. The incidence density (ID) of catheter-related bacteremia was 5.5, 92.8% from the fourth day of ICU admission; ID of ventilator-associated pneumonia (VAP) was 5.94, 88.9% since the fourth day; and ID of urinary tract infections (UTI) related to urinary catheter was 2.88, 80% of them since the fourth day. From all patients who developed intra-ICU infections, mean APACHE II in admission was 21.3 (SD ±9.6) with a mean time stay of 23.4 days (SD ±12.9) and a mortality percentage of 19.6%.

Conclusion In our ICU the main cause of admission was the polyvalent patient, who is younger and has more severity with not much difference in mean time of stay compared with the coronary patient. The intra-ICU infections provide an increase of morbi-mortality risk and consumption of resources.

P95

Emergence of isolates that are intrinsically resistant to colistin in critically ill patients: are we selecting them out?

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Introduction Poor infection control practices along with irrational usage of antibiotics lead to emergence of multidrug-resistant (MDR) organisms. Increasing use of colistin for treating MDR infections leads to selection of organisms that are intrinsically resistant to colistin. There are limited Indian literatures which evaluated the incidence of intrinsically resistant isolates to colistin in critically ill patients. Our study aimed to investigate the incidence of true pathogen or colonizer with the prior antibiotic exposure and patient's clinical outcome.

Methods The prospective, cross-sectional study was carried out from March 2013 to April 2014. Clinical samples included culture positivity for isolates intrinsically resistant to colistin from patients who were admitted to the ICU or had a prior ICU stay in the same admission.

Results A total of 93 unusual Gram-negative rods were isolated from 76 patients. This included 19.4% (n = 18) *Serratia marcescens*, 12.9% (n = 12) *Stenotrophomonas maltophilia*, 14% (n = 13) *Burkholderia cepacia*, 24.7% (n = 23) *Proteus mirabilis*, 17.2% (n = 16) *Morganella morganii*, 9.7% (n = 9) *Elizebethkingia meningoseptica* and 2.1% (n = 2) *Providencia* species. A total of 68.4% (n = 52) patients had prior exposure to either colistin or carbapenems or both. In total, 71% (n = 66) of the total isolates from patients had previous antibiotic exposure. Among the total 93 intrinsically resistant isolates to colistin, 37.6% (n = 35) of isolates from all clinical sources (endotracheal, pus, urine and blood samples) were true pathogens and the remaining 62.3% (n = 58) were colonizers. There was a statistically significant increase in length of ICU stay and duration of hospitalization in the presence of true pathogen.

Conclusion Selection pressure due to extensive use of higher antibiotics may lead to emergence of intrinsically resistant isolates, which narrows the therapeutic options in the ICU. Our study emphasizes the paramount importance of establishing clinical relevance of these organisms before treating them as true pathogens. This calls for judicious use of higher antibiotics, implementation of an antibiotic stewardship program and strict infection control practices.

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P96

In vitro antimicrobial susceptibility of fosfomycin against organisms isolated from various clinical specimens: a multicentre trial from Kolkata

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Introduction In the era of rising prevalence of serious infections caused by multidrug-resistant (MDR) organisms and the paucity of in-flow of newer antimicrobial agents, the relatively older antibiotics that had been left out of clinical practice for various reasons are now being increasingly considered as the potential agents to combat such infections. Fosfomycin, known for almost four decades, has a broad spectrum of activity against several Gram-negative and Gram-positive bacteria.

Methods This study, conducted in the Microbiology Department of Medica Superspecialty Hospital between July and November 2014, was aimed at testing the *in vitro* sensitivity of fosfomycin against isolates identified from various clinical specimens from different parts of Kolkata. After confirming the identity and antibiogram by Microscan Autoscan 4, the isolates were tested for fosfomycin sensitivity by the Epsilometer test. MIC values were interpreted in accordance with the currently recommended Clinical and Laboratory Standards Institute (CLSI) criteria for urinary tract isolates of *Escherichia coli* and *Enterococcus faecalis* and the European Committee on Antimicrobial Susceptibility Testing (EUCAST) criteria for Enterobacteriaceae and *Staphylococcus aureus*.

Results Out of the 1,895 isolates tested, fosfomycin displayed an overall *in vitro* susceptibility against 90%, but only 64% against MDR strains. Among the MDR organisms nearly 78% of *E. coli* and 70% of *Klebsiella* spp. and 40% of MRSA isolates showed provisional MICs in the sensitive range while among the sensitive strains fosfomycin showed around 92% susceptibility. Our study results were comparable with the results obtained from an Indian study published from CMC Vellore in 2013 showing a fosfomycin susceptibility of around 75% among MDR uropathogenic *E. coli*.

Conclusion Being a broad-spectrum bactericidal agent usable both orally and parenterally with low toxicity profiles and lesser prevalence of cross-resistance with other antimicrobials, fosfomycin can be an alternative to other broad-spectrum agents to treat uncomplicated infections as well as in the case of infections with MDR organisms where treatment options are very few. This study possibly reveals a much-needed solution for the rising carbapenem resistance and also for the treatment of infections with such MDR pathogens, thereby bringing down the length of stay in hospital, cost of therapy and suffering on the part of the patients.

P97

Antibiotic synergy testing for multidrug-resistant Gram-negative pathogens in a Greek ICU

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Introduction The emergence of multidrug-resistant (MDR) pathogens is a major cause of infection-related mortality among critically ill patients. The synergistic effect between commonly used antibiotics against difficult to treat nosocomial MDR Gram-negative strains, if present, could provide a viable option as an alternative therapy. The aim of this study was to investigate the potential of antibiotic synergy against MDR *A. baumannii*, *K. pneumonia* and *P. aeruginosa* strains, isolated from critically ill patients in a Greek ICU.

Methods We tested 59 *A. baumannii*, 41 *K. pneumoniae* and 64 *P. aeruginosa* strains, isolated during the period 2010 to 2013. All strains were resistant to carbapenems and showed reduced susceptibility or resistance to tigecycline or colistin (MIC >2), in accordance with CLSI guidelines. We evaluated double-drug combinations of carbapenem (CRB)/colistin (COL), tigecycline (TG)/COL, rifampicin (RIF)/COL, CRB/gentamicin (GEN), CRB/amikacin (AMK) for *A. baumannii*, TG/COL,

CRB/COL, piperacillin–tazobactam (PIP/TAZ)/GEN, CRB/GEN for *K. pneumoniae* and AMK/(PIP/TAZ), AMK/aztreonam (AZT), AMK/cefepime (CEF), AMK/CRB and CRB/COL for *P. aeruginosa* strains. In order to perform synergy tests, the E-test methodology (BioMerieux, Marcy l'E'toile, France) was used. Synergy was defined as a fraction inhibitory concentration (FIC) index ≤0.5, additive effect 0.5 to 1, indifferent or antagonistic effect >2 (Lorian definition).
Results Against 59 MDR *A. baumannii* strains, the synergy effect of CRB/COL was 55.9%, RIF/COL 38.9%, CRB/GEN 22%, CRB/AMK 20.3% and TG/COL 16.9%, respectively. Against 41 *K. pneumoniae* strains, synergy rates were: CRB/COL 43.9%, CRB/GEN 31.7%, PIP/TAZ/GEN 29.2% and TG/COL 24.4% respectively. Against 64 *P. aeruginosa* strains, synergy rates were: AMK/PIP/TAZ 64.6%, AMK/AZT 64.6%, AMK/CEF 58.3%, CRB/COL 52%, AMK/CRB 25%.
Conclusion The most effective combination for both the *A. baumannii* and *K. pneumoniae* strains tested was CRB/COL. The next most effective combination was RIF/COL and CRB/GEN respectively. No competitive effect was observed for RIF/COL combination in all cases tested. The most effective combinations for *P. aeruginosa* strains were AMK plus PIP/TAZ or AZT or CEF. The next most effective combination was CRB/COL. We recommend implementation of an antibiotic synergy test for MDR pathogens as a routine antimicrobial test in the hospitals' microbiology laboratories, especially for critically ill patients, since some combinations seem to excel. Further studies are needed for the correlation of these combinations with clinical efficacy.

P98

Development of antibiotic treatment algorithms based on Gram stain to restrict use of broad-spectrum antibiotics in the treatment of ventilator-associated pneumonia: a retrospective analysis

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Introduction Ventilator-associated pneumonia (VAP) is a common and serious problem in ICUs. Several studies have been conducted to determine the effectiveness of Gram stain of tracheal aspirates for diagnosing VAP. However, the effectiveness for predicting causative microorganisms and guiding appropriate initial antibiotic therapy has not been evaluated. The purpose of this study is to determine whether Gram stain of tracheal aspirates can guide appropriate initial antibiotic therapy for VAP.
Methods We retrospectively assessed two hypothetical empirical antibiotic treatment algorithms for VAP on an 18-bed ICU. Data on consecutive episodes of microbiologically confirmed VAP were collected over a period of 22 months and divided into a derivation (1 February 2013 to 30 November 2013) and validation (1 December 2013 until 15 November 2014) cohort. We constructed two algorithms in the derivation cohort. One is a local ecology-based algorithm (LEBA), according to clinical risk factors for MDR and susceptibility results in our hospital. The other is a Gram stain-based algorithm (GSBA). The selection of antibiotics on GSBA was directed against pathogens predicted from the results of bedside Gram staining of tracheal aspirates collected just before antibiotic therapy. Subsequently, LEBA and GSBA were retrospectively reviewed and compared with actually prescribed antibiotics in the validation cohort.
Results The first 50 VAP episodes made up the derivation cohort and the subsequent 50 VAP episodes the validation cohort. Antibiotic coverage rates by applying LEBA and GSBA were identical (96% vs. 96%). GSBA proposed more narrow spectrum therapy as compared with LEBA (P <0.001). GSBA recommended carbapenems in significantly less episodes than LEBA (P <0.001) and the same episodes as actually prescribed initial therapy (P = 1). However, there was significant increase of antibiotic coverage rates in GSBA compared with the actually prescribed initial therapy (96% vs. 78%, P = 0.015).
Conclusion Antibiotic coverage rates on GSBA were comparable with LEBA. The use of GSBA would result in a significant reduction of the administration of broad-spectrum antibiotics. Bedside Gram staining may be useful to guide appropriate initial antibiotic therapy for VAP.

P99

Skewed antibiogram of community-acquired urinary isolates and the therapeutic dilemma

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Introduction Urinary tract infection (UTI) is one of the most common bacterial infections in humans. Gram-negative organisms being the most common causative agent, the rising prevalence of resistance to a number of antibiotics and more importantly the production of extended spectrum beta-lactamase (ESBL) by these organisms is a growing concern worldwide. As the scenario is no better in community isolates, the choice of empirical antimicrobials for such infections becomes a great challenge for the clinicians.
Methods In this retrospective observational study we aimed at knowing the prevalence of ESBL production by organisms causing UTI in the community and to study the antibiogram of such isolates. Urine samples from patients with suspected UTI in the community were cultured for uropathogen by routine microbiological methods and susceptibility testing was done on Microscan Autoscan 4 (Siemens).
Results Out of 527 isolates of Enterobactereaceae, 314 (59.58%) were ESBL producers from the community samples compared with 315 (67.30%) from hospital samples, with *Escherichia coli* being the most commonly isolated pathogen. *Enterobacter* spp. showed highest prevalence (80%) of ESBL production from the community samples. Among the ESBL producing strains from the community, the sensitivity to ciprofloxacin, levofloxacin and nitrofurantoin was 18%, 21% and 44% respectively while in the non-ESBL producers the sensitivity rates were 52%, 51% and 73% respectively.
Conclusion Organisms producing the ESBL phenotype present with an added possibility of being resistant to other broad-spectrum antimicrobial agents which are commonly prescribed in the community to empirically treat such infections. This makes the choice of empirical antibiotic much more challenging in the community, drawing errors in judgment. A possibility of frequent overcorrection lies on the other side of the coin. This study also shows the possible need for empirical institution of class I carbapenems as one of the treatment options and outpatient parenteral antimicrobial therapy.

P100

Is it possible to predict multidrug-resistant organism colonization and/or infection at ICU admission?

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Introduction We tried to develop a predictive model for patients colonized/infected by any multidrug-resistant organism (MDRO-C/I) at ICU admission based on risk factors easy to obtain (not depending on complex clinical records), being aware that foreseeing MDRO-C/I at ICU admission is key for appropriate empirical treatment and infection control.
Methods Data were collected prospectively from admission to discharge of 16,950 patients admitted consecutively (at least >24 hours) to 147 Spanish ICUs of the ENVIN (National Surveillance Study of Nosocomial Infections in ICUs) registry, from April to June 2010. To create the predictive model, 11,998 (2/3) patients were used for univariable and multivariable logistic regression model and 4,952 (1/3) for subsequent validation.
Results With a MDRO prevalence of 2.12% (359 MDROs at ICU admission were detected in 314 patients), 87.58% patients had only one MDRO, meanwhile 12.42% were MDRO-C/I by two or more simultaneously. Risk factors used in the development of the predictive model and independently associated with MDRO-C/I at ICU admission were

(relative risk not shown due to space limitation): age 65 to 74, medical or surgical critical patient (especially urgent surgery), admitted from other ICU or long-term facility, immunosuppression and deep postsurgical skin or skin-soft tissue infections. Admitted from the community and female gender emerged as protective factors. Although the predictive model showed good discrimination (AUC-ROC = 0.775 (95% CI, 0.744 to 0.807)), sensitivity was only 67.4%. Validation with the remaining 4,952 patients (1/3) showed an AUC-ROC = 0.712 (95% CI, 0.665 to 0.759) and a *P* value on the Hosmer–Lemeshow goodness of fit test of 0.855. Even creating a new model, including variables obtained after ICU admission (severity by APACHE score, mechanical ventilation, central venous, arterial or urinary catheter, immunodeficiency, parenteral nutrition, ventricular derivation, extrarenal depuration, non-invasive ventilation, tracheotomy, enteral nutrition and nasogastric tube), prediction capability did not improve (AUC-ROC = 0.801 (95% CI, 0.774 to 0.828), sensitivity 71.4%).

Conclusion MDRO prediction at ICU admission could not be based merely on clinical–demographic risk factors. Taking into account local particularities and combining risk factors with a rapid laboratory test might be the most effective way forward.

P101

Methicillin-resistant *Staphylococcus aureus* in the ICU: risk factors and a predictive model to detect it at ICU admission

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Introduction Being capable of predicting MRSA on ICU admission is crucial to enhance infection control and to avoid inappropriate empirical treatment. Two objectives were studied: to describe risk factors for MRSA colonization/infection (MRSA-C/I) once admitted to the ICU; and to develop a predictive model at ICU admission, based on easy-to-obtain admission factors.

Methods Data were collected prospectively from 69,894 patients admitted consecutively (stay >24 hours) to 147 Spanish ICUs participating in the National Surveillance Study of Nosocomial Infections in ICU registry (ENVIN) during April to June 2006 to 2010. Univariable and multivariable analysis was performed for both objectives but we used only easy-to-obtain variables for the predictive model exclusively from those admitted in 2010 (n = 16,950, 2/3 for analysis and 1/3 for subsequent validation).

Results In the 2006 to 2010 period, 1,046 were C/I by MRSA (note that relative risks are not included due to space limitations). First objective: previous antibiotic, APACHE II score >18, skin-soft tissue or postsurgical superficial skin infections, trauma or medical patient, age >65 (especially >75), urinary catheter and admitted from a long-term care facility were independent risk factors for MRSA-C/I in ICU. Multicolonization increased significantly the risk of MRSA-C/I, and immunodeficiency and gender male emerged as protective factors. Second objective: independent risk factors on ICU admission were male gender, trauma critical patient, urgent surgery, admitted from other ICU, community or long-term facility, being immunosuppressed and skin-soft tissue infection. All configured the risk model for which, although showing good discrimination (AUC-ROC, 0.77; 95% CI, 0.72 to 0.82), sensitivity (67%) and specificity (76.5%) were insufficient for the ICU setting. Afterwards validation with the remaining 4,952 (1/3) showed AUC-ROC = 0.72 (95% CI, 0.65 to 0.79) and *P* value on the Hosmer–Lemeshow goodness of fit test = 0.539. The model did not improve even after including more complex variables (AUC-ROC = 0.82; 95% CI, 0.77 to 0.86, sensitivity 63.64%, specificity 78.48%).

Conclusion Independent risk factors for MRSA-C/I in the ICU and at ICU admission are described. To predict MRSA-C/I at ICU admission we should not rely on clinical–demographic risk factors alone. Its combination with a rapid laboratory test could be the way to proceed in future studies.

P102

Protective effect of a fecal incontinence management system against bacteremia for out-of-hospital cardiac arrest patients undergoing extracorporeal membrane oxygenation

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Introduction Recently, extracorporeal cardiopulmonary resuscitation (ECPR) has become a common measure against cardiopulmonary arrest. In cases with ECPR, we usually insert cannulae for extracorporeal membrane oxygenation (ECMO) via the femoral artery and vein. However, the cannulation site is often contaminated by feces due to incontinence. Moreover, patients tend to be compromised by hypothermia due to the target temperature management, so we often experience central line-associated bloodstream infection of patients undergoing ECMO. We investigated the protective effect of a fecal incontinence management system (FMS) against bacteremia in patients undergoing ECMO.

Methods We studied 41 consecutive patients undergoing ECMO for out-of-hospital cardiac arrest (OHCA) between April 2010 and May 2014. Patients were divided into two groups according to the use or no use of FMS (Flexi-Seal™). Patients who died within 48 hours or from whom cannulae for ECMO were removed within 48 hours were excluded. Patients' characteristics, underlying disease, target temperature management, prophylactic antibiotic use and incidence of bacteremia during admission were recorded and analyzed retrospectively.

Results Among 41 patients, 15 (37%) underwent FMS. There was no difference in age, sex, underlying disease, target temperature management, and prophylactic antibiotic use between two groups. Mean duration of ECMO was 4 days in both groups. The incidence of bacteremia was none in the group with FMS and five (19%) in the group without FMS. Within five cases of bacteremia, three were caused by enterobacterium.

Conclusion FMS may be protective against bacteremia for OHCA patients undergoing ECMO.

P103

Novel influenza A antibodies reduce severity of secondary pneumococcal pneumonia after influenza infection in mice

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Introduction Secondary bacterial pneumonia after influenza infection can cause severe disease with a high mortality. Recently, a new group 2 influenza A antibody (AT10_002) has been developed, which binds to multiple H3 and H7 subtypes. In a mouse model of primary influenza infection, treatment with AT10_002 as a fusion antibody protects against lethal infection, and reduces loss of bodyweight [1]. We hypothesized that treatment with AT10_002 reduces weight loss, lung injury and bacterial outgrowth, in a mouse model of viral infection followed by secondary pneumococcal infection.

Methods Male C57Bl/6 mice were intranasally inoculated with 400 TCID50 Influenza A (H3N2). Two days after infection, mice were injected with either AT10_002 i.v. (n = 8) or a control antibody (n = 7). After 7 days, both groups were intranasally inoculated with 5×10^3 *S. pneumoniae* type 3 and were sacrificed 18 hours later. Outcome measures were weight loss, wet lung weight, cell count in bronchoalveolar lavage fluid (BALF), and colony-forming units (CFUs) in lung homogenate. Data are represented as medians, and treatment groups are compared using nonparametric tests.

Results Mice receiving AT10_002 showed significantly lower weight loss at the time of sacrifice compared with the control group (+1% vs. –12% change in weight; P = 0.0003). Also wet lung weight was lower (68 vs. 96 mg; P = 0.0003), cell counts in BALF were lower (4.9×10^5 vs. 7.0×10^5 cells/ml; P = 0.0037) and CFUs in lung homogenate were lower (33 vs. 25×10^4 CFUs/mg; P = 0.0003) compared with controls.

Conclusion Early treatment with influenza antibody AT10_002 significantly reduces weight loss, lung injury and bacterial outgrowth,

in a mouse model of influenza infection followed by secondary pneumococcal pneumonia.

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P104

Prevalence of viral respiratory tract infections in acutely admitted and ventilated ICU patients: a prospective multicenter observational study

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Introduction The prevalence of viral respiratory tract infections in critically ill patients is uncertain, as well as the optimal diagnostic method to detect these. The aim of this study was to assess the prevalence of viral respiratory tract infections in mechanically ventilated patients, in both the upper and lower respiratory tract.
Methods A prospective observational study was performed in five ICUs in the Netherlands. From September 2013 to April 2014, consecutive acutely admitted, mechanically ventilated patients were included, regardless of diagnosis at admission. Nasopharyngeal (NP) swabs and tracheal aspirates (TA) were collected at intubation, and were tested via multiplex RT-PCR for the following viruses: influenza A and B, parainfluenzaviruses, RSV, human metapneumoviruses, bocaviruses, coronaviruses, rhinoviruses, enteroviruses, parechoviruses and adenoviruses. Viral DNA/RNA copies were expressed by crossing-point (cp) values.
Results In total, 1,499 patients were included, of whom 265 patients (18%) had a viral respiratory tract infection with at least one virus. In 17 patients, two viruses were found; two patients had an infection with three viruses. The most prevalent was parainfluenzavirus-3 (5.7%); 17 patients (1.1%) had an infection with influenza. The lowest prevalence of viral infections occurred in September (12%), the highest in October and February (both 26%). Of the patients tested positive in TA, only 46% also tested positive in NP. The median cp values were not significantly different between TA and NP swabs (31.1 vs. 31.6, $P = 0.75$).
Conclusion The prevalence of viral respiratory tract infections is high in unselected ICU patients. Testing tracheal aspirate in combination with nasopharynx greatly increased detection of viruses, and yields similar cp values. Whether these viral infections are associated with prolonged mechanical ventilation and worse outcomes remains to be determined.

P105

Adequate initial antimicrobial therapy as the factor assessing treatment efficacy in human septic shock

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Introduction The early identification of severe sepsis and septic shock and early implementation of the SSC bundles were associated with reduced mortality [1]. The failure to initiate appropriate antimicrobial therapy increased mortality of septic shock patients [2]. We hypothesized that the parameter 'Consensus initial antimicrobial therapy with microbial cultures' correlates with outcome of septic shock patients.
Methods We analyzed 535 consecutive patients with septic shock (sepsis-induced hypotension persisting despite adequate fluid resuscitation) from the EPOSS database (Data-based Evaluation and Prediction of Outcome in Severe Sepsis), which was developed to monitor and assess treatment efficacy in patient with severe sepsis and septic shock. Patients were admitted to participating ICUs (12 hospitals – 17 high-volume care units) in the Czech Republic from 1 January 2011 to 5 November 2013. Patients were divided into two groups: survivors ($n = 274$) and nonsurvivors ($n = 261$).
Results Survivors versus nonsurvivors were similar in: age 65.8 (64.2; 67.5) versus 66.5 (64.7; 68.3) $P = 0.583$, men 159 (58.0%) versus 160 (62.0%) $P = 0.376$, APACHE II score 27 (15 to 40) versus 28 (15 to 40) $P = 0.737$. Statistically significant differences between survivors versus nonsurvivors were found in the parameter 'Consensus initial antimicrobial therapy with microbial cultures' 178 (79.5%) versus 128 (58.4%) $P < 0.001$ and in the parameter 'Administration antimicrobials within the first hour' 163 (59.9%) versus 171 (70.7%) $P = 0.001$. Administration of 30 ml/kg crystalloid for hypotension or lactate 4 mmol/l (3 hours) and application of vasopressors (6 hours) were in both groups without statistically significant differences.
Conclusion We found that correct choice of antibiotics improves outcome of septic shock patients. The choice of empirical antimicrobial therapy depends on complex factors related to the underlying disease, susceptibility of pathogens, patient's history and clinical syndrome. Adequate initial antimicrobial therapy as an important factor of survival along with suitable initial fluid resuscitation and application of vasopressors should be a priority for healthcare in human septic shock.
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P106

Source of MDR infections in an ICU: busting the myth

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Introduction MDR infections in the ICU are not nosocomial all the time, as perceived commonly. We performed a 2-year retrospective study to analyze the source of culture positivity in a medical ICU and to identify which types of infections are more prevalent.
Methods The data of a 35-bed medical ICU were analyzed from November 2012 to October 2014. The source of culture positivity was divided into three groups: patients admitted from the ER to the ICU who were referred from other hospitals or direct admissions, the second group was patients admitted within the hospital but outside the ICU for the first 48 hours, and the third group was ICU-acquired infections. We also analyzed the data for type of infections, whether Gram-negative, Gram-positive or fungal.
Results There were 1,051 cultures positive in a 2-year period. In total, 46.8% ($n = 492$) of cultures were already positive on admission, which denotes community-acquired and referred patients from other hospitals. A total of 31.1% ($n = 327$) of cultures were positive from patients admitted to general wards for more than 48 hours and then transferred to the ICU. Twenty-two percent ($n = 232$) of cultures were ICU-acquired infections. The data show community-acquired and hospital-acquired infections are the bulk of the culture load in an ICU. This could be attributed to increased surveillance and adherence to infection control practices in the ICU which may not be followed stringently in other parts of the hospital. Overuse of broad-spectrum antibiotics in community and primary care hospitals has resulted in a spurt in growth of resistant infections. This has reached an alarming level in developing countries. Out of total cultures positive 78.3% ($n = 822$) were Gram-negative infections which included community-based and non-ICU infections.
Conclusion Antibiotic stewardship and strict adherence to infection control protocols in hospitals and guidelines for general practitioners can significantly reduce the load of resistant organisms in the ICU. This may eventually improve patient outcomes and help in preserving the antibiotics for future generations.
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P107

Concordance between a new molecular real-time approach and traditional culture in suspected VAP patients

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Introduction Early microbiological documentation may reduce attributable mortality and excessive use of broad-spectrum antibiotics in ventilator-associated pneumonia (VAP). Using bronchoalveolar lavage (BAL) and endotracheal aspirates (ETA), we studied a new molecular biology-based approach to detect and quantify bacteria in less than 3 hours. This prospective multicenter trial aimed at comparing the microbiological results obtained using this molecular protocol (easyMAG® system) and semiquantitative culture in suspected VAP.
Methods ETA and BAL samples were consecutively collected during 10 months in adult patients in four ICUs of France. The molecular method includes a preprocessing liquefaction for ETA before DNA extraction. DNAs were extracted using the easyMAG® system. Real-time PCR (qPCR) was run using the ABI7500FastDx PCR instrument. The results presented here concern: *Staphylococcus aureus*, *Pseudomonas aeruginosa* and Enterobacteriaceae. Quantification was performed using qPCR standard curves, by converting the cycle threshold to CFU/ml.
Results A total of 125 suspected VAP were included from 122 patients. In total, 125 BAL and 107 ETA were collected. Sex ratio (M/F) was 76%, and CPIS ≥6 was calculated in 74.6% of the suspected VAP patients. Mean ventilation duration before sampling was 6 days. Seventy-eight percent and 65% of the BAL and ETA culture were positive respectively. Correlations between molecular method and culture on BAL and ETA are reported in Table 1.

Table 1 (abstract P107). Concordance between qPCR and culture on BAL/ETA in VAP patients

	Positive culture	qPCR	Agreement (%)	Sensitivity (%)	Specificity (%)
S. aureus (BAL/ETA)	28/20	31/25	96.7/89.7	96.6/76.9	96.8/93.8
P. aeruginosa (BAL/ETA)	23/20	20/23	97.6/93.5	100/100	97.1/92.4
Enterobacteriaceae (BAL/ETA)	27/7	36/18	90.3/85.0	90.0/58.3	90.4/88.4

Conclusion Sensitivity and specificity of the new molecular approach for these main bacteria found in VAP could enable targeted first-line antibiotic therapy. In the future, the development of this approach will aim at obtaining a bedside diagnostic in only a few hours.

P108

Use of Cepheid Xpert Carba-R® for rapid detection of carbapenemase-producing bacteria in critically ill, abdominal surgical patients: first report of an observational study

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Introduction Xpert Carba-R® (Cepheid®, USA) is a PCR-based assay for rapid (<1 hour) detection of bacteria carrying carbapenem-resistance genes (KPC, NDM, VIM, OXA-48, IMP-1). The aim of the study is to compare PCR with microbiological cultures in critically ill, abdominal surgical patients.
Methods We performed an observational study at University Hospital 'P. Giaccone' Palermo. We enrolled abdominal surgical patients admitted to the ICU with suspected abdominal sepsis or developing sepsis during the ICU stay. We obtained two rectal swab specimens and two drainage samples to perform PCR assay and classic culture tests. We used Cohen's *K* to test concordance of results. We considered concordant those results of positive detection of carbapenemase-producing bacteria by both methods (even if a polymicrobial growth was observed by cultures) or negative results by both methods. Concordance was studied for rectal swab and drainage specimens. Antibiotic susceptibility testing was performed through a semiquantitative method.
Results Eight complete samples sets were collected from seven patients. Seven rectal swab specimens were negative for both PCR and cultures. In one patient a positive culture from carbapenem-resistant *P. aeruginosa* was detected from the rectal swab resulting negative to PCR. In one patient a positive culture from carbapenem-resistant *A. baumanii* was detected by drainage culture resulting negative to PCR. In two cases a positive result was observed from both PCR and cultures of rectal swab and drainage specimens. Vim and KPC genes were detected in one case and *A. baumanii* and *K. pneumoniae* with carbapenem resistance were isolated from cultures. A KPC gene was detected by PCR in the other case, and *K. pneumoniae* with carbapenem resistance was isolated from cultures. In all other cases a negative result was observed by both PCR and cultures. Cohen's *K* of 0.71 (95% CI = 0.21 to 1) was observed for rectal swab and drainage specimens.
Conclusion We need more data to evaluate the performance of PCR for rapid detection of carbapenemase-producing bacteria from rectal swabs and drainage of critically ill surgical patients even though its concordance with cultures seems to be good.

P109

Use of an electronic medical record system to improve antimicrobial stewardship

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Introduction Antimicrobial resistance constitutes a growing global threat, driven in part by inappropriate antimicrobial prescribing [1]. Most hospitals implement antibiotic policies to promote antimicrobial stewardship. This audit examined the Royal Cornwall Hospital Trust (RCHT) Critical Care Department's compliance with the current standard defined in our local antimicrobial policy. This states that all antimicrobial prescriptions are to have an indication and review date recorded [2]. Sequential strategies to improve compliance were introduced prior to re-auditing the effects.
Methods The RCHT Critical Care Department utilizes the Phillips Care Vue electronic patient record. Data from this system were interrogated at three stages to assess our compliance with the trust's antimicrobial policy. The first data interrogation was performed prior to any intervention, and reflected baseline antimicrobial prescribing habits. The second data interrogation was performed during a period of active antibiotic stewardship promotion. The third data interrogation was performed following the addition of a care bundle to the prescribing module of Care Vue. This daily tick-box prompt reminded clinicians to check that all antimicrobial prescriptions had an indication and review date recorded. The records of all of the patients admitted to the critical care department during the periods of data interrogations were assessed for antimicrobial indication and review date transcription.
Results From the first data interrogation, antimicrobial prescriptions had an indication and review date transcription in 57% and 60% of cases respectively. Following the awareness campaign, the indication and review date transcription rate increased to 78% and 85% respectively. A daily electronic prompt was then added to our care bundle list. The final data interrogation, performed after this intervention, demonstrated that the transcription rates for both the indication and the review date had increased to 96%.
Conclusion We have demonstrated that the use of a daily prompt within an electronic patient record can greatly improve compliance in recording the indication and review date for all antimicrobials. These data support the widespread implementation of an electronic prescribing system where daily reminders are integrated in an effort to improve compliance with antimicrobial stewardship.

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P110

Factors associated with survival of ICU patients with pneumonia caused by multidrug-resistant Gram-negative bacteria

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Introduction Multidrug-resistant (MDR) bacterial pneumonia is associated with significant morbidity and mortality in severely ill ICU patients. The assessment of factors associated with the onset and clinical course of MDR pneumonia may improve treatment effectiveness. The purpose of this study is to identify factors associated with outcome in mechanically ventilated patients with ventilator-associated pneumonia (VAP) caused by MDR bacteria.
Methods We studied retrospectively all mechanically ventilated patients treated in the A' ICU of KAT General Hospital in Athens from 1 January 2011 to 31 December 2013 and showed ventilator-associated pneumonia from MDR Gram-negative bacteria. Standard demographic and clinical data, the causative organisms and outcome were recorded. For statistical significance, chi-square and Student *t* tests were used.
Results A total of 102 mechanically ventilated patients, 75 men and 27 women, were included in the study. All patients showed VAP caused by MDR bacteria. They were stratified by outcome into survivors and nonsurvivors. ICU mortality was 55%. Gender, cause of admission, the causative microbe, colonization of bronchial secretions and secondary bacteremia had no correlation with outcome. Age and APACHE II score were higher in nonsurvivors (P <0.01 and P <0.05 respectively). The time-onset of pneumonia after admission was longer in patients with VAP caused by Klebsiella or Pseudomonas than those with VAP caused by acinetobacter (P <0.01). Patients with Klebsiella or Pseudomonas pneumoniae needed more time on mechanical ventilation than those with pneumonia from acinetobacter (P <0.01).
Conclusion VAP caused by MDR bacteria is a leading cause of ICU death. Age and APACHE II score are significant risk factors of death.
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P111

Epidemiological cohort study of systemic antifungal therapy for suspected or confirmed invasive candidiasis in the ICU: the Amarcand2 study

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Introduction Prescription of antifungal treatments (AFT) in ICUs in case of suspected or confirmed invasive candidiasis (SIC or CIC) has been challenged by different guidelines. The study aimed to describe the epidemiology of the invasive candidiasis (IC), analyze the criteria for the AFT initiation, the AFT type, and its changes during patient follow-up.
Methods A prospective observational multicenter cohort study. Consecutive adult patients with SIC or CIC and treated with systemic AFT were included between October 2012 and September 2013 in 104 French ICUs.
Results In total, 870 patients were included and 835 evaluable, the IC was confirmed at study inclusion for 291 and suspected for 544 patients. Eventually, the IC was confirmed for 403/835 patients (peritonitis: 177; candidaemia: 141; deep candidiasis: 61; mixed infection sites: 24). *Candida albicans* was the main pathogen (67%), then *C. glabrata* (16%). At inclusion, CIC were treated with caspofungin (Cas): 55%, and fluconazole (Flu): 34%, whereas these antifungals were administered to 46% and 45% of SIC, respectively. Patients with SIC were more severe than those with CIC. The two main criteria for initiating empirically an AFT were a central venous catheter (79%) and severe septic shock (70%). The rate of change of the initial AFT was higher in the CIC group (49%) than in the SIC group (33%, P <0.0001). In the CIC group, it was mostly for changing the antifungal agent (de-escalation Cas → Flu in half of the patients) based on mycological tests results. In the SIC group, the AFT was modified almost as often for changing the drugs (including 22% de-escalation Cas → Flu) as for stopping the AFT. The 28-day mortality of candidaemia was 42% in cases of *C. glabrata*, 40% in cases of *C. albicans*, and 20% in cases of *C. parapsilosis*. Among survivors, the median duration of treatment was 17 to 21 days according to the infection site in cases of CIC, and 10 days in cases of SIC.
Conclusion French ICU patients are treated with antifungal agents selected according to the candidiasis severity, contrary to ESCMID guidelines which recommend initiating with echinocandins regardless of severity. As recommended, the therapy was secondarily adapted to microbiological results.

P112

Micafungin concentrations 100 mg daily in plasma and burn eschars in patients with severe burn injuries

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Introduction Micafungin (MCF) is an echinocandin agent with broad activity against *Candida* spp., which are frequently isolated in blood and eschar cultures of burned patients, who present different pharmacokinetics (PK) characteristics. Due to the limited information about its PK, we investigate MCF levels in plasma and burn eschar tissues in this population.
Methods A PK study of MCF at standard dosage (100 mg/day). Cmax (end of the infusion) and Cmin (before next dose) plasma levels of MCF were obtained after first dose and at steady state (days 4 and 5 of therapy); and on day 5 in eschars (1 to 3 hours after infusion). They were measured by HPLC. Spearman's rho test was used for bivariate correlations between MCF exposure and patient's clinical factors.
Results There were 10 patients (eight men; age: 18 to 77 years). Patients' characteristics and PK are shown in Table 1. A high interindividual variability was observed in the concentrations of MCF. Peak plasma concentrations after the first and repeated doses of MCF were inversely correlated with % burned TBSA (Spearman's $\rho = -0.695$ and -0.750 (P <0.05), respectively), but not with the time from burn injury. MCF concentrations in burn eschars were not correlated with % burned TBSA. MCF was well tolerated. One patient had candidemia. The crude mortality was 40%.
Conclusion This is the largest PK study of 100 mg daily of MCF in severely burned critically ill patients. The inverse correlation between MCF exposure and % burned TBSA suggests that patients with large burned TBSA may need higher doses of MCF. Nevertheless, MCF levels in plasma and burn eschar tissues after the first and multiple doses were above the MIC90 against most clinically important *Candida* species.

P113

Tedizolid clearance by *in vitro* continuous renal replacement therapy model

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Introduction Tedizolid is an oxazolidinone antibiotic approved to treat acute bacterial skin and soft tissue infection and is under investigation

Table 1 (abstract P112). Clinical and pharmacokinetic characteristics of patients

Patient	% burned TBSA	% FT	ABSI	MCF dose (mg/kg body weight)	Plasma Cmax/Cmin after first dose (µg/ml)	Plasma Cmax/Cmin at steady state (µg/ml)	Burn eschar tissue on day 5 (µg/g)	Days from admission to the start of MCF	SOFA at the beginning of MCF	LOS in BICU (days)
1	35	20	9	1.3	8.6/0.8	7.4/1.0	2.3	38	1	75
2	40	35	8	2.0	8.5/1.1	9.4/1.8	<LQ	15	6	23
3	23	16	8	1.3	6.4/0.8	10.3/1.2	<LQ	12	2	17
4	70	40	12	1.1	3.9/0.5	4.5/0.8	0.4	8	6	43
5	23	12	7	1.3	7.5/1.8	8.0/1.4	0.6	10	5	19
6	70	60	11	1.2	3.4/0.5	5.0/0.9	1.5	12	5	70
7	80	70	12	1.1	3.8/0.4	4.0/0.4	0.2	34	2	61
8	60	50	10	1.4	4.8/0.5	4.3/1.0	0.2	34	2	90
9	44	34	10	1.3	4.5/1.1	9.1/2.3	0.2	8	6	34
10	34	28	9	1.3	4.1/0.7	5.4/1.0	0.7	10	5	35
Median	42	34.5	9.5	1.3	4.7/0.7	6.4/1.0	0.5	12	5.0	39
IQR	31.3 to 70.0	19.0 to 52.5	8 to 11.3	1.1 to 1.4	3.9 to 7.5/0.5 to 1.1	4.5 to 9.1/0.9 to 1.4	0.3 to 1.1	9.5 to 19.8	3.5 to 5.6	22.7 to 71.3

ABSI, Abbreviated Burn Severity Index; BICU, burn intensive care unit; FT, full thickness; IQR, interquartile range; LOS, length of hospital stay; LQ, limit of quantification (<0.1 µg/ml); SOFA, Sequential Organ Failure Assessment; TBSA, total body surface area.

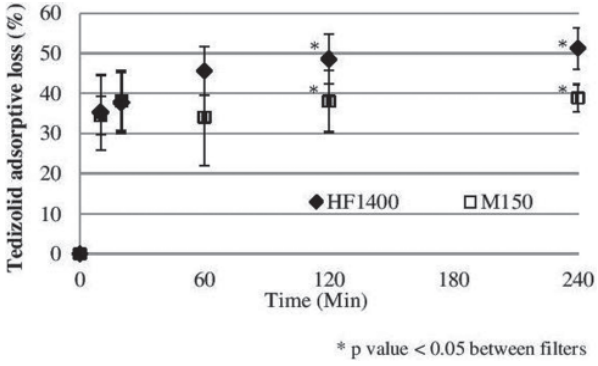


Figure 1 (abstract P113).

for treatment of nosocomial pneumonia, common in critically ill patients with acute kidney injury. There are limited data on tedizolid disposition in continuous renal replacement therapy (CRRT). This study's purpose was to assess continuous hemofiltration (CHF) and continuous hemodialysis (CHD) influence on tedizolid clearance.

Methods Validated, bovine blood-based, *in vitro* CHF and CHD models were used with six new HF 1400 (polysulfone) and six new Multiflow 150 (AN 69) hemodiafilters. Tedizolid's transmembrane clearances (CLTM) during CHF and CHD were assessed by measuring sieving (SC) and saturation (SA) coefficients at various ultrafiltrate (Quf) (1, 2, 3 l/hour) and dialysate flow rates (Qd) (1, 2, 3 and 6 l/hour), using a blood flow rate (Qb) of 200 ml/minute. Tedizolid adsorption was tested in a 1 l recirculating CHF model at Quf of 2 l/hour and Qb of 200 ml/minute over 4 hours. Adsorption (%) was calculated after correcting for the dilution by CHF priming volume. Urea was added as a control in all experiments.

Results Urea SC and SA were ~1 in all experiments. In CHF, mean tedizolid SC ranged from 0.52 to 0.57 for HF1400 and from 0.50 to 0.54 for M150. CLTM did not differ between filter types for Quf of 1, 2, and 3 l/hour. In CHD, mean tedizolid SA ranged from 0.46 to 0.56 for HF1400 and from 0.38 to 0.44 for M 150. Tedizolid CLTM with the HF1400 was higher than M150 values at Qd of 6 l/hours (P <0.02). Tedizolid exhibited irreversible adsorption within 10 minutes. See Figure 1.

Conclusion Tedizolid's CLTM is dependent on hemodiafilter type and Qd for CHD and Quf in CHF. At conventional CRRT rates, tedizolid CLTM appears modest relative to total body clearance and is unlikely to require dose adjustments. CRRT adsorption in the clinical setting is likely less than what we observed in this *in vitro*, continuously recirculating blood model.

P114

Stability of crushed tedizolid phosphate tablets for nasogastric tube administration

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Introduction Tedizolid phosphate, a novel oxazolidinone antibacterial prodrug recently approved by the US Food and Drug Administration for the treatment of acute bacterial skin and skin structure infections, is available as oral (that is, tablets) and intravenous formulations. The clinical pharmacokinetics of tedizolid, the active moiety of tedizolid phosphate, are similar when orally administered tedizolid phosphate is given as powder in a capsule or as tablets. This suggests that crushing tablets prior to administration is unlikely to alter tedizolid pharmacokinetics, provided no drug is lost during administration. To determine whether the expected dose of tedizolid phosphate can be delivered via nasogastric (NG) tube in critically ill patients who have difficulty swallowing, this study evaluated the stability and recovery of tedizolid phosphate 200 mg tablets after crushing, dispersion in water, and passage through an NG tube.

Methods For each assay, run in triplicate, one 200 mg tablet of tedizolid phosphate was crushed, dispersed in water, drained under gravity through one of two types of NG tubes (type 1, Kangaroo Nasogastric Feeding Tube, 10 Fr 43" (109 cm); type 2, Salem Sump Dual Lumen Stomach Tube, 18 Fr/CH (6.0 m) 48" (122 cm)), and collected for recovery analysis by high-performance liquid chromatography with UV detection. To analyze the chemical stability of the crushed tablet dispersed in water, the aqueous preparation was assayed initially after dispersion and again after 4 hours at room temperature, without NG tube passage. The prespecified limit for tedizolid phosphate in recovery samples was 90 to 110% of the dose. Limits were also specified for levels of certain impurities.

Results The average and individual recovery values of tedizolid phosphate were within 90 to 110% of the 200 mg dose when crushed tablets, dispersed in water at room temperature, were transferred through the 2 NG tubes (type 1: 95.8%; type 2: 93.6%). There was

no significant change in recovery values after 4 hours of storage at room temperature (93.9% initially and 94.7% after 4 hours). Results for degradation products and impurities were also within specified limits in NG recovery samples and in the 0-hour and 4-hour aqueous preparations.
Conclusion The stability and recovery of tedizolid phosphate were not influenced by crushing the tablets and passing through an NG tube. Therefore, administration of crushed tedizolid phosphate tablets to patients is unlikely to alter the pharmacokinetics of tedizolid compared with whole tablets.

P115

Antiviral prophylaxis inhibits cytomegalovirus reactivation in critical illness

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Introduction Reactivation of latent cytomegalovirus (CMV) can lead to viraemia or CMV disease and has been detected in up to 30% of critically ill patients without prior history of immune suppression. However, the clinical importance of this observation remains unclear. We report a proof-of-concept randomised controlled trial of two antiviral drugs in intensive care patients to determine their impact on CMV reactivation.
Methods We conducted a single-centre randomised controlled study of high-dose valaciclovir or low-dose valganciclovir prophylaxis, as compared with standard care, in CMV seropositive patients in the ICU at Queen Elizabeth Hospital Birmingham, UK. Patients were excluded if CMV seronegative. Study participants randomised to a study drug received either 450 mg valganciclovir daily enterally (or ganciclovir intravenously) or 2 g valaciclovir four times daily enterally (or aciclovir intravenously) for a period of up to 28 days. Blood was collected for CMV viral load during the 28-day study period. The primary outcome measure was reactivation of CMV in blood above 20 copies.ml^{-1} (assay detection limit) by day 28.
Results A total of 124 patients were randomised; 44 control, 34 valaciclovir, and 46 valganciclovir. Recruitment to the valaciclovir arm was halted early because of an imbalance in mortality (44% mortality vs. 19% in other arms). Independent blinded review of all deaths did not reveal any deaths attributable to unexpected causes. Fourteen patients were excluded from the primary analysis because of baseline CMV reactivation. CMV reactivation occurred in 30% (12/40) of the control arm but only 3% (1/39) in the valganciclovir arm (RR: 0.09 (95% CI: 0.01, 0.6)). When the two treatment arms were considered together, reactivation was observed in only 4% (3/70) (RR: 0.1 (95% CI: 0.04, 0.5)). See Figure 1.
Conclusion This is the first study in critical care to assess the feasibility of antiviral prophylaxis to prevent CMV reactivation in a mixed population of critically ill patients. Low-dose valganciclovir was shown to suppress CMV reactivation as effectively as higher-dose valaciclovir.

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P116

Pharmacokinetics of daptomycin in patients undergoing low-flow continuous venovenous hemodiafiltration

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Introduction In daptomycin (DAP), 1,061 mg hour/l of the area under the concentration–time curve (AUC)/MIC was required to obtain clinical success [1], and a trough serum concentration (Cmin) cutoff point of 24.3 g/ml was most significantly associated with CPK elevation [2]. Reportedly, DAP at a recommended dosage of 8 mg/kg is removed in patients undergoing high-flow continuous venovenous hemodiafiltration (CVVHDF) (blood flow and filtration rates were 150 ± 48 and 2 l/hour). In Japan, CVVHDF is preferentially performed with lower flow rates. Investigating effects of flow rate on DAP removal during continuous renal replacement therapy is essential to adjust therapeutic dosages. We aimed to investigate the pharmacokinetics of DAP in CVVHDF patients in this setting.
Methods DAP (6 mg/kg) was administered intravenously every 48 hours to CVVHDF patients in the ICU. Blood and filtrate samples were collected at 0, 1, 1.5, 2, 5, 12, 24, and 48 hours after infusion. All collected samples were analyzed using HPLC according to the method of Tobin and colleagues [3]. Maximum concentration (Cmax), elimination half-life (t1/2), area AUC, Cmin, volume of distribution (Vd), clearance (CL), fraction unbound, and sieving coefficient (Sc) were evaluated. Patient characteristics and CVVHDF parameters including blood, dialysate, and filtration flow rates were recorded.
Results Three patients were included in the study. Mean blood, dialysate, and filtration flow rates were 86.7 ± 11.5 ml/minute, 417 ± 29 ml/hour, and 417 ± 29 ml/hour, respectively, confirming that CVVHDF was performed under low-flow setting. Cmax was 50.1 ± 12.7 mg/l (31.9, 70.5, 49.7 mg/l); t1/2, 35.1 ± 34.8 hours (18.6, 11.5, 70.5 hours); AUC, 889 ± 399 mg hour/l (471, 967, 1,260 mg hour/l); Cmin, 16.0 ± 10.3 mg/l (2.3, 24.7, 14.0 mg/l); Vd, 26.0 ± 20.9 l (23.8, 6.34, 47.9 l); CL, 9.47 ± 4.56 ml/minute (14.7, 6.35, 7.37 ml/minute); and fraction unbound, 5.8% (5.7, 4.1, 7.6%). Sc and CL of dialyzer were 0.08 ± 0.03 (0.11, 0.04, 0.07) and 1.20 ± 0.39 ml/minute (1.70, 0.88, 0.96 ml/minute), respectively.
Conclusion DAP (6 mg/kg daptomycin every 48 hours) in patients receiving low-flow CVVHDF resulted in showing variability of AUC and avoiding accumulation. Owing to small case numbers, it needs further study.

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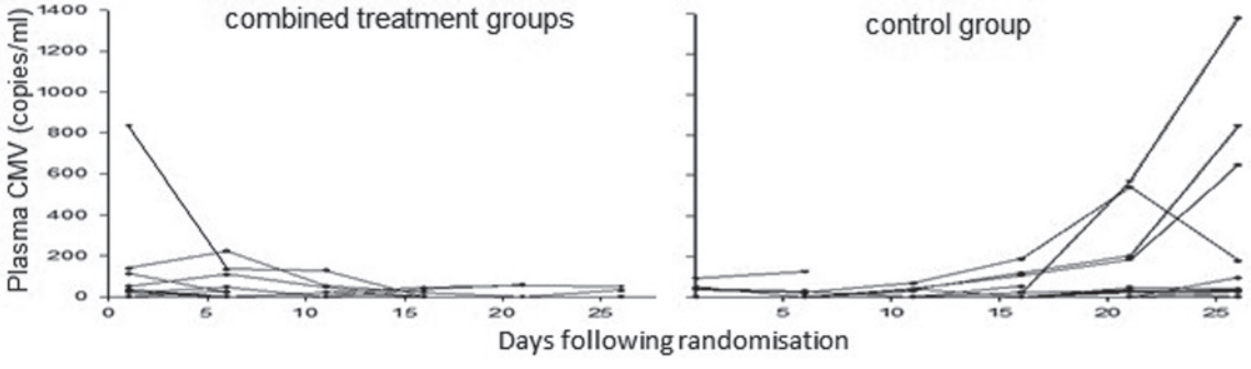


Figure 1 (abstract P115). CMV reactivation over time. Each line represents a single patient.

P117

Adsorption of amikacin during continuous venovenous haemofiltration in a swine model of acute renal failure

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Introduction *In vitro* studies suggest that there is significant adsorption of amikacin, netilmicin, gentamicin and tobramycin to polyacrylonitrile haemofilters. This occurs rapidly and has the potential to substantially reduce the peak aminoglycoside concentration, which will reduce efficacy [1]. However, whether significant adsorption occurs *in vivo* is unknown. We therefore carried out a controlled *in vivo* study of the effect of amikacin adsorption by polyacrylonitrile filters during haemofiltration, using a porcine model of acute renal failure.
Methods A porcine model of acute renal failure was created by bilateral ligation of the renal arteries and veins. Eight pigs underwent haemofiltration using a 0.6 m^2 polyacrylonitrile filter, blood flow 200 ml/minute, ultrafiltration rate 1,000 ml/hour. All ultrafiltrate was returned to the pigs via a separate venous catheter so that any elimination of amikacin by haemofiltration could only be due to adsorption. Another eight pigs underwent sham haemofiltration in which blood was pumped around a haemofiltration circuit without a haemofilter and without ultrafiltration. Both groups of pigs were given intravenous amikacin, 15 mg/kg body weight over 30 minutes, and blood samples were taken from the arterial limb of the haemofilter circuit at 0, 5, 10, 15, 20, 25, 30, 40, 50, 60, 75, 90, 105, 120, 150, and 180 minutes after the start of the amikacin administration to assay amikacin concentrations.
Results Post-distribution peak concentration of amikacin was slightly, but significantly, lower in the CRRT group than that in sham group (55.0 ± 4.5 vs. 61.1 ± 5.9 mg/l, P <0.05).
Conclusion This study shows that the effect of adsorption by polyacrylonitrile haemofilters on *in vivo* amikacin peak concentrations is small, and less than would be expected from *in vitro* data.
Acknowledgement This work was supported by a grant from the Hong Kong Research Grants Committee, CUHK 4644/08M.
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P118

PK/PD of single-dose amikacin in emergency department patients with severe sepsis/shock: should we apply the ICU-based higher loading dose?

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Critical Care 2015, **19(Suppl 1):**P118 (doi: 10.1186/cc14198)

Introduction Studies in the ICU showed that a single amikacin dose of ≥25 mg/kg should be used in conditions of increased distribution volume (Vd) such as severe sepsis/shock [1]. However, no data are available for emergency department (ED) patients in the early phase of sepsis/septic shock. The purpose of this study was to determine whether a single amikacin dose of 25 versus 15 mg/kg results in PK/PD target attainment for ED patients.
Methods ED patients with severe sepsis/shock were randomly treated with a single amikacin dose of 25 versus 15 mg/kg. Blood samples were collected at +1 (peak), +6 hours and +24 hours (trough) after the start of infusion. Primary outcome was PK/PD target attainment defined as a peak/MIC >8, corresponding with both actual MIC values documented from isolated pathogens, as well as EUCAST susceptibility breakpoints for Enterobacteriaceae and *P. aeruginosa*; that is, 8 mg/l. Noncompartmental analysis was used to calculate PK parameters.
Results During a study duration of 20 months, 50 patients were enrolled in each dosing regimen resulting in 100 peak concentrations, 92 and 88 +6 hours and +24 hours concentrations respectively. Target attainment using local MIC values (median 2 mg/l, documented in 56 isolated Gram-negative pathogens) was achieved in 95% in both groups (P = 0.98). Using EUCAST susceptibility breakpoints, the target was attained in 76% versus 40% in the 25 versus 15 mg/kg group, respectively (P < 0.0001). Single-dose PK parameters are displayed in Table 1 and compared with the ones reported in the ICU [1].

Table 1 (abstract P118)

PK parameter	15 mg/kg ED	25 mg/kg ED	25 mg/kg ICU
Peak (mg/l)	58 (47 to 70)[a]	91 (72 to 105)[a]	73 (62 to 90)
Trough (mg/l)	6 (3 to 12)	5 (3 to 15)	7 (2 to 15)
Vd (l/kg)	0.3 (0.3 to 0.5)	0.4 (0.2 to 0.6)	0.4 (0.3 to 0.5)
Cl (ml/minute/kg)	1.6 (1 to 2.3)[a]	2.2 (1.4 to 3)[a]	1.9 (1.3 to 3.5)

Cl, clearance. [a]Mann–Whitney U <0.05, 15 versus 25 mg/kg ED patients.

Conclusion The EUCAST-based PK/PD target was only attained in 76% of patients treated with 25 mg/kg. However, in contrast to ICU patients, the majority of ED patients are treated for community-acquired infections, so MIC values are significantly lower than the EUCAST susceptibility breakpoints, warranting PK/PD target attainment in both 25 and 15 mg/kg dosing regimens when local epidemiology is taken into account.
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P119

Intravenous fosfomycin therapy in critically ill patients infected with colistin-resistant enterobacteriacae

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Introduction Carbapenem-resistant enterobacteriacae emerged in recent years as one of the most challenging groups of antibiotic-resistant pathogens. Polymyxins are considered as the last resort for the treatment of infections with carbapenem-resistant Gram-negative bacilli (GNB). Inadequate or extensive use of colistin leads to emergence of colistin resistance in GNB, jeopardizing treatment options in ICUs, potentially increasing mortality and morbidity and necessitating prudent use of alternative antibiotics. Fosfomycin, a phosponic acid derivative which acts primarily by disrupting bacterial cell wall synthesis, is a broad-spectrum antibiotic. Fosfomycin tromethamine is an oral formulation approved for the treatment of uncomplicated urinary tract infection caused by multidrug-resistant (MDR) bacteria. Recently fosfomycin is also available as a sodium/disodium formulation for intravenous use, which is showing promising result against MDR/potentially drug-resistant pathogens.
Methods A total of four colistin-resistant (MIC ≥4) GNB were isolated from ICU patients with nosocomial MDR infections. All four isolates were Klebsiella pneumonia. Among these isolates three were from blood and one from endotracheal aspirate and all four isolates were sensitive to fosfomycin *in vitro*. All of these patients had multiple comorbidities with recent history of colistin exposure. Intravenous fosfomycin sodium (inj Fosmicin; Meiji, Japan) was started as a combination therapy with carbapenem.
Results Among the three bacteremic patients, two recovered completely from sepsis as well as the patient with ventilator-associated pneumonia. There was clinical as well as microbiological cure with normalization of sepsis markers. The only one bacteremic patient who died during the course of therapy was later diagnosed to have azole-resistant fungemia as a superinfection.
Conclusion Based on the evidence of clinical experience and available studies, intravenous fosfomycin therapy may be considered as the last option for the treatment of MDR GNB infection where there is documented colistin resistance and where there is literally no other choice of antibiotic therapy.
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P120

Performance of amikacin inhale: impact of supplemental oxygen and device orientation

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Introduction Amikacin Inhale is an integrated drug–device combination in development by Bayer HealthCare through a collaboration with Nektar Therapeutics, to improve clinical outcome in intubated and mechanically ventilated patients with Gram-negative pneumonia. It is available in two configurations: on-vent for intubated patients and hand-held for extubated patients to complete aerosolized antibiotic therapy. Amikacin Inhale is a smart system that consists of the pulmonary drug delivery system with a vibrating mesh nebulizer and the specially formulated Amikacin Inhalation Solution (400 mg every 12 hours for 10 days). The objectives of this study were to evaluate the performance of the Amikacin Inhale hand-held configuration with supplemental O_2 concentration supplied at different flow rates and in different orientations. We hypothesize that the delivered dose of amikacin will not significantly change with increased O_2 flow rate or varying orientation.
Methods In the hand-held configuration of Amikacin Inhale, amikacin is aerosolized into a holding chamber. Amikacin aerosol is inhaled with ambient air entering the bottom of the chamber through the inhalation valve. Supplemental O_2 may be supplied through the O_2 port and mixes with ambient air entering through the inhalation valve. O_2 concentration and delivered dose at the mouthpiece exit were characterized *in vitro* at various O_2 flow rates (2 to 10 l/minute). O_2 concentrations were measured every minute until the end of dosing. A ventilator was connected to the set up to simulate patient breathing. The delivered dose was measured at the exit of the mouthpiece. Drug distribution within the test setup compartments was analyzed using HPLC. The *in vitro* delivered amikacin dose was also measured at nebulizer orientations of 0° and 45° (n = 3 per orientation) using a simulated breathing profile with no supplemental O_2.
Results The mean O_2 concentration ranged from 36 to 70% over 2 to 10 l/minute and was ≥40% at ≥3 l/minute. The delivered dose did not change substantially with increasing enriched O_2 flow rate (72 to 82% of nominal dose). At 0° and 45° orientations, the delivered dose of amikacin was 74 to 80% and 73 to 76% of the nominal dose (400 mg), respectively.
Conclusion Amikacin Inhale was shown *in vitro* to be suitable for extubated patients who require supplemental O_2. The delivered dose was independent of supplemental O_2 and device orientation.

P121

Early preventive administration of inhaled tobramycin in severe polytrauma

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Introduction Nosocomial pneumonia (NP) occurs in 30 to 50% of multiple trauma patients. It is mostly caused by multiresistant Gram-negative bacteria. Use of inhaled antibiotics as adjuncts to systemic antibiotics presents a great outlook for the prevention of NP in multiple trauma patients. The aim of the study was to evaluate the efficacy of early administration of inhaled tobtamycin (IT) as an adjunct to systemic antibiotics for the prevention of NP in polytrauma.
Methods Fifty-four ICU mechanically ventilated patients with multiple trauma (ISS >30; car accident 55.6%; fall 29.6%; train accident 11.1%; domestic 3.7%) were enrolled in the single-center randomized trial. Groups were comparable in ISS, age, sex, type of trauma, and blood loss. Patients were randomized into two groups: Group 1 (n = 27), addition of IT to systemic antibiotics (ciprofloxacin 800 mg/day; metronidazol 1,500 mg/day); Group 2 (n = 27), only systemic antibiotics (same regimen). Inhaled tobramycin (300 mg twice daily via nebulizer) and systemic antibiotics were administered within the first 24 hours after ICU admission. After obtaining the results of bronchoalveolar lavage microbiology, the antibiotic regimen was switched according to the sensitivity. The primary outcome measure was new onset of NP and duration of ICU stay. Microbiological, X-ray, CPIS, signs of sepsis and oxygenation index were used as objective indicators of the clinical progress. The secondary outcome measure was 30-day mortality. Diagnosis of NP was made according to the standard clinical and CPIS criteria. The data were statistically analyzed by SPSS 11.5 (M, σ, Newman–Keuls test; chi-square-test P <0.05).
Results Preventive administration of IT as an adjunct to systemic antibiotics was associated with a lower incidence of NP in group 1 (group 1 33.3%, group 2 66.7%, χ^2 = 6,000; P = 0.014) and a shorter duration of ICU stay (group 1 8.0 ± 4.6 days vs. 17.1 ± 18.4 days, P = 0.03). The mortality did not differ between groups: 11.1% in group 1 and 22.2% in group 2 (P ≥0.99). On day 3 *Acinetobacter* spp. (30.5%), *K. pneumoniae* (22.0%), *B. cepacia* (13.2%) and *P. aeruginosa* (34.3%) were detected in BAL, there were no differences between groups. In group 1 CPIS remained stable and APACHE II decreased. CPIS and APACHE II were lower in group 1 on day 5 (P = 0.0004).
Conclusion Early administration of IT as an adjunct to systemic antibiotics is effective in prevention of NP in multiple trauma patients: it promotes decrease of NP incidence and decrease of ICU stay.

P122

Intrathecal administration of colistin, vancomycin and amikacin for central nervous system infections in ICU neurosurgical patients

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Introduction Central nervous system (CNS) infections in ICU patients after neurosurgery are a difficult and life-threatening complication demanding immediate action. In many cases intravenous (i.v.) administration of antibiotics is not sufficient; thus, intrathecal (i.t.) administration is required.
Methods From January 2013 to November 2014 all cases with CNS infections were recorded. Inclusion criteria were the presence of fever ≥38.5°C, increased inflammatory markers, compatible lumbar puncture (LP) findings (increased number of polymorphonuclear leukocytes, increased protein and low glucose compared with serum levels) and no evidence of other site of infection. All subjects were receiving appropriate i.v. antibiotic treatment based on cultures. Intrathecal administration of 300,000 iu colistin, 25 mg vancomycin and 25 mg amikacin was performed taking under consideration that neurosurgical patients in the ICU have CNS infection attributed to Gram-negative bacteria or/and to *Staphylococcus* species.
Results Overall, nine cases with CNS infection were recorded aged from 22 to 74, all males. LP was performed between the second and 17th day (average 8.3 days) and the CSF analysis showed 40 to 6,000 cells – mainly PMNs, protein 161 mg% to 287 mg% and glucose from 3 to 58 mg/dl. They were all colonized with *Acinetobacter baumannii* sensitive only to colistin. CSF cultures were negative for all patients besides one, who grew *A. baumannii*. Of those, seven (77%) were receiving i.v. colistin, eight (88%) carbapenems, and eight (88%) glycopeptides, all in combination with other antibiotics. Median i.t. administration time was 9.1 days. All patients responded to i.v. and i.t. antibiotics but there was one case in which fever relapsed and increased number of cells in subsequent LP was observed which was attributed to colistin, which was withdrawn. All these patients survived, and were discharged to the ward.
Conclusion Patients treated with the abovementioned regime showed clinical and biochemical improvement. The above drug combination turned out to be successful in neurosurgical ICU patients with CNS infection.

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P123

Efficacy and safety of heparin in patients with sepsis: a systematic review and meta-analysis

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Introduction Septic shock is characterized by systemic inflammation coupled with upregulation of coagulation. Heparin is an inexpensive and widely available anticoagulant with anti-inflammatory properties. The objectives our study were to evaluate the efficacy and safety of heparin in patients with sepsis, septic shock or disseminated intravascular coagulation (DIC) associated with infection.
Methods We included randomized controlled trials from MEDLINE, EMBASE, CENTRAL, Global Health, Scopus, Web of Science, the International Clinical Trials Registry Platform (inception to April 2014), conference proceedings, and reference lists of relevant articles. Two reviewers independently identified and extracted trial-level data from randomized trials investigating unfractionated or low molecular heparin administered to patients with sepsis, severe sepsis, septic shock or DIC associated with infection. Internal validity was assessed in duplicate using the Risk of Bias tool. Our primary outcome was mortality. Safety outcomes included hemorrhage, transfusion and thrombocytopenia.
Results We included nine trials enrolling 2,637 patients. Eight trials were of unclear risk of bias and one was classified as having low risk of bias. In trials comparing heparin with placebo or usual care, the risk ratio for death associated with heparin was 0.88 (95% CI = 0.77 to 1.00, I^2 = 0%, 2477 patients, six trials). In trials comparing heparin with other anticoagulants, the risk ratio for death was 1.30 (95% CI = 0.78 to 2.18, I^2 = 0%, 160 patients, three trials). In trials comparing heparin with placebo or usual care, major hemorrhage was not statistically significantly increased (risk ratio 0.79, 95% CI = 0.53 to 1.17, I^2 = 0%, 2,392 patients, three trials). In one small trial of heparin compared with other anticoagulants, the risk of major hemorrhage was significantly increased (2.14, 95% CI = 1.07 to 4.30, 48 patients). Important secondary and safety outcomes, including minor bleeding, were sparsely reported.
Conclusion Heparin in patients with sepsis, septic shock, and DIC associated with infection may be associated with decreased mortality; however, the overall impact remains uncertain. Safety outcomes have been under-reported and require further study. Large randomized trials are needed to evaluate the efficacy and safety of heparin in patients with sepsis, severe sepsis, and septic shock.

P124

Use of intravenous immunoglobulin to treat sepsis in a general ICU

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Introduction Sepsis is a major cause of admission to the ICU, and a leading cause of death for ICU patients. Intravenous immunoglobulin (IVIg) is indicated in the treatment of some patients with sepsis, although the evidence for this remains controversial. The use of IVIg is regulated due to its high cost, and prescription guidelines have been revised by the NHS, coordinated by the National Demand Management Programme for Immunoglobulin.
Methods We conducted a retrospective audit of pharmacy records of IVIg prescriptions issued to ICU patients with severe sepsis and septic shock from 2009 to 2014 against national prescription guidelines. Microbiology results were examined to support prescriptions, and admission APACHE II scores and unit outcomes were examined.
Results From 2009 to 2014, 644 patients were admitted to the ICU with severe sepsis and septic shock, with a mortality rate of 41%. Seventeen patients received IVIg. Of these, eight patients met the national guidelines for prescription, with a mortality rate of 25%. Nine patients did not meet the national guidelines for prescription, with a mortality rate of 44%. The difference in mortality rates between the two groups did not reach statistical significance (P = 0.6). There was no significant difference in APACHE II scores between the two groups. There was also no difference in mortality between those receiving IVIg and those who did not. We also found no difference in those receiving single or double doses of IVIg.
Conclusion The use of IVIg does not appear to affect mortality in sepsis. There was also no statistical benefit or harm demonstrated by using IVIg. This also holds true whether IVIg is given either according to the guidelines or not; however, stricter adherence to the guidelines does have financial implications.
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P125

Adjunct prednisone therapy for patients with community-acquired pneumonia: a randomized, placebo-controlled multicenter trial

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Introduction Clinical trials yielded conflicting data about the benefit of adding systemic corticosteroids for community-acquired pneumonia (CAP). We evaluated whether short-term corticosteroid treatment reduces time to clinical stability in patients hospitalized for CAP.
Methods This randomized, placebo-controlled multicenter trial compared prednisone 50 mg for 7 days with placebo in patients hospitalized with CAP. The primary endpoint was time to clinical stability.
Results Overall, 802 patients were randomized in seven Swiss hospitals from December 2009 to May 2014. Time to clinical stability was shorter in the prednisone group compared with placebo (3.0 vs. 4.4 days, HR = 1.33, 95% CI = 1.15 to 1.50, P <0.001). The prednisone group as compared with the placebo group had a shorter time to hospital discharge (6 vs. 7 days (HR = 1.19, 1.04 to 1.38), P = 0.012) and a shorter duration of intravenous antibiotic treatment (4 vs. 5 days (difference, –0.89 days, –0.20 to –1.57 days), P = 0.011). All-cause mortality, ICU stay, recurrent pneumonia and rehospitalization rate were similar in both groups. Incidence of pneumonia-associated complications until day 30 tended to be lower in the prednisone group (2.8% vs. 5.6%, OR = 0.49, 0.23 to 1.02, P = 0.06). The prednisone group had a higher rate of in-hospital hyperglycemia needing insulin treatment (19.4% vs. 10.9%, OR = 1.96, 1.31 to 2.93, P = 0.001). Other adverse events compatible with corticosteroid use were rare and similar in both groups.
Conclusion Prednisone treatment for 7 days in hospitalized patients with CAP shortens time to clinical stability, time to hospital discharge and duration of intravenous antibiotic treatment without an increase in complications.

P126

Pharmacokinetics, safety and tolerability of human recombinant alkaline phosphatase in healthy volunteers

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Introduction Clinical trials showed renal protective effects of bovine intestinal alkaline phosphatase in critically ill patients with

sepsis-associated acute kidney injury (AKI) [1,2]. Recently, human recombinant AP (recAP) was developed as a pharmacological attractive replacement. We conducted a phase I clinical trial to evaluate tolerability, safety and pharmacokinetics of recAP in healthy volunteers.
Methods In a randomized, double-blind, placebo-controlled phase I trial, healthy volunteers received via a 1-hour i.v. infusion a single dose of recAP (200, 500, 1,000 or 2,000 U/kg; n = 33) or multiple doses of recAP (500 or 1,000 U/kg; n = 18) on three consecutive days (n = 18). Serum recAP concentrations, AP activity levels and anti-drug antibodies were measured, and safety parameters were monitored.
Results RecAP administration resulted in a terminal elimination half-life and plasma clearance of 49 to 58 hours and 2.8 to 3.4 l/hour after single ascending doses, respectively, and 63 to 66 hours and 3.1 to 3.8 l/hour after multiple ascending doses. Peak recAP concentrations and AP activity levels were reached at the end of the 1-hour infusion and showed a rapid decline with about 10% of the maximum concentration remaining at 4 hours and less than 5% at 24 hours post start. Although the maximal concentration and total systemic exposure of recAP and AP activity increased slightly more than dose proportionally this is of no significance in the estimated therapeutic dose range. RecAP treatment was generally well tolerated and anti-drug antibodies could not be detected in serum.
Conclusion RecAP is characterized by a long serum terminal half-life, by stable serum AP levels and did not exert any safety concerns when administered to healthy volunteers. These results pave the way to investigate the potential of recAP as a new treatment option for sepsis-associated AKI in a phase II clinical trial, which will start at the end of 2014 [Clinical Trial Register:NCT02182440].
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P127

Rat polymyxin B hemoperfusion model: preventive effect on renal tubular cell death in a rat cecal ligation and puncture model

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Introduction Direct hemoperfusion with a polymyxin B immobilized column (PMX-DHP) adsorbs endotoxin and has been used for the treatment of septic shock [1]. However, the mechanisms of action behind PMX-DHP are not fully understood. Therefore, the purpose of this study was to elucidate mechanisms of action behind PMX-DHP in a rat model of cecal ligation and puncture.
Methods Sprague–Dawley rats were anesthetized and were mechanical ventilated after tracheostomy. The right internal carotid artery was cannulated with a catheter for continuous measurement of the arterial pressure and heart rate. The right femoral vein was cannulated with a catheter for infusion of saline (10 ml/kg/hour) during the study period. The rats were randomized into three experimental groups: cecal ligation and puncture (CLP) + dummy column (Dummy-DHP) group (n = 10), CLP + PMX-DHP group (n = 10), and sham group (n = 4). Four hours after CLP, Dummy-DHP or PMX-DHP was performed for 1 hour. Blood was drawn from the right internal carotid artery, perfused through PMX column or dummy column, and returned to the right femoral vein. The heart rate, mean arterial pressure, arterial blood gases, and plasma concentrations of creatinine, lactate, potassium, and cytokines (IL-6 and IL-10) were measured at baseline and at 4, 5, and 8 hours after CLP. At the completion of the experiment, the rats were killed overdose of pentobarbital. The kidney, liver, and lung were harvested, and histopathologic examinations of these organs were performed.
Results Hypotension and metabolic acidosis occurred in the CLP + Dummy-DHP group, whereas hemodynamics and acid–base balance were better maintained in the CLP + PMX-DHP group. Plasma concentrations of lactate, creatinine, potassium, and cytokines were significantly higher in the CLP + Dummy-DHP group than in the CLP + PMX-DHP group at 8 hours. Renal tubular cell death was observed in the CLP + Dummy-DHP group, but not in the CLP + PMX-DHP group.
Conclusion PMX-DHP improved hemodynamics, acid–base balance, and creatinine levels through reducing cytokines and renal tubular cell death in a rat model of cecal ligation and puncture. These findings suggest the preventive role of PMX-DHP in the development of sepsis-related acute kidney injury.
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P128

White blood cell counts have an impact on septic patient outcome followed by polymyxin-B immobilized fiber with direct hemoperfusion

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Introduction The mortality rate of severe sepsis and septic shock is varied and high (25 to 70%). In our institute, the indication for polymyxin-B immobilized fiber with direct hemoperfusion (PMX-DHP) has been that circulatory failure (systolic blood pressure <90 mmHg or required catecholamines and high lactacidemia) continued despite following early goal-directed therapy by the Surviving Sepsis Campaign guidelines 2012.
Methods This study included 80 patients with severe sepsis or septic shock due to abdominal infection retrospectively. These subjects were divided into two groups: those with WBC counts <4,000 (L-group: 64 patients) and those with WBC counts >12,000 (H-group: 16 patients). Mean arterial pressure, WBC counts, platelet counts, interleukin-6 (IL-6), and plasminogen activator inhibitor-1 (PAI-1) were measured immediately before the initiation and after the completion of PMX-DHP. Statistical analysis was performed using the chi-squared test for background factors, with Wilcoxon's rank-sum test for comparison within a group, and Mann–Whitney's U test for comparison between groups. The significance level was set at P <0.05.
Results The mortality rate of 28 days in the L-group was 32.8%, and was 18.8% in the H-group. Mean arterial pressure increased significantly (P <0.01) in the H-group compared with the L-group. WBC counts in the L-group increased and in the H-group decreased (P <0.01) during PMX-DHP treatment. Platelet counts in both groups decreased significantly (P <0.01).There was no significant difference between before and after PMX-DHP in IL-6 levels. On the other hand, IL-1ra decreased significantly before and after PMX-DHP. Also, IL-6 and IL-1ra in the L-group were significantly higher than those in the H-group at the start of PMX-DHP. PCT values in the L-group were increased compared with the H-group at the start of PMX-DHP (P <0.01). PCT in the L-group increased significantly (P <0.01), but no significant changes in the H-group. PAI-1 showed no significant changes before and after PMX-DHP and no changes in both groups at the start of PMX-DHP.
Conclusion The mortality rate of the L-group tended to be higher than that of the H-group. Inflammatory and anti-inflammatory cytokines in the L-group were higher than those of the H-group. These results indicate that leukopenia (WBC <4,000) in severe sepsis patients leads to more severe outcome and hypercytokinemia than leukocytosis (WBC >12,000) in severe sepsis patients.

P129

Use of therapeutic plasma exchange in children with thrombocytopenia-associated multiple organ failure in the Turkish TAMOF network

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Introduction Thrombocytopenia-associated multiple organ failure (TAMOF) can lead to high mortality in critically ill children, possibly related to consequences of thrombotic microangiopathy. Plasma

exchange therapy may improve thrombotic microangiopathy [1]. The purpose of this observational cohort study is to describe whether there is an association between use of plasma exchange therapy and outcome in the Turkish TAMOF network.

Methods We performed a retrospective cohort analysis in patients with TAMOF at three different pediatric ICUs comparing those who received plasma exchange (+) plus standard therapies with those who did not receive plasma exchange (–) and only received standard therapies.

Results Among the 42 TAMOF patients enrolled, all had a primary or secondary sepsis diagnosis. Fifteen received plasma exchange therapy (PE(+) group) and 27 received standard medical treatment without plasma exchange (PE(–) group). The mean age was 17.69 months (8.24 to 54.22) in the PE(+) group, and 13.46 months (6.47 to 20.55) in the PE(–) group. Age (P = 0.232), gender (P = 0.206), thrombocyte count (P = 0.09), OFI score (P = 0.111) and Pelod score (P = 0.177) on admission were not statistically different between groups. The overall 28-day mortality was higher in the PE(–) group 70.37% compared with 26.67% in the PE(+) group (univariate P =0.006; multivariate controlling for Pelod, OFI, PRISM scores and neurological failure P = 0.048). Length of stay was increased in the PE(+) group (P = 0.004).

Conclusion The positive association found between use of plasma exchange therapy and improved survival supports the potential of this therapy in Turkish children with TAMOF. The positive, although less so, associated treatment effect observed after controlling for illness severity provides further rationale for performing a randomized controlled trial in the pediatric Turkish TAMOF network. Sample size calculations call for a 100-patient trial with a *pre hoc* interim analysis after enrollment of 50 TAMOF patients.

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P130

Clinical experience of using a novel extracorporeal cytokine adsorption column for treatment of septic shock with multiorgan failure

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Introduction Severe sepsis and multiorgan failure (MOF) are major causes of death in the ICU. The extracorporeal cytokine adsorption column (ECAC; Cytosorb®, CytoSorbents Corporation, USA), a critical care focused therapeutic device, results in rapid *in vitro* and *in vivo* elimination of several key cytokines and prevents organ failure. Use of ECAC in patients with sepsis is a new area of research with insufficient data to promote large prospective RCTs. Studies published to date have shown promising results. We report our clinical experience with ECAC for severe sepsis/septic shock/MOF patients.

Methods A retrospective evaluation of ECAC in patients admitted to a tertiary ICU from November 13 to October 14 to analyze: clinical safety; selection of a subgroup of patients where it could be used; selection of timing for initiation; number of device filters required per patient; and selective markers to identify above initiation. Patients were managed with standard of care (SOC; antibiotics, vasopressors, i.v. fluids, sepsis dosed steroids) and ECAC as adjuvant therapy. Vitals, APACHE II and SOFA scores were measured.

Results Nineteen ICU patients (14 men, five women; 24 to 72 years; average ICU stay 10 days; average ventilator days 9) with APACHE II >17 (except one with dengue shock syndrome), SOFA score ≥11 (n = 16) and the majority having infection largely in the lung (n = 8; alone or with UTI and blood infection) followed by the abdomen (n = 4), UTI (n = 3) and others (n = 4) were given ECAC (total ECAC = 31). Predicted mortality (PM) was >40% in 16, >30% in two and <30% in two (tropical infections) patients. Duration of therapy was 6 hours (no. of ECAC = 18) and 8 hours (n = 4; no. of ECAC = 5) for the majority of patients. Overall, four patients (two with tropical infections and two with PM >40%) survived; three of them had were ECAC early (<24 hours of admission). The majority of patients (n = 11) who died could be given ECAC only once. Of patients who died, seven were given ECAC late (>24 hours). APACHE scores before and after ECAC therapy were available for eight patients who died; APACHE score decreased >5 points in five patients after single application of ECAC.

Conclusion ECAC can be used as adjuvant therapy in treatment of severe sepsis/septic shock/MOF. Our patients had high PM and four could be saved with use of ECAC. We could expect a better outcome if ECAC was used early (<24 hours) during treatment. However, future well-designed studies are needed to clarify the role of ECAC in patients with MOF/septic shock.

P131

Effectiveness of polymyxin B immobilized fiber hemoperfusion in patients with septic shock due to Gram-negative bacillus infection: the PMXHP study

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Introduction Mortality from septic shock in the ICU remains high, ranging from 30 to 50%. In particular, Gram-negative bacilli (GNB) account for 40% of the causative bacteria of severe sepsis, which progresses to multiorgan failure due to significant inflammation. Hemoperfusion with polymyxin B-immobilized fiber (PMX) adsorbs endotoxin and can reduce the inflammatory cascade of sepsis due to GNB. However, the clinical efficacy of this treatment has not been demonstrated. We aimed to verify the efficacy of endotoxin adsorption therapy by using PMX.

Methods We retrospectively evaluated 387 patients who received a broad-spectrum antimicrobial treatment for septic shock due to GNB between January 2009 and December 2012 in the ICU of 10 Japanese tertiary hospitals. After alignment of the treatment time phase for each patient, we divided the patients into two groups according to whether PMX treatment was performed within 24 hours after ICU admission (PMX group: n = 129 and non-PMX group: n = 258). The primary endpoint was 28-day mortality.

Results The mean (SD) age and SOFA scores on ICU admission were 72.5 (12.5) years and 10.0 (3.4), respectively. The infection site was intra-abdominal (47.0%), pulmonary (17.6%), and urinary tract (27.8%). Two-thirds of all patients had bacteremia due to GNB. No difference in 28-day mortality was observed between the two groups (PMX: 33.9% vs. non-PMX: 33.1%, P = 0.87). In the Cox regression analysis adjusted for age, sex and facilities, the PMX treatment (hazard ratio = 0.87; 95% confidence interval, 0.53 to 1.43) did not improve the outcome.

Conclusion No difference in mortality rate was observed after adjustment for the endotoxin adsorption therapy with PMX in the patients with septic shock due to GNB.

P132

Impact of evolving cardiac catheterisation services on admissions to a regional ICU

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Introduction National UK audit data demonstrate cardiac catheterisation services, including percutaneous coronary intervention and noncoronary interventions, are increasing [1-3]. National mortality rates post cardiac catheterisation are also increasing, reflecting an increasing proportion of sicker patients undergoing interventional procedures [3]. National audit procedures do not evaluate patients admitted to intensive care post cardiac catheterisation. We aimed to

evaluate the impact of an evolving regional cardiac catheterisation service on a regional intensive care unit (RICU) serving a population of 1.8 million.
Methods A retrospective review was carried out. Patients admitted from the regional cardiac catheterisation laboratory to the regional ICU, between September 2009 and September 2014, were identified using validated RICU admission records. Clinical data were extracted from computerised patient records.
Results A total of 170 patients were identified (representing 2.9% of critical care admissions during this time). Baseline characteristics: 71.7% male, median age 66 (IQR 55 to 74), median APACHE score 18 (IQR 15 to 23). Seventy-one patients (41.7%) had an APACHE score >20. Fifteen patients (8.8%) were aged >80 years. Admissions increased yearly – 20 in 2010, 26 in 2011, 35 in 2012, 47 in 2013, 37 at the end of the third quarter of 2014 (projected 59 admissions by year end 2014). Median length of stay was 3.5 days (IQR 1.8 to 7.2). Average length of stay reduced yearly (9.14 days in 2010 to 5.01 days in 2014). ICU bed-days per year remained static over the 5-year period. Critical care and hospital mortality rates were 33% and 39% respectively. There was a trend towards increasing mortality yearly, and with increasing age and APACHE score.
Conclusion An evolving cardiac catheterisation service is having a significant impact on intensive care services within a regional centre. Increasing mortality trends in this critical care population reflects post-cardiac catheterisation mortality trends nationally. We suggest intensive care admissions post cardiac catheterisation should be included in the national audit, to allow forward planning of intensive care services and to promote quality improvement within this population.
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P133

Impact of the introduction of e-learning prior to a basic transthoracic echo course

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Critical Care 2015, **19(Suppl 1):**P133 (doi: 10.1186/cc14213)

Introduction Focused Intensive Care Echo accreditation is a nationally approved pathway for training and accreditation in basic transthoracic echocardiography (TTE) in the UK. Recently, an e-learning module, the Intensive Care Echo and Basic Lung Ultrasound (ICE-BLU), has been introduced to facilitate TTE learning [1]. Previous work from our group has shown that incorporating simulation-based teaching elements into a basic TTE course improves candidates' satisfaction [2]. We assessed the impact of introducing the ICE-BLU e-learning programme prior to our simulation-based basic TTE course.
Methods Prior to the August 2014 course, all candidates were required to complete the ICE-BLU e-learning module. On the morning of the course, the candidates completed a questionnaire to assess the impact of the e-learning module. The survey included questions on the quality of content, user friendliness, whether the content was pitched at the right level and any problems faced whilst accessing the e-learning module. We also analysed candidates' feedback from our January and August 2014 courses (Figure 1).
Results The response rate of the survey was 100%. Eighty per cent of candidates completed the e-learning module. The e-learning module was rated high by most candidates (80%). However, nearly one-half of the candidates faced problems accessing the module, online. Analysis of candidates' feedback (from the January and August 2014 courses) revealed that candidates' overall impression was better with the introduction of e-learning prior to the course.

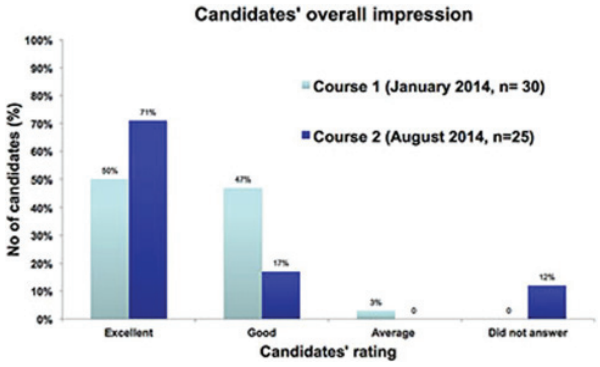


Figure 1 (abstract P133).

Conclusion Our survey has shown that the e-learning initiative was welcome by the candidates. We conclude that introduction of e-learning prior to a simulation-based basic TTE course enhances candidates' satisfaction and feedback.
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P134

Diagnostic concordance of emergency doctor-performed bedside ultrasonography versus specialist-performed echo-Doppler ultrasonography in the diagnosis of deep venous thrombosis of lower limbs

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Introduction Deep venous thrombosis (DVT) is an increasing major cause of mortality and morbidity. There is a need for quick, easy, cheap, convenient and reliable diagnostic tools. The objectives were to ascertain the diagnostic concordance of emergency doctor-performed ultrasound (EDUS) of the lower extremities with specialist doctor-performed (radiologist or vascular surgeon) echo-Doppler (SDED), in the diagnosis of DVT, and to identify possible causes of nonconcordance.
Methods A prospective, multicentre study. Adult patients (>18 years old) with clinical suspicion of DVT, with high or moderate risk (on Wells scoring), or low risk with increased D-dimer levels, were eligible for the study. Emergency doctors performed two EDUS in femoral and popliteal areas (these results were blinded). After this, echo-Doppler was performed by specialist doctors. Both procedures were done within 24 hours of each other. The final result was considered nonconcordant if one or both of the EDUS did not match with the SDED. These SDED were used as reference (as standard clinical practice).
Results From September 2013 to September 2014, a total of 328 patients were enrolled. Fifty-one investigators from seven hospitals performed the EDUS. Each patient had the EDUS (femoral and popliteal areas) and SDED (also in femoral and popliteal areas). Of 328 pairs of US studies, 37 were nonconcordant between EDUS and SDED. Two EDUS were incomplete, so the concordance analysis was performed with 326 US studies, with 35 discordant. The percentage of agreement between EDUS and SDED was 89.26%. The kappa index was 0.76 (95% CI = 0.69 to 0.84), and this means a substantial agreement.
Conclusion There is substantial agreement between EDUS and SDED in the diagnosis of DVT, in routine clinical practice. This confirms the results of previous papers. The largest nondiagnostic concordance in thrombus occurs in the early performances of emergency doctors,

especially until the fifth performance. After the sixth one, the incidence of mismatches falls dramatically. It seems advisable to mentor the training programmes with at least five shadowed performances in order to lower the incidence of mistakes.

P135

Cardiac abnormalities in patients with septic shock detected by speckle tracking echocardiography

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Critical Care 2015, **19(Suppl 1):**P135 (doi: 10.1186/cc14215)

Introduction Sepsis-induced myocardial dysfunction is a well-recognized condition and confers worse outcomes in septic patients. However, the diagnostic criteria remain poorly described. Echocardiographic assessment by conventional parameters such as left ventricular ejection fraction (LVEF) is often affected by ongoing changes in preload and afterload conditions. Novel echocardiographic technologies such as speckle tracking imaging have evolved for direct assessment of the myocardial function. In this study, we investigate the measurement of myocardial strain by speckle tracking imaging for the diagnosis of sepsis-induced myocardial dysfunction.
Methods This is a prospective, case–control study at a university-affiliated tertiary care adult medical ICU. Consecutive patients admitted with a diagnosis of septic shock meeting the international consensus criteria were included. Patients with other causes of myocardial dysfunction were excluded. They are compared with age-matched, gender-matched, and cardiovascular risk factor-matched controls, who were admitted to hospital for sepsis but did not develop septic shock. Conventional echocardiographic parameters, as well as speckle tracking imaging of myocardial function, were obtained within 24 hours of diagnosis. Offline analyses of endocardial tracings were performed by two independent operators.
Results From January 2014 to December 2014, 32 patients with septic shock (study group) and 20 patients with sepsis but no septic shock (control group) were recruited. The baseline characteristics were similar. Conventional echocardiographic measurements, including LVEF (59.53% vs. 60.67% in the control group, $P = 0.450$) and fractional shortening (31.98% vs. 32.98%, $P = 0.323$), did not differ between the two groups. The study group had a greater degree of myocardial dysfunction measured by left ventricular global longitudinal strain (–14.6 vs. –17.6, $P = 0.005$, with a less negative value implying worse myocardial contractility). The hemodynamic profiles (cardiac index 3.49 l/minute/m^2 vs. 3.41 l/minute/m^2 respectively, $P = 0.764$) were not statistically different.
Conclusion This is a first study in the adult population to show that the use of speckle tracking imaging can diagnose significant sepsis-induced myocardial dysfunction, which was not otherwise detectable by conventional echocardiography.

P136

Evaluating the effect of sepsis and septic shock on myocardial functions by echocardiography and serum biomarker level in peripheral veins and coronary sinus

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Critical Care 2015, **19(Suppl 1):**P136 (doi: 10.1186/cc14216)

Introduction Sepsis is a leading cause of death in critically ill patients despite the use of modern antibiotics and resuscitation therapies. Biomarkers and cardiovascular changes have an important place in this process. Myocardial depression occurs in 40% of septic patients.
Methods Twenty patients (group I) with sepsis or septic shock were included and 10 patients (group II) served as the nonseptic group. Group I morbidity and mortality at day 28 in the ICU were targeted as the endpoint. Laboratory investigations, APACHE IV, SAPS II and SOFA scores were calculated. Biomarkers IL-1α, IL-1β, IL-6, IL-10, TNFα, CRP, NT-proBNP and troponin level were estimated on admission and day 7 in the peripheral vein (PV) and coronary sinus (CS). Transthoracic echocardiography and tissue Doppler imaging was done on admission and on day 7.
Results Comparing group I versus group II, the mortality rate was 45%, and there was a statistically significant difference for temperature ($P = 0.001$), HR ($P = 0.001$) and WBC count ($P = 0.01$) on admission. Upon comparing survivors versus nonsurvivors in group I there was a statistical difference in HR on day 7 ($P = 0.02$), successful vasopressor withdrawal ($P = 0.02$), P/F ratio ($P = 0.02$) and $ScVO_2$ on day 7 ($P = 0.03$). Regarding IL-1α, IL-1β, TNFα and troponin I there was no statistical significant difference between groups I and II but IL-6, IL-10 and CRP showed statistically significant difference on admission PV and CS. Pro-BNP shows statistically significant difference in all CS samples between septic and nonseptic groups. Regarding echo upon comparing the survivors versus nonsurvivors, E'd/t on day 0 shows a statistically significant difference between both groups. SAPS II and seventh-day SOFA are good predictive scores for mortality in sepsis.
Conclusion Diastolic dysfunction was seen in 90% of patients. Fever, HR, and WBC counts are still good early indicators for diagnosis of sepsis. Vasopressor withdrawal on the seventh day was a good predictor for survival. Admission serum IL-6, IL-10 and CRP from PV were better indicators for sepsis than IL-1, pro-BNP and troponin I. Admission TNFα and seventh-day IL-6 levels were highly prognostic for mortality. CS samples proved that NT pro-BNP is a good indicator for sepsis diagnosis and a good predictor for survival. TNFα from CS samples was also a good predictor of mortality. SAPS II and a slower E'd/t on admission was a good predictor of mortality.
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P137

Sepsis survivors present with higher values of cardiac index and velocity time integral in the emergency department

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Critical Care 2015, **19(Suppl 1):**P137 (doi: 10.1186/cc14217)

Introduction Myocardial depression is common among septic patients [1]. The aim of this study was to assess whether the values of cardiac index (CI) and velocity–time integral (VTI) calculated by echocardiography differ between survivors and nonsurvivors of sepsis.
Methods This was a prospective observational study. We included adult newly admitted septic patients, regardless of disease severity. Exclusion criteria were concomitant pregnancy or obstetric/gynecological sepsis and co-existing or terminal diseases that may limit life expectancy. At the moment of recruitment, additional exclusion criteria included: concomitant pulmonary embolism, trauma or acute ischemic coronary disease; pericardial tamponade; aortic valve disease; tachyarrhythmias and absence of adequate echocardiographic windows. Echocardiographic evaluations were made within the first 10 minutes of initiation of fluid therapy in the emergency room. All measurements and images were obtained with a 1.5 to 3.5 MHz phased array transducer using a standard cardiac preset. CI is the quotient of the cardiac output (CO) divided by the body surface area. The CO is the product of the stroke volume by the heart rate. Stroke volume is calculated as the product between aortic VTI (measured using pulsed-wave Doppler) and aortic cross-sectional area. The latter is calculated in the long axis parasternal window using the left ventricular outflow tract diameter measurement.
Results In 3 months, 58 patients were included. The average age was 46.6 years, and 36 were male. Overall mortality was 14%. We included 16 patients with sepsis syndrome, 27 patients with severe sepsis and 15 patients with septic shock. Severe sepsis patients presented with higher values of CI, when compared with sepsis syndrome and septic shock patients (3.46, 3.08 and 2.92 l/minute/m^2, respectively, P = NS). The same occurred with VTI (19.27, 18.81 and 16.74 cm for severe sepsis, sepsis syndrome and septic shock, respectively; P = NS). Mean values of CI were lower in nonsurvivors of sepsis (2.51 vs. 3.35 l/minute/m^2, $P = 0.018$). Mean values of VTI were also lower in nonsurvivors (14.83 vs. 19.01 cm, $P = 0.022$).
Conclusion In our study, nonsurvivors of sepsis presented with lower values of both CI and VTI in the emergency department. Therefore, CI

and VTI may be good markers of sepsis severity and mortality in newly admitted patients. In addition, further studies are warranted to assess the role of CI and VTI as therapeutic targets.

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P138

Speckle tracking imaging for evaluation of effects of positive end-expiratory pressure level on right ventricular function

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Critical Care 2015, **19(Suppl 1):**P138 (doi: 10.1186/cc14218)

Introduction Positive end-expiratory pressure (PEEP) is commonly used to correct hypoxemia in the ICU. However, PEEP may impair right ventricular functions by increasing its afterload. Speckle tracking imaging (STI) is a new echocardiography strain analysis technique that provides direct assessment of myocardial contractility during systole and diastole. The aim of this study was to evaluate the effects of different PEEP levels on right ventricular functions by using STI in patients undergoing coronary artery bypass grafting surgery.
Methods After ethics committee approval and patients' written consent, we prospectively analyzed 20 CABG surgery patients. After initiation of mechanical ventilation and before sternotomy, 5, 10, and 20 cmH_2O PEEP were applied in 5-minute intervals consequently. After stabilization at each PEEP level, four-chamber and two-chamber images of the right ventricle were recorded using TEE. The right ventricle diameter, velocity, longitudinal strain, SR, and fractional area change (RVFAC) were calculated and evaluated from the recorded images.
Results The mean age of study patients (85% male) was 59.7 ± 10.5 years. Intraoperative mean, systolic, and diastolic arterial blood pressures and heart rate were similar at the three PEEP levels. Compared with 5 and 10 cmH_2O PEEP, mean RVFAC significantly decreased at 20 cmH_2O PEEP (P = 0.001). Right ventricle velocity reduced with incremental PEEP increases (P <0.05). Mean SR values decreased at 20 cmH_2O PEEP when compared with 5 cmH_2O PEEP (P = 0.03). Mean right ventricle diameter measurements decreased with incremental PEEP increases; however, this decrease was significantly different between 20 cmH_2O PEEP and other two PEEP levels (P = 0.01). The mean right ventricle strain value significantly decreased at 20 cmH_2O PEEP when compared with other two PEEP levels (P <0.001 for both).
Conclusion Compared with 5 and 10 cmH_2O PEEP levels, right ventricle functions in terms of strain, SR, right ventricle diameter, and RVFAC were significantly impaired at 20 cmH_2O PEEP level.

P139

Absence of lung sliding is not a reliable indicator of pneumothorax in patients who require high PEEP

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Critical Care 2015, **19(Suppl 1):**P139 (doi: 10.1186/cc14219)

Introduction The objective of our study was to estimate correlation between PEEP and disappearance of lung sliding (LS) due to lung overdistension in the absence of pneumothorax.
Methods We performed a prospective study from September 2013 to May 2014 in adult patients with respiratory failure who required mechanical ventilation, lung CT and recruitment manoeuvre. Lung CT was used as the gold standard to exclude pneumothorax. A staircase recruitment manoeuvre was used with 5 cmH_2O increases of PEEP from baseline to 35 cmH_2O and decreases in reverse order. The duration of each step was 1 minute. Lung ultrasound was performed to evaluate LS at each step in one intercostal window in the highest point of left and right hemithoraces by physicians trained in lung ultrasound and blinded to changes in PEEP.
Results In all, eight patients were included; five (62.5%) males, mean age 70.1 ± 7.4 years. Mean auto-PEEP was 0.7 ± 0.4 cmH_2O. The values of

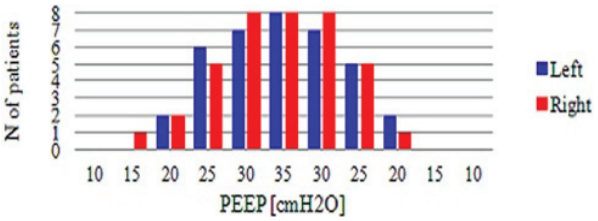


Figure 1 (abstract P139). Absence of LS during increasing and decreasing PEEP.



Figure 2 (abstract P139). Values of PEEP above which LS was not present.

PEEP at which LS disappeared or reappeared were compared using the Wilcoxon signed-rank test to assess the influences of anatomical side and PEEP increase or decrease. The values of PEEP at disappearance of LS for the right lung were not statistically significantly different from the left lung (P = 0.844 for increases, P = 0.938 for decreases). The values of PEEP at which LS disappeared obtained during increases were not statistically significantly different from values obtained during decreases (P = 1.000 for left lung, P = 0.875 for right lung; Figure 1). From data pooled from both sides and protocols, the median value of PEEP at which LS disappeared as a false positive sign of pneumothorax was 25 cmH_2O (interquartile range = 20 to 30 cmH_2O). At PEEP = 10 cmH_2O, no patient showed absence of LS, whereas at PEEP = 35 cmH_2O, all patients showed absence of LS (Figure 2).
Conclusion According to this study, higher PEEP levels correlate with disappearance of LS without pneumothorax. Absence of LS in patients with high PEEP should be interpreted with caution and other signs of pneumothorax should be sought before therapeutic interventions are attempted.

P140

Lung ultrasound in quantifying lung water in septic shock patients

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Critical Care 2015, **19(Suppl 1):**P140 (doi: 10.1186/cc14220)

Introduction Quantification of lung ultrasound (LUS) artifacts (B-lines) is used to assess pulmonary congestion in emergency medicine and cardiology [1,2]. We investigated B-lines in relation to extravascular lung-water index (EVLWI) from invasive transpulmonary thermodilution in septic shock patients. Our aim was to evaluate the role of LUS in an intensive care setting.
Methods Twenty-one patients admitted with septic shock to a general ICU underwent LUS of eight zones, four per hemithorax, within 24 hours after ICU admission. EVLWI was calculated simultaneously by transpulmonary thermodilution using a pulse-contour continuous cardiac output system, and NT-proBNP and clinical data were collected. Two physicians blinded to other data independently quantified the number of B-lines. Spearman's rho was used to test the correlation of B-lines to EVLWI and clinical data, and linear regression and Bland–Altman analysis were used to assess the agreement between B-lines and EVLWI. Interobserver variability was tested using Bland–Altman analysis and intraclass correlation coefficient (ICC).
Results Fourteen patients (67%) were male, the median age was 62 years (IQR 55 to 68) and eight (38%) patients had cardiac comorbidities. In median, SAPS 3 was 64 (IQR 60 to 74), ICU length of stay was 3 days (IQR 2 to 8) and seven patients (33%) died within 30 days of ICU admission. All patients were mechanically ventilated and treated according to

guidelines [3]. The median number of B-lines was 15 (IQR 10 to 30) and the median (IQR) NT-proBNP, EVLWI and oxygenation index (OI) were 7,800 ng/l (3,690 to 15,050), 11 ml/kg (IQR 8 to 18) and 9.2 (5.7 to 15.7), respectively. None of the characteristics differed significantly between survivors and nonsurvivors. The number of B-lines correlated to EVLWI ($\rho = 0.45$, $P = 0.04$; $r^2 = 0.20$, $P = 0.04$), but not to NT-proBNP ($\rho = -0.42$, $P = 0.06$), OI ($\rho = 0.25$, $P = 0.31$) or ICU length of stay ($\rho = 0.14$, $P = 0.57$). On Bland–Altman analysis, mean differences and 95% limits of agreements between B-lines and EVLWI was 4.9 (–14.5 to 24.5), and 5.9 (–3.5 to 15.3) when assessing observer agreement. The ICC between methods was 0.52 (95% CI = –0.17 to 0.81) and 0.90 (95% CI = 0.73 to 0.92) between observers.

Conclusion LUS non-invasively and user-independently quantifies lung water in concordance with, but does not replace, invasive measurements. Further studies are needed establish the role of LUS as a monitoring and diagnostic tool in septic shock patients.

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P141

Variations in near-infrared spectroscopy-derived oxygen downslope during a vascular occlusion test in critically ill patients: relationship with outcome

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Critical Care 2015, **19(Suppl 1):**P141 (doi: 10.1186/cc14221)

Introduction Near-infrared spectroscopy (NIRS) with a vascular occlusion test (VOT) can be used to extrapolate information regarding the tissue oxygen extraction rate. We explored the meaning of variations in tissue oxygen saturation downslope (StO_2down) during a VOT in critically ill patients.

Methods In this prospective observational study, NIRS (thenar eminence) was applied every day in 93 patients admitted to the ICU. A VOT was performed using a 40% StO_2 target. The slope of the desaturation curve was assessed separately for the first part (StO_2 Down1) and the last part (StO_2 Down2) of the curve and the difference between Down2 – Down1 was calculated.

Results No significant differences were seen in StO_2 Down1 or Down2 between ICU survivors (n = 76) and ICU nonsurvivors (n = 17) over the first 10 days in the ICU, while Down2 – Down1 was higher in ICU nonsurvivors (Figure 1). Patients in the upper quartile of mean Down2 – Down1 showed the highest 90-day mortality ($P = 0.014$).

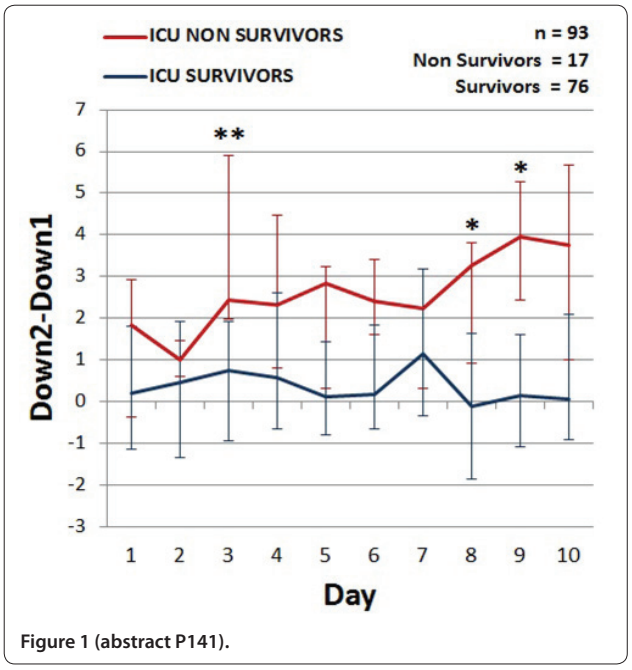


Figure 1 (abstract P141).

Conclusion ICU nonsurvivors tended to show a flattening in the last part of the desaturation curve during a VOT, suggesting a reduced tissue oxygen extraction. This may depend on microvascular dysfunction and/or cellular hypometabolic status.

P142

Normobaric hyperoxia and the microcirculation in critically ill patients: a prospective observational study

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Critical Care 2015, **19(Suppl 1):**P142 (doi: 10.1186/cc14222)

Introduction It is well known that oxygen acts as a vasoconstrictor. We evaluated the impact of normobaric hyperoxia on the sublingual microcirculation in critically ill patients.

Methods Forty mechanically ventilated (FiO_2 ≤50%) patients with hemodynamic stability were enrolled in a prospective observational study. The first 20 patients underwent a 2-hour period of hyperoxia (FiO_2 = 100%), and 20 patients were studied as controls (no FiO_2 variations). The sublingual microcirculation (three sites) was evaluated with sidestream dark-field imaging at baseline (t0), after 2 hours of hyperoxia (t1), and 2 hours after return to baseline (t2). Continuous video recording was also performed during FiO_2 variations on one and the same area (2-minute video).

Results No changes in mean arterial pressure were observed. The perfused small vessel density tended to decrease at t1 and normalize at t2 (Figure 1) in the hyperoxia group. These variations appeared early after 2 minutes of FiO_2 changes. A significant increase in lactate levels over time (from 1.1 (0.9 to 1.7) at t0 to 1.4 (1.1 to 1.9) mmol/l at t2, $P = 0.01$) was seen in the hyperoxia group.

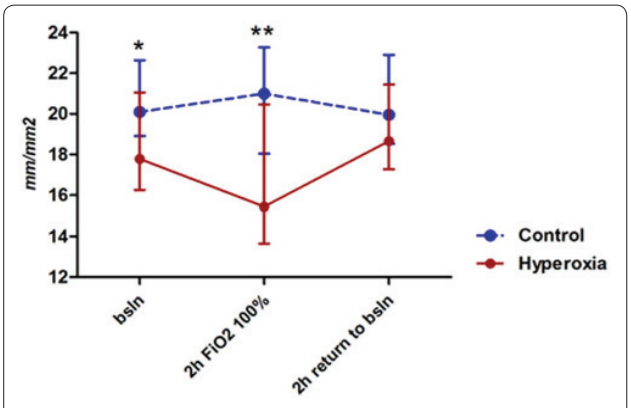


Figure 1 (abstract P142).

Conclusion Hyperoxia induces an early decrease in microvascular perfusion, which appears to go back to normality at return to normoxia.

P143

Near-infrared spectroscopy for assessing the tissue oxygen extraction rate during sepsis: relationship with outcome

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Critical Care 2015, **19(Suppl 1):**P143 (doi: 10.1186/cc14223)

Introduction Microcirculatory dysfunction impairs tissue oxygenation during sepsis. We applied near-infrared spectroscopy (NIRS) to evaluate the tissue oxygen extraction rate in sepsis and its relationship with outcome.

Methods A prospective observational study; 14 septic patients underwent NIRS monitoring (thenar eminence) with a vascular occlusion test (using a 40% StO_2 target) at admission to the ICU.

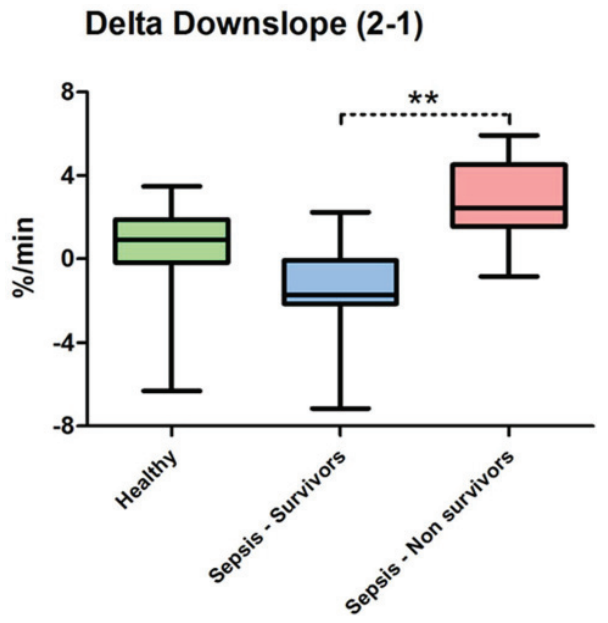


Figure 1 (abstract P143).

Healthy volunteers (n = 27) were studied as controls. The slope of the desaturation curve was assessed separately for the first (StO_2 Down1) and the last part (StO_2 Down2) of the curve and the difference between, Down2 – Down1, was calculated.

Results StO_2 Down1 was lower in healthy volunteers as compared with septic patients (P <0.05); no difference was seen between ICU survivors (n = 7) and nonsurvivors (n = 7). StO_2 Down2 was similar between healthy volunteers and ICU survivors, while it was higher in nonsurvivors (P <0.01 vs. healthy). ICU nonsurvivors showed higher Down2 – Down1 as compared with ICU survivors (P <0.01, Figure 1).

Conclusion Tissue oxygen extraction was reduced in septic patients. Nonsurvivors showed a flattening in the last part of the desaturation curve during a VOT, while the first part of the StO_2 downslope did not show any difference between survivors and nonsurvivors. This may reflect a tissue hypometabolic status, which may be better elicited in the final part of the ischemic challenge.

P144

Prospective nonrandomized observational study of the use of an impedance threshold device in patients with spontaneous respiration and hemodynamic instability

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Introduction The use of an impedance threshold device (ITD) in cardiac arrest victims has been shown to increase the systolic arterial pressure (SAP) by increasing venous return [1]. There are limited studies concerning the use of ITD in patients with spontaneous respiration and hemodynamic instability. The purpose of this study is to evaluate changes of hemodynamic parameters with the use of ITD in patients with spontaneous respiration and hemodynamic instability.

Methods A 5-month prospective nonrandomized observational study that included 50 adult patients with spontaneous respiration and hypotension in the emergency room and the wards of multiple causes except trauma. After measurement of the SAP and verification of hypotension (SA*P* ≤90 mmHg), a mask-style ITD was added. Hemodynamic parameters were evaluated every 1 minute and for 10 minutes after the intervention. Endpoint of the study was a change of patient's SAP after application of ITD.

Results The SAP of patients that were included in the study increased 15 to 22 mmHg (P <0.05). Heart rate remained unchanged. Eighty percent of patients declared good to very good tolerance from ITD application.

Conclusion In this observational study of patients with spontaneous respiration and hypotension, ITD increased the SAP, while it seems that it was well tolerated by patients. Additional and larger studies will be needed in the future in order to investigate the benefits of ITD when used to patients with spontaneous respiration and hemodynamic instability.

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P145

Lactate in the burn patient

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Introduction Severe burns result in rapid loss of intravascular volume due to development of a severe capillary leak and hypovolemic shock. It is widely accepted that traditional markers, such as blood pressure and urinary output, are useful but do not sufficiently reflect global perfusion, regional microcirculation or reversal shock. Blood lactate concentration is widely used in ICUs as a reliable prognostic marker of global tissue hypoxia. Our aim is to determine whether the percentage of lactate clarified in the first 24 hours is valid as a guide for resuscitation.

Methods We prospectively studied 143 consecutive burn patients admitted to our Burn Unit. Sociodemographics and comorbidities data were recorded. Clinical data were collected to calculate the Acute Burn Severity Index. Resuscitation according to the Parkland formula was guided by a urinary output of 0.5 to 1 ml/hour and the results of monitoring the blood pressure. Crystalloid solution (Ringer´s acetate) was given exclusively during the first 24 hours. Early surgical excision of burn eschar and early coverage of excised burn wounds with autografts was performed. Initial and subsequent serum lactate levels were measured to calculate lactate clearance according to the formula: lactate basal – lactate at 24 hours / lactate basal × 100. The primary outcome was mortality.

Results During a period of 2 years we studied 143 patients; their mean age was 46.98 ± 19.38 years, mean TBSA burn injury of the study population was 22.82 ± 20.25. The flame was the most frequent mechanism. A total of 83 patients were in mechanical ventilation and 13.6% of them developed ARDS. The mortality range in the study group was 17%. Serum lactate at admission ≥2 mmol/l was associated with 31.3% mortality versus 6% in patients with a serum lactate at admission <2 mmol/l (P <0.05). Length of time to lactate normalization variable is associated with mortality (P <0.02). The average lactate normalization time was 4.6 days in nonsurvivors while in survivors it was 2.02 days. A relation does not exist between the lactate clearance and mortality in all patients.

Conclusion The length of time to lactate normalization in the severe burn patient is a marker of survival and a simple parameter to guide the endpoint of resuscitation; however, the percentage of lactate clarified in the first 24 hours is not valid.

P146

Blood lactate normalization following venoarterial ECMO institution for refractory cardiogenic shock

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Introduction Venoarterial (VA) ECMO is used to support patients with refractory cardiogenic shock (CS). Elevated lactate level (>2 mmol/l)

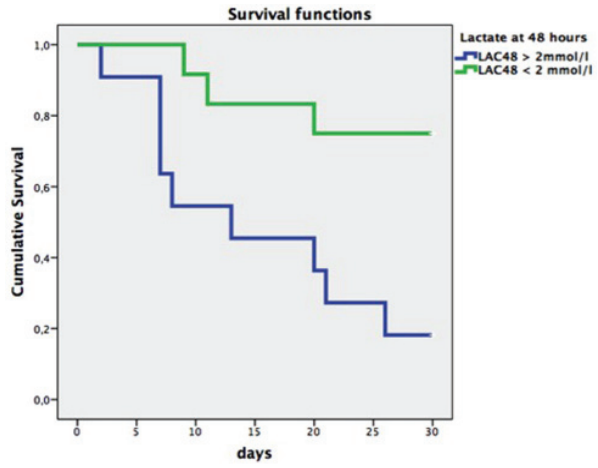


Figure 1 (abstract P146).

is an indicator of end-organ hypoperfusion. We hypothesize that the lactate (LAC) normalization had prognostic value in this cohort of patients.

Methods We performed a retrospective observational study on patients admitted to the ICU for refractory CS from January 2010 to November 2014. Patients with postcardiotomy and/or post-transplant CS were excluded. Demographics, clinical, hemodynamic and biochemical values were collected. LAC was measured on arterial blood before ECMO institution (LAC0) and after 48 hours (LAC48). Lactate clearance was calculated as follows: (LAC0 – LAC48) / LAC0 × 100. Data were analyzed by comparative statistic; sensibility and specificity were tested with ROC.

Results Twenty-three patients underwent VA ECMO for refractory CS in the study period. Etiologies of CS were: 11 acute myocarditis, five acute myocardial infarction and seven acute decompensation of chronic cardiomyopathy. The median time of ECMO was 10 days (4 to 15). Thirteen patients died during hospital stay and 10 survived. Three patients were bridged to LVAD and two to heart transplant; eight were bridged to recovery. The main cause of ICU death was multiple organ dysfunction (12/13). Nonsurvivors showed significantly higher LAC0 (5 (2 to 6) vs. 8 (5 to 11), $P = 0.021$). Lactate clearance at 48 hours was not significantly different between survivors and nonsurvivors (79%, 95% CI = 67 to 86 vs. 60%, 95% CI = 32 to 72, $P = 0.08$). However, LAC48 was predictive for ICU mortality (AUC 0.82; 95% CI = 0.64 to 1.0; $P = 0.011$). ROC curve analysis identified the accuracy was highest by setting the lactate <2 mmol/l. Patients that did not normalize lactate (LAC <2 mmol/l) after 48 hours despite hemodynamic restoration had poorer outcome at 30 days, as is shown in the Kaplan–Meier curve (log-rank $P = 0.006$) (Figure 1).

Conclusion Failing to normalize patient's LAC in the first 48 hours of VA ECMO assistance for CS is a predictor of ICU mortality. Targeting LAC level <2 mmol/l at 48 hours post ECMO institution might be a reasonable goal for these patients.

P147

Is an inotrope score a predictor of mortality and morbidity in children with septic shock?

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Critical Care 2015, **19(Suppl 1):**P147 (doi: 10.1186/cc14227)

Introduction Inotropes and vasoactive drugs in septic shock are commonly used to maintain cardiac output, tissue perfusion and oxygenation. We undertook this study with the purpose of evaluating an inotropic score as a predictor of mortality and morbidity among children who diagnosed septic shock.

Methods A multicenter retrospective chart review was performed in two pediatric ICUs. A total of 93 children with septic shock were recruited. Hourly doses of following inotropes were recorded for the first 48 hours after admission: dopamine, dobutamine, adrenaline and noradrenaline. The inotrope score for every hour, minimum, maximum and mean values for the first 24 hours, and subsequent 24 hours were calculated. In our analysis, the inotrope score was calculated as described by Wernovsky. We expanded this formula to include norephinephrine as follows: Wernovsky Inotrope Score = dopamine dose (μg/kg/minute) + dobutamine dose (μg/kg/minute) + 100 × epinephrine dose (μg/kg/minute). Our adjusted inotrope score = Wernovsky Inotrope Score + 100 × norepinephrine dose (μg/kg/minute).

Results Forty-two of 93 patients died. Age and sex were not different between survivors and nonsurvivors. Significantly higher mean and maximum inotropic score for the first 24 hours and first 48 hours were found in nonsurvivors than those of survivors ($P < 0.05$). Using 15 as a cutoff point for predicting mortality, the sensitivity and specificity were 69.76% and 50.98% respectively. The association between Prism scores and minimum, mean and maximum inotrope scores were statistically significant for 0 to 24 hours, 25 to 48 hours and 0 to 48 hours. Mean 0 to 24 hours and maximum 0 to 48 hours inotrope scores were weakly associated with prolonged ICU stay ($P = 0.047$, $P = 0.042$ respectively). There were no significant relationships between inotrope scores and receiving mechanical ventilation.

Conclusion The mean and maximum inotropic scores in the first 24 hours and 0 to 48 hours are an independent predictor of mortality in critically ill children with septic shock.

P148

Is the shock index a universal predictor in the emergency department? A cohort study

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Introduction The shock index (SI; heart rate/systolic blood pressure) is a widely reported tool to identify acutely ill patients at risk for circulatory collapse in the emergency department (ED). Because old age, diabetes, essential hypertension, and β-/Ca^{2+} channel-blockers might reduce the compensatory increase in heart rate and mask blood pressure reductions in shock or pre-shock states, we hypothesized that these factors weaken the association between SI and mortality, reducing the utility of SI to identify patients at risk.

Methods This was a cohort study from Odense University Hospital of all first-time visits to the ED between 1995 and 2011 ($n = 111{,}019$). The outcome was 30-day mortality. We examined whether age ≥65 years, diabetes, essential hypertension, and use of β-/Ca^{2+} channel-blockers modified the association between SI and mortality. The prognostic value of SI ≥1 was evaluated with diagnostic likelihood ratios.

Results We observed a 30-day mortality of 3%. With SI <0.7 as reference, a SI of 0.7 to 1 was associated with an adjusted OR of 2.9 (CI 2.7 to 3.2) for 30-day mortality while the adjusted OR for SI ≥1 was 10.3 (CI 9.2 to 11.5). ORs for SI ≥1 were reduced (but still significant) in patients who were older, hypertensive, or on β-/Ca^{2+} channel-blockers, whereas diabetes had no effect. The OR for SI ≥1 in patients ≥65 years was 8.2 (CI 7.2 to 9.4) compared with 18.9 (CI 15.6 to 23.0) in younger patients. β-/Ca^{2+} channel-blocked patients had an OR of 6.4 (CI 4.9 to 8.3) versus 12.3 (CI 11.0 to 13.8) in nonusers, and the OR for hypertensive patients was 8.0 (CI 6.6 to 9.4) versus 12.9 (CI 11.1 to 14.9) in nonhypertensive patients. The OR for SI ≥1 of 9.3 (CI 6.7 to 12.9) in diabetics did not differ from the OR of 10.8 (CI 9.6 to 12.0) in nondiabetic patients. A SI of 0.7 to 1 was associated with ORs significantly greater than 1 (range: 2.2 to 3.1) with no evident differences within the subgroups. A SI measurement ≥1 was associated with lower positive likelihood ratios in patients ≥65 years, with hypertension, diabetes or using β-/Ca^{2+} channel-blockers (range 4.9 to 6.5) compared with patients not exposed to these factors (range 7.6 to 11.6).

Conclusion SI is independently associated with 30-day mortality in a broad population of ED patients. Old age, hypertension and β-/Ca^{2+} channel-blockers weaken this association, but the association remains prognostic. SI ≥1 suggests substantial risk of 30-day mortality in all ED patients.

P149

Risk factors for severe vasodilatory shock after cardiac surgery

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Introduction Vasodilatory shock is a well-known complication in patients who undergo cardiac surgery with cardiopulmonary bypass (CPB) and its occurrence is associated with higher morbidity and mortality. Despite that, clinical characteristics of vasoplegic shock and its spectrum of severity are poorly described. The aim of this study was to compare patients who developed mild to moderate vasoplegic shock with patients who developed a severe form and to identify predictive factors for the severe form of vasoplegic shock.
Methods We performed an observational study in 300 patients who underwent cardiac surgery with CPB and presented within the first 24 hours after surgery with refractory hypotension and used a vasopressor agent. Severe vasoplegic shock was defined as a requirement of norepinephrine higher than 1 μg/kg/minute or the use of two or more vasopressors. Baseline characteristics, laboratorial, clinical and intraoperative data, such as amount of fluids, bleeding, blood transfusion, inotropes and length of CPB were collected at ICU admission. Logistic regression was performed using severe vasodilatory shock as the outcome.
Results There were 46 (15%) patients who develop the severe form of vasodilatory shock within 24 hours after cardiac surgery. In a univariate analysis, patients with the severe form were more likely to be older, to receive more blood transfusion and inotropic agents, to have higher levels of serum lactate, lower hemoglobin concentration and lower SvO_2 at the end of the procedure, lower cardiac output index, higher heart rate and higher levels of reactive C protein at ICU admission. These patients also experienced more postoperative organ dysfunction, had a longer length of ICU stay and higher mortality. There were no differences between patients regarding amount of fluids and length of CPB. In a multivariate analysis we identify age (OR = 1.04, 95% CI = 1.01 to 1.08, P = 0.016), intraoperative use of epinephrine (OR = 5.49, 95% CI = 2.42 to 12.43, P <0.001), higher serum lactate at the end of the procedure (OR = 1.04, 95% CI = 1.01 to 1.06, P = 0.001) and intraoperative blood transfusion (OR = 5.06, 95% CI = 2.19 to 11.69, P <0.001).
Conclusion This study demonstrated that older patients, intraoperative blood transfusion and utilization of epinephrine were independently associated with a more severe form of vasodilatory shock after cardiac surgery with CPB. Also, we identified that a higher lactate at the end of the procedure was an independent predictive factor for this severe form of shock.
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P150

Preoperative treatment with levosimendan helps to evaluate myocardial reserves in cardiosurgical patients with chronic heart failure

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Introduction The aim of the study was to assess the possibility of preoperative levosimendan (LS) administration in myocardial reserve evaluation and choice of the method of surgical treatment in patients with chronic heart failure (CHF).
Methods LS was used in 107 (female and male) patients (mean age 53 ± 3 years) as a component of CHF therapy to prepare them for the surgical intervention (2 to 4 days before surgery). In total, 44.9% of the patients had CHF caused by noncoronarogenic dilated cardiomyopathy and 55.1% by ischemic cardiomyopathy. Indication for LS therapy was left ventricular ejection fraction (EF) <35% (28 ± 6%). Seventy percent of patients had mitral insufficiency (MI), grades II to IV, 63% tricuspid insufficiency (TrI), grades II to III, 84% pulmonary hypertension (PH), 47% arterial hypertension, grades II to III, and 27% of the patients had left ventricular aneurysm. Mean level of BNP was 1,803 ± 124 pg/ml. LS was administered as i.v. infusion in doses of 0.025 to 0.1 μg/kg/minute without previous bolus injection. Mean duration of infusion was 27.5 ± 5.3 hours. After infusion all patients underwent control assessment of values. All patients were operated: 25 (23.3%) underwent reverse cardiac remodeling, 63 (58.9%) myocardium revascularization (MR) with mitral or aortic valve replacement, 17 (15.9%) MR and/or resection of left ventricular aneurism and two (1.9%) heart transplantation.
Results Heterogeneity of LS effects was registered in a number of values. The most significant positive effect which allowed one to evaluate myocardial reserve was demonstrated by decrease of PPA (93.5% of patients) and increase of EF (77.6% of patients). The most significant changes were also noted in decrease of TrI, PH and MI (in 53.2%, 36.6% and 36% of patients, respectively). In 69.2% of patients with noncoronarogenic dilated cardiomyopathy the effect of LS exposure was marked. In the majority of patients with ischemic cardiomyopathy the effect was moderate. In case of the absence of LS-positive effect, perioperative use of mechanical circulatory support was considered.
Conclusion Preoperative use of LS allows one to evaluate myocardial reserves and prepare high-risk patients with CHF for surgery. Our findings may serve as one of the additional criteria to choose the type of surgical treatment: reconstructive surgery (with or without perioperative mechanical circulatory support) or heart transplantation.

P151

Levosimendan versus dobutamine in cardiac surgery

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Critical Care 2015, **19(Suppl 1):**P151 (doi: 10.1186/cc14231)

Introduction Early studies suggested a significant increase in survival in patients treated with levosimendan compared with dobutamine or placebo (LIDO, RUSSLAN and CASINO trials). However, two subsequent studies (SURVIVE and REVIVE II) have not confirmed these findings.
Methods A prospective observational study of all patients undergoing cardiac surgery at Malaga's Regional Hospital from March 2009 to March 2013. We analyzed patients who used levosimendan compared with those that used dobutamine in the first hours after cardiac surgery, discarding patients in which neither of these two drugs were used or surgical cases that arrived at the ICU with both inotropics. We analyzed demographic variables as well as clinical complications in the ICU and overall perioperative mortality of patients. We performed a second analysis using the propensity score, obtaining the probability of patients being treated with either drug, pairing each patient who received levosimendan with its nearest neighbor receiving dobutamine.
Results We collected 875 patients: 331 received one of the two drugs, 50 received both drugs and 494 did not receive any drug. ICU mortality was 7.2% (levosimendan group) and 12.5% (dobutamine group), P = 0.1. After adjustment for severity and type of surgery, the use of levosimendan in the postoperative period was not a protective factor for ICU mortality (P = 0.18, OR = 0.5, 95% CI = 0.18 to 1.3). In the matched sample, mortality was 7.4% (levosimendan group) and 5.9% (dobutamine), P = 0.73. After logistic regression adjusted for severity, measured with EuroSCORE and type of surgery, levosimendan was not a protective factor for ICU mortality (P = 0.8, OR = 1.2, 95% CI = 0.26 to 5.45).
Conclusion In our environment, we have observed differences in the use of levosimendan compared with dobutamine (higher rate of men undergoing CABG, diabetes and worse EF). After homogenizing the sample of patients by propensity score, an effect on mortality is discarded and we observed a significant need for use of norepinephrine and a nonsignificant trend for prolonged mechanical ventilation and renal failure requiring renal replacement therapy, both probably related with the greatest need for vasopressors observed.

P152

Levosimendan: use, cost-effectiveness and outcome in a tertiary cardiothoracic centre

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Introduction Levosimendan was originally developed for the treatment of decompensated heart failure in situations for which conventional therapy is not sufficient. It is an effective calcium-sensitising drug with vasodilatory and inotropic effects and improves cardiac contractility. Trials have shown positive outcome benefit with the use of levosimendan [1]. We reviewed the usage levosimendan at our institution and outcome of these patients.
Methods We reviewed the use of levosimendan at Harefield from January 2013 through December 2013. Patient demographics, logistic EuroSCORE (Figure 1), diagnosis, surgical or intervention details, inotropic support, dosage and duration of levosimendan use, length of stay in the ICU, cost (Table 1) and patient outcome were collected.
Results Levosimendan was used in 30 patients, 23 (77%) male and seven (23%) female. Median age was 69 (59 to 72.8). Levosimendan was used post cardiac surgery, post angioplasty and in patients with ventricular assist devices (VAD) and extracorporeal membrane oxygenator (ECMO). Most of the patients received a standard regimen of 12.5 mg administered at a dose of 0.1 μg/kg/minute for 24 hours. Concurrent noradrenaline was used in most of the patients ranging from 0.02 to 0.2 μg/kg/minute. The median length of stay in the ICU was nine (6 to 14.5) days for survivors and 23.5 (7.5 to 36) days in nonsurvivors. Sixteen patients (55%) survived and were discharged from the hospital.

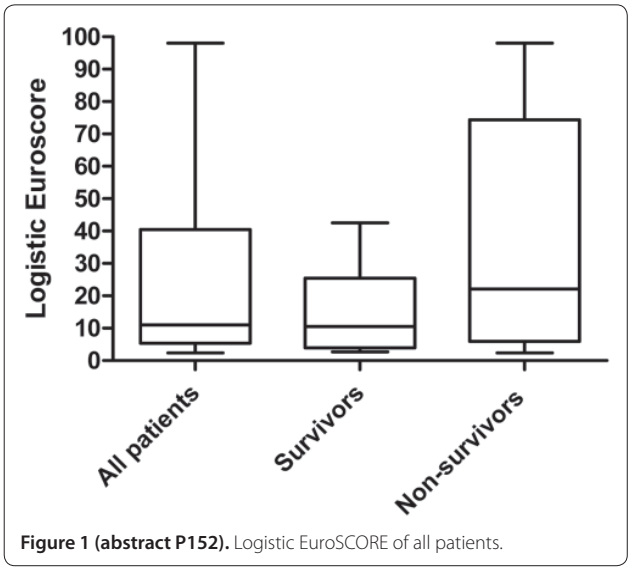


Figure 1 (abstract P152). Logistic EuroSCORE of all patients.

Table 1 (abstract P152). Cost of levosimendan based on a 70 kg patient

	Levosimendan	Adrenaline	Milrinone
Maximum dose (μg/kg/minute)	0.2	1	0.7
Cost per vial (£)	894	2.30	16
Cost per 24 hours (£)	894	7	112

Conclusion We have successfully used this drug in high-risk patients during the perioperative period with good results without major complications. Levosimendan seems to reduce catecholamine requirement, the need for mechanical circulatory support, and the duration of critical care, which can justify the cost of this drug. It can be also useful in weaning patients from short-term VAD and ECMO. Larger studies are required in this area.

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P153

Levosimendan in the emergency department: a useful tool to improve cellular perfusion

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Introduction Levosimendan is an inotropic seldom used in emergency departments (EDs). It has shown improved mortality in patients with shock [1] with few adverse effects [2]. This work denotes the experience of levosimendan use in the ED of Hospital Universitario Mayor between 2012 and 2014.
Methods We present a retrospective study which analyzes the effect, after 24 hours, of levosimendan administration on perfusion parameters of 166 ED patients. Patients had to have shock diagnosis of any cause. Differences between the initial and final mean value of the following parameters were evaluated: lactate, central venous oxygen saturation ($ScvO_2$) and venoarterial difference of CO_2 ($DvaCO_2$). Data were stratified according to levosimendan categories (initial or rescue). In addition, association between different variables with mortality was sought. Differences were considered statistically significant at probability levels below 0.05.
Results There were no differences in APACHE II values between patients who received levosimendan as initial therapy from those who received it as a rescue measure. A total of 41 patients fulfilled lactate normalization requirements (lactate <2.0 or clearance >50%) (Table 1). Forty-four patients reached normal values of $SvcO_2$ and 37 patients of $DavCO_2$ after levosimendan initiation. There were no associations between the normalization of lactate, SvO_2 and $DvaCO_2$ and different types of shock. Twenty-nine patients who received initial therapy with levosimendan normalized their lactate values and 12 who received it as a rescue therapy (P <0.05). Sixty-three patients developed hypotension, and none had adverse effects requiring discontinuation of the drug. Hospital mortality was 47.7%. Variables associated with mortality in the study group were lactate value at admission (OR = 1.3, 95% CI = 1.0 to 1.7), the use of vasopressin after start levosimendan (OR = 7.5, 95% CI = 1.9 to 28.6) and the use of norepinephrine before starting (OR = 10.8, 95% CI = 1.9 to 60.7).

Table 1 (abstract P153). Perfusion variables before and after levosimendan

Variable	Initial	Final
Lactate (mmol/l)	3.3 (0.5 to 18)	2.38 (0.4 to 17)*
$SvcO_2$ (%)	56.3 (23 to 85)	65.2 (37 to 91)*
$DvaCO_2$ (mmHg)	8.2 (–16 to 26)	7.3 (–2 to 21)

*P <0.01. McNemar test.

Conclusion Levosimendan use in the ED, as initial or rescue therapy, normalizes lactate values and improves the $SvcO_2$ after 24 hours, without an increase in adverse effects.
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P154

Milrinone role in treatment of septic shock

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Critical Care 2015, **19(Suppl 1):**P154 (doi: 10.1186/cc14234)

Introduction The inotropic agents used in the ICU are dobutamine and milrinone; unfortunately, they have shown significant side effects when used for myocardial depression during septic shock. Our objective is to describe Mn behavior in septic shock.

Methods We reviewed 72 clinical records of patients with diagnosis of septic and mixed shock who received Mn through January to December 2013. Demographic, hemodynamic, metabolic and gasometric data were recorded before and after Mn infusion. The PiCCO monitoring system was used. Data were expressed as mean and standard deviation. The statistical analysis used Student's *t* test. $P < 0.05$ was considered significant.
Results Seventy-two patients were studied: 36.5% were women, mean and SD of age, APACHE II, mechanical ventilation days and long ICU stay were: 67 ± 16 years, 18.5 ± 5.9 points, 14.9 ± 12.9 and 24.5 ± 21.9 days, respectively. A total 20.3% of the patients received dobutamine. Thirty-nine percent presented mixed shock. Global mortality was 23%. After Mn infusion: cardiac index (CI) increased: 3.1 ± 1 to 3.3 ± 1.1, cardiac rate increased: 82.4 ± 14.4 to 88.3 ± 18 and $ScvO_2$ increased: 71.1 ± 10.3 to 76.1 ± 7.3 ($P < 0.05$). $PaCO_2$ arteriovenous difference and lactate were reduced: 7.36 ± 3.3 to 6.04 ± 3.6 and 18.7 ± 14.9 to 13.1 ± 9.1 ($P < 0.05$). CVP, MAP, RVSI, VSTI, EVLWI and base excess showed no significant difference. Mn initial average dose was 0.35 ± 0.13. NE before and after Mn infusion showed no significant difference: 0.11 ± 0.20 versus 0.12 ± 0.22.
Conclusion Mn optimizes cardiovascular performance in septic shock and mixed shock, without affecting hemodynamic variables and global tissue perfusion. In addition, we observed that the IC, $ScvO_2$, $PaCO_2$ arteriovenous difference and lactate are related variables.
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P155

False arrhythmia alarms can be reduced by algorithm improvements while the magnitude of the reduction is affected by alarm settings

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Introduction The ECRI Institute has identified alarm fatigue as the number one health technology hazard [1]. A recent study on 461 ICU patients investigated 2,558,760 alarms [2]. In total, 88.8% of the annotated 12,671 arrhythmia alarms were false positives (FPs). It was concluded that the excessive number of alarms is 'a complex interplay of inappropriate user settings, patient conditions, and algorithm deficiencies'. Nine conditions causing alarms, four of which were ECG algorithm related, were reported [2]. In this study, we investigated a new algorithm in which improvements targeting three of the reported four ECG-related conditions were implemented: low amplitude QRS; wide QRS; nonactionable ventricular tachycardia (VT).
Methods The false alarm rate of the new algorithm (GE Carescape, 2012) was compared with that of the algorithm evaluated in the study (GE Solar, 2003) [2] on the collected ECG waveform data. User settings such as QRS detection sensitivity (high/normal) were not available. Therefore, normal sensitivity was assumed for both versions. With the old algorithm, 10 patients with low QRS amplitudes gave a significantly higher number of FPs than were reported [2]. For those patients, both sensitivity modes were tested with the old algorithm. Sixty-six percent of patients with a pacemaker did not have the pacemaker mode selected [2]. Outlier patients in which false alarms were due to user settings (20 patients with a pacemaker) or patient condition (four patients with a bundle branch block) rather than algorithm deficiency were excluded.
Results Improved algorithm resulted in 66% reduction of FP alarms. When using the high-sensitivity mode for the 10 patients with low QRS, FP reduction was 18%. No compromises regarding detection of true events were found. The 24 outlier patients contributed to 81.3% of FP alarms. The algorithm changes responsible for the reduced FPs were: adaptive threshold for low amplitude QRS detection; QRS filter with an extended frequency range; management of VT alarm priorities.
Conclusion A majority of the FPs was linked to user settings and patient conditions. The algorithm changes resulted in a clear reduction of ECG algorithm-related FP alarms, while the magnitude of the reduction depends strongly on the settings at the bedside.
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P156

Arrhythmia incidence and risk factors in critically ill patients

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Introduction Cardiac arrhythmias may be observed at any time during the ICU stay. The prognosis may suffer due to these arrhythmias. In our study, we aimed to evaluate incidence and risk factors of arrhythmias occurring in patients in the ICU.
Methods Patients treated in the ICU were included in the study if they fulfilled the following: age >18, no cardiac valvular disease, no cardiac surgery in the recent 6-month period, no history of myocardial infarction (MI), need for mechanical ventilation, and one or more organ failure. Demographic, hemodynamic and laboratory parameters, APACHE II score, presence of sepsis, acute renal failure, MI, and VIP during the ICU stay were recorded. Therapies used for arrhythmia and response to therapies were also recorded.
Results Two hundred and fourteen patients were included in the study. Twenty-six percent ($n = 56$) of patients had arrhythmias. Incidence was higher in females ($P = 0.045$). Average age of arrhythmic patients was 69 (19 to 86), and they were older than nonarrhythmic patients ($P < 0.001$). APACHE II scores were higher in arrhythmic patients ($P = 0.001$).
Admission to the ICU with cerebrovascular event (CVE) and trauma was related to arrhythmia ($P = 0.021$, $P = 0.032$, respectively). There was a significant relationship between VIP and sepsis presence ($P < 0.001$, $P < 0.001$). Atrial fibrillation was the most frequent type of arrhythmia (53%), and the most frequently used medication was diltiazem (28.5%). The patients who had arrhythmias had a longer ICU stay ($P = 0.021$). The mortality rate for all patients was 48.1%. There was no statistically significant relationship between arrhythmia and mortality ($P > 0.05$).
Conclusion Older age, higher APACHE II scores, trauma, CVE, VIP and sepsis increases arrhythmia risk in critically ill patients. Atrial fibrillation is most common and the most preferred treatment for all arrhythmias is diltiazem.
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P157

Pulmonary hypertension, right ventricular dysfunction and acute heart failure: a portentous consortium

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Introduction Pulmonary hypertension and right ventricular dysfunction (RVD) are frequently encountered in patients with acute heart failure. We sought a better understanding of the coupling between RVD and pulmonary hypertension in the setting of acute decompensated heart failure (ADHF) as it might improve the prognostic stratification and influence the survival rates.
Methods Echocardiography was performed in 329 patients with ADHF and right ventricular function was assessed by measuring the right ventricular fractional area, and a right ventricular ejection fraction (RVEF) <35% was taken as the cutoff value for RV systolic dysfunction. The systolic pulmonary pressure (PASP) was calculated from the tricuspid regurgitation signal applying the modified Bernoulli equation,

and pulmonary hypertension was considered as PASP >35 mmHg. Based on the values of PASP and RVEF the study group was classified into four subgroups: group 1, normal PASP/preserved RVEF; group 2, high PASP/preserved RVEF; group 3, normal PASP/ low RVEF; group 4, high PASP/low RVEF. The primary endpoint was all-cause mortality. The median follow-up was 18 months. Survival analysis was performed according to the Cox regression method, adjusted for age, gender, LV function, estimated glomerular filtration rate, troponin I, hemoglobin, serum sodium and BNP levels.

Results Pulmonary hypertension was found in 78% of the patients (median PASP: 53 mmHg). As compared with the patients with normal PASP the patients with pulmonary hypertension were more likely to be in New York Heart Association functional class (NYHA) III or IV (86% vs. 49%, P <0.001), had a lower RVEF (23 ± 9% vs. 32 ± 8%, P <0.001), and had significantly higher BNP levels (280 ± 107 pg/ml vs. 540 ± 320 pg/ml, P <0.001). In a Cox model, compared with patients with normal right ventricular function and without pulmonary hypertension (group 1), the adjusted hazard ratio for mortality was 3.1 (95% CI: 1.6 to 4.2, P <0.01) in group 2, 0.3 (95% CI: 0.2 to 1.9, P = 0.3) in group 3 and 4.2 (95% CI: 1.9 to 6.1, P <0.001) in group 4.

Conclusion Among ADHF patients, the coupling of pulmonary hypertension and RVD carries an incremental risk, having a portentous impact on the survival rate.

P158

High-sensitive cardiac troponins and CK-MB concentrations in patients undergoing cardiac surgery

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Introduction Hs-cTn is the new standard cardiac biomarker for the diagnosis of myocardial necrosis. We conducted a prospective study to compare the course and values of Hs-cTn and CK-MB after CABG and OPCAB. We also evaluated the relationship between values >10 × 99th percentile URL of CK-MB and Hs-cTn as a possible marker for perioperative myocardial infarction.

Methods All adult patients undergoing cardiac surgery between February and August 2014 were included. Exclusion criteria were urgent surgery, GFR <60 ml/minute/1.73 m^2, CK-MB >4 µg/l and/or Hs-cTn >14 ng/l at baseline (BL). Hs-cTn and CK-MB were measured before induction (BL), upon arrival in the ICU and at fixed times after arrival. Patients with perioperative AMI as defined by the third universal definition of AMI were excluded for *post hoc* analysis [1].

Results Of the 93 patients admissible for inclusion, 40 in the CABG and 14 in the OPCAB group met all inclusion criteria in this preliminary dataset. CK-MB values are higher from ICU arrival up to T24 versus baseline in both CABG and OPCAB (P <0.0001) with a peak at T3. For Hs-cTn, ICU up to T48 values are higher (P <0.01) in CABG with a peak at T6, and from T3 to T48 in OPCAB (P <0.05) versus baseline (Figure 1). In CABG patients CK-MB levels are higher versus OPCAB from ICU up to T12 (P <0.03), and from ICU to T48 for Hs-cTn levels (P <0.02). In 39 CABG patients (97.5%) and 10 OPCAB patients (71.4%) all individual Hs-cTn values are above 140 ng/l (= 10 × 99th percentile of URL).

Conclusion Both CK-MB and Hs-cTn levels increase significantly after cardiac surgery. Postoperative Hs-cTn levels exceed the 10 × 99th percentile of URL in nearly all CABG patients. Our data show an important discrepancy between the 10 × 99th percentile for both biomarkers, and suggest that a different definition for postoperative AMI may be needed when Hs-cTn is used.

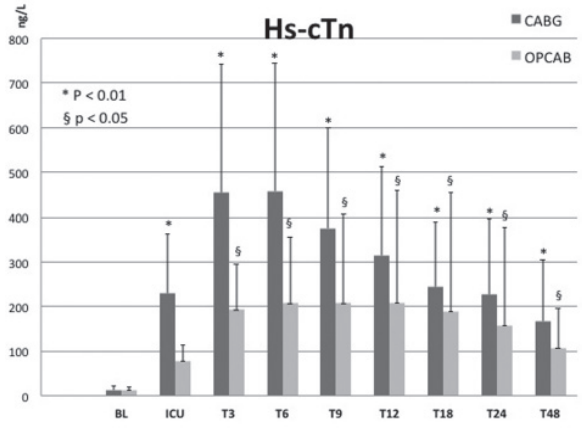


Figure 1 (abstract P158).

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P159

Analytical and diagnostic characteristics of the high-sensitivity PATHFAST troponin I assay

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Introduction The POC PATHFAST cTnI assay (Mitsubishi Medience, Japan) has shown promising analytical validity. We thought to evaluate whether the assay could be classified 'highly-sensitive'.

Methods cTnI was determined using PATHFAST in 120 healthy individuals (60 men and 59 women, 21 to 69 years old, median 42 years). Cardiac disorders were excluded by cardiac magnetic resonance imaging. The diagnostic characteristics were investigated by determination of cTnI and cTnT (Roche hs-cTnT) in 181 patients admitted to the chest pain unit at presentation, and 3 and 6 hours later. The results were related to the discharge diagnoses.

Results The cTnI concentrations measured in the control group ranged from 0.4 to 17.2, mean 2.1 (95% CI: 1.6 to 2.6) ng/l, without age dependency. Men revealed higher levels than women, means (IQR) were 2.8 (1.2 to 2.6) and 1.1 (0.7 to 1.3) ng/l. The CLSI nonparametric method revealed a 99th percentile value of 16 ng/l. The quantification of cTnI above the LoD (1.0 ng/l) and below the 99th percentile was possible in 79 of 120 individuals. The imprecision profile according to NCCLS revealed 20%, 10% and 5% CVs at concentrations of 2, 3 and at 20 ng/l, respectively. The discharge diagnosis was NSTEMI in 71 patients. The cTnI median values at 0, 3 and 6 hours were 46, 166 and 399 ng/l, respectively. AUC values at 0, 3 and 6 hours were 0.923, 0.964 and 0.969 for hs-cTnT and 0.919, 0.962 and 0.958 for cTnI, respectively. cTnI revealed AUC values of absolute changes from admission to 3 hours and from admission to 6 hours were 0.920 and 0.931, respectively.

Conclusion The PATHFAST cTnI demonstrated complete fulfillment of the analytical criteria for high-sensitive cTn assays: The imprecision (CV) at the manufacturer-recommended 99th percentile value was 5%. The quantification of cTnI in was possible in 65.8% of healthy individuals. The examination of the diagnostic characteristics revealed complete concordance with the hscTnT assay for detection of NSTEMI and for assessment of absolute changes of cTn values (rise and/or fall) in NSTEMI patients. PATHFAST cTnI showed highly sensitive detection of NSTEMI with increasing sensitivity at admission and after 3 to 6 hours, not going along with decreased specificity. The PATHFAST cTnI might be useful at the point-of-care setting for early rule-in and rule-out diagnosis of NSTEMI.

P160

Combining therapeutic hypothermia and primary coronary intervention in comatose survivors of ventricular fibrillation due to ST-elevation myocardial infarction

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Introduction Primary percutaneous coronary intervention (PPCI) is the preferred reperfusion strategy for ST-elevation acute myocardial infarction (STEMI). In comatose survivors of cardiac arrest, mild induced hypothermia (MIH) improves neurological recovery.

Methods A total of 112 patients undergoing PPCI and MIH were compared with 32 comparable consecutive patients who underwent PPCI but no MIH. We hypothesized that combining both methods lead to better survival rate. MIH was induced (propofol, fentanyl, saline 4 ml/kg BW, 2°C) and maintained for 24 hours, targeting 32 to 34°C. Spontaneous rewarming was allowed (0.5°C).
Results There were no significant differences between the MIH and Control group in general characteristics, cardiac arrest circumstances and angiographic features. Except for decreases in heart rate during MIH, there was no difference between MIH and no MIH groups in arterial pressure, peak lactate (7.7 vs. 6.2 mmol/l; $P = 0.36$), need for vasopressors (57% vs. 41%; $P = 0.09$), aortic balloon counterpulsation (13% vs. 22%; $P = 0.19$), repeat cardioversion/defibrillation (17% vs. 25%; $P = 0.30$). There was lower incidence of inotropic use (36% vs. 59%; $P = 0.01$) and use of antiarrhythmics (11% vs. 53%; $P = 0.002$). There was no difference in FiO_2 during mechanical ventilation and in renal function. See Table 1.

Table 1 (abstract P160). Survival after 12 months

	MIH	Control	*P*
CPC 1/2	50 (45%)	5 (15%)	0.002
CPC 3/4	0	0	NS
Cardio	20 (18%)	6 (19%)	0.95
CNS	18 (16%)	17 (53%)	0.00001

Conclusion Hospital survival with CPC 1/2 was significantly better in the MIH group (45% vs. 15%; $P = 0.01$). Our study clearly demonstrates that PPCI and MIH are feasible and may be combined safely in comatose survivors of ventricular fibrillation in STEMI setting. Such strategy improves survival with good neurological recovery.
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P161

Synthesized 18-lead electrocardiogram as routine myocardial ischemia detection in an emergency department: a preliminary evaluation in Europe

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Introduction Standard 12-lead electrocardiogram (ECG) is, with biomarkers, the most accurate method in the diagnosis of acute coronary syndrome (ACS). However, posterior (V7-V8-V9) and right (V3R-V4R-V5R) derivations are not systematically performed due to the time-consuming procedure involved, despite major therapeutic implications (fluid loading instead of nitrates use in right ventricular involvement) and published guidelines [1]. Recently, an 18-lead ECG system, standard 12-lead ECG and six additional synthesized leads (assessing posterior and right ventricular areas) in only one recording procedure has been developed. The reliability of this material (ECG 2550; Nihon Kohden Co. Ltd, Japan) was already validated in this indication in an Asian population [2,3].
Methods We conducted a prospective, observational study with patients admitted to our emergency department (ED), during a 6-month period. Requirement for ECG was guided by physician's discretion according to patient's history. All patients with chest pain, dyspnea, palpitations, disturbance of consciousness, malaise or abdominal complaint underwent synthesized 18-lead ECG within 10 minutes of ED arrival. The aim of the study was to evaluate the effectiveness of the synthesized 18-lead ECG as an ischemia triage tool in the ED, and particularly the ability to early detect a right ventricular involvement.
Results Of the 3,835 nontraumatic patients treated in the ED, 3,196 were adults. In this adult population, 500 ECGs were performed in patients whose symptoms suggest ACS. The median age was 62.3 years and the sex ratio was 1.16. Clinical presentation was chest pain (31%), dyspnea (14%), palpitations (5%), disturbance of consciousness (3%) or others (47%). Fifty-six (11.2%) were diagnosed as ACS, including 20 ST-elevation myocardial infarction (STEMI), 28 non-STEMI and eight unstable angina. Of the 20 STEMI patients, eight (40%) and five (25%) were diagnosed as STEMI complicated by right ventricular and posterior wall ischemia respectively, which means that these complications could have been missed by standard 12-lead ECG.
Conclusion Eighteen-lead ECG with synthesized right-sided and posterior precordial leads was an efficient method to diagnose ACS in a Caucasian population within 10 minutes of ED arrival. It is particularly performant to detect right ventricular ischemia early, which can modify acute therapeutic strategy.
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P162

Global longitudinal strain value for predicting left ventricular remodeling after primary percutaneous reperfusion therapy in acute myocardial infarction

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Introduction After an acute myocardial infarction with ST-segment elevation (STEMI) treated with percutaneous coronary intervention (PCI), the left ventricle (LV) can undergo negative remodeling (R–). We aimed to investigate whether global longitudinal strain (SGL) of the left ventricle (LV) predicts remodeling.
Methods Transthoracic echocardiography with speckle tracking imaging (TTE-STI) was performed 2 to 3 days after primary PCI and 6 months later in patients with diagnosis of STEMI. LV R– criteria were: LVEF increase ≤5% and end-diastolic volume increase ≥15%. Logistic regression and ROC curve analysis was used for the statistical analysis.
Results Eighty-three patients (56 ± 11 years) with STEMI at any LV localization and subjected to primary PCI were studied during 2012: LV

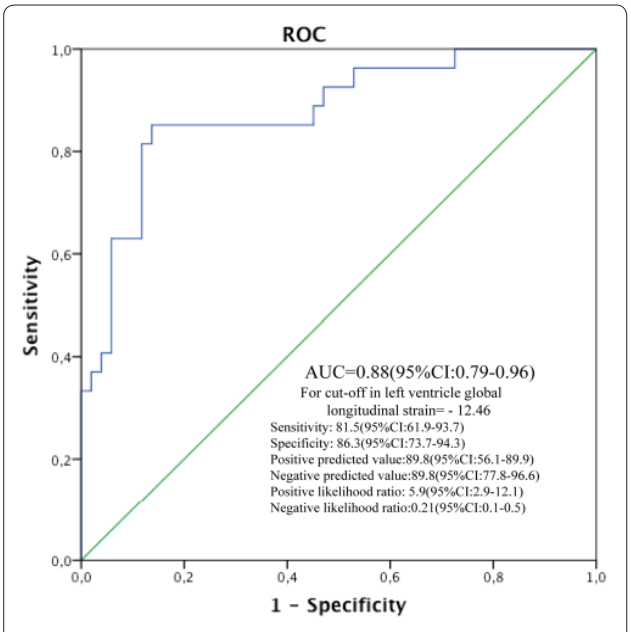


Figure 1 (abstract P162).

R– patients (n = 35, 42%) and no LV R– patients (n = 48, 58%). Diabetes mellitus (41% vs. 19%; P <0.001) and TnI levels (1.2 ± 2.1 μg/l vs. 0.4 ±0.3 μg/l; P = 0.005) showed higher incidence in LV R– patients. SGL was –12.5 ± 5.6% in no LV R– patients and –6.5 ± 3.4 in LV R– patients. In the regression analysis just LV SGL and SL in left anterior descending territory remained significant, OR: 1.85 (1.24 to 2.76) (P <0.001) and OR: 1.63 (1.15 to 2.31) (P <0.001), respectively. The analysis of ROC curves revealed that at the cutoff level of –12.46%, SGL identifies LV R– with a sensibility of 81% and a specificity of 86% (AUC = 0.88: 95% CI: 0.79 to 0.96; P <0.001) (Figure 1).
Conclusion SGL assessment in the first days after primary PCI is useful in the prediction of LV R– independently of the myocardial infarction localization.

P163

Analysis of the interhospital transfer times in patients with ST-elevation acute coronary syndrome for undergoing urgent coronariography

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Introduction The aim was to analyze the related assistance times to transfer patients with ST-elevation acute coronary syndrome (STEMI) referred to another hospital with a hemodynamics unit (HU) for performing emergency catheterization (primary or rescue PCI).
Methods A consecutive registry of patients seen in 2013 (January to October) in the ICU of a hospital without a HU. The total transfer time is considered from the call to the Emergency Coordination Center until arrival at the HU. In turn, this time is divided into activation time, arrival time of the relocation team, patient preparation time and transfer time. In the case of primary PCI, the door-to-balloon time was estimated by adding to the total transfer time the initial assessment and completion time of catheterization and balloon inflation. The times are expressed in minutes, as the median and interquartile range.
Results During 10 months of 2013, we treated 162 STEMI. Of these, 104 had evidence of reperfusion (64%). Primary PCI was performed in 24 patients (23%), of which 10 were transferred from the hospital to the HU. Fibrinolytic therapy was used in 62 patients (59%), of these 20 (32.2%) required rescue PCI. The transfer time for primary PCI was 0:39:44 (0:31:41 to 0:44:32) minutes. The transfer time for rescue PCI was 0:38:56 (0:37:25 to 0:51:29) minutes. The door-to-balloon time estimated for primary PCI was 80 minutes.
Conclusion Times for interhospital transfer of patients with STEMI who had undergone urgent catheterization are within the range considered optimal. In the case of primary PCI, times are lower than the 90 to 120 minutes recommended practice guidelines.

P164

Cerebrovascular haemodynamics in preeclamptic patients

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Introduction The goal of the study was to analyse cerebral blood flow in pregnancy complicated by preeclampsia.
Methods This was a prospective study. I group: 45 patients, 17 to 38 years (mean age 27.5 ± 5.3 years) with verified diagnosis of severe preeclampsia; control group: 72 healthy women with normal pregnancy, third trimester, 19 to 34 years (mean age 24.5± 4.3 years). Exclusion criteria: potentially haemodynamically significant stenosis; congestive heart disease; arrhythmia; large changes in haemorheology; diabetes mellitus; and craniospinal trauma and syncope. Study of cerebral flow was improved by the method of transcranial dopplerography (TCD). All patients underwent duplex scan of extracranial portions of brachiocephalic arteries and transcranial duplex scan in the area of middle cerebral artery (MCA) (segment M1). During duplex scan of brachiocephalic arteries lumen, the presence of extravasal causes for basic blood flow disturbances was estimated. We determined lumen of large basilar arteries and quantitative features of blood flow in MCA. By the transtemporal approach in the MCA M1 segment, peak systolic flow velocity (Vps), maximal end-diastolic velocity (Ved), time-adjusted maximal velocity (TAMX), resistance index (RI), pulsative index (PI), and systolic/diastolic ratio (S/D) were determined. Significance of mean value differences were calculated using the STATISTICA 6.0 program with determination of Student's t criteria with normal spread in the group.
Results All haemodynamic values in the M1 segment of MCA in preeclamptic patients were decreased in comparison with the same values in healthy pregnant women with different significance: PI (mean 0.77 vs. 0.84, P <0.01); RI (mean 0.52 vs. 0.54, P <0.05); Vps (mean 90.22 vs. 104.74 cm/second, P <0.001); Ved (mean 43.25 vs. 48.53 cm/second, P <0.001); TAMX (mean 61.48 vs. 67.30 cm/second, P <0.01); and S/D (mean 2.02 vs. 2.06, P <0.05). Found pathophysiological changes of cerebral haemodynamics were consistent with a dopplerographic pattern of diminished perfusion and are typical for vascular segments, which are located proximally to the zone of abnormally high haemodynamic resistance: prestenotic arterial segments, episodes of arterial hypertension and distal vasoconstriction.
Conclusion With TCD we obtained a possibility to determine and estimate changes in cerebrovascular flow in pregnant patients with severe preeclampsia. This enhances diagnostic possibilities of some serious pregnancy complications, and gives us deep understanding of some components of pathogenesis and increased treatment efficacy.

P165

Prognostic comparison of tissue Doppler indices of diastolic dysfunction and cardiac biomarkers in septic shock

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Introduction Diastolic dysfunction as evaluated by tissue Doppler imaging (TDI), particularly by E/E' ratio (peak early diastolic transmitral velocity/peak early diastolic mitral annular velocity) and mitral annular E'-wave, is common and crucial in critical illness. Our prospective observational study assessed the prognostic significance of TDI variables versus cardiac biomarkers, B-type natriuretic peptide (BNP), troponin-T (TnT) and investigated determinants of plasma BNP rise, in septic shock.
Methods Twenty-seven mechanically ventilated adult patients admitted to our ICU were evaluated within 72 hours of evolving septic shock. Patients underwent two transthoracic echocardiographies within 72 hours of the onset of septic shock: shortly after diagnosis and 24 hours later (confirmatory), alongside relevant measurements of cardiac biomarkers. Peak mitral inflow E and A velocity waves were recorded using pulsed-wave Doppler at the mitral valve tips from the apical four-chamber view, peak early (E') and late (A') diastolic myocardial velocities were obtained by TDI at the septal mitral annulus in the apical four-chamber view. E/E' was calculated. P ≤0.01 was reported as statistically significant.
Results Mean ± SD APACHE II score was 21.22 ± 7.28, mean ± SD admission SOFA score was 10.25 ± 2.76. Hospital mortality was 55%. Nonsurvivors had increased E/E' (15.56 ± 1.48; P <<0.00001) and reduced E' 6.32 ± 0.68 cm/second (P <<0.00001) compared with survivors, who exhibited inverse correlations with an E/E' significantly lower (9.30 ± 2.88) and higher E' (9.01 ± 0.85 cm/second). In contrast, BNP and TnT levels displayed remarkably lower statistical significance in nonsurvivors (P = 0.005, P = 0.007 respectively). The ROC curves had an area under the curve of 0.98 for the E', and 0.92 for the E/E'. Vasopressor management (noradrenaline dose) (P = 0.0001), fluid balance (P <0.001) and E/E' (P = 0.00004) were independent predictors of plasma BNP concentration.
Conclusion Diastolic dysfunction as evaluated by E/E' and E' constitutes a major independent predictor of outcome in septic shock, compared with cardiac biomarkers, suggesting that echocardiographic techniques assessing diastolic dysfunction in sepsis may replace cardiac biomarkers for mortality prediction. Fluid balance, vasopressor management and diastolic dysfunction are independent predictors of BNP elevation in septic shock. Our findings should be confirmed by an extended prospective study.

P166

Accidental intra-arterial injection: an under-reported preventable never event

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Introduction Depending upon the medication administered, accidental administration of medication into the arterial line can cause devastating complications. This wrong-route injection is a never event in the UK but may be under-reported especially when occurring in the unconscious patient who may not notice associated pain temporally. Under-reporting may occur because resultant complications may be delayed a number of hours and the accountable healthcare worker may not recognise or choose not to report the error. In 2008 the UK National Patient Safety Agency (NPSA) reported only 76 incidents related to poor sampling technique but few wrong route arterial injections. Of these 21% suffered moderate to severe harm [1]. The NPSA suggests that training and the use of clear labelling alongside red arterial tubing and standard red lock caps be used to prevent arterial sampling errors.
Methods In 2014, we conducted a national postal survey of ICUs in the UK to attempt to determine the rate of accidental intra-arterial injections. The survey was sent to the clinical director of every ICU and they were asked whether they were aware of any unintentional arterial line injection having occurred in their hospital in the last 5 years.
Results Of the 56 ICUs that responded, 16 (28.5%) reported that they had personally seen an accidental injection into the arterial line.
Conclusion Despite the arterial line safety recommendations made by the NPSA in 2008, we demonstrate that intra-arterial injection is still a problem and that it remains under-reported. Our incidence is likely to be an underestimate as it relies on the recollections of a single individual in each institution. Medical errors can be mitigated by consideration of human factors and system engineering to improve patient safety. A focus on clinical awareness, colour coding and training may lead to improvements; however, institutions and clinical directors also bear a responsibility to prevent never events and a number of engineered solutions are now available such as needle-free non-injectable arterial sampling devices to protect the healthcare environment and make this error impossible [2,3].
Acknowledgement Funding from Eastern Academic Health Science Network, UK.
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P168

Room temperature transpulmonary thermodilution (TPTD) with increased indicator 20 ml TPTD bolus compared with standard TPTD with 15 ml iced saline: a prospective observational study

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Critical Care 2015, **19(Suppl 1):**P168 (doi: 10.1186/cc14248)

Introduction Use of ice-cold saline is assumed to provide best accuracy of TPTD to obtain the cardiac index (CI), global end-diastolic volume (GEDVI) and extravascular lung-water (EVLWI). However, room-temperature injectate might facilitate TPTD outside the ICU. A recent study [1] showed acceptable bias and percentage error (PE) for CI-room derived from TPTD with 15 ml room temperature saline compared with CI-cold using 15 ml iced saline for TPTD. However, GEDVI-room and EVLWI-room had borderline PE values close to 30%, and the bias of GEDVI-room markedly increased with higher values of GEDVI and in case of femoral CVC. Since imprecision of TPTD-room might be reduced by a larger volume of injectate, it was the aim of our study to compare CI, GEDVI and EVLWI derived from TPDT using 20 ml room temperature injectate with standard TPTD with 15 ml iced saline.
Methods In 31 patients 236 sets with two 20 ml TPTDs with 21°C and subsequently two standard TPTDs with 4°C saline were obtained using the PiCCO-2 device with the latest algorithm correcting GEDVI for femoral TPTD (Pulsion Medical Systems, Germany).
Results Fifteen female and 16 male patients, APACHE II score 21 ± 7. Mean values of CI (4.02 ± 0.98 vs. 3.96 ± 0.91 l/minute*m^2; P <0.001), GEDVI (800 ± 166 vs. 796 ± 163 ml/m^2; P = 0.011) and EVLWI (10.3 ± 3.7 vs. 9.7 ± 3.6 ml/kg; P <0.001) were slightly higher when measured at room temperature compared with cold saline. Mean bias and PE values were 0.06 ± 0.37 l/minute*m^2 and 18.6% for CI, 4 ± 81 ml/m^2 and 20.2% for GEDVI and 0.5 ± 1.1 ml/kg and 22.7% for EVLWI. Bias values in case of femoral compared with jugular indicator injection were not significantly different for CI (0.04 ± 0.41 vs. 0.11 ± 0.30 l/minute*m^2; P = 0.161) and EVLWI (0.56 ± 1.19 vs. 0.42 ± 1.07 ml/kg; P = 0.492). Bias for GEDVI-room was significantly lower for femoral CVC compared with jugular indicator injection (–6.0 ± 81.1 vs. 18.9 ± 78.3 ml/m^2; P = 0.008).
Conclusion Compared with previous data using 15 ml room-temperature injectate, our data with 20 ml room-temperature injectate in general provide acceptable bias and percentage error when compared with standard TPTD with 15 ml iced saline. This also applies for femoral CVC room-temperature TPTD which might also be related to a new PiCCO-2 algorithm correcting for femoral CVC site.
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P169

Transpulmonary thermodilution-derived haemodynamics in patients with liver failure: a prospective study in 351 patients

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Introduction Patients with acute or chronic liver failure are considered to have an altered pattern of haemodynamics. Nevertheless, there is a lack of studies systematically investigating haemodynamics in patients with liver failure. Therefore, it was the aim of this study to compare transpulmonary thermodilution (TPTD)-derived haemodynamics of 112 patients with acute or chronic liver failure with 239 patients without liver failure.
Methods We analyzed a prospectively maintained database including 6,016 TPTD measurements in 351 patients. To account for different numbers of TPTDs in different patients, comparison of first measurements of patients with and without liver failure was the primary endpoint. Statistics: Wilcoxon test for unpaired samples; IBM SPSS Statistics 22.
Results A total of 207 male and 144 female patients, APACHE II score 21 ± 7, 62 ± 14 years old, one to 126 TPTDs per patient. Diagnosis: cirrhosis/liver failure n = 112 patients (31.9%), sepsis 55 (15.7%), ARDS 46 (13.1%), GI affection 21 (6.0%), cardiogenic shock 19 (5.4%), various 98 (27.9%). Patients with liver failure were slightly younger than the other patients (58 ± 11 vs. 64 ± 15 years; P <0.001). All other baseline characteristics were comparable including APACHE II (20 ± 7 vs. 21 ± 8; NS), SAPS (39 ± 12 vs. 41 ± 14; NS), height (172 ± 9 vs. 170 ± 9 cm; NS) and weight (76 ± 20 vs. 73 ± 17 kg; NS). Among haemodynamic parameters, preload markers GEDVI (753 ± 168 vs. 790 ± 226 ml/m^2; P = 0.182) and CVP (14.4 ± 8.8 vs. 14.9 ± 7.1 mmHg; P = 0.250) were comparable. Despite comparable preload parameters, the following parameters were significantly different: patients with acute or chronic liver failure had significantly higher cardiac index (4.3 ± 1.3 vs. 3.3 ± 1.3 l/minute/m^2; P <0.001), stroke volume index (50 ± 15 vs. 37 ± 15; P <0.001), pulse pressure (75 ± 19 vs. 65 ± 21 mmHg; P = 0.021) and cardiac power index (0.7 ± 0.24 vs. 0.60 ± 0.28 W/m^2; P <0.001). By contrast, MAP (77 ± 15 vs. 80 ± 15 mmHg; P = 0.045), SVRI (1,305 ± 638 vs. 1,877 ± 898 dyn*s/cm^5*m^2; P <0.001) and heart rate (84 ± 19 vs. 92 ± 22/minute; P <0.001) were significantly lower in patients with liver failure.
Conclusion Our data derived from a large TPTD database demonstrate markedly different haemodynamics in patients with cirrhosis or acute liver failure with the only exception of static preload markers GEDVI and CVP. These findings should be considered in instable patients with liver failure.

P170

Measurement of cardiac output in children: comparison between direct Fick method and pressure recording analytical method: preliminary report

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Introduction There are few methods of cardiac output (CO) estimation validated in children. The aim of this study is to investigate the reliability of an uncalibrated pulse contour method of CO estimation, the pressure recording analytical method (PRAM), in pediatric patients scheduled for diagnostic right and left heart catheterization, compared with the oxygen-direct Fick method.
Methods Cardiac index (CI) was simultaneously estimated by Fick, and PRAM applied to pressure signals recorded invasively from a femoral catheter. All measurements were performed in steady-state condition. PRAM CI measurements were obtained for 10 consecutive beats simultaneously during the Fick CI estimation. Agreement between Fick and PRAM was assessed using the Bland–Altman method. Correlation coefficient, bias, and percentage of error were calculated.
Results Forty-three CI measurements were performed in 43 patients. The data showed good agreement between CIFick and CIPRAM: r^2 = 0.98; bias –0.0074 l/minute/m^2; limits of agreement from –0.22 to 0.22 l/minute/m^2. The percentage error was 8%. Figure 1 shows the Bland–Altman plot.

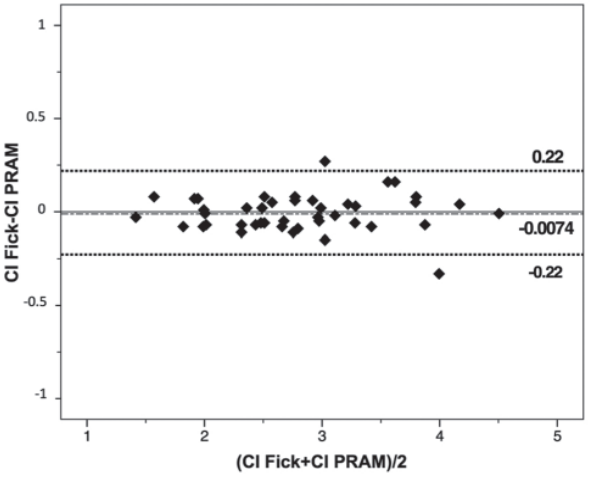


Figure 1 (abstract P170). Bland–Altman plot of the cardiac index measured with Fick versus PRAM.

Conclusion PRAM provides reliable estimates of cardiac output in hemodynamically stable pediatric cardiac patients compared with the Fick method.

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P171

Potential role of jugular vein echographic assessment for central venous pressure estimation

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Introduction Although recognized as a questionable indicator of the intravascular volume, central venous pressure (CVP) is integrated in many therapeutic algorithms for hemodynamic resuscitation of critically ill patients [1]. In an attempt to simplify CVP estimation, several clinical and ultrasonographic approaches have been suggested [2-5].

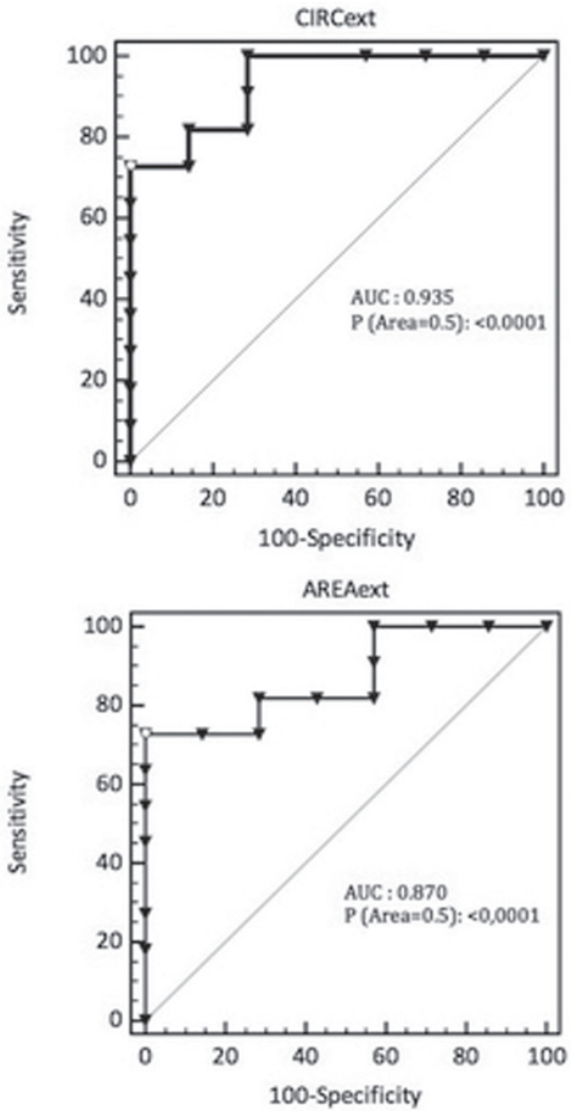


Figure 1 (abstract P171).

Nonetheless, the external jugular vein (EJV) circumference and area have not been evaluated. Considering the role of EJV visual assessment in the clinical estimation of CVP, we hypothesized that EJV ultrasound evaluation could be used to reliably estimate CVP.
Methods Patients with a CVC placed as part of clinical management were evaluated. EJV and internal jugular vein (IJV) measurements were performed at the left cricoid level. IJV and EJV were visualized in short axis view; diameters, circumferences and areas were obtained at end expiration with simultaneous CVP measurement. Measures were performed by a single trained operator, who was blind to CVP values.
Results Forty-eight patients were included. A poor correlation was found between CVP and IJV and EJV circumference and area in mechanically ventilated patients. A strong correlation was found between CVP and EJV circumference (*r*: 0.74; *P* = 0.0004; 95% CI: 0.421 to 0.897) and area (*r*: 0.702; *P* = 0.0012; 95% CI: 0.35 to 0.88) in spontaneously breathing patients. Conventional receiver-operating characteristic curves were generated to assess the utility of EJV circumference and area to predict low (≤8 mmHg) versus high (>8 mmHg) CVP values. AUC for EJV circumference and area was 0.935 (*P* <0.0001; 95% CI: 0.714 to 0.997) and 0.87 (*P* <0.0001; 95% CI: 0.63 to 0.98) respectively (Figure 1).
Conclusion These results highlight a potentially evolving role of EJV circumference and area in the hemodynamic management

of spontaneously breathing patients. An important aspect of the suggested approach is its simplicity, requiring basic technical skills and making it suitable in any scenario where an ultrasound machine is available.

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P172

Do intravascular hypovolaemia and hypervolaemia result in changes in pulmonary blood volume?

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Introduction Hypovolaemia is generally believed to induce centralisation of blood volume. Therefore, we evaluated whether hypovolaemia and hypervolaemia result in a change in central blood volume (that is, pulmonary blood volume (PBV)) and we explored the effects on the distribution between PBV and circulating blood volume (Vd circ).
Methods After local District Governmental Animal Investigation Committee approval, blood volume was altered in both directions randomly in steps of 150 ml (mild) to 450 ml (moderate) either by haemorrhage, retransfusion of blood, or infusion of colloids in six Foxhound dogs. The anaesthetised dogs were allowed to breathe spontaneously. Blood volumes were measured using the dye dilution technique: PBV was measured as the volume of blood between the pulmonary and aortic valve, and Vd circ by two-compartmental curve fitting [1,2]. The PBV/Vd circ ratio was used as a measure of blood volume distribution. A linear mixed model was used for analysing the influence of blood volume alterations on the measured haemodynamic variables and blood volumes.
Results A total of 68 alterations in blood volume resulted in changes in Vd circ ranging from −33 to +31% (Figure 1). PBV decreased during mild and moderate haemorrhage, while during retransfusion PBV increased during moderate hypervolaemia only. The PBV/Vd circ ratio remained constant during all stages of hypovolaemia and hypervolaemia (Figure 1).

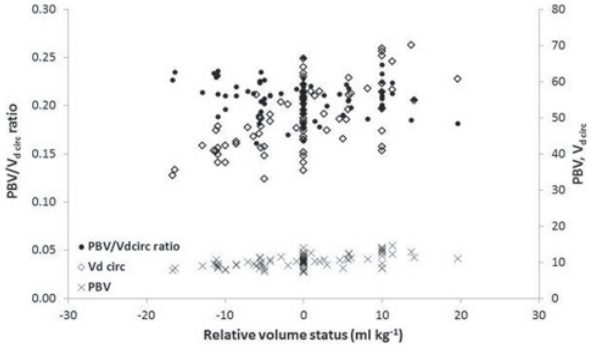


Figure 1 (abstract P172).

Conclusion Mild to moderate alterations of blood volume result in changes of PBV and Vd circ. However, against the traditional belief of centralisation we could show that the cardiovascular system preserves the distribution of blood between central and circulating blood volume in anaesthetised dogs.

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P174

Comparative study between fluidless resuscitation with permissive hypotension using the impedance threshold device versus aggressive fluid resuscitation with Ringer lactate in a swine model of hemorrhagic shock

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Introduction Permissive hypotension, which results in avoidance of intravascular overpressure and thereby avoidance of platelet plug dislodgement early in the clotting mechanism, improves the results after trauma and hemorrhage. The research hypothesis is that augmentation of negative intrathoracic pressure with the use of an impedance threshold device (ITD) will improve hemodynamic parameters, without affecting permissive hypotension or causing hemodilution. On the other hand, aggressive resuscitation with Ringer lactate will cause hemodilution and intravascular pressures that are very high for permissive hypotension, capable of platelet plug dislodgement.
Methods Twenty anesthetized Landrace/Large-White pigs (19 ± 2 kg, 10 to 15 weeks) were subjected to a fixed hemorrhage (50% over 30 minutes). The pigs were randomly allocated into two groups (n = 10 per group). In group A, ITD was the only treatment for hypotension, while in group B, an intravenous administration of 1 l Ringer lactate was applied for treatment of hypotension. Hemodynamic parameters were continuously assessed for the first 30 minutes after blood loss.
Results Mean systolic arterial pressures (SAPs) 30 minutes after the intervention in each group were as follows: group A 80 ± 5 mmHg and group B 90 ± 4 mmHg. Maximum SAPs during the assessment period were: group A 89 ± 2 mmHg and group B 128 ± 5 mmHg. Mean pulse pressure was higher in the ITD group versus the fluid resuscitation group (P <0.05). After the assessment period, mean hematocrit in group A was 24 ± 2%, while in group B it was 18 ± 1% (P <0.001).
Conclusion In our study, the ITD increased SAP and pulse pressure without overcompensation. On the other hand, aggressive fluid resuscitation led to a significant increase of SAP >100 mmHg capable of clot dislodgement and in addition led to hemodilution.

P175

Relation between global end-diastolic volume and left ventricular end-diastolic volume

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Introduction Measurement of global end-diastolic volume (GEDV) is provided by cardiovascular monitoring devices using thermodilution procedures. The aim of this study was to assess the relation between this clinically available index and left ventricular end-diastolic volume (LVEDV), which is typically not available at the patient bedside.
Methods Measurements were performed on six anaesthetised and mechanically ventilated pigs. Volume loading via successive infusions of saline solution was first performed and was followed by dobutamine infusion. These two procedures provided a wide range of LVEDV values. During these experiments, GEDV was intermittently measured using the PiCCO monitor (Pulsion AG, Germany) during thermodilutions and LVEDV was continuously measured using an admittance catheter (Transonic, NY, USA) inserted in the left ventricle.
Results Table 1 presents the linear correlations obtained between LVEDV and GEDV. These correlations are good to excellent, with r^2 values from 0.59 to 0.85. However, the coefficients of the linear regressions present a large intersubject variability, which prevents the precise estimation of LVEDV using GEDV. Nevertheless, variations in LVEDV are well reproduced by the GEDV index. The variations in LVEDV actually equal 21 to 48% of those in GEDV. The coefficient b is always nonzero, indicating that some proportion of the GEDV index is actually not linked to LVEDV.

Table 1 (abstract P175). Linear regressions between LVEDV and GEDV

Subject	*a*	*b* (ml)	r^2
1	0.26	7.64	0.82
2	0.43	–47.10	0.66
3	0.21	–12.99	0.75
4	0.25	–11.42	0.59
5	0.41	–65.42	0.85
6	0.48	–65.75	0.68

LVEDV = $a \times$ GEDV + b.

Conclusion The results show that GEDV and LVEDV are generally well correlated, but the correlation coefficients are subject specific. A preliminary calibration step (for instance using echocardiography) is thus necessary to infer LVEDV from GEDV.

P176

Volume assessment in critically ill patients: echocardiography, bioreactance and pulse contour thermodilution

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Introduction We performed an evaluation of three devices used for assessment of volume status in critically ill patients in our institution: transthoracic echocardiography (TTE) (CX50; Philips Ultrasound), bio reactance (NICOM; Cheetah Medical) and pulse contour-based thermodilution (PiCCO; Pulsion Medical).
Methods Ten mechanically ventilated critically ill patients with PiCCO monitoring *in situ* and a good quality of images on transthoracic view were included. All study measurements were made in triplicate. A single trained cardiologist, blinded to the results from the other monitors, performed the TTE study. Differences among the three methods were assessed for significance using one-way ANOVA, Spearman's coefficient and Bland–Altman analysis. All statistical analyses were performed using Graph-pad Prism 5 and $P < 0.05$ was taken as significant.
Results Ninety measurements were obtained. NICOM and TTE-derived stroke volume appeared well matched but PICCO-derived values showed significant variation ($F = 2.4$, $P = 0.09$). There was no correlation between TTE velocity time integer (VTI) and NICOM stroke volume variation (SVV) ($r = 0.24$, $P = 0.20$; Figure 1A) but a good correlation and small bias between TTE-VTI and PiCCO-SVV ($r = 0.76$, $P < 0.0001$; Figure 1B). Applying the following indications for volume expansion (PiCCO and NICOM SVV >15% and TTE VTI variability >15%) we found an agreement in 71% of cases between TTE and PiCCO and in 42% of cases between echocardiography and NICOM.
Conclusion Stroke volume produced by bioreactance appeared to be comparable with that measured by echocardiography but not with PiCCO. There was a good agreement between decision-making as regards fluid administration between PiCCO and echocardiography. NICOM appeared unreliable in this setting.

P177

Bioreactance-based passive leg raising test can predict fluid responsiveness in patients with sepsis

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Introduction Fluid administration is always important and difficult during the therapy of patients with sepsis. Accurately predicting fluid responsiveness and thus estimating whether the patient will benefit from fluid therapy seems particularly important. The present study intended to predict fluid responsiveness in patients with sepsis using a bioreactance-based passive leg raising test, and to compare this approach with the commonly used central venous pressure (CVP) approach.
Methods This prospective, single-center study included 80 patients with sepsis from the Department of Critical Care Medicine of Zhejiang Hospital. Patients were randomly assigned to either Group A or Group B, with patients of in Group A first taking the passive leg raising test and then taking the fluid infusion test, while patients in Group B followed the opposite protocol. NICOM was used to continuously record hemodynamic parameters such as cardiac output (CO), heart rate (HR) and central venous pressure (CVP), at baseline1, PLR, baseline2, and volume expansion (VE). Fluid responsiveness was defined as the change in CO (ΔCO) ≥10% after VE.
Results CO increased during PLR (from 5.21 ± 2.34 to 6.03 ± 2.73 l/minute, $P < 0.05$); and after VE (from 5.09 ± 1.99 to 5.60 ± 2.11 l/minute, $P < 0.05$). The PLR-induced change in CO (ΔCOPLR) and the VE-induced change in CO (ΔCOVE) were highly correlated ($r = 0.80$ (0.64 to 0.90)), while the CVP and ΔCOVE were uncorrelated ($r = 0.12$ (–0.16 to 0.32)). The areas under the ROC curves of ΔCOPLR and ΔCVP for predicting fluid responsiveness were 0.868 and 0.514 respectively. ΔCOPLR ≥10% was found to predict fluid responsiveness with a sensitivity of 86% and a specificity of 79%.
Conclusion Bioreactance-based PLR could predict fluid responsiveness in patients with sepsis, while CVP could not.

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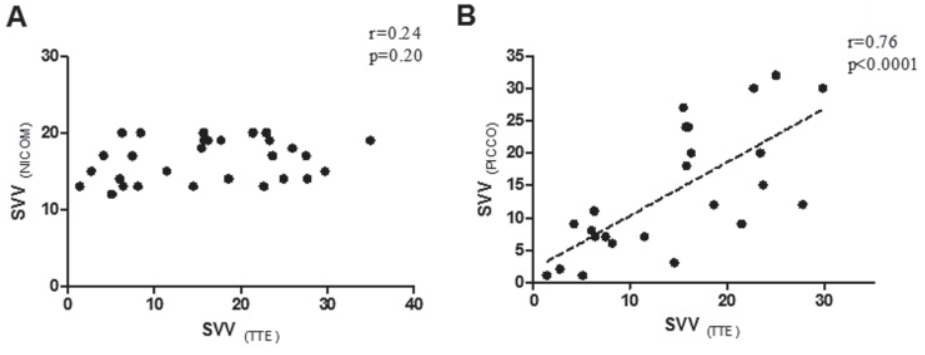


Figure 1 (abstract P176).

P178

Acute changes of metabolic parameters after fluid challenge

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Critical Care 2015, **19(Suppl 1):**P178 (doi: 10.1186/cc14258)

Introduction The detection of heart response to fluid administration is still a challenge in clinical practice. Changes in metabolic parameters may be useful to detect changes in cardiac output (CO) after fluid expansion.
Methods This is a prospective observational study in adult critically ill patients. CO was measured either by echocardiography or by a thermodilution method (PiCCO, Swan–Ganz catheter). Hemodynamic measurements and blood gas analysis were obtained before and after a fluid challenge with either 1,000 ml crystalloid or 500 ml colloid. Arterial and central venous blood gas samples were taken simultaneously. Oxygen delivery (DO_2), oxygen consumption (VO_2) and carbon dioxide production (VCO_2) were calculated according to well-known formulas. Patients were divided into three groups (high responders, mild responders and nonresponders) according to their change in CO (>20%, 10 to 20%, <10%, respectively).
Results We evaluated 27 patients, age 68 (95% CI: 61 to 74) and APACHE II score 22 (95% CI: 18 to 26). Seven patients were high responders, eight patients were moderate responders and 12 were nonresponders. DO_2 was significantly increased in high responders (37 ± 35%, P <0.01) as compared with moderate responders or nonresponders. Furthermore, nonresponders had a decrease in their DO_2 (–10 ± 7%, P <0.01), while moderate responders showed no change in their DO_2 (1.6% ± 10, P = 0.73) after fluid challenge. We found no differences in changes in lactate levels and central venous oxygen saturation ($ScvO_2$) between high responders, moderate responders and nonresponders. No differences in the changes of VCO_2 or VO_2/VCO_2 ratio were found between high responders, mild responders and nonresponders too. Changes in DO_2/VCO_2 ratio were found to be significantly increased only in high responders (47 ± 73% vs. –14 ± 31%, P = 0.02) and not in mild responders (15 ± 54% vs. –14 ± 31%, P = 0.15) as compared with nonresponders.
Conclusion Only significant increases of CO (>20%), after fluid administration, lead to improved oxygen delivery; DO_2 may be decreased in nonresponders. The changes of $ScvO_2$ and lactate levels do not track the changes of CO after fluid challenge. The DO_2/VCO_2 ratio may be a useful index to identify significant increases of CO after fluid challenge in cases where CO measurement is not feasible.

P179

Global end-diastolic volume: a better indicator of cardiac preload in patients with septic shock

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Critical Care 2015, **19(Suppl 1):**P179 (doi: 10.1186/cc14259)

Introduction The aim of the study was to assess the value of the global end-diastolic volume (GEDV) evaluated by transpulmonary thermodilution as an indicator of cardiac preload comparing with stroke volume variation (SVV) in patients with septic shock.
Methods A prospective, observational study performed in an interdisciplinary ICU including 91 patients with septic shock. Hemodynamic monitoring was performed with a new calibrated pulse wave analysis method (VolumeView/EV1000; Edwards Lifesciences) in 37 patients (group EV1000) or with an uncalibrated method (FloTrac/Vigileo; Edwards Lifesciences) in 54 patients (group Vigileo) during the first 72 hours. All patients were receiving mechanical ventilation and vasopressors. Measurements were performed before and immediately after volume loading using 500 ml Ringer solution over a short period (<30 minutes).
Results A total of 211 fluid challenges were studied in 91 patients. We observed a significant relationship between the GEDV index before volume loading and the percentage increase in GEDV index in the EV1000 group and changes in GEDV index were significantly correlated with changes in stroke volume index (r = 0.75, P <0.001), but an insignificant relationship between SVV variation and cardiac index variation (P >0.05) in the Vigileo group.
Conclusion The transpulmonary thermodilution GEDV is a better indicator of cardiac preload than SVV in patients with septic shock.
Acknowledgements This paper was cofinanced from the European Social Fund, through the Sectorial Operational Programme Human Resources Development 2007–2013, project number POSDRU/159/1.5/S/138907 'Excellence in scientific interdisciplinary research, doctoral and postdoctoral, in the economic, social and medical fields – EXCELIS'; coordinator, The Bucharest University of Economic Studies.
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P180

Predicting fluid responsiveness in ICU patients: comparison of different parameters and cutoff limits using pulse power analysis assessment

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Introduction Dynamic parameters are becoming standard for fluid responsiveness assessment. Cutoff values are different in the literature. The aim was to assess the accuracy of different preload parameters to predict fluid responsiveness using pulse power analysis and to compare different levels of hemodynamic response due to passive leg raising (PLR) against the effect of a fluid challenge (FC).
Methods A prospective study in a 17-bed mixed ICU. Patients were fully ventilated and CO monitored with LiDCOplus® and underwent a FC due to hypotension and/or hypoperfusion and preload dependence (SVV and/or PPV >10%). PLR was performed before FC. Hemodynamic data were recorded prePLR, postPLR and postFC with 0.5 l crystalloids. We compared different cutoff values of increase in CO and SV (10 to 15%) to assess the ability of PLR, SVV, PPV and CVP to predict the response to FC. Statistical analysis: continuous variables expressed as mean ± SD. Comparison before and after was done using a paired Student's t test, and receiver operating characteristic (ROC) curves were generated by varying the discriminating threshold of each variable.
Results Thirty-one patients were included. Baseline parameters: MAP 70.5 mmHg (SD 13.3) 87% under catecholamine, SV 55.32 ml (SD 20.2), CO 5.2 l (SD 2), SVV 16.8% (SD 12), PPV 19.1% (SD 14), HR 96 bpm (SD 18) and CVP 9.2 mmHg (SD 2.5). In total, 41.9% of patients increased 15% CO after FC (selected as responders), 38.7% after the PLR. Differences in responders versus nonresponder patients were: baseline SVV (23.9 vs. 11.6; P = 0.02) and PPV (28.4 vs. 12.4; P = 0.01). Differences in SV and CO were not statistically significant. The best parameter to predict positive response to FC was PLR with cutoff 12.6% for CO increase: sensitivity 84.6% (95% CI = 65 to 104), specificity 94.4% (95% CI = 84 to 105) and AU ROC 0.94 (95% CI = 0.86 to 1.0). ROC was also good for SVV 0.835 (95% CI = 0.66 to 1.0; P = 0.002) and PPV 0.833 (95% CI = 0.681 to 0.985; P = 0.002) in this cutoff value. In SV increase, PLR, SVV and PPV had P <0.05, but with worse ROC. In addition, SVV <13% identified patients who will not increase MAP with FC: sensitivity 91.7% (95% CI = 76 to 107.3%), negative predictive value 93.5 (95% CI = 80.7 to 106). CVP failed to distinguish responders from nonresponders.
Conclusion Our results support the idea that a reversible FC (PLR; CO cutoff 12.6%) is best at identifying responder patients to a FC. Dynamic parameters (SVV/PPV) are also effective when appropriate. Beat-to-beat SV and CO using pulse power analysis is a valid tool for these tests.

P181

Respiratory variations in aortic blood flow velocity and inferior vena cava diameter as predictors of fluid responsiveness in mechanically ventilated children using transthoracic echocardiography in a pediatric PICU

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Introduction Volume expansion remains the first treatment step for most children with acute circulatory failure in order to assess blood

volume status. In this way, dynamic echocardiographic parameters have been proposed in mechanically ventilated children [1,2], using the heart–lung interactions. This study aimed to investigate whether respiratory variations of aortic blood flow velocity (DELTA Vpeak ao) and inferior vena cava diameter (DELTA IVC) by transthoracic echocardiography (TTE) could accurately predict fluid responsiveness in ventilated children.

Methods A prospective observational and interventional study conducted in a pediatric ICU investigated 40 mechanically ventilated children with preserved left ventricular (LV) function using TTE. Each patient had tachycardia, hypotension, oliguria, delayed capillary refilling or hemodynamic instability despite vasopressor drugs. Intervention: standardized volume expansion (VE).

Results The VE-induced increase in LV stroke volume was ≥10% in 28 patients (responders) and <10% in 12 patients (nonresponders). Before VE, the DELTA Vpeak ao and DELTA IVC in responders was respectively higher than that in nonresponders (18.75% (12 to 32) vs. 13.5% (6 to 16) and 31% (18 to 57) vs. 17.5% (14 to 25)). The prediction of fluid responsiveness was higher with DELTA Vpeak ao (ROC curve area 0.894 (95% CI = 0.756 to 0.969), $P = 0.0001$) and DELTA IVC (ROC curve area 0.869 (95% CI = 0.717 to 0.957), $P = 0.0001$). The best cutoff value for DELTA Vpeak ao was 16% with sensitivity and specificity predictive values of 71.6% and 83.3%, respectively, and DELTA IVC was 20% with sensitivity and specificity predictive values of 88.5% and 90.9%, respectively.

Conclusion In this study, DELTA Vpeak and DELTA IVC were appropriate variables to predict fluid responsiveness by TTE in ventilated children.

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P182

Prediction of fluid responsiveness in mechanically ventilated children using dynamic and static parameters by esophageal Doppler in a pediatric ICU

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Introduction Prediction of fluid responsiveness is defined by an increase in stroke volume (SV) of at least 10% after volume expansion. Dynamic [1] and static [2] esophageal Doppler (OD) parameters have been proposed in mechanically ventilated children to guide fluid therapy. This study aimed to compare dynamic parameters using the respiratory variation in aortic blood flow with static parameters using Doppler corrected flow times (FTc) obtained by OD.

Methods A prospective, observational and interventional study was conducted in our pediatric ICU from March 2012 to September 2014. We investigated 18 mechanically ventilated children with acute circulatory failure (ACF) – tachycardia, hypotension, oliguria, delayed capillary refilling or hemodynamic instability despite vasopressor drugs – using OD for each patient. Intervention: standardized volume expansion (VE).

Results The VE-induced increase in stroke volume was ≥10% in 14 patients (responders) and <10% in four patients (nonresponders). Before VE, the DELTA Vpeak ao in responders was higher than in nonresponders (19.5% (12 to 29) vs. 11.5% (7 to 13)), whereas FTc was lower in responders than in nonresponders (262.5 milliseconds (180 to 340) vs. 285 milliseconds (205 to 300)). The prediction of fluid responsiveness was higher with DELTA Vpeak ao (ROC curve area 0.964 (95% CI = 0.756 to 1.000); $P = 0.0001$) than with FTc (ROC curve area 0.562 (95% CI = 0.314 to 0.790); $P = 0.7203$). The best cutoff value for DELTA Vpeak ao was 13% with sensitivity and specificity predictive values of 85.7% and 100%, respectively; and the best cutoff value for FTc was 265 milliseconds with sensitivity and specificity predictive values of 57.1% and 75%, respectively.

Conclusion In our study, DELTA Vpeak was the most appropriate variable to predict fluid responsiveness by OD in ventilated children with ACF.

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P183

Fluid management in mechanically ventilated children with acute circulatory failure based on the pleth variability index in a pediatric ICU

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Introduction The pleth variability index (PVI) is a new dynamic index obtained by automatic estimation of respiratory variations in the pulse oximeter waveform amplitude. This noninvasive and continuous hemodynamic monitoring has been recently proposed in mechanically ventilated patients to guide fluid therapy. We recently acquired a PVI monitor in 2014. PVI is calculated by measuring changes in perfusion index (PI) during the respiratory cycle as follows: PVI = ((PImax – Pimin) / PImax) × 100. This study aimed to investigate whether PVI at baseline can predict fluid responsiveness.

Methods In our pediatric ICU we started a prospective and observational study. Between January and November 2014, nine mechanically ventilated children were investigated using PVI and transthoracic echocardiography for each patient with acute circulatory failure (ACF): tachycardia, hypotension, oliguria, delayed capillary refilling or hemodynamic instability despite vasopressor drugs. Intervention: standardized volume expansion.

Results Significant changes in stroke volume were observed after volume loading (VL) ≥10% in eight patients (responders (R)) and <10% in one patient (nonresponder (NR)). Before VL, PVI was significantly higher in R than NR at baseline ((19.75 ± 3.15%) vs. (9% ± 0.00%), P <0.0001), and decreased significantly in R from baseline to after VL ((19.75% ± 3.15) vs. (12.5% ± 2.828), P <0.0001).

Conclusion In this study, PVI seems to predict fluid responsiveness in ventilated children with ACF.

P184

Collapsibility of jugular veins, subclavian veins and inferior vena cava as predictors of fluid responsiveness in patients on pressure support ventilation: a prospective cohort study

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Introduction The accuracy of predicting fluid responsiveness (FR) using IVC collapsibility is high in patients on controlled mechanical ventilation, but remains unknown in spontaneously breathing patients with mechanical ventilation. Also, adequate ultrasound images of IVC are difficult to obtain in a substantial number of patients. The aim of the current study is to evaluate utility of collapsibility of jugular veins (IJV) and subclavian veins (SCV) in comparison with collapsibility of IVC in patients on pressure support ventilation.

Methods Patients on pressure support ventilation were prospectively included when fluid challenges were clinically indicated. Bilateral IJV were examined at the level of cricoid cartilage. Bilateral SCV were measured where the veins crossed the clavicle. Anteroposterior diameter, cross-sectional area (CSA) of IJV and SCV were measured using frame by frame analysis. IVC was measured 2 cm from the right atrial border in a long axis view. Fluid responsiveness was defined as 8% increase of stroke volume calculated by the Vigileo monitor (Vigileo, FloTrac; Edwards Lifesciences) after passive leg raising (started from supine position). Receiver operating characteristic (ROC) curves were generated using EZR.

Results Twenty-nine patients (35 measurements) were included. Nineteen measurements had fluid responsiveness. The mean tidal

volume was 9.8 ml/predicted body weight. The area under the ROC curve of IVC collapsibility was 0.576 (95% confidence interval (CI): 0.38 to 0.77), while the area under the ROC curves of right IJV, left IJV, right SCV and left SCV collapsibility were 0.870 (95% CI: 074 to 1.0), 0.54 (95% CI: 0.34 to 0.74), 0.62 (95% CI: 0.43 to 0.81) and 0.54 (95% CI: 0.34 to 0.74), respectively. Greater than 11% of right jugular vein collapsibility predicted fluid responsiveness with a sensitivity of 79% and a specificity of 94%.

Conclusion Our results suggest collapsibility of the right jugular vein can be a useful predictor of fluid responsiveness in patients on pressure support ventilation, compared with other central large veins. Collapsibility of IVC does not predict FR in those patients.

P185

Passive leg raising cannot predict volume responsiveness in septic shock patients having cardiac arrhythmia

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Introduction The passive leg raising test (PLRT) is a self-volume challenge used in order to predict volume responsiveness (VR) in both spontaneous and mechanically ventilated critically ill patients. However, there were small numbers of arrhythmic patients included in previous studies. Therefore, the accuracy of the PLRT for prediction of VR in arrhythmic patient is still inconclusive. We hypothesized that the PLRT can predict VR in mechanically ventilated patients having cardiac arrhythmia.

Methods Mechanically ventilated patients having cardiac arrhythmia who have been considered for volume expansion were recruited in this prospective study. Each patient was sedated, paralyzed and monitored with a central venous catheter and a thermistor-tipped femoral arterial VolumeView catheter connected to the EV1000 monitor. We assessed hemodynamic changes after PLRT via a pulse wave contour analysis method. Then we compared it with hemodynamic changes after volume expansion (NSS 500 ml in 15 minutes) via the transpulmonary thermodilution (TPTD) method.

Results A total of 17 patients were included in this study. Six patients were volume responders (TPTD cardiac index change ≥15%). A PLRT change cardiac index ≥10% from the pulse wave contour analysis method had predicted VR with a sensitivity of 50%, a specificity of 72.7% and an area under the ROC curve of 0.591 ($P = 0.546$).

Conclusion The PLRT may not be used for prediction of VR in mechanically ventilated patients having cardiac arrhythmia; however, further and larger studies are needed to confirm this finding.

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P186

Return on investment for implementation of perioperative goal-directed therapy in major surgery: a nationwide database study

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Introduction Preventable postsurgical complications are increasingly recognized as a major healthcare burden. A recent meta-analysis showed a 17 to 29% decrease in complications after major surgery with perioperative goal-directed therapy (PGDT) [1]. We assessed the financial consequences of postsurgical complications in a large population from 541 US hospitals in order to predict potential savings with PGDT.

Methods Data from adults who had any one of 10 major noncardiac surgical procedures between January 2011 and June 2013 were selected from the Premier research database. Twenty-six postsurgical complications were tabulated. Hospital costs, length of stay, and readmission rates were compared in patients with and without complications. Risk ratios reported by Pearse's meta-analysis were used to estimate the expected reduction in postsurgical morbidity with PGDT. Potential cost-savings were calculated from the actual and anticipated morbidity rates using the mean difference in total costs.

Results A total of 204,680 patients met the search criteria, and 76,807 patients developed one or more postsurgical complications (morbidity rate 37.5%). In patients with and without complications, hospital costs (including 30 days readmission costs) were $27,607 ± 32.788 and $15.783 ± 12,282 ($P$ <0.0001), median (interquartile range) hospital lengths of stay (first stay) were 7 (4 to 10) days and 4 (3 to 5) days (P <0.0001), and 30-day readmission rates were 17.2% and 11.9% (P <0.0001), respectively. With PGDT, the morbidity rate was anticipated to decrease from 26.6 to 31.1%, yielding gross cost savings of $153 million to 263 million for the study period, $61 million to 105 million per year, or $754 to 1,286 per patient.

Conclusion Postsurgical complications occurred in more than one-third of our study population and had a dramatic impact on hospital costs, length of stay, and readmission rates. Potential cost savings with PGDT were $754 to 1,286 per patient. These projections should help hospitals estimate the return on investment for implementation of PGDT.

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P187

Assessing fluid status with the vascular pedicle width: relationship to IVC diameter, IVC variability and lung comets

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Introduction This study attempts to determine a vascular pedicle width (VPW) cutoff value that identifies a fluid replete state defined as an IVC diameter ≥2 cm and ≤15% respiratory variation.

Methods In a cross-sectional design, consecutive, critically ill patients underwent simultaneous chest radiographs and ultrasounds. The Research Ethics Committee approved the study.

Results Eighty-four data points on 43 patients were collected. VPW correlated with IVC diameter ($r = 0.64$, $P \leq 0.001$) and IVC variation ($r = -0.55$, $P \leq 0.001$). No correlation was observed between VPW and number of lung comets ($r = 0.12$, $P = 0.26$) or positive fluid balance ($r = 0.3$, $P = 0.058$). On multivariate linear regression, standardized coefficients demonstrated that a 1 mm increase in IVC diameter corresponded to a 0.28 mm (Beta) increase in VPW. ROC curve analysis yielded an AUC of 0.843 (95% CI = 0.75 to 0.93), $P \leq 0.001$ and provided the best accuracy with a cutoff VPW value of 64 mm (sensitivity 81%, specificity 78%, PPV = 88.5%, NPV = 66%, correct classification rate = 79.6%). See Figure 1.

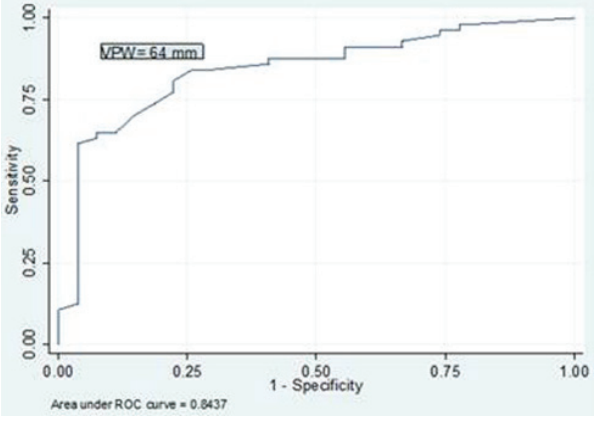


Figure 1 (abstract P187). ROC curve for VPW discriminating fluid repletion by IVC ultrasound.

Conclusion A VPW value of 64 mm accurately identifies a fluid replete state. Increased extravascular lung water, however, was not relatable to the VPW measurements. The VPW can be confidently used to discriminate fluid repletion from fluid responsiveness.

P188

Bioimpedance as a measure of fluid overload in patients recently admitted to intensive care

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Introduction Fluid overload is associated with adverse outcomes in critical illness; however, better methodology is required for its quantification. Bioelectrical impedance analysis (BIA) represents a non-invasive method for quantification of fluid overload [1], but has not been widely taken up in the ICU.
Methods We assessed changes in fluid balance and performed daily BIA (using a Maltron BioScan 920-II; Maltron International Ltd, UK) over 3 days in consecutive ICU admissions with LOS >72 hours.
Results Of 24 patients 71% were male, median age was 65 years and APACHE II score was 15. Eleven patients had a medical diagnosis and 13 a surgical or trauma reason for admission. Seventy-one percent were mechanically ventilated and 67% were on vasopressors or inotropes. Median BIA-estimated extracellular water was 25.2 l (IQR 22 to 28) on day 1, equating to excess fluid of 7.2 l (IQR 5 to 13.9). Median right body resistance normalized to height at 50 kHz (R50/h) on day 1 was 214 Ω/m (IQR 187 to 256). Daily change in ECW and R50/h correlated with daily fluid balance between BIA measurements (R^2 = 0.48 and 0.37 respectively) (Figure 1).
Conclusion BIA suggests many patients already have significant fluid overload on the first day of ICU admission. Overall, changes in device-specific algorithms for ECW estimation and measured resistances correlated with recorded fluid balance; however, there were inconsistencies in the number of individual patients. Prospective assessment is required to establish whether BIA measurements can be used to assist fluid management in the ICU.
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P189

Minimal volume for a fluid challenge in postoperative patients

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Introduction An effective fluid challenge should increase the mean systemic filling pressure (Pmsf) in order to increase the venous return. The objective of this study was to determine the minimum volume of intravenous fluid required to significantly increase the Pmsf.
Methods Patients following cardiac surgery were randomly allocated to receive 1, 2, 3 or 4 ml/kg (body weight) of crystalloid over 5 minutes using a 60 ml syringe. Pmsf was measured using the arterial pressure after stopping blood flow in the arm with a pneumatic tourniquet inflated for 1 minute. Cardiac output (CO) was also recorded at baseline and immediately after the fluid infusion. CO was measured with LiDCO or pulmonary artery catheter, and a positive response was considered an increase of 10% from baseline. From previous data, the least significant change for Pmsf was 15%. Medians were compared using the independent samples media test, and proportions were compared using a chi-square test. Statistical significance was considered when P <0.05.
Results Fifty patients were included, 40.8% of them were responders. The proportion of responders increases with the increase of dose of fluids (Table 1). The regression equation was: change of Pmsf (%) = 4.4 (dose of fluids ml/kg, 95% CI 2.3 to 6.5) – 1.6 (95% CI 7.4 to 4.3, R^2 = 0.28, F(1.47) = 17.8, P <0.001). The predicted dose of fluids required to achieve a change in Pmsf of 15% is 3.7 ml/kg crystalloids.

Table 1 (abstract P189). Change of Pmsf-arm and CO

	1 ml/kg (n = 12)	2 ml/kg (n = 12)	3 ml/kg (n = 13)	4 ml/kg (n = 13)	P
ΔPmsf-arm (%)	0.0 (–4 to 9)	6.5 (3 to 21)	9.0 (8 to 16)	18 (9 to 21)	0.05
ΔCO (%)	3.9 (0.4 to 10)	6 (2.1 to 9.1)	9.9 (–1.6 to 14.3)	12.9 (2.6 to 23.5)	0.1
Responders (%)	25.0	18.2	46.2	69.2	0.04

Values are median (interquartile range).

Conclusion The minimum volume required to perform an effective fluid challenge is 4 ml/kg infused in 5 minutes. However, only 30% of the variation of change in Pmsf can be explained by the dose of i.v. fluid given. The proportion of responders increases with the volume of fluids.

P190

Positive fluid balance is an independent risk factor for acute kidney injury in critically ill patients: results of a prospective, cross-sectional study

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Introduction In critical illness, fluid overload may predispose to acute renal dysfunction by a number of mechanisms. Once acute kidney

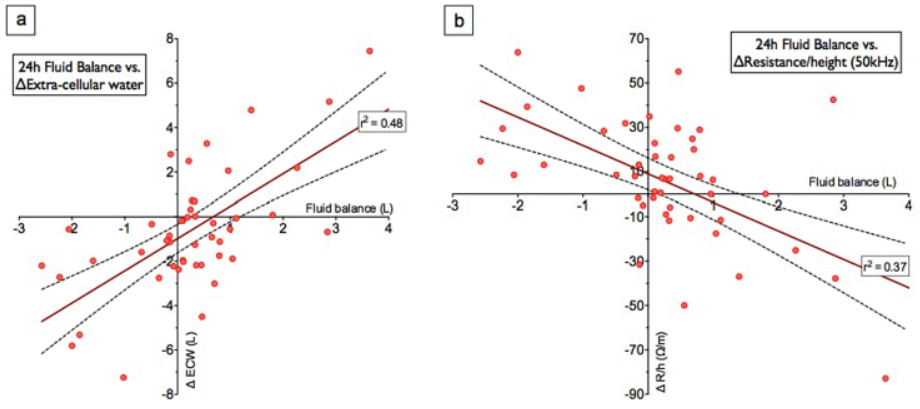


Figure 1 (abstract P188). Change in BIA-measured ECW **(a)** or R/h at 50 kHz **(b)** versus daily fluid balance.

injury (AKI) develops, positive fluid balance has been described as a risk factor for overall mortality and delayed renal recovery. We hypothesized that fluid overload may be an independent risk factor for AKI in the critically ill.
Methods In a cross-sectional design, we collected data on consecutive, critically ill, adult patients admitted over a 5-month period to the medical and surgical ICUs of a single center. AKI was defined according to the RIFLE Classification. Logistic regression analysis was performed to determine the predictive ability of variables for AKI. The institutional Research Ethics Committee approved the study.
Results Three hundred and thirty-nine patients were included; mean age was 51 ± 20.4 years, 167 (49%) patients were male. Mean APACHE II score was 22 ± 12.8 and SAPS II score was 35.4 ± 18.9. Severe sepsis/septic shock was the admitting diagnosis in 129 (38%) patients, 108 (32%) patients were postoperative. AKI developed in 148 (44%) patients; Risk 29 (9%); Injury 26 (8%); Failure 89 (26%) by the RIFLE criteria. On univariate regression analysis; positive fluid balance >2 l on the first ICU admission day, OR 2 (95% CI = 1.3, 3.3, P = 0.002); age, OR 2.7 (95% CI = 1.7, 4.2, P = 0.000); CHF, OR 3.1 (95% CI = 1.2, 7.9, P = 0.013); APACHE II score, OR 1.02 (95% CI = 1.0, 1.04, P = 0.006); SAPS II score, OR 1.04 (95% CI = 1.02, 1.05, P = 0.000); mean MAP on admission, OR 0.98 (95% CI = 0.96, 0.99, P = 0.033); need for vasopressors on admission, OR 2.7 (95% CI = 1.7, 4.2, P <0.001) and for >24 hours, OR 2.7 (95% CI = 1.7, 2.5, P <0.001); and vancomycin use, OR 1.5 (95% CI = 1.02, 2.53, P = 0.04) significantly predicted the development of AKI. On multivariate regression, CHF, OR 3.8 (95% CI = 1.4, 10, P = 0.007); age, OR 1.02 (95% CI = 1.01, 1.03, P = 0.001); vasopressors for >24 hours, OR 2.6 (95% CI = 1.6, 4.2, P <0.001) and a >2 l positive fluid balance on the first ICU day, OR 1.6 (95% CI = 1.02, 2.7, P = 0.04) remained significant predictors.
Conclusion Fluid overload, defined as a >2 l positive fluid balance on the first day of ICU admission, is an independent risk factor for the development of AKI in the general ICU population.

P191

Positive fluid balance as a risk factor for mortality and acute kidney injury in vasoplegic shock after cardiac surgery

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Introduction After cardiac surgery, about 15% of patients develop vasoplegic shock, characterized by systemic vasodilation, increased capillary permeability and edema. We hypothesized that large-volume resuscitation, resulting in positive fluid balances in the first 24 hours of ICU admission, would be associated with mortality and would not be protective against AKI in this subset of patients.
Methods This is a retrospective analysis of 362 patients submitted to cardiac surgery at the Heart Institute of University of São Paulo in a period of 2 years. Of a total of 2,383 patients, we enrolled 362 patients. Vasoplegic shock was diagnosed if in the 24 hours of ICU admission patients had hypotension, need of vasoactive drugs after fluid replacement and cardiac index ≥2.2 l/minute/m^2. Data were analyzed in logistic regression models for 30-day mortality and acute kidney injury through Acute Kidney Injury Network (AKIN) score as outcomes.
Results The mean age of patients was 57 years. Of 362 patients, 53 died at 30 days (14.6%). Nonsurvivors as compared with survivors were slightly older (59 ± 12 vs. 55 ± 13, P = 0.063), had a higher prevalence of AKI through AKIN score ((0) 6.9%, (1) 11.1%, (2) 28.9%, (3) 31.9%, P <0.001), a higher 24-hour fluid balance (421 ml (–55 to 695) vs. 2,686 ml (1,321 to 2,856), P <0.001), and higher lactate levels at the intraoperative and at 48 hours (5 mmol/l (4.0 to 7.6) vs. 4.4 (3.33 to 6.55), P <0.001; and 8.11 (5.49 to 12.3) vs. 1.5 (1.33 to 1.88), P <0.001). In the multivariate analysis, positive fluid balance in the first 24 hours (OR = 1.006, 95% CI = 1.003 to 1.008, P <0.001) and higher lactate after 48 hours (OR = 1.204, 95% CI = 1.072 to 1.353, P = 0.002) were predictors of 30-day mortality. Forty-three percent of patients developed AKI during 30 days. In the multivariate analysis, positive fluid balance in the first 24 hours (OR = 1.001, 95% CI = 1.000 to1.001, P <0.001) and higher lactate at 48 hours (OR = 1.011, 95% CI = 1.000 to 1.021, P = 0.0043) were predictors of 30-day AKI.
Conclusion Positive fluid balance after cardiac surgery is an independent risk factor for mortality and for acute kidney injury in patients presenting vasoplegic shock.

P192

Impact of postsurgical complications on hospital costs and margins

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Introduction The impact of postsurgical complications (PSC) on hospital cost has been studied but the impact on margins remains controversial [1]. We assessed economic consequences of PSC in US Medicare patients, and benefits expected from reducing PSC by 14% to 40% with Enhanced Recovery Programs [2].
Methods Data from patients with ≥1 comorbidity and major cardiac, vascular, gastrointestinal and orthopedic surgeries in 2011 were extracted from Medicare Standard Analytic Files. Hospital margin was calculated as payment minus cost. Patients with and without PSC were compared, and the economic impact of a 14 to 40% relative reduction in PSC was calculated.
Results Of 303,432 patients, 37% had ≥1 PSC. Median length of stay was 10 days for patients with ≥1 PSC and 6 days without (P <0.0001 with vs. without PSC), with readmissions for 21% and 16%, respectively (P <0.0001 with vs. without PSC). Average margins for cases with PSC converted into without PSC would be $1,870 higher. A 14 to 40% reduction in patients with PSC (from 37% to 32% to 22%) would result in saving $153 million to $438 million, and increase hospital margins overall by $28 million to $79 million. See Table 1.

Table 1 (abstract P192)

Mean 2011 US$/patient	With PSC		Without PSC	
	Cost ($)	Margin ($)	Cost ($)	Margin ($)
Cardiac	46,535	–2,286	32,887*	–778*
Gastrointestinal	33,280	–3,088	18,942*	–752*
Orthopedic	20,798	–3,567	15,194*	–1,872*
Vascular	31,042	–4,782	17,667*	–2,267*

*P <0.0001 with versus without PSC.

Conclusion Postsurgical complications have a significant impact on hospital margins. Enhanced Recovery Programs have the potential not only to improve quality of care but also to improve hospital margins.
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P193

Lactate levels after major cardiac surgery are associated with hospital length of stay

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Introduction The objective of the study was to evaluate whether postoperative lactate values are associated with hospital length of stay in patients undergoing major cardiac surgery. Previous studies have shown an association between postoperative lactate levels and increased morbidity and mortality after major cardiac surgery. However, the association between lactate and hospital length of stay has not been adequately characterized.
Methods We performed a retrospective analysis of all patients presenting for coronary artery bypass grafting and/or valve surgery between 2002 and 2014 at a tertiary care center in Boston, who had a lactate level measured within 3 hours of skin closure. Lactate values

were categorized into clinical meaningful categories: 0 to 2 mmol/l (normal), 2 to 4 mmol/l (elevated) and ≥4 mmol/l (high) to allow for nonlinear effects. The unadjusted association between lactate group and length of stay was assessed with the Kruskal–Wallis test and *post hoc* Wilcoxon rank-sum tests. To assess the association between postoperative lactate levels and hospital length of stay we performed multivariable Poisson regression with robust variance estimates. We adjusted for more than 30 variables including patient demographics, comorbidities, cardiac characteristics (for example, New York Heart Association class and ejection fraction), and surgical characteristics (for example, year, status (elective, urgent, emergent), type of procedure, perfusion time, and cross clamp time).
Results We included a total of 1,267 patients. The median age was 68 (quartiles: 59, 76), 32% were female, 68% underwent coronary artery bypass grafting and 59% underwent valve surgery. Median length of hospital stay was 6 days (quartiles: 5, 9). Median length of stay in the normal, elevated and high lactate groups were 5 days (quartiles: 4, 7), 6 days (quartiles: 5, 9) and 9 days (quartiles: 6, 17), P <0.001 for comparison. In multivariable analysis, patients with an elevated lactate had a 1.12 times (95% CI: 1.02 to 1.23, P = 0.02) longer length of stay compared with those with normal lactate. Patients with a high lactate had a 1.30 times (95% CI: 1.10 to 1.53, P = 0.002) longer length of stay compared with those with normal lactate.
Conclusion Postoperative lactate levels are associated with increased length of hospital stay in patients undergoing major cardiac surgery. Interventions aimed at decreasing postoperative lactate levels may decrease hospital length of stay.

P194

Hemodynamic behavior in a randomized trial of intensive alveolar recruitment after cardiac surgery

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Critical Care 2015, **19(Suppl 1):**P194 (doi: 10.1186/cc14274)

Introduction The potential benefits of a protocol of intensive alveolar recruitment may be outweighed by its detrimental effects in hemodynamic stability after cardiac surgery. The aim of this study was to analyze the hemodynamic behavior of patients included in a trial of intensive alveolar recruitment after cardiac surgery.
Methods In this randomized trial, we assigned adult patients with PaO_2/FIO_2 <250 at a PEEP of 5 cmH_2O to either intensive alveolar recruitment or a standard protocol, both using low-tidal volume ventilation (6 ml/kg/ibw) after adequate volemia status. Our hypothesis was that an intensive alveolar recruitment protocol with controlled pressure of 15 cmH_2O and PEEP of 30 cmH_2O during 1 minute, repeated three times at 1-minute intervals between each maneuver, would not cause hemodynamic instability.
Results In total, 163 patients were included in the standard and 157 in the intensive group. Patients of the intensive group had a significant reduction of the MAP at T1, T2 and T3 (1 hour, 2 hours and 3 hours of the protocol), returning to baseline after T4 (Figure 1). No patients had severe hypotension (MAP <65 mmHg) and the study was not stopped in any case. The length of the hospital stay was shorter among patients in the intensive group (10.9 (9.9 to 11.9) vs. 12.4 days (11.3 to 13.6); P = 0.045).
Conclusion An intensive alveolar recruitment protocol did not result in hemodynamic instability in hypoxemic patients after cardiac surgery (NCT01502332).

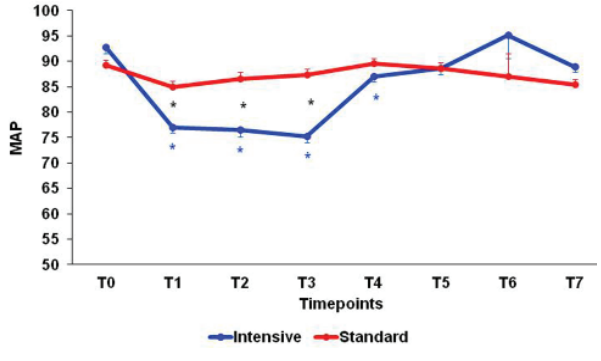


Figure 1 (abstract P194).

P195

Team-based extubation protocol in cardiac surgical patients reduces ventilation time and reduces length of stay in the ICU

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Critical Care 2015, **19(Suppl 1):**P195 (doi: 10.1186/cc14275)

Introduction National University Hospital, Singapore, recently formed a Division of Critical Care – Respiratory Therapy. This service rapidly expanded to provide 24/7 Respiratory Therapy Services in the cardiothoracic intensive care unit (CTICU). One goal of service expansion was a reduction in duration of mechanical ventilation after cardiac surgery. We hypothesized that introduction of a team-based extubation protocol would reduce the duration of mechanical ventilation and ultimately affect ICU length of stay.
Methods A multidisciplinary group created a team-based extubation protocol. The protocol was applied to all elective postoperative cardiac surgery patients. To assess the protocol's impact, data were collected in a registry 3 months before and 3 months after protocol initiation. Data collection included cardiopulmonary bypass time, McCormack airway assessment, ICU admission time, initial pH, lactate, inotropes upon arrival at the CTICU, blood gas analysis prior to extubation, time of extubation and length of stay. Patients were excluded from data analysis if they experienced events which contraindicated application of the protocol, such as significant intraoperative or postoperative complications. These events were explicitly stated in the extubation protocol. Singapore's Domain-specific review board granted waiver of patient consent to analyze and present these data.
Results A total of 201 patients undergoing elective open cardiac surgery were included; 99 patients before protocol implementation (pre-protocol) and 102 patients after implementation (post-protocol). There was no significant difference in mean age (60 vs. 61 P = 0.823), gender (79.8% vs. 79.4% P = 1.00), EuroSCORE (26 vs. 32 P = 0.576) and proportion receiving bypass surgery (72% vs. 80% P = 0.206) or valve surgery (21% vs. 19% P = 0.722) between the two groups. Median extubation time was reduced by 3.5 hours (620 minutes vs. 408 minutes P <0.001). ICU length of stay was also reduced following introduction of the pre-protocol 48 hours versus 24 hours post protocol (P <0.05).
Conclusion A team-based extubation protocol significantly reduced the duration of mechanical ventilation and this translated to reduced ICU length of stay in patients undergoing elective open-heart surgery.

P196

Impact of patient frailty on outcome in cardiothoracic surgery

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Introduction Frailty is defined as a multidimensional syndrome involving loss of physical and cognitive reserve leading to greater vulnerability to adverse events [1]. Such events include susceptibility to unplanned hospital admissions, and death [1-3]. Frailty is associated with increased ICU and 6-month mortality, and reduced quality of life [4]. The aim of this study is to investigate the impact of baseline frailty on postoperative quality of life indicators and postoperative frailty following cardiothoracic surgery.
Methods Adult patients undergoing cardiac surgery or thoracic surgery (involving thoracotomy) were included in this study. Baseline measures of frailty [4] and performance status were prospectively recorded using validated tools. Informed consent was obtained prior to inclusion. Outcome measures of APACHE II scores, duration of ventilation, length

of ICU stay and mortality were recorded. Follow-up at 6 months was conducted by telephone to assess recovery patterns.
Results A total of 120 patients were included in this study, including 100 patients who underwent cardiac surgery and 20 patients who underwent thoracic surgery. Eighty-five patients (70.8%) were male. The mean age was 65.4 years (range 25 to 89 years). The mean baseline frailty score also varied widely within our cohort. Four patients died in the ICU following their surgery (3% ICU mortality rate). Mean length of ICU stay was 2.7 days (range 0 to 20 days), with a mean duration of ventilation of 20 hours (range 0 to 264 hours). Follow-up of these patients at 6 months following their surgery is currently underway.
Conclusion Owing to advances in life expectancy, health and perioperative medicine, it has become more difficult to determine fitness for major surgery. Our data suggest that frailty may be a useful prognostic measure to help inform such decisions.
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P197

Preoperative intra-aortic balloon counterpulsation in cardiac surgery: propensity analysis of data obtained from the ARIAM Registry of Cardiac Surgery

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Critical Care 2015, **19(Suppl 1):**P197 (doi: 10.1186/cc14277)

Introduction The aim of our study was to assess whether the preoperative use of IABP is beneficial in patients undergoing cardiac surgery of any kind.
Methods An observational, retrospective, multicenter study of all patients undergoing cardiac surgery and included in the ARIAM-ANDALUCIA Registry of Cardiac Surgery from March 2008 to July 2012. The probability of placing IABP in the preoperative period has been calculated, making a propensity analysis to obtain two homogeneous groups treated with or without the IABP, based on personal history, functional status and type of surgery. Seventy-seven patients with preoperative IABP were matched with 77 patients without BCIAO with the nearest propensity score. We used the chi-square test or Student *t* test as needed and binary logistic regression for multivariate analysis so we can rule out possible confounding variables. We used the statistical package R v2.12 for MAC.
Results A total of 8,026 were recorded, in 77 of them an IABP was inserted before the surgery. We performed a propensity score analysis by pairing 72 patients with and without BCIAO based on epidemiological factors and type of surgery. In the analysis of all-cause 30-day mortality, 27% of patients in whom IABP was inserted prior surgery died versus 13.1% of patients without IABP preoperative implantation ($P = 0.043$). A combined endpoint that included need for prolonged mechanical ventilation over 24 hours or reoperation or mediastinitis or stroke after surgery or 30-day mortality was performed and occurred in 58.3% of patients with preoperative IABP versus 41.7% without it ($P = 0.046$). When stratified by preoperative risk (analyzed with EuroSCORE), no difference between groups was observed ($P = 0.62$, OR 0.75 (0.23 to 2.35)) for mortality rate and ($P = 0.11$, OR 0.47 (0.19 to 1.18)) for the combined endpoint. The patients with preoperative IABP implantation had a higher ICU length of stay (10.6 ± 7.7 vs. 4.6 ± 6.7, $P = 0.046$) with no differences in terms of overall hospital stay (21.8 ± 18.7 vs. 18.9 ± 22.08, NS).
Conclusion The use of IABP prior to cardiac surgery in patients at high risk does not reduce the mortality rate nor the combined endpoint described above. ICU length of stay was greater in those patients in whom IABP was implanted prior to surgery; there were no differences in overall hospital stay.

P198

Intraortic balloon pump use in cardiac surgery: analysis of data from the ARIAM Registry of Cardiac Surgery

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Introduction The aim of the study is to analyze IABP use in patients undergoing cardiac surgery included in the ARIAM Registry of Cardiac Surgery.
Methods An observational, retrospective, multicenter study of all patients undergoing cardiac surgery included in the ARIAM-ANDALUCIA database of Cardiac Surgery from March 2008 to July 2012. We used the chi-square test and Student *t* test as needed, establishing the level of statistical significance at 95%.
Results Of the 8,026 patients who underwent cardiac surgery during the study period, BCIAO was implemented in 358 (4.5%) of them. In total, 65.4% were male. Surgical times in those patients where IABP was implanted were 146 ± 81 minutes and 90 ± 66 minutes (cardiopulmonary and aortic clamping times, respectively). The in-surgery room mortality was 4.7%, 30-day mortality in these patients was 40.2%. Patients in whom IABP was implanted had a mortality rate eight times higher than those who did not require it during surgery or postoperatively (40.2% vs. 8.4%, $P = 0.0001$. OR 8.1, 95% CI (6.4 to 10.3)). Besides mortality was higher, the later IABP was implanted the higher the mortality rate was (29.6% of the preoperative, 44.2% of surgical and 54.4% of those starting in ICU, $P = 0.015$). The ICU length of stay was 9 ± 22 days while the hospital length of stay was 21 ± 28 days. In patients who needed IABP, the ICU stay was higher than for those who did not need it (9 ± 22 vs. 5 ± 10 days, $P = 0.002$) whereas there was no difference in hospital stay (21 ± 28 vs. 20 ± 24 days, $P = 0.054$).
Conclusion The intra-aortic balloon pump was used by 4.5% of surgeries performed during the study period and in patients with an increased risk of perioperative complications, estimated by EuroSCORE. ICU length of stay was higher in patients requiring IABP, with no differences in overall hospital stay. Mortality rate was 40% higher, and increases with the delay in the implantation.

P199

Vasoplegic syndrome in cardiac surgery: role of synergism between polymorphism of tumor necrosis factor beta and plasminogen activator inhibitor type 1

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Introduction Cardiopulmonary bypass can lead to postoperative hemodynamic disorders. Several genetic polymorphisms have been studied in this setting. We investigated the possible existence of a synergism between polymorphisms of plasminogen activator inhibitor type 1 (PAI-1) and tumoral necrosis factor beta (TNF-B) on hemodynamic response after cardiac surgery.
Methods We prospectively studied the association between hemodynamic response and polymorphisms of TNF-B and PAI-1 in 563 patients undergoing elective cardiac surgery during the years 2008 to 2011. We tested the Hardy–Weinberg equilibrium in the sample. V18 SPSS was used.
Results We studied 563 patients. We found significant differences in TNF-B polymorphisms regarding norepinephrine requirements at 4 hours (F: 15.9; $P < 0.001$), *post hoc* Scheffé (GG vs. AA, 0.32 (0.11 to 0.65) vs. 0.06 (0.04 to 0.09) μg/kg/minute, $P < 0.001$; GG vs. AG, 0.32 (0.11 to 0.65) vs. 0.06 (0.03 to 0.08), $P < 0.001$)) and at 24 hours (F: 8; $P = 0.005$), *post hoc* Scheffé (GG vs. AA, 0.27 (0.01 to 0.52) vs. 0.10 (0.06 to 0.14), $P = 0.019$; GG vs. AG, 0.27 (0.01 to 0.52) vs. 0.07 (0.04 to 0.09), $P = 0.003$)). Unfavorable TNF-B (G homozygous vs. allele A) and PAI-1 unfavorable (4G homozygous vs. allele 5G) were grouped, after adjusting for perioperative significant variables. The homozygous GG and 4G alleles were significant for NA 4 hours (F: 5.5; $P = 0.02$ and F: 4.1; $P = 0.04$, respectively) and GG–4G allele interaction (F: 6; $P = 0.01$) (Figure 1),

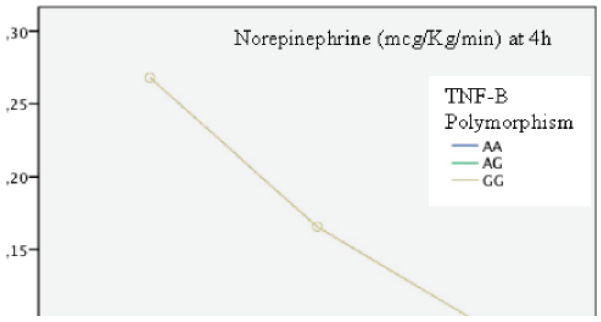


Figure 1 (abstract P199).

while for NA at 24 hours statistics showed GG (F: 3.2; $P = 0.07$), 4G allele (F: 2; $P = 0.15$) and interaction (F: 3.6, $P = 0.05$).

Conclusion GG homozygous polymorphism TNF-B is associated with an increased dependence on norepinephrine after cardiopulmonary bypass, showing a synergistic action with the 4G allele of PAI-1.

P200

Pharyngeal oxygenation during apnoea following conventional pre-oxygenation and high-flow nasal oxygenation

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Introduction We hypothesised that pharyngeal oxygen concentrations would be maintained higher and for longer with transnasal humidified rapid insufflation ventilatory exchange (THRIVE) than conventional bag-mask pre-oxygenation (CPO). CPO requires the mask to be removed during laryngoscopy; this means that air may enter the mouth so subsequent apnoeic oxygenation will be less effective. Oral suctioning could exacerbate this process. However, if high pharyngeal oxygen concentrations and an open airway are maintained, apnoeic oxygenation could be substantially improved. Methods used have included NO-DESAT [1] and recently THRIVE [2], which has been shown to extend apnoea times for up to 1 hour.

Methods A volunteer with a nasopharyngeal sampling catheter underwent simulated emergency airway management (EAM), using both CPO and THRIVE, with and without suction. Following 3 minutes of pre-oxygenation with CPO ($FiO_2 = 1$, $FEO_2 > 0.8$) or THRIVE (60 l/minute; Optiflow, Fisher and Paykel), EAM was simulated by voluntary apnoea and pharyngoscopy with the laryngoscope blade tip placed 2 cm from the posterior pharyngeal wall. Capnography at the laryngoscope tip confirmed apnoea. Pharyngeal gas samples (20 ml) were collected during apnoea, and after 5 seconds of oropharyngeal suctioning. Pre-oxygenation was repeated between sampling. Samples ($n = 100$) were analysed using calibrated fuel cells.

Results Pharyngeal oxygen concentrations (mean and SEM) are shown in Figure 1 (all points are significant $P < 0.05$).

Conclusion Pharyngeal oxygen concentration rapidly falls following CPO. This may be detrimental for apnoeic oxygenation during conventional laryngoscopy. Conversely, THRIVE maintains high pharyngeal oxygen concentrations over time. Suction has an immediate negative effect on pharyngeal oxygen concentration that is attenuated by THRIVE. Assessment of NO-DESAT (15 l/minute) was abandoned due to discomfort.

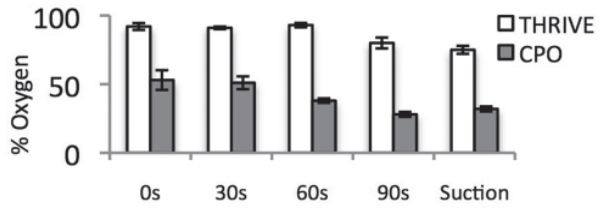


Figure 1 (abstract P200). Pharyngeal oxygen concentration.

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P201

Effects of high-flow nasal cannula therapy on oxygenation, lung volumes and CO_2 removal in critically ill hypoxemic patients: preliminary results

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Critical Care 2015, **19(Suppl 1):**P201 (doi: 10.1186/cc14281)

Introduction High-flow nasal cannula (HFNC) is increasingly proposed as respiratory support for hypoxemic non-intubated acute respiratory failure patients. Clinically, HFNC therapy decreases dyspnea, improves patient's comfort, improves oxygenation and enhances clearance of upper airway secretions [1]. We present preliminary results from a clinical study aimed at measuring the effects of HFNC on gas exchange, lung volumes and inspiratory effort in hypoxemic non-intubated critically ill patients.

Methods We performed a prospective randomized cross-over study on hypoxemic non-intubated patients ($PaO_2/FiO_2 \leq 300$ mmHg) admitted to the ICU of the San Gerardo Hospital and prescribed to receive oxygen by facial mask. We delivered the same air/oxygen mix by HFNC (Optiflow; Fisher & Paykel Healthcare, Auckland, New Zealand) and facial mask (20 minutes per step). Continuous recordings of regional lung volumes by EIT (Pulmovista 500; Drager Medical GmbH, Lubeck, Germany) and of inspiratory effort by esophageal pressure (Pes) were obtained and analyzed offline by dedicated software.

Results We enrolled 15 patients (10 male), age 57 ± 16 years. Compared with standard facial mask, HFNC significantly improved PaO_2/FiO_2 (199 ± 60 vs. 150 ± 46, $P < 0.001$) and end-expiratory lung impedance (corresponding to aeration) (866 ± 568 au vs. baseline, $P < 0.001$). Moreover, HFNC decreased the respiratory rate (22 ± 5 bpm vs. 20 ± 5 bpm, $P < 0.001$), as well as negative Pes swings (ΔPes 8.3 ± 5 mmHg vs. 6.6 ± 1 mmHg, $P < 0.01$) and corrected minute ventilation (that is, actual MV × actual $PaCO_2$ / 40 mmHg) (49,887 ± 16,176 au vs. 41,811 ± 14,042 au, $P < 0.001$). Finally, central venous pressure increased (6 ± 5 mmHg vs. 4 ± 5 mmHg, $P < 0.01$), possibly indicating positive end-expiratory pressure effect.

Conclusion In non-intubated hypoxemic critically ill patients, HFNC improves oxygenation and end-expiratory aeration; moreover, HFNC reduces the inspiratory effort and the minute ventilation needed to maintain normal arterial CO_2 tension.

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P202

New assembled video laryngoscope: a study on efficacy and cost-effectiveness

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Introduction Video laryngoscopes have been introduced in recent years as an alternative choice to facilitate tracheal intubation. Difficulties with tracheal intubation are mostly caused by difficult direct laryngoscopy with impaired view to the vocal cords. Many endoscopic intubation laryngoscopes have been designed to visualize the vocal cords around the corner looking through a proximal viewfinder. Although they are useful devices, they have limitations for doing direct laryngoscopy and are very expensive, hence they are not used for routine tracheal intubation.

Methods A Macintosh intubating laryngoscope has been modified by attaching a waterproof USB camera with a inbuilt light source, which

is located in the same position as the light source on the standard Macintosh blade thus providing a view angle of up to 290° and the USB camera is connected to a laptop. A total of the first 50 patients who presented to the emergency department over a period of 6 months in need of intubation were included in the study and every alternate patient participated in the evaluation of the assembled video laryngoscope (VAL). Information about patient demographics and airway characteristics, Cormack-Lehane (C/L) views and the ease of intubation using the VAL was collected. Failure was defined as more than one attempt at intubation.

Results Excellent (C/L1) or good (C/L2) laryngeal exposure was obtained in 92% and 8% of patients respectively. In 25 patients in whom VAL was performed, there was a comparable or superior view. Intubation with direct laryngoscopy was successful in 95.2% of patients and VAL was successful in 95.4% of patients. Three patients from the VAL group and four patients from the direct laryngoscopy group were excluded. See Figure 1.



Figure 1 (abstract P202). New video laryngoscope connected to laptop.

Conclusion This new assembled VAL is the cheapest video-assisted laryngoscope available costing around $60, which can even be introduced into primary healthcare setup in developing countries. VAL consistently yielded a comparable or superior glottic view compared with direct laryngoscopy despite the limited or lack of prior experience with the device. Because the device can be used for both routine as well difficult tracheal intubation, it may be a helpful tool to intubate trauma cases where C-spine immobilization is unavoidable. The presented video-assisted laryngoscope is a useful tool for documentation, teaching and monitoring tracheal intubation.

P203

Availability of appropriate airway monitoring at UK in-hospital cardiac arrest

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Critical Care 2015, **19(Suppl 1):**P203 (doi: 10.1186/cc14283)

Introduction Airway complications are more common outside the operating theatre and in emergency situations. Capnography remains the gold standard of confirming correct endotracheal tube (ETT) placement, retaining high sensitivity and specificity in cardiac arrest [1]. The 2010 European Resuscitation Council guidelines for adult advanced life support recommended waveform capnography in this setting [2]. Failure to use capnography was also identified as a major contributor to airway-related morbidity and mortality in a national UK audit [3]. We sought to investigate current practice relating to the availability and use of capnography equipment cardiac arrest within UK hospitals.

Methods Between June and November 2014, a telephone survey was conducted of all UK acute hospitals with adult level 3 ICUs and an emergency department (ED). Hospitals were identified using nationally available data. A standardised telephone questionnaire was developed examining practice regarding intubation for cardiac arrest and the availability and utilisation of capnography within the ED, ICU and general wards. Questions were directed at the anaesthetist or intensive care doctor 'responding to cardiac arrest calls'. The respondent was given the option to decline participation. All data were anonymised.

Results A total of 211 hospitals met the inclusion criteria. The response rate was 100%. Arrest calls were mainly attended by anaesthesia (47.8%) and ICU doctors (38.3%) with around 2% physicians only. Most were a registrar grade (56.3%). The ability to measure $ETCO_2$ was available in all but four EDs; most used waveform capnography. A similar pattern was seen was seen in the vast majority of ICUs: a single institution reported no capnography available. However, in 141 (66.8%) of the hospitals surveyed, no facility to measure $ETCO_2$ was present on the general wards. Where available, 86.7% used capnography to confirm ETT placement. Less than 50% used $ETCO_2$ to determine CPR effectiveness and 8% to prognosticate.

Conclusion We believe this is the first study of its kind to follow NAP4 and investigate the availability of capnography throughout for use during cardiac arrest. Whilst equipment levels appear adequate (albeit not perfect) in resuscitation areas, there appears a lack of availability of suitable devices on general wards.

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P204

Using a laryngoscope and endotracheal tube succeeds in a difficult case of nasogastric tube insertion

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Critical Care 2015, **19(Suppl 1):**P204 (doi: 10.1186/cc14284)

Introduction Nasogastric (NG) tube insertion is necessary in a variety of critically ill patients for intra-abdominal decompression, prevention of aspiration, route of medication administration and nutrition. However, it often fails in patients who showed sedated or comatose mentality with poor cooperation during the procedure. Although there are many reports inserting a NG tube in difficult cases, most methods need a special guide wire, tube or nasoendoscope. We report a case of NG tube insertion in a comatose patient using a laryngoscope and endotracheal tube which are easily available.

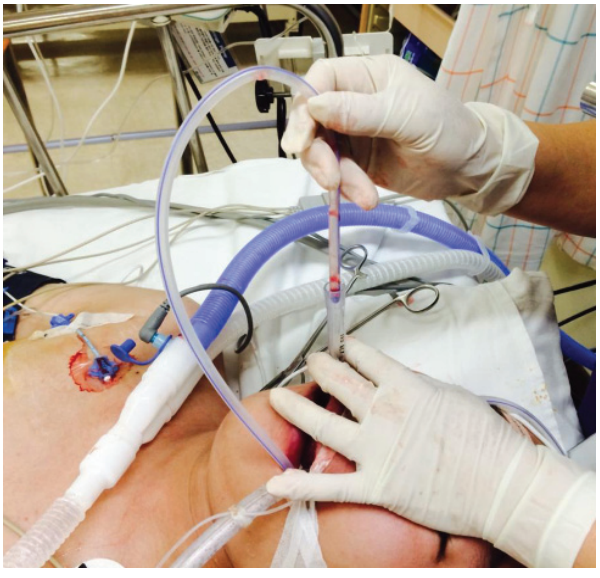


Figure 1 (abstract P204). Insertion of a nasogastric tube through an endotracheal tube in the esophagus.

Methods A NG tube was inserted using a laryngoscope and endotracheal tube.
Results A 15-year-old male patient admitted due to abrupt mental change and brain imaging showed severe subdural hemorrhage. NG tube insertion was done for enteral feeding but failed several times though changing position. As we had no guide wire and no nasoendoscope, an endotracheal tube was used as guidance for the NG tube. After making a longitudinal midline cut on the endotracheal tube, it was inserted into the esophagus under a laryngoscope. The NG tube was pushed into the endotracheal tube, and then the endotracheal tube was removed through the cut, reserving the NG tube. We checked the position of the NG tube by air sound and X-ray, and started enteral feeding without complication, such as nasal bleeding, emphysema, and gastric perforation. See Figure 1.
Conclusion We report a new method of NG tube insertion using a laryngoscope and endotracheal tube.

P205

Admissions with airway emergencies in the ICU at a tertiary referral centre

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Introduction As a tertiary referral centre for ENT and maxillo-facial surgery, our ICU receives complex elective and emergency cases. The frequency, aetiology and outcomes of airway emergencies are poorly described. Understanding these factors is key to improving management.
Methods We conducted a retrospective review of the ICU electronic patient database examining unplanned admissions with airway emergencies between December 13 and November 14. Data on demographics, aetiology of airway obstruction (including postprocedural), APACHE II score, therapeutic intervention(s) administered, and outcomes were collected.
Results Of 1,516 unplanned admissions, airway emergencies represented 6.3% (96 patients) of whom 40 (41.7%) had malignancy (26 maxillo-facial/trachea, three pulmonary, four haematological, seven other) and 24 infection (abscesses, epiglottitis, Ludwig's angina). Referring specialties were maxillo-facial surgery (n = 34), internal medicine (n = 25), ENT (n = 21) and other surgical specialties (n = 16). Thirteen patients had complications post bronchoscopy (vocal cord palsy, need for NIV or intubation), one post microlaryngoscopy, and 20 were admitted after difficult intubation. Eighteen were admitted post drainage of abscess (dental, retropharyngeal) and seven for observation for epiglottitis. Thirteen patients had stridor (three tracheal stenosis, one vocal cord cyst, one post CVA, four post vocal cord palsy, one post oesophagoscopy, one post thyroidectomy, two post decannulation). Seven were admitted after emergency tracheostomy, one after blocked tracheostomy, one after emergency laryngectomy, six post bleeding (epistaxis, haemoptysis, bleed form laryngectomy site), and four post evacuation haematoma. Three were admitted following anaphylaxis/angioedema and one after laryngospasm. Twenty-nine patients required medical management only (for example, steroids, nebulisers, and so forth), 25 were extubated post difficult intubation and six needed haemostasis control. Ten (nine surgical) tracheostomies were performed during their ICU stay. Sixteen patients died in hospital, of whom five were in the ICU at the time; 14 of these had an underlying malignancy. Twenty-three patients deteriorated during their ICU stay including HAP (n = 3), bleeding from airway (n = 3), PEA arrest (n = 1), airway swelling (n = 2), blocked laryngectomy (n = 1), and tracheostomy dislodgement (n = 1).
Conclusion Marked variation was seen in the type and aetiology of airway emergencies admitted to the ICU. A broad training programme is thus required to offer wide-ranging awareness of potential problems, communication (including an emergency airway plan), and acute management.

P206

Outcomes of medical patients requiring emergency intubation in a rural Irish hospital

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Introduction Bantry General Hospital (BGH) is a small rural hospital serving a large, geographically isolated part of southwest Ireland. Following an influential national review of adult critical care services [1], a protocol was introduced in late 2010 mandating the immediate transfer of all medical patients intubated on an emergency basis to a large critical care centre 100 km away. Similar mandatory transfer protocols were introduced at the same time throughout the island of Ireland but few data are available regarding patient outcomes. We designed a study to look at the outcomes of all patients encompassed by the protocol at BGH.
Methods We retrospectively reviewed the charts and electronic data of medical patients requiring emergency intubation at BGH from November 2010 to December 2013. We recorded the following data: age, sex, admission diagnosis, comorbidities, time delay to transfer, in-transit mortality, length of stay, survival to discharge and 1-month and 6-month mortality.
Results Forty-five patients (31 male) were included with a mean age of 67 ± 15 years. The commonest admission diagnoses were sepsis (10), cardiogenic shock (10), primary respiratory failure (nine) and intracranial haemorrhage (eight). The median transfer delay time was 47 minutes. Only 27 (60%) patients were actually transferred and they were significantly younger than nontransferred patients (62 vs. 73 years, P = 0.02). In-transit mortality was zero. Mean length of stay in the critical care centre was 14.8 ± 16.8 days. Survival to discharge was significantly higher in transferred (14/27) compared with nontransferred (3/18) patients (52% vs. 17%, P = 0.017). Overall mortality rates were 62% and 69% at 1 and 6 months respectively and were significantly lower in the transferred group (P = 0.02).
Conclusion Overall mortality rates of medical patients intubated urgently at BGH were high. Forty per cent of intubated patients were not transferred, indicating significant modification of the protocol over time. Patients transferred to the critical care centre were younger and had significantly better outcomes than patients remaining in BGH, probably due to decisions not to transfer patients with poor prognoses. Most patients who survived to discharge were still alive 6 months later.
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P207

Comparison of video laryngoscopy with direct laryngoscopy in patients with good glottic visualization: an observational study of 348 emergency intubations

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Critical Care 2015, **19(Suppl 1):**P207 (doi: 10.1186/cc14287)

Introduction Video laryngoscopy (VL) is known to improve glottic visualization and the first-attempt success rate compared with direct laryngoscopy (DL) in emergency tracheal intubations (ETIs). Since VL does not align the oral, pharyngeal, and laryngeal axes of the upper airway, it sometimes leads to failed intubation despite good glottic visualization. We tested the hypothesis that VL has a lower first-attempt success rate of ETI than DL among patients with good glottic visualization.
Methods We performed a prospective observational study examining ETIs at our tertiary care institution from July 2012 to June 2014. All consecutive patients who underwent ETIs in the emergency department and ICU were included. Patients under 18 years of age, intubated with VL not using C-MAC, were excluded. After each ETI effort, the operator completed a standardized data collection form. We classified glottic visualization as good (C-L grade 1 or 2), and poor (C-L grade 3 or 4). The primary outcome was the first-attempt success rate.

The primary exposure was use of VL. Potential confounders of success rate examined were age, sex, primary indication of intubation, methods of intubation, and operator level of training and specialty. Among patients with good glottic visualization, we conducted a multivariable logistic regression adjusted for potential confounders.
Results A total of 348 patients were included. VL attained better glottic visualization than DL (92.3% vs. 82.6%, respectively: P <0.001). In total, 299 patients with good glottic visualization were included in the analysis. Of these patients, 185 (61.9%) were male, median age and body mass index were 69 (interquartile range (IQR), 51 to 77) and 22 (IQR, 20 to 24) respectively. In univariate analysis, VL group had less respiratory failure (18.3% vs. 46.8%: P <0.001) and included more trauma patients (21.1% vs. 7.9%: P <0.001). The first-attempt success rates were similar between two groups (82.6% vs. 77.4%: P = 0.286). Multivariable logistic regression analysis adjusted for potential confounders showed that the success rate of VL was similar to that of DL (odds ratio, 1.17; 95% confidence interval, 0.57 to 2.39).
Conclusion Despite the possible poor alignment of airway, the first-attempt success rate of VL is similar to that of DL among patients with good glottic visualization.

P208

Transnasal humidified rapid insufflation ventilatory exchange for pre-oxygenation and apnoeic oxygenation during rapid sequence induction

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Introduction Rapid sequence induction (RSI) in the ICU, emergency department (ED) and operating room (OR) carries the risk of hypoxemia if laryngoscopy is prolonged especially in high-risk patients. Bag and mask pre-oxygenation is normally used to extend the apnoea time; however, arterial desaturation may still rapidly occur. Transnasal humidified rapid insufflation ventilatory exchange (THRIVE) is a new technique that provides modest CPAP during pre-oxygenation and crucially also continuous oxygenation of the pharyngeal space throughout the apnoeic period. In elective surgery, THRIVE provides apnoea times as long as 60 minutes due to apnoeic oxygenation [1]. We report the first implementation of THRIVE with emergency patients into the ICU, ED and OR.
Methods Following training a THRIVE system was installed in each location either as a fixed system on the anaesthetic machine (OR) or a mobile solution on a wheeled stand (ICU, ER). This was a simplified Optiflow system (Fisher and Paykel, New Zealand) consisting of a high-flow rotameter, a reusable humidifier, a reusable circuit and a disposable nasal interface. Anaesthetists of all grades were encouraged to use THRIVE (60 l/minute) prior to and during all high-risk intubations. Prospective data of pre and post intubation SpO_2 and time to intubate were collected. Anaesthetists were interviewed on acceptability of the technique.
Results There were 62 RSI intubations using THRIVE (ICU and ED = 30; OR = 33). Difficult airway equipment used in 36 cases (videolaryngoscopy in 23). Mean apnoea time was 118 seconds (30 to 480 seconds), with a median SpO_2 fall of 1% (0 to 33%). There was no correlation between arterial desaturation and apnoeic time. OR cases had a mean apnoea of 113 seconds with a median SpO_2 fall of 0% (0 to 13%). ICU and ED cases had a mean apnoea time of 119 seconds and median SpO_2 fall of 1% (0 to 33%). THRIVE was universally readily accepted. Reasons cited included: simplification of pre-oxygenation (hands free) and increased confidence. Six outlying arterial desaturation events suggested poor airway maintenance at induction or use in particularly high-risk patients. Many anaesthetists reinstituted THRIVE following extubation in selected patients (for example, obesity). No complications occurred during implementation.
Conclusion We conclude that THRIVE provides a convenient, safe and easy to implement technique for pre-oxygenation and apnoeic oxygenation during laryngoscopy.
Reference

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P209

Airway hygiene in the ICU: can ipratropium plus salbutamol help?

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Introduction β-Adrenergic agonists increase the ciliary beat frequency in experimental models, raising the possibility that they may be useful for airway hygiene [1]. Salbutamol increases large airway mucociliary clearance [2], although this may not be true for smaller airways [3]. There are no data from ICU patients, so we decided to test the effectiveness of transtracheal instillation of a mixture of ipratropium and salbutamol, assessing the reduction of the number of aspirations and hours of ventilation.
Methods An open randomized prospective study was held during 2014. All admitted patients were alternately selected as the study or control group and included if submitted to invasive ventilation for at least for 24 hours. Four patients who had secondary cardiac rhythm effects attributable to β-adrenergic agonists were excluded. In the study group, 3 ml of a dilution of 2.5 ml ipratropium (0.52 mg) plus salbutamol (2.5 mg) with 2.5 ml distilled water was instilled after the aspiration of secretions. During the ventilation period we noted for both groups, in addition to the demographic data, the number of tracheal aspirations by day and hours of ventilation. The statistical analysis was done with XLSTAT 2014 and we used the Kolmogorov–Smirnov test to compare the normal distribution of the groups.
Results These preliminary results included 107 patients. The only normal distribution, according to the Kolmogorov–Smirnov test, was for the number of hours of ventilation: 76.3 ± 100 (24; 478) in the study group versus 111 ± 167 (24; 780) in the control group.
Conclusion The preliminary analysis, referring to the first 6 months of study, showed a tendency in the reduction of both ventilation hours and length of stay in the study group. No significant difference was found in the number of aspirations, which may be explained by ICU nursing routines. Further studies will try to find whether significant differences in the incidence of VAP exist, allowing this procedure to be implemented in ICU routines.
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P210

Simultaneous use of a heat and moisture exchanger and a heated humidifier causes critical airway occlusion in less than 24 hours

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Introduction We hypothesised that the simultaneous use of a heat and moisture exchanger (HME) and a heated humidifier (HH) would increase the incidence of airway occlusion over a 24-hour period in comparison with each device in isolation. This bench study compares the incidence of airway occlusion when using (group 1) no airway humidification, (group 2) a HME alone, (group 3) a HH alone and (group 4) both a HME and a HH in combination. Tracheal intubation requires the use of artificial humidification systems. HMEs are less efficient but convenient especially for a short period of intubation and HHs are commonly more expensive. Both devices are often used in close proximity on the ICU depending on the particular clinical scenario and/or clinical practitioner. Following a critical incident of HME obstruction due to waterlogging on our ICU we realised that HH and HME may be used together inadvertently. This airway obstruction was only resolved by the removal of the HME from the patient's breathing circuit.
Methods A lung simulator underwent pressure-controlled ventilation (Pinsp = 25 cmH_2O; PEEP = 5 cmH_2O; Vt = 500 ml) for 24 hours for seven

test periods for each group (n = 24). A HME (Filta-Therm; Intersurgical, Berkshire, UK) was placed between the breathing circuit and catheter mount or the HH (MR850; Fisher & Paykel, Auckland, New Zealand) was used, or both in combination. Circuit manipulation was performed 4-hourly to simulate patient movement. Hourly Vt was recorded to determine airway occlusion. Critical airway occlusion (defined as a drop on the TV to <50 ml) was assessed using a Fisher's exact test.

Results In all seven of the breathing circuits in group 4 (both a HME and a HH in combination), critical airway occlusion occurred suddenly between 19 and23 hours. No episodes occurred in the other three groups (P <0.0001).

Conclusion The combination of the use of HME and HH within a single ICU risks inadvertent dual use in a single patient and if uncorrected this is likely to result in a ventilator circuit obstruction. Medical errors can be mitigated by consideration of human factors and system engineering to improve patient safety. A focus on clinical awareness and training may lead to improvements; however, the numbers, experience and turnover of critical care staffing would indicate that a systems approach is appropriate and either HME or HH should be used exclusively in an ICU.

P211

Endobronchial streptokinase for airway thrombus: a case series

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Critical Care 2015, **19(Suppl 1):**P211 (doi: 10.1186/cc14291)

Introduction Pulmonary haemorrhage (PH) is common in patients receiving mechanical ventilation and especially during ECMO, due to severe lung pathology and systemic anticoagulation. Whilst PH manifests as worsening ventilation and gas exchange, in ECMO patients who already have low tidal volume and who do not rely on pulmonary gas exchange, deterioration may not be evident until extensive airway thrombus (AT) has developed. Management of AT is challenging, with lavage, suctioning, mechanical disruption and extraction of limited efficacy in severe cases. Limited reports suggest that topical thrombolytics may have a role in the management of AT [1]. We report the safety and efficacy of endobronchial streptokinase (EBSK) in patients with extensive AT.

Methods A retrospective case series in a UK ECMO centre. Patients who received EBSK between 2010 and 2014 were identified from pharmacy records.

Results Five patients were identified, 80% were male. Median age was 40 years, APACHE II score 36.5 and Murray score 3.75. Four were on ECMO with systemic heparin. All had ARDS secondary to lung infections (community-acquired pneumonia (two), lung abscess (one), TB (one) and PJP (one)). All had extensive AT, diagnosed on bronchoscopy, causing occlusion of the trachea or major bronchi, refractory to physiotherapy, lavage, suctioning ± rigid bronchoscopy. Patients received up to three administrations of EBSK, 1,000 u/ml in saline 0.9% under bronchoscopic guidance. Dose per administration was 30,000 to 80,000 u and total dose was 30,000 to 150,000 u (375 to 1,500 u/kg), with interval bronchoscopy after several hours for lavage and suctioning of lysed clot. In all cases EBSK was well tolerated with no immediate complications and no clinically significant change in systemic laboratory coagulation parameters at 12 or 24 hours compared with pretreatment baseline. In all cases, significant clearance of airway thrombus was achieved. Median tidal volume increased from 60 ml pre treatment to 170 ml at 24 hours. Median PaO_2 during the 'FiO_2 1.0 test' improved from 9.0 to 17.6 kPa at 24 hours. No major bleeding, intracerebral haemorrhage or ECMO cannulae bleeding was seen up to 7 days post treatment.

Conclusion In this series, the largest reported to date, and the first on ECMO, EBSK was highly effective in achieving clearance of AT with subsequent improvements in pulmonary mechanics and gas exchange. No major disturbance of systemic coagulation parameters or major haemorrhagic complications occurred. The use of EBSK may be considered for refractory AT.

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P212

Reduction of ventilator-associated pneumonia using the AnapnoGuard system

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Critical Care 2015, **19(Suppl 1):**P212 (doi: 10.1186/cc14292)

Introduction Ventilator-associated pneumonia (VAP) is a common complication in mechanically ventilated patients. Frequently the pathogens responsible derive from aspirated secretions of the upper respiratory tract or the stomach. In order to prevent aspiration, two missions should be attained: a good tracheal cuff seal with a well-tolerated pressure, together with continuous evacuation of secretions from the subglottic space. These two goals can be achieved using the AnapnoGuard system and its related endotracheal tube (ETT).

Methods A single-center, open-label study in a general ICU. Control group: (retrospective data) mechanically ventilated patients on standard of care regular ETT, manual suction of the trachea and oral–pharyngeal space by nursing staff. Study group: (prospective data) connected at all times to the AnapnoGuard system: an ETT with two above-the-cuff suction ports and a third port and lumen for rinsing and CO_2 measurement. A triple lumen harness is connected to a control system designed to measure CO_2 levels above the cuff (to identify leaks), inflate the cuff accordingly, rinse and suction secretions above the cuff. To be included in the study patients had to have no pneumonia on admission and at least 3 days of mechanical ventilation. VAP was diagnosed for a new chest X-ray infiltrate accompanied by fever, leucocytosis and positive sputum culture. The study was approved by the hospital IRB.

Results Control group: 100 patients who received standard intubation and treatment in 2009 to 2010. Of these, four dropped out due screening failure of pneumonia on the day of enrollment. Study group: in 2011 to 2014, 192 patients were screened. Of these, 49 were found eligible and were enrolled. Of these, 14 dropped out (four screening failures with pneumonia on day of enrollment and 10 withdrawals with MV of less than 24 hours). Mean age was 51 (control) and 49 (study). Males were 75% of both groups and mean weight was 81 kg in both. VAP was diagnosed in 26 (27%) of controls and only three (8.5%) of the study group (P = 0.03). Mean time from admission to VAP diagnosis was 4.7 days in controls versus 5.12 in the study group (NS). No serious adverse events occurred.

Conclusion Patients connected to the AnapnoGuard system demonstrated a statistically significant lower VAP rate compared with the control group (8.5% vs. 27% respectively, P = 0.03). The estimated relative risk of VAP occurring in the control group was more than three times higher than the study group. Rinsing and aspiration of subglottic secretions combined with cuff pressure and seal management may be an effective method to prevent VAP.

P213

Risk factors for bleeding complications after percutaneous dilatational tracheostomy: a 10-year institutional analysis

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Critical Care 2015, **19(Suppl 1):**P213 (doi: 10.1186/cc14293)

Introduction Percutaneous dilatational tracheotomy (PDT) is the standard airway access in critically ill patients who require prolonged mechanical ventilation. Bleeding complications after PDT are infrequently observed but have a tremendous impact on further clinical course CFA risk stratification for patients scheduled for PDT.

Methods We retrospectively reviewed the records of all patients who underwent PDT (using the Ciaglia technique with bronchoscopic guidance) on our cardiothoracic ICU between 2003 and 2013. Patients were stratified into two groups: patients suffering from acute moderate, severe or major bleeding (Group A) and patients who presented none or only mild bleeding (Group B).

Results A total of 1,001 patients (46% male, mean age 68.1 years) that underwent PDT were analyzed. In the majority of patients, no or

only mild bleeding during PDT occurred (none: 425 (42.5%), mild: 488 (48.8%)). In 84 patients (8.4%), bleeding was classified as moderate. Three patients suffered from severe bleeding, only one major bleeding with need for emergency surgery was observed. Study groups showed significant differences in Simplified Acute Physiology Score (SAPS) on the day of PDT (Group A: 47.0 ± 13.1, Group B: 32.9 ± 11.2, $P = 0.042$), renal replacement therapy on the day of PDT (Group A: 53 (60.2%), Group B: 439 (48.1%), $P = 0.026$), presence of coagulopathy (Group A: 48 (54.5%), Group B: 393 (43.0%), $P = 0.043$), platelet count (Group A: 91.6 ± 59.2, Group B: 111.5 ± 79.8 × 1,000/µl, $P = 0.037$), fibrinogen levels (Group A: 373.6 ± 159.1, Group B: 450.6 ± 259.0 mg/dl, $P = 0.012$), proportion of PDTs performed by residents (Group A: 72 (81.8%), Group B: 632 (69.2%), $P = 0.034$) and moderately to very difficult PDT (Group A: 31 (35.2%), Group B: 141 (15.4%), $P = 0.001$). Using logistic regression analyses, difficult PDT, low-experienced operator, SAPS >40 and low fibrinogen were independent predictors of relevant bleedings after PDT.

Conclusion Periprocedural bleeding complications during PDT are rare. However, low fibrinogen levels as well as difficult PDT, low-experienced operator and SAPS >40 are associated with an increased risk for bleeding complications. Therefore, preprocedural risk evaluation for bleeding complications should include these factors and further studies are necessary to prove whether modification of risk factors – for example, substitution of fibrinogen prior to PDT – is able to reduce incidence of bleeding complications.

P214

Percutaneous dilatational tracheostomy: complications and safety without the use of bronchoscopic guidance

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Introduction Since the introduction and development of percutaneous dilatational tracheostomy (PDT), this procedure is accepted and incorporated in ICUs worldwide. In spite of obvious benefits for the patients, who obtain more comfort and mobility and less use of sedatives, the procedure also implies the risk of several complications, some of which may be lethal. Severe complications include hemorrhage, displacement and pneumothorax. Different methods of PDT are described in the literature, each with disadvantages and benefits. The aim of this study was to analyze complications due to PDTs performed without the use of bronchoscopic assistance.

Methods The study was conducted in a Danish eight-bed, non-university ICU. Since 2007, all patients admitted to the ICU have been registered on an electronic patient record system, in which daily vital values, diagnoses, procedures and healthcare providers' notes are entered. When searching for 'percutaneous dilatation tracheostomy' in the electronic system, we found all patients who had undergone this specific procedure. Afterwards we analyzed each of these patients' hospital records, looking for any periprocedure or postprocedure complications noted within 7 days. In addition we registered patients' age, sex, BMI, SOFA score, methods used in procedures and experience of operators.

Results A total of 136 patients admitted to the UCI had undergone a PDT between 2007 and 2014. Of these, two were excluded due to the PDT being performed in another hospital before admission to our ICU. All 134 PDTs were performed with the Ciaglia Blue Rhino Method. No PDTs were performed with bronchoscopic guidance. In 12 cases some kind of complication due to the PDT was registered: six cases with need of surgical hemostasis, three cases of bleeding with need of transfusion of blood products, one case of PDT displacement, one case of ventilation-related problems during procedure and, finally, one case of tracheal cartilage fracture. There were no incidents of pneumothorax. No PDTs had a lethal outcome due to the procedure itself. The total complication rate was 9.0%. Of the 12 cases, four (33%) complications occurred during the procedure, the rest (66%) occurred after the procedure. The overall periprocedure complication rate was 3%.

Conclusion In this study, PDTs without the use of bronchoscopic guidance were performed safely with a low rate of complications.

P215

Decision-making algorithm for TS in the ICU

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Introduction Nowadays more percutaneous dilatational tracheostomy (PDT) methods are in use, but there is no ideal risk-free technique. We

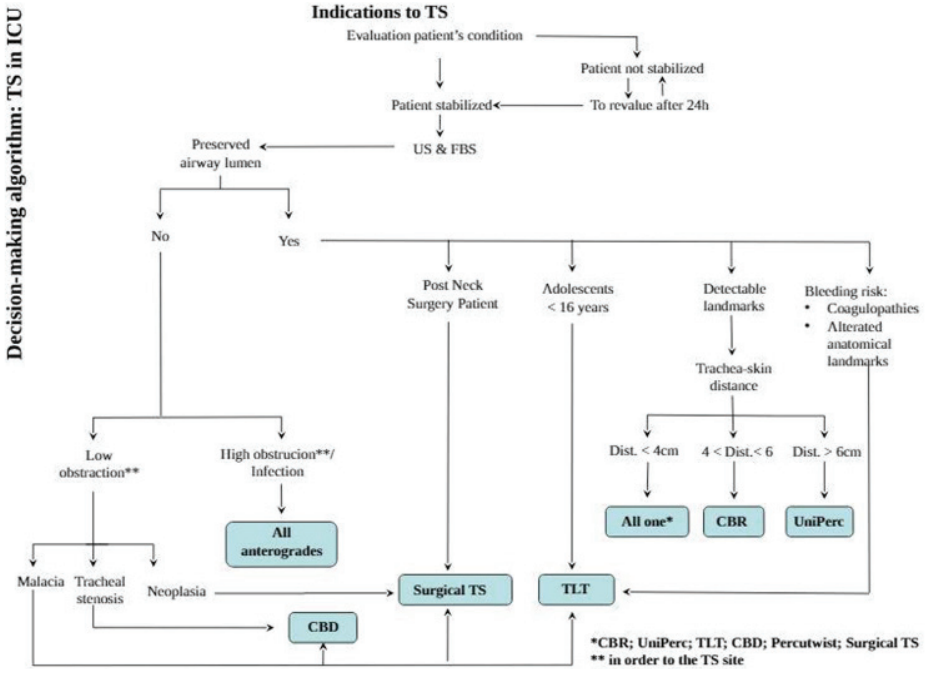


Figure 1 (abstract P215).

have outlined a decisional algorithm to choose the most appropriate technique in each case to reduce the incidence of complications.

Methods A retrospective review was performed using data from the last 14 years. Two hundred patients were selected. Patients were divided into two groups: one including the first 100 PDTs treated without the algorithm (nA-group) and the other including the last 100 patients treated with the algorithm (A-group). Valuation of clinical and anatomical features of the patients, neck ultrasound and fibrobronchoscopy came before the procedure [1]. The algorithm was formulated by our experience with PDT techniques, comparing the specific characteristics of each one with the physiopathological characteristics of each patient.

Results We recorded complications (bleeding, tracheoesophageal fistula, subglottic stenosis, tracheal rings' fracture, difficulty of placement, change of procedure) related to PDTs performed with and without applying the algorithm. We considered complications that occurred in our experience and we changed our modality in technique choice (Figure 1). Compared with the complications reported in the nA-group, use of the algorithm as a guide to choose the kind of PDT technique seems to reduce the incidence of complications (37% vs. 19%; $P = 0.001$ chi-square test).

Conclusion In our experience the application of the proposed algorithm may reduce the incidence of complications related to PDT in the ICU. However, a randomized controlled multicenter study would be necessary in order to confirm the efficiency and validity of the proposed algorithm.

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P216

Impact of antibiotic therapy during a bedside percutaneous tracheotomy procedure in an ICU

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Critical Care 2015, **19(Suppl 1):**P216 (doi: 10.1186/cc14296)

Introduction Percutaneous bedside tracheostomy (PBT) is a frequently done procedure in the ICU. PBT is a clean-contaminated procedure, and the duration of the procedure is 15 to 20 minutes depending on the physician's procedural skills. The rate of infectious complications and efficacy of perioperative therapy in reducing infections after PBT is currently unknown. Currently there have been no definitive recommendations for prophylactic antibiotic therapy before PBT in the ICU.

Methods All clinical and microbiological data were retrospectively collected and analyzed during the ICU stay before PBT performance and 72 hours after the PBT procedure from 110 patients in our ICU. Controls were defined as patients in whom the PBT procedure was performed in the ICU, with antibiotics administered 72 hours prior to and during the procedure (Group 1, $n = 82$). Cases were defined as patients in whom the PBT procedure was performed in the ICU without antibiotics administered 72 hours prior to and during the procedure (Group 2, $n = 28$). Secondary bacteremia, line sepsis and VAP during the 72 hours after PBT were considered infectious complications. Two-tailed $P < 0.05$ was considered to be significant.

Results No differences were found in age, gender, admission diagnoses, length of ICU stay and in-hospital mortality rate between the two study groups. Overall Gram-negative, Gram-positive and fungal flora were similar in both groups before and after PBT. Patients who received antibiotic therapy had a lower incidence of new ventilator-associated pneumonia (VAP) episodes (15/82 (18.2%) in Group 1 vs. 14/28 (50%) in Group 2, $P < 0.001$ (0.23, 0.87 to 0.13)) (Table 1). There were no differences in the incidence of bacteremia or line sepsis (Table 1).

Table 1 (abstract P216). Clinical data of new infections 72 hours after the PBT procedure

Infection	Group 1	Group 2	*P* value OR
Bacteremia	21/82(25.6%)	11/28(39.3%)	0.149
Colonization	67/82(82.7%)	23/28(82.1%)	0.718
Line sepsis	10/82 (12%)	4/28 (14.3%)	0.39
New VAP (%)	15/82(18.2%)	14/28 (50%)	0.001

Conclusion Our findings highlight the importance of conducting a prospective randomized control trial to better understand the role of antibiotic prophylaxis in PBT.

P217

Outcomes of patients with tracheostomy discharged from ICU to Transitional Care Unit and general wards

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Introduction Patients with a tracheostomy (TQ) tube in place discharged from the ICU to a general ward (GW) are a fragile group and the TQ may be a risk factor for morbidity and mortality [1,2]. For this reason they need closer monitoring and more airway care. The Transitional Care Unit (TCU) assists patients with serious medical conditions and bridges the gap between the ICU and home or long-term care facilities providing the necessary medical, nursing, psychological and rehabilitative care. The purpose of this study was to evaluate the impact of the TCU on outcomes of tracheostomized patients discharged from the ICU.

Methods We retrospectively reviewed medical records of ICU adults patients who had TQ when discharged to a new TCU and to a GW. The study was carried out in two tertiary care university hospitals from January 2007 to November 2014. Study variables were age, sex, APACHE II score, principal diagnosis, associated major procedures, length of stay in ICU and out in hospital, TCU and GW, Sabadell score, in-hospital mortality, types of tracheotomy procedure, decision to decannulate and discharge to home or long-care facilities.

Results In total 12,839 records of patients discharged from the ICU were analyzed. Tracheostomy was present in 133 patients. Two groups were defined: (1) TCU ($n = 56$) and (2) GW ($n = 77$). Patients of the TCU group were older (60.1 ± 13.1 vs. 54.9 ± 15.8 years; $P < 0.05$) with higher APACHE II score (23 (CI: 21.5 to 25.6) vs. 18.5 (CI: 17.1 to 19.9); $P < 0.001$), and had longer stay in the ICU (45.8 (CI: 38.2 to 53.3) vs. 28.4 (CI: 24.2 to 32.6) days; $P < 0.001$) and on the ward (71.1 (CI: 57.4 to 84.8) vs. 46.1 (CI: 33.7 to 58.2) days; $P < 0.001$) than those of the GW group. The GW group had category 1 of Sabadell score more frequently than the TCU group (25.9% vs. 8.9%; $P = 0.019$). Rates of nosocomial infections were similar in both groups. No significant differences on vasoactive use (50% vs. 40.2%), renal failure (23.2% vs. 20.7%), blood transfusions (25% vs. 23.2%), parenteral nutrition (10.7% vs. 12.9%), in-hospital deaths (14.3% vs. 24.6%), decannulation (55% vs. 50%), or discharge to home (53.6% vs. 37.7%) were found between groups 1 and 2, respectively.

Conclusion In our setting the TCU helps to care more safely for severe tracheostomized patients after ICU discharge, and furthermore facilitates discharge home.

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P218

Rapid amelioration of respiratory parameters in severely obese patients after percutaneous dilatational tracheotomy

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Introduction Incidence of obesity in developed countries is rising. Currently, Europe has a prevalence of 9 to 30% with significant impact on public health systems. Obese patients in the ICU require special management and treatment. Altered anatomy in obese patients complicates procedures such as mechanical ventilation. Obesity affects cardiopulmonary physiology and requires elevated ventilation pressures. In our retrospective study, we determined the effect of early

percutaneous dilatational tracheotomy (PDT) and cessation of sedation on respiratory parameters in severely obese patients.
Methods From June 2010 to July 2014, we included all patients with a body weight of >130 kg, respiratory failure and PDT who were admitted to the ICU of the University Hospital of Muenster. We compared respirator parameters and blood gas analysis before and after PDT. Parameters were recorded on days –1, 0, 1, 3, 5, and 10, with day 0 describing the day of PDT.
Results Twenty-one patients were included in the study. Mean age was 56 ± 10.3 years and 14 (66.7%) of the patients were male. Body weight was 164.5 ± 39.4 kg, body height accounted for 176.8 ± 8.7 cm (n = 20) and body mass index was 49.7 ± 16.9 kg/m^2. Patients stayed in the ICU for 18.4 ± 13.8 days. Mean time of mechanical ventilation by endotracheal tube was 2.4 ± 1.5 days (n = 20) and via tracheostomy 9.8 ± 7.0 days. After PDT, peak inspiratory pressure (P <0.0001), positive end-expiratory pressure (P <0.0001) and insufflated oxygen concentration (P <0.0001) could significantly and rapidly be reduced. Respiratory minute volume increased significantly (P = 0.004). PDT was not associated with relevant complications.
Conclusion Early PDT rapidly improves respiratory distress in severely obese patients due enabling of spontaneous breathing and reduction of dead space ventilation.

P219

Early postoperative use of CPAP reduces need for unplanned IPPV in elective vascular patients

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Introduction Respiratory failure is a well-known complication of aortic aneurysm surgery. We describe the impact of a protocol, using CPAP after elective surgery to reduce the need for unplanned invasive ventilation.
Methods In 2012 we introduced a CPAP protocol for patients undergoing elective aortic aneurysm surgery, either open (AAA) or as an endovascular repair (EVAR). According to pre-existing risk factors (see Table 1) and arterial blood gas analysis in the anaesthetic room, they were assigned to two alternative options on the ITU: prophylactic CPAP for 9 hours in each of the first two postoperative nights or oxygen via face mask. CPAP was applied at any time in the patients stay, if their P/F ratio dropped below 40. Criteria to stop CPAP were also predefined. Previously, CPAP was initiated at the discretion of nursing staff, P/F ratios were not utilised.

Table 1 (abstract P219). Criteria for the use of prophylactic CPAP

Current smoker
FEV1: <1.5 l/minute
Poor exercise tolerance (<100 yards) due to chest problems
SpO_2 <92% on air
SpO_2 <92% on FiO_2 >0.4 in theatre

Results We compare patient cohorts in the years 2010 and 2011 (pre protocol) with 2013 and 2014 (post protocol). Results are reported as the split between open surgery and endovascular repair. Table 2 presents requirements for invasive ventilation (IPPV) and length of stay (LOS) for both patient groups.

Table 2 (abstract P219). IPPV requirements and length of stay data

	2010 to 2011			2013 to 2014		
IPPV	LOS ITU (days)	LOS hospital (days)	IPPV	LOS ITU (days)	LOS hospital (days)	EVAR
2/67 (3%)	2	6	1/77 (1.3%)	2	5	AAA
10/46 (21.7%)	5	9	6/37 (16.2%)	5	12	

Conclusion There is a clear reduction in the need for unplanned IPPV in both patient groups. An audit in 2013 showed incomplete protocol adherence in the ITU, therefore benefits may be underestimated.

P220

Is the gastric tube a burden for noninvasive ventilation?

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Critical Care 2015, **19(Suppl 1):**P220 (doi: 10.1186/cc14300)

Introduction The application of noninvasive ventilation (NIV) in ICUs has spread widely during the years. It is used in the treatment of different forms of acute respiratory failure and COPD exacerbations. Although NIV is thought to be more comfortable for patients than invasive mechanical ventilation, its failure rates in the ICUs range between 10 and 40%. Except for the interface-related problems, there are some specific considerations for the patient–ventilator interaction and the applied mechanical forces. During NIV there is a predisposition for the stomach to be inflated with gas, which could cause severe respiratory complications, especially in COPD patients, and thus prolong the mechanical ventilation and the weaning process. This remains one of the major causes for NIV failure. Although a lot of face masks with different interfaces are available on the market, just a few have additional ports for a NGT. They are characterized by higher price and a complex setup. In order to perform NIV in patients, requiring NGT placement, without additional air leaks and to be able to ensure their enteral nutrition and/or stomach drainage, we installed a port for a NGT on a standard face mask.
Methods In this study, six of the COPD patients admitted to our ICU, who required NGT placement, were ventilated with the Draeger Evita 2 dura through a modified reusable silicone face mask (UMDNS code: 12-453 with 22 mm ID connection; sizes 4 and 5) with silicone headgear and a hook ring. All of them had a NGT during their stay in the ICU. We evaluated the efficacy of our modification comparing the achieved Vt with modified and unmodified face mask, during two periods of 10 minutes. The mode and parameters of ventilation were not changed. We assessed patient comfort with a visual analogue scale.
Results The average duration of NIV was 3.5 days (SD = 1.6). We examined two sets of 10 consequent breathing cycles for every patient. The mean Vt was 472 ml (SD = 76 ml) with standard face mask and 460 ml (SD = 86 ml) with the modified one. There was statistically significant correlation between the two datasets (P <0.05). No additional leaks were detected. According to the VAS evaluation, five of the patients (83%) had comfort improvement with the modified mask.
Conclusion With this modification of the face mask we achieved adequate drainage of the stomach and/or the enteral nutrition of the patients and improvement in their comfort during NIV, compared with the ventilation with a standard mask, without additional air leaks and at a low cost.

P221

Lung ultrasonography as a marker of pulmonary edema in cardiac surgery patients: visual versus quantitative evaluation

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Introduction Lung ultrasonography (LUS) has been used for non-invasive detection of pulmonary edema. LUS visual scores (V-LUS) based on B-lines are poorly correlated with either pulmonary capillary wedge pressure (PCWP) or extravascular lung water (EVLW). A new quantitative LUS analysis (Q-LUS) has been recently proposed [1,2]. The aim of the study was to investigate whether Q-LUS is better correlated with PCWP and EVLW than V-LUS, and to what extent positive end-expiratory pressure (PEEP) affects the assessment of pulmonary edema by Q-LUS and V-LUS.

Methods Thirty-nine patients mechanically ventilated with PEEP of 5 cmH_2O ($n = 47$) or 10 cmH_2O ($n = 30$) and PCWP ($n = 77$) or EVLW ($n = 38$) monitored were studied.
Results PCWP was significantly and strongly correlated with Q-LUS Grey Unit value ($r^2 = 0.64$) but weakly with V-LUS B-line score ($r^2 = 0.19$). EVLW was significantly and strongly correlated with QLUS Grey Unit mean value ($r^2 = 0.65$) more than with V-LUS B-line score ($r^2 = 0.42$). Q-LUS showed a better diagnostic accuracy than V-LUS for the detection of PCWP >15 mmHg or EVLW >10 ml/kg. With a PEEP of 5 cmH_2O, the correlations with PCWP or EVLW were stronger with Q-LUS than V-LUS. With a PEEP of 10 cmH_2O, the correlations with PCWP or EVLW were still significant for Q-LUS but insignificant for V-LUS. Intraobserver repeatability and interobserver reproducibility were much better for Q-LUS than V-LUS.
Conclusion Both V-LUS and Q-LUS are acceptable indicators of pulmonary edema in patients mechanically ventilated with low PEEP but at high PEEP only Q-LUS provides data that are significantly correlated. Computer-aided Q-LUS has the advantages of being not only independent of operator perception but also of PEEP.
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P222

Lung ultrasound aeration assessment: comparison of two techniques

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Critical Care 2015, **19(Suppl 1):**P222 (doi: 10.1186/cc14302)

Introduction Lung ultrasound (LUS) allows semiquantification of lung aeration in PEEP trials [1], pneumonia [2] and weaning [3]. LUS score is based on number/coalescence of vertical artifacts (B-lines) in longitudinal scan (LONG) [4]: the pleura is identified between two ribs and its visualization limited by intercostal space (ICS) width. We hypothesized that a transversal scan (TRANSV) aligned with ICS would visualize longer pleura and a higher number of artifacts, with better assessment of loss of aeration (LoA).
Methods LONG and TRANSV were performed in six areas per lung (anterior, lateral and posterior, each divided into superior and inferior). Once LONG was performed, TRANSV was obtained by a probe rotation until the ribs disappeared. We considered pleural length, B-line number/coalescence, and subpleural/lobar consolidations. LUS score was assigned: 0 normal lung, 1 moderate LoA (≥3 well-spaced B-lines), 2 severe LoA (coalescent B-lines), 3 complete LoA (tissue-like pattern).
Results We enrolled 38 patients (21 males, age 60 ± 16 years, BMI 24.7 ± 4.7 kg/m²) corresponding to 456 ICSs. In 63 ICSs, a tissue-like pattern was visualized in both techniques. In the other 393, LONG versus TRANSV pleural length was 2.0 ± 0.6 cm (range 0.8 to 3.8; variance 0.31) versus 3.9 ± 0.1 cm (range 3.0 to 4.3; variance 0.1) ($P < 0.0001$), B-lines per scan were 1.1 ± 1.6 versus 1.8 ± 2.5 ($P < 0.0001$), coalescent B-lines were detected in 24 versus 30% ($P < 0.05$) and subpleural consolidations in 16 versus 22% ($P < 0.05$), respectively. LUS scores' prevalence significantly differed in LONG versus TRANSV (Figure 1).

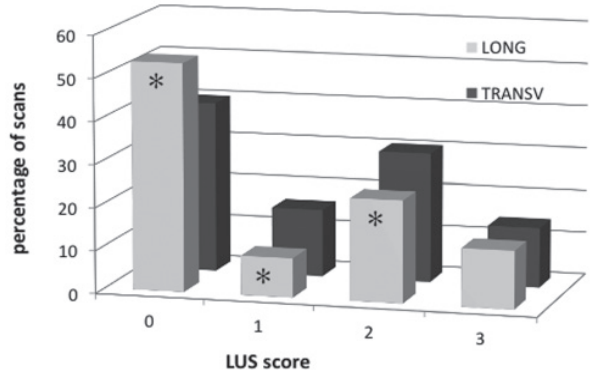


Figure 1 (abstract P222). LUS scores. *$P < 0.01$ TRANSV versus LONG.

Conclusion TRANSV visualizes significantly longer pleura and greater number of artifacts useful for lung disease assessment.
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P223

Ultrasound assessment for extravascular lung water in patients with septic shock

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Critical Care 2015, **19(Suppl 1):**P223 (doi: 10.1186/cc14303)

Introduction Extravascular lung water (EVLW) refers to fluid within the lung but outside the vascular compartment. Increment of EVLW was associated with mortality in critically ill patients. Extravascular lung water index (EVLWI) >10 ml/kg was found in patients with cardiogenic pulmonary edema and correlated with pulmonary capillary wedge pressure >20 mmHg. Measurement of EVLW needs sophisticated tools and an invasive method by transpulmonary thermodilution (TPTD) technique. In contrast, multiple B-lines by lung ultrasound (LUS) have been recently proposed to correlate with increased EVLW in patients with pulmonary edema. This study aims to compare three methods of LUS and EVLWI measured by TPTD to assess pulmonary edema in patients with septic shock.
Methods The authors prospectively enrolled 17 patients with septic shock who were admitted to the medical ICU, Phramongkutklao Hospital between September 2013 and June 2014. EVLWI was measured by TPTD (VolumeView Set, EV1000; Edwards Lifesciences) method. According to international evidence-based recommendations for point-of-care lung ultrasound 2012, three methods of LUS (LOGIQ e ultrasound; GE Healthcare) were compared to assess EVLW daily in each patient until no indication for invasive blood pressure monitoring [1]. Firstly, B-lines were measured in 28 lung zones. The total numbers of B-lines seen in each patient were counted as total B-line scores (TBS). Secondly, upper and lower BLUE points were anterior two-region scans each side marked by physician hands. Pulmonary edema was diagnosed if three or more B-lines were presented in all regions. Lastly, scanning eight regions, two anterior and two laterals per side, was considered abnormal if more than one scan per side had three or more B-lines.
Results A total of 40 comparisons were obtained. Significant positive linear correlations were found between TBS and EVLWI determined by TPTD ($r = 0.637$, $P < 0.001$). The TBS ≥39 has sensitivity of 91.7% and specificity of 75.0% to define EVLWI >10 ml/kg. There was low sensitivity (33.3% and 50.0% respectively) but high specificity (100% and 96.0% respectively) of the positive BLUE points and eight regions to define EVLWI >10 ml/kg.
Conclusion TBS is the best method for assessing EVLW compared with BLUE points and eight regions. These data support the benefit of LUS with summation of B-line scores of 28 rib interspaces for assessment of the increment of EVLW in septic shock patients.
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P224

Atrophy of diaphragm muscle visualized with ultrasound in mechanically ventilated patients

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Critical Care 2015, **19(Suppl 1):**P224 (doi: 10.1186/cc14304)

Introduction Mechanical ventilation (MV) induces diaphragmatic muscle atrophy and contractile fibre dysfunction, the so-called ventilator-induced diaphragm dysfunction (VIDD). Although

diaphragmatic atrophy can be assessed using ultrasound, the biggest trial in humans published so far included seven patients and only measuring the thickness at two moments during the disease process [1]. We aimed to assess the time course of diaphragm atrophy in a larger cohort of MV patients using ultrasound.

Methods A total of 54 patients from an adult ICU were included in this prospective single-centre cohort trial. Patients who needed <72 hours of MV or had been recently admitted to an ICU were excluded. Patients were ventilated in a controlled, assisted, and/or hybrid ventilation mode. The thickness of the diaphragm was assessed daily; the first recording was within 24 hours after the start of mechanical ventilation and we continued the measurements until the patients were extubated or tracheotomised. We measured the diaphragm at the zone of apposition, as described by McCool and colleagues [2] using a linear 13 MHz ultrasound probe. Figure 1 shows a sample measurement.

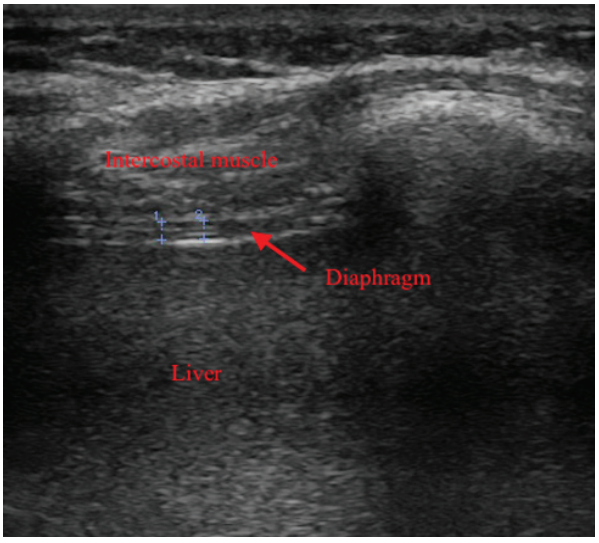


Figure 1 (abstract P224). Sample ultrasound recording. Lines 1 and 2 are diaphragm thickness measurements.

Results We were successfully able to record the diaphragm thickness in all included patients. Median time on the ventilator was 9 days (IQR 4 to 15 days). Mean baseline thickness was 1.9 mm (SD ±0.4 mm), and mean nadir was 1.3 mm (SD ±0.4 mm), corresponding with a mean change in thickness of 32% (SD ±18%). As early as after only 72 hours of MV, we already noted an average drop of diaphragm thickness of 20%, illustrating the rapid progression of the atrophy in VIDD.

Conclusion On average, diaphragm thickness decreased 32% in our cohort. The decrease occurred rapidly, with two-thirds of the maximal thinning already present after 72 hours of MV.

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P225

Quantitative ultrasonography for pneumonia

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Introduction Chest-X-ray is recommended for routine use in patients with suspected pneumonia, but its use in emergency settings is limited. In this study, the diagnostic performance of a new method for quantitative analysis of lung ultrasonography was compared with bedside chest X-ray and visual lung ultrasonography for detection of community-acquired pneumonia, using thoracic computed tomography as a gold standard.

Methods Thirty-two spontaneously breathing patients with suspected community-acquired pneumonia undergoing computed tomography examination were consecutively enrolled. Each hemithorax was evaluated for the presence or absence of abnormalities by chest X-ray and quantitative or visual ultrasonography.

Results Quantitative ultrasonography showed higher sensitivity (93%), specificity (95%), and diagnostic accuracy (94%) than chest X-ray (64%, 80%, and 69%, respectively), or visual ultrasonography (68%, 95%, and 77%, respectively), or their combination (77%, 75%, and 77%, respectively).

Conclusion Quantitative lung ultrasonography was considerably more accurate than either chest X-ray or visual ultrasonography in the diagnosis of community-acquired pneumonia and it may represent a useful first-line approach for confirmation of clinical diagnosis in emergency settings.

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2. Quanta Imaging Technology. www.quanta.camelotbio.com.

P226

Effect of lung recruitment on oxygenation in patients with acute lung injury ventilated in CPAP/pressure support mode

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Critical Care 2015, **19(Suppl 1):**P226 (doi: 10.1186/cc14306)

Introduction One of the aims of lung recruitment is to improve oxygenation [1], but it has not yet been investigated in spontaneously breathing patients. Our objective was to evaluate the effects of recruitment maneuvers on oxygenation in patients ventilated in CPAP/pressure support (CPAP/PS) mode.

Methods In a prospective, observational study, 30 patients with a Lung Injury Score ≥2 were recruited. Following baseline measurements (t_0) PEEP was increased by 5 cmH_2O (t_1). Recruitment maneuver was applied for 40 seconds with 40 cmH_2O PS. Measurements were taken immediately after recruitment (t_2) then 15 minutes (t_3) and 30 minutes later (t_4).

Results According to the difference of PaO_2/FiO_2 between t_2 and t_0, three groups were defined: nonresponders (NR: difference of PaO_2/FiO_2 ≤0%, $n = 8$), low responders (LR: difference of PaO_2/FiO_2 = 0 to 50%, $n = 11$) and high responders (HR: difference of PaO_2/FiO_2 >50%, $n = 11$). In the NR-group, PaO_2/FiO_2 decreased significantly: median (interquartile), PaO_2/FiO_2 = 178 (159 to 240) versus 165 (118 to 210) mmHg; in the LR-group and in the HR-group there was significant improvement: 119 (98 to 164) versus 161 (123 to 182) mmHg and 141 (130 to 183) versus 239 (224 to 369) mmHg, $P < 0.05$, respectively. Dynamic compliance (C_{dyn}) significantly dropped at t_2 as compared with t_0 in the NR-group, C_{dyn} = 62 (48 to 87) versus 53 (43 to 78) ml/cmH_2O, while there was no significant change in the LR- and HR-groups, $P < 0.05$. At the same time points the dead space to tidal volume ratio (Vds/Vte) significantly increased in the NR-group, Vds/Vte = 30 (23 to 37) versus 37 (26 to 42)%, but not in the LR- and HR-groups, $P < 0.05$.

Conclusion Recruitment maneuvers improved PaO_2/FiO_2 in the majority of patients (73%) without affecting C_{dyn} or Vds/Vte; therefore it may be a safe approach to improve oxygenation in patients ventilated in CPAP/PS mode.

Reference

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P227

A better way to determine sample size to detect changes in length of mechanical ventilation?

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Critical Care 2015, **19(Suppl 1):**P227 (doi: 10.1186/cc14307)

Introduction Estimation of effective sample size (*N*/arm) is important to ensure power to detect significant treatment effects. However,

traditional parametric sample size estimations depend upon restrictive assumptions that often do not hold in real data. This study estimates *N* to detect changes in length of mechanical ventilation (LoMV) using Monte-Carlo simulation (MCS) and mechanical ventilation (MV) data to better simulate the cohort.

Methods Data from 2,534 MV patients admitted to Christchurch Hospital ICU from 2011 to 2013 were used. *N* was estimated using MCS to determine a sample size with power of 80%, and compared with the Altman's nomogram for two patients groups, (1) all patients and (2) targeted patients with 1 <LoMV ≤15 days. MCS allows any range of intervention effect to be simulated, where this study tested a 10 and 25% difference in LoMV (0.5 to 1.25 days for mean LoMV of 5 days). The simulated LoMV for the intervention group is compared with the LoMV in a control group using the one-sided Wilcoxon rank-sum test, Student *t* test, and Kolmogorov–Smirnov test to assess central tendency and variation.

Results The distribution of LoMV is heavily skewed. Altman's nomogram assumes a normal distribution and found *N* >1,000 to detect a 25% LoMV change. Figure 1 panels (1) and (2) show *N* for 80% power if all patients were included, and panels (3) and (4) for the targeted patient group. Panels (1) and (3) show that it is impossible to achieve 80% power for a 10% intervention effect. For 25% effect, MSC found *N* = 400/arm (all patients) and *N* = 150/arm (targeted cohort).

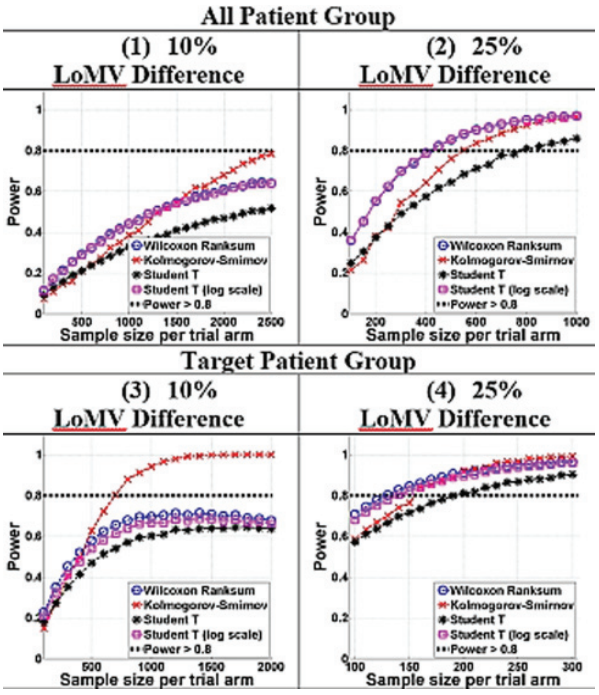


Figure 1 (abstract P227).

Conclusion Traditional parametric sample size estimation may overestimate the required patients. MCS can estimate effective *N*/arm and evaluate specific patient groups objectively, capturing local clinical practice and its impact on LoMV. It is important to consider targeting specific patient groups by applying patient selection criteria that can be easily translated into trial design.

P228

Non-invasive respiratory volume monitoring for quantification of respiratory depression after benzodiazepine administration

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Critical Care 2015, **19(Suppl 1):**P228 (doi: 10.1186/cc14308)

Introduction Benzodiazepines are used in many of settings to induce sedation, but can cause a reduction in respiratory drive. Objective monitoring of the effect of benzodiazepines on respiratory status in non-intubated patients has been difficult, putting patient safety at risk. A non-invasive respiratory volume monitor (RVM) that provides continuous measurement of minute ventilation (MV), tidal volume (TV) and respiratory rate (RR) was used to quantify the effects of midazolam on respiratory status in spontaneously breathing patients.

Methods An impedance-based RVM (ExSpiron; Respiratory Motion Inc., Waltham, MA, USA) was used in 30 patients who received 2 mg midazolam prior to induction of anesthesia and were sedated but spontaneously breathing. Eleven of these patients (58 ± 19 years, average BMI 27.7) received midazolam at least 20 minutes prior to induction. Digital RVM data were collected and MV, TV and RR calculated and evaluated from 30-second segments 10 minutes before and after the first dose of midazolam. Ten patients were analyzed as a group and one patient was analyzed separately (due to idiosyncratic reaction).

Results Following administration of midazolam, the group MV and TV decreased an average of 19 ± 7% and 16 ± 5%, respectively (mean ± SEM, *P* <0.01, both) while RR remained essentially unchanged (decrease of 3 ± 8%, *P* >0.3). In the younger half of the cohort (45 ± 16 years), the decreases in MV and TV were not significant, only 6 ± 3% and 8 ± 5%, respectively. The older half of the cohort (72 ± 8 years) displayed fourfold greater MV and TV decreases (32 ± 11%, *P* <0.05 and 25 ± 6%, *P* <0.05), when compared with the younger cohort, *P* <0.01, Figure 1).

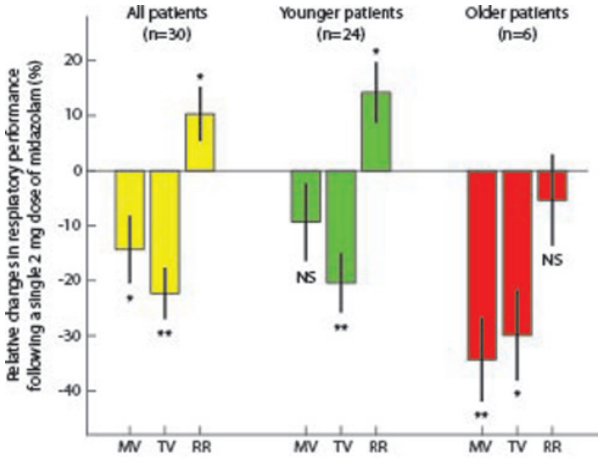


Figure 1 (abstract P228).

Conclusion Continuous monitoring with RVM provides a valuable depiction of hypoventilation from benzodiazepines, not demonstrated by other methodologies such as pulse oximetry and RR alone. RVM monitoring can help uncover potentially life-threatening hypoventilation in older patients. Further studies are ongoing to quantify hypoventilation after administration of other anesthetic medications.

P229

Nebulized heparin for patients under mechanical ventilation: a conventional data meta-analysis

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Critical Care 2015, **19(Suppl 1):**P229 (doi: 10.1186/cc14309)

Introduction Mechanical ventilation has the potential to induce pulmonary coagulopathy. Local treatment by nebulization of heparin could be beneficial in ventilated patients. The aim of this data meta-analysis is to determine the association between nebulization of heparin and outcome of mechanically ventilated critically ill patients.

Methods PubMed, Scopus, EMBASE, and Web of Science were searched for relevant articles. Articles were selected if they compared

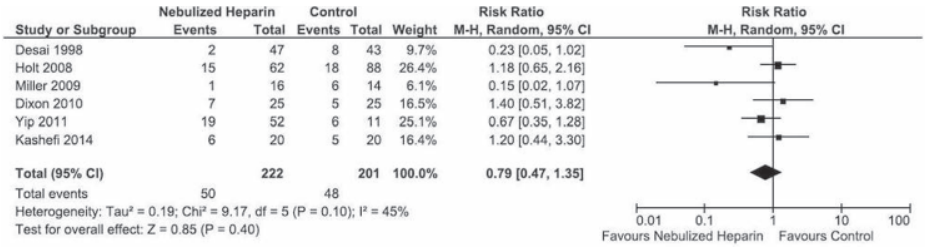


Figure 1 (abstract P229). Effect of heparin nebulization on mortality.

nebulization of heparin with standard care. The primary endpoint was overall mortality. Secondary endpoints included occurrence of pneumonia and number of ventilator-free days and alive at day 28.

Results Six articles were found: five retrospective cohorts with historical controls, one randomized controlled trial, covering 423 patients. Dosages of nebulized heparin varied from 30,000 to 150,000 IU/day. Fifty out of 222 patients (22.5%) receiving nebulized heparin and 48 out of 201 patients (23.9%) receiving standard care died (risk ratio (RR) 0.79 (95% CI 0.47 to 1.35)) (see Figure 1). Occurrence of pneumonia (RR 1.36 (95% CI 0.54 to 3.45); $I^2 = 59\%$), and number of ventilator-free days and alive at day 28 (standardized mean difference 0.11 (95% CI –0.14 to 35); $I^2 = 0\%$), were not different between the two groups.

Conclusion Nebulization of heparin is not associated with improved outcome in mechanically ventilated critically ill patients. This meta-analysis is limited by methodological problems in most included studies. Only one randomized controlled trial could be included. Also, most patients in the meta-analyzed studies suffered from inhalation trauma, and heparin dosages differed widely.

P230

Diagnosis of obstructive sleep apnea with respiratory polygraph in hypercapnic ICU patients

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Introduction The most frequent reasons for hypercapnic respiratory failure (HRF) in ICUs are COPD and in recent years obesity hypoventilation syndrome (OHS) and obstructive sleep apnea (OSA). Even 15 to 30% of COPD patients also have accompanying OSA. Due to increased upper airway resistance, those patients require higher expiratory pressures (EPAP) during noninvasive ventilation (NIV). In order to prescribe optimal mode and pressures during the ICU stay and at discharge, the intensivist should diagnose the underlying OSA. Portable recording devices have been developed and they were approved at least for the diagnosis in high pretest probability patients with results equal to in-laboratory polysomnography. The aim of this study is to assess whether respiratory polygraph (RPLG) can be used for obtaining diagnostic information of OSA in hypercapnic ICU patients.

Methods Patients, with HRF requiring NIV, were included in the study. RPLG studies were conducted under nasal oxygen before NIV, using the Philips Respironics Alice PDx® device, which provides the records of pulse oximetry with derived heart rate; snoring and nasal airflow with nasal pressure transducer and nasal thermistor; rib cage, abdominal motion and body position with abdominal and thoracic belts. American Academy of Sleep Medicine 2014 recommendations were used for the diagnosis of OSA and OHS. Because of the diagnostic difficulties of hypopnea in hypoxemic patients, we evaluated only the obstructive apnea index (OAI) instead of the apnea hypopnea index (AHI).

Results Thirty-one patients with the mean age of 67 ± 9 years were included in the study. Their mean APACHE II score was 16 ± 5 and BMI was 33 ± 9 kg/m^2. Admission arterial blood gases were as follows (mean ± SD); pH: 7.33 ± 0.07, PaO_2: 74 ± 12 mmHg, $PaCO_2$: 69 ± 11 mmHg, HCO_3^-: 31 ± 5, O_2Sat%: 92 ± 4. Admission diagnoses of the patients were OHS (36%) and COPD (68%). Mean OAI was 13 ± 6 in patients with OAI >5. Eighty-one percent ($n = 25$) of the recordings were interpretable and clinical and RPLG data supported a new diagnosis of OSA in 14 (56%) patients, and EPAP levels were increased. Laboratory sleep study was recommended to 19% of the patients. At the end of the study 56% of the COPD and 72% of the OHS patients were identified to have OSA.

Conclusion Although it underestimates AHI, RPLG is important and technically feasible in ICU patients in suggesting the presence of OSA and in providing information for appropriate NIV management.

P231

Respiratory muscle training during mechanical ventilation: a systematic review

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Introduction Respiratory muscle weakness is common in mechanically ventilated patients and impairs liberation from ventilation. Inspiratory muscle training (IMT) might accelerate liberation from mechanical ventilation. We undertook to summarize previously published IMT protocols and the impact of IMT on respiratory muscle function and clinical outcomes.

Methods We searched multiple databases using a sensitive search strategy combining MeSH headings and keywords for studies of IMT during MV. Studies were adjudicated for inclusion and data were abstracted independently and in duplicate. Methodological quality was assessed using the GRADE system.

Results Eleven studies met the inclusion criteria; of these, six were randomized controlled trials and five were observational studies.

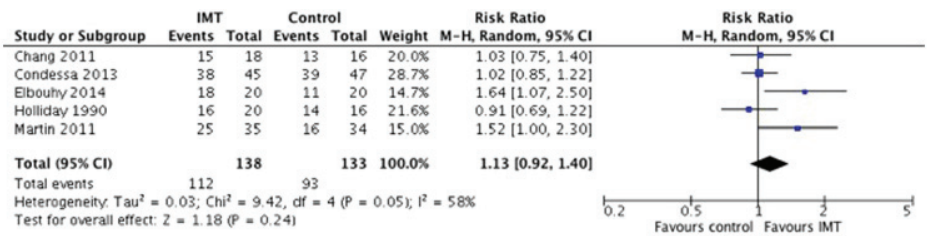


Figure 1 (abstract P231). Effect of IMT on the rate of successful weaning from mechanical ventilation.

A variety of IMT techniques were employed including inspiratory threshold loading (eight studies), biofeedback to increase inspiratory effort (one study), chair-sitting (one study) and diaphragmatic breathing pattern training (one study). Threshold loading was achieved by application of an external device (six studies) or increases in the inspiratory pressure trigger setting (two studies). Most studies implemented IMT in the weaning phase ($n = 5$) or after difficult weaning ($n = 5$); one study implemented IMT within 24 hours of intubation. IMT was associated with greater increases in maximal inspiratory pressure compared with control (six studies, mean difference 7.6 cmH_2O (95% CI 5.8, 9.3), $I^2 = 0\%$). There were no significant differences in the duration of MV (six studies, mean difference –1.1 days (95% CI –2.5, 0.3), $I^2 = 71\%$) or the rate of successful weaning (Figure 1; five studies, risk ratio 1.13 (95% CI 0.92, 1.40), $I^2 = 58\%$). The GRADE quality of evidence was low for all these outcomes; risk of bias was high for most studies and summary effects were imprecise and inconsistent. No serious adverse events related to IMT were reported.

Conclusion IMT in mechanically ventilated patients appears safe and well tolerated and improves respiratory muscle function. IMT was not associated with accelerated liberation from mechanical ventilation. However, because the included studies had important methodological limitations and employed varying methods of IMT, we cannot draw firm conclusions about the effect of IMT on clinical outcomes.

P232

Prospective assessment of the ability of rapid shallow breathing index computed during a pressure support spontaneous breathing trial to predict extubation failure in ICU

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Introduction As the objective clinical criteria [1] are imperfect to assess patients before extubation, simple physiological parameters are used to try to improve extubation failure (EF) prediction. The rapid shallow breathing index (RSBI) (respiratory rate (RR) over tidal volume (VT) ratio) recorded during a T-piece spontaneous breathing trial (SBT) is known as the most reliable physiologic predictor. However, RSBI is nowadays usually computed during a pressure support (PS) SBT using the values displayed on the ventilator screen and not based on spirometry measurements without any assist as initially published. The aim of the present study was to prospectively assess the ability of currently measured RSBI to predict EF.

Methods Retrospective analysis of prospectively collected data from patients intubated for more than 48 hours admitted in the medico-surgical ICU of Lausanne, Switzerland, from January 2007 to December 2008. EF was defined as the need for reintubation within 48 hours after extubation. Reintubations for a procedure requiring general anesthesia were not considered as EFs. RR and VT during the PS SBT were recorded from the ventilator and RSBI was computed accordingly. Baseline characteristics and currently measured RSBI were compared between patients who experienced EF versus success (*t* test or chi-square test as appropriate). The ability of currently measured RSBI to predict EF was assessed using ROC curve analysis.

Results A total of 478 extubated patients were included, 25 of whom (5.2%) were reintubated. ICU mortality (ICU-m) and in-hospital mortality (H-m) were higher in reintubated patients: ICU-m = 6 (24) versus 22 (5), $P = 0.002$ and H-m = 9 (36) versus 63 (15), $P = 0.009$. The reasons for EF were: acute lung failure ($n = 15$), congestive heart failure ($n = 4$) and aspiration/bronchial congestion ($n = 6$). Demographic data were similar between patients successfully and nonsuccessfully extubated: age: 58 ± 17 versus 58 ± 19 years, $P = 0.85$; male gender: 15 (60) versus 263 (61), $P = 0.99$. SAPS II score was higher in the EF group: 30 ± 22 versus 42 ± 27, $P = 0.04$. RSBI were significantly higher in patients who experienced EF: RSBI=59 ± 44 versus 43 ± 26, $P = 0.04$. The area under the ROC curve for currently measured RSBI was: 0.617 (95% CI = 0.571 to 0.662), $P = 0.035$.

Conclusion In a cohort of 458 medico-surgical ICU patients, RSBI measured during a pressure support SBT was higher in patients experiencing EF but very imperfect to predict EF.

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P233

Presence of neutrophil extracellular traps in bronchial aspirate of patients diagnosed with acute respiratory distress syndrome or acute exacerbation of idiopathic pulmonary fibrosis

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Introduction Neutrophil extracellular traps (NETs) are fibrous structures that are produced extracellularly from activated neutrophil. They can trap and kill various pathogens, and their release is one of the first lines of immune system. Meanwhile, recently it was reported that NETs also exert adverse effects in inflammatory diseases. Acute respiratory distress syndrome (ARDS) and acute exacerbation of idiopathic pulmonary fibrosis is acute-onset respiratory failure. It is characterized by excessive neutrophil infiltration into the alveolus, and great amounts of neutrophil elastase are released. The purpose of this study is to evaluate whether NETs are produced in bronchial aspirate of patients with ARDS or acute exacerbation of idiopathic pulmonary fibrosis, and to identify correlations with the respiratory function.

Methods This was a prospective observational study of seven patients admitted to the ICU of a large urban tertiary referral hospital. All patients were mechanically ventilated at the time of admission. The bronchial aspirates were collected serially from the patients by suction through a tracheal tube. To identify NETs, extracellular components including DNA, histone H3, and citrullinated histone H3 were simultaneously detected using immunohistochemistry. The respiratory function was evaluated by PaO_2/FiO_2 ratio (P/F ratio).

Results The study group was comprised of four men and three women. Median age was 69 (IQR: 61.0 to 72.5) years old. The reason for admission was ARDS ($n = 5$) and acute exacerbation of idiopathic pulmonary fibrosis ($n = 2$). The reasons for ARDS are bacterial pneumonia ($n = 3$), necrotizing fasciitis ($n = 1$) and extensive burn ($n = 1$). We identified NETs in the bronchial aspirates of all the patients. NET formation had persisted in four cases during the study period, their P/F ratio did not improve and all patients were dead due to respiratory failure. On the other hand, NETs decreased and vanished in three cases, their P/F ratio improved and all patients recovered from ARDS.

Conclusion NET formation was observed in bronchial aspirates of all the patients diagnosed with ARDS or acute exacerbation of idiopathic pulmonary fibrosis. It may be one of the prognostic factors of ARDS or acute exacerbation of idiopathic pulmonary fibrosis.

P234

New molecules controlling endothelial barrier

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Introduction Acute lung injury (ALI) and its hypoxemic form, acute respiratory distress syndrome (ARDS), has no approved pharmacological treatment and is a condition with high mortality. Vascular leakage is one of the early events of ALI/ARDS. CD73 activity (ecto-5′-nucleotidase) maintains the endothelial barrier function of lung capillaries via its enzymatic endproduct adenosine. Interferon-beta (IFNβ) increases synthesis of CD73 and has been effective in a mouse model of ALI [1].

Methods Therefore we conducted a phase I/II trial [2], in which intravenously administered human recombinant IFNβ1a (FP-1201) was used in the study, which consisted of dose escalation (phase I) and expansion (phase II) parts to test the FP-1201 safety, tolerability and efficacy in ALI/ARDS patients. CD73, MxA (a marker for IFN β response) and other biomarkers were measured to follow pharmacokinetics/dynamics of the intravenously administered FP-1201 and therapeutic efficacy.

Results The optimal tolerated dose of FP-1201 (10 μg/day for 6 days) resulted in maximal MxA stimulation. Also soluble CD73 values increased, while IL-6 decreased in sera of the FP-1201-treated ALI/ARDS patients. The overall mortality of the 37 patients treated with FP-1201

was only 8.1%, fourfold to fivefold less than the expected rate based on APACHE II score values of 21.9. The control group (n = 59), which was eligible for the trial but not possible to recruit, had mortality of 32.2% (P = 0.01) and APACHE II score 23.0.

Conclusion Restriction of vascular leakage with FP-1201 seems to significantly benefit ALI/ARDS patients. Our results suggest that FP-1201 could be the first effective, mechanistically targeted, disease-specific pharmacotherapy for patients with ARDS. However, these findings warrant conduction of a large multicenter study to establish safe and effective FP-1201 treatment of ARDS.

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P235

Endocan can be a predictive marker of severity of sepsis but cannot be a marker of acute respiratory distress syndrome in ICU patients

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Introduction Endocan (endothelial cell specific molecule-1), a 50 kDa dermatan sulfate proteoglycan, is expressed by endothelial cells in the lung and kidney. It was reported that the serum Endocan level is related to the severity of sepsis and positive correlation with the mortality rate. On the other hand, it was also reported that lower levels of serum Endocan are associated with subsequent development of chronic kidney disease, and chronic liver disease acute lung injury (ALI) in trauma patients. The aim of this study is confirmation of the relationship between serum Endocan level and the severity of sepsis, and also the severity of acute respiratory distress syndrome (ARDS) in septic patients.

Methods This study was conducted as a single-center, retrospective, observational study in the emergency department of Fukuoka University Hospital from April 2010 to August 2013. Blood samples were collected within 2 hours when the patients were diagnosed with ARDS. In this time we adopted the Berlin definition as the categorized of ARDS severity. Furthermore, we evaluated the extravascular lung water index (EVLWi) and pulmonary vascular permeability index (PVPI) as a condition of ARDS using the transpulmonary thermodilution method. Additionally, 10 healthy donors were entered as a control. The patients were divided into nonsepsis, severe sepsis and septic shock using the ACCP/SCCM guidelines.

Results We enrolled 70 ARDS patients during the investigation periods. We met six patients with nonsepsis, 27 with severe sepsis and 37 with septic shock. The serum Endocan levels were significantly higher in patients with septic shock (3.7 to 3.9 ng/ml) than in patients with severe sepsis (1.7 to 2.3 ng/ml, P <0.05), nonsepsis (0.6 to 0.3 ng/ml, P <0.05) and healthy donors (0.4 to 0.1 ng/ml, P <0.05). However, there was no significant correlation between the Endocan level and the severity of ARDS. In addition, significant correlation between the Endocan level and EVLWi and PVPI was not observed.

Conclusion These results suggested that there was good relationship between the Endocan level and the severity of sepsis. But unlike the trauma patients, correlation between the severity of ARDS and Endocan value was not recognized.

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P236

Mesenchymal stem cell and endothelial cell interaction restores endothelial permeability via paracrine hepatocyte growth factor *in vitro*

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Introduction Mesenchymal stem cells (MSCs) have potent stabilizing effects on the vascular endothelium injury, inhibiting endothelial permeability in lung injury via paracrine hepatocyte growth factor (HGF). Recently, it has been indicated that MSCs secreted more factors by MSC–endothelial cell (MSC-EC) interaction. We hypothesized that MSC-EC interaction restored endothelial permeability induced by lipopolysaccharide (LPS) via paracrine HGF.

Methods We investigated the endothelial permeability induced by LPS under two co-culture conditions in transwells. HPMECs were added into the upper chambers of cell-culture inserts, while there two different co-culture conditions in the lower side of transwells as follows: MSC-EC interaction group: MSCs and HPMEC contact co-culture in the lower chambers; and MSC groups: MSCs only in the lower chambers. The endothelial permeability in the upper side of transwells was detected. Then the concentration of HGF was measured in the culture medium using an enzyme-linked immunosorbent assay kit, following by neutralizing HGF with anti-HGF antibody in the co-culture medium. In addition, VE-cadherin protein expression were measured under the co-culture conditions by western blot, adherens junctions (AJs) protein including F-actin and VE-cadherin were detected by immunofluorescence technique as well.

Results The permeability significantly increased after LPS stimulation in a dose-dependent and time-dependent manner (P <0.01). Meanwhile, MSC-EC interaction more significantly decreased endothelial permeability induced by LPS (P <0.05 or P <0.01). Moreover, HGF levels in the MSC-EC interaction group were much higher than those of the MSC group (P <0.01). However, neutralizing HGF with anti-HGF antibody inhibited the role of MSC-EC interaction in improving endothelial permeability (P <0.05). Compared with the MSC group, MSC-EC interaction increased VE-cadherin protein expression (P <0.01), and restored remodeling of F-actin and junctional localization of VE-cadherin. However, the MSC effect was significantly blocked by anti-HGF antibody (P <0.05 or P <0.01).

Conclusion These data suggest that MSC-EC interaction decreased endothelial permeability induced by LPS, which was mainly attributed to HGF secreted by hMSCs. The main mechanisms of HGF restoring the integrity of EC monolayers are remodeling of endothelial intercellular AJs and decreasing caveolin-1 protein expression.

P237

Elevated levels of soluble RAGE predict impaired alveolar fluid clearance in a translational mouse model of acute respiratory distress syndrome

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Introduction Receptor for advanced glycation endproducts (RAGE) is a transmembrane receptor expressed in the lung and primarily located on alveolar type I cells. RAGE is implicated in acute respiratory distress syndrome to alveolar inflammation and, when its soluble form sRAGE is assayed in plasma or pulmonary edema fluid, as a marker of AT I cell injury. Functional activity of AT 1 cells can be assessed by the measurement of the alveolar fluid clearance (AFC) rate [1], but the relationship between sRAGE plasma levels of sRAGE and AFC rates has never been investigated. Our objectives were to report plasma levels of sRAGE in a mouse model of direct acid-induced epithelial injury, and to test their correlation with AFC rates.

Methods Forty-one CD-1 mice were divided into two groups: an HCl group underwent orotracheal instillation of hydrochloric acid on day 0, and a group control. Mice were evaluated on days 0, 1, 2 and 4 after a 30-minute period of mechanical ventilation. Blood and lung edema fluid (EF) were sampled. Before initiation of MV, all mice received a tracheal instillation of bovine serum albumin (5%) to detect changes in alveolar protein levels over 30 minutes. Plasma levels of sRAGE and total protein levels were measured. AFC rate values were corrected after measurement of mouse serum albumin in EF.

Results Basal AFC rate was 35% over 30 minutes in HCl-injured mice, but it was significantly depressed on day 1 (16% over 30 minutes; P = 0.02). Over time, AFC reached basal levels again. Plasma levels of sRAGE were higher in HCl-treated animals than in control animals on day 1

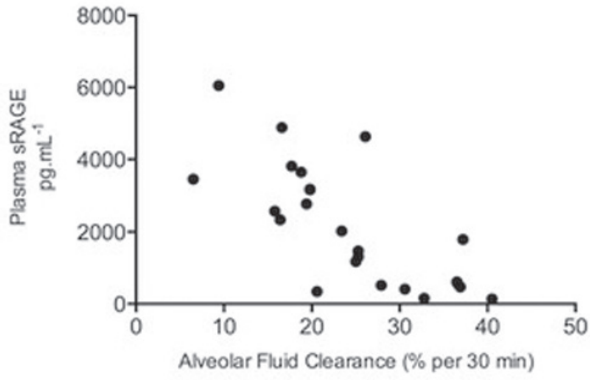


Figure 1 (abstract P237). Relation between AFC rates and sRAGE plasma levels.

($P = 0.03$) and day 2 ($P = 0.02$). The rate of AFC was inversely correlated with sRAGE levels in the plasma (Spearman's $\rho = -0.73$, $P < 0.001$). See Figure 1.

Conclusion The highest impairment in AFC is reported on day 1. sRAGE levels are also higher in injured mice and may be a good surrogate marker of AT I cell injury. This is a newly described relationship between AFC rates and sRAGE plasma level in a mouse model of direct epithelial injury. Our results support further translational investigation on the role of RAGE in alveolar injury and recovery.

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P238

Smoking increased risk of ARDS in surgical critically ill patients: results from the multicenter THAI-SICU study

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Introduction Cigarette smoking slowly and progressively damages the respiratory system [1]. In surgical critically ill patients, whether active cigarette smoking until admission to the surgical intensive care unit (SICU) is associated with increased risk of acute respiratory distress syndrome (ARDS) is not clearly identified.

Methods We conducted a cohort study using the THAI-Surgical Intensive Care Unit (THAI-SICU) study databases [2], which recruited 4,652 Thai patients admitted to the SICUs from nine university-based hospitals in Thailand (April 2011 to November 2012). The enrolled patients were divided into three groups (active smokers, exsmokers, and nonsmokers). Primary outcome was the incidence of patients diagnosed with ARDS and the secondary outcomes included 28-day mortality, incidence of systemic inflammatory response syndrome (SIRS), SICU length of stay (LOS), and total SICU cost.

Results Of those 4,652 patients, there were 2,947 nonsmokers, 1,148 exsmokers, and 557 active smokers. There was no difference of APACHE II score between three groups of patients. The active smokers exhibited the highest incidence of ARDS (active smokers 5.4%, exsmokers 4.8%, and nonsmokers 3%, $P = 0.003$). There was no difference of 28-day mortality between the three groups of patients. Active smokers had the highest incidence of SIRS (active smokers 41%, exsmokers 37%, and nonsmokers 34%, $P = 0.006$). Compared with nonsmokers and exsmokers, active smokers had a longer SICU LOS ($P < 0.01$) and higher total SICU cost ($P = 0.02$). Patients who smoked more than 15 pack-years were 2.5 times more likely to develop ARDS than patients who smoked ≤15 pack-years (95% CI: 1.65 to 3.66, $P < 0.001$). In multivariate analysis we found that every 1 pack-year of cigarette smoking before admission to the SICU is associated with increased risk of new ARDS with a hazard ratio of 1.02 (95% CI: 1.01 to 1.02, $P = 0.001$) after adjustment for APACHE II score, age, gender, and chronic obstructive pulmonary disease.

Conclusion In surgical critically ill patients, active smokers are associated with increased risk of new ARDS, longer SICU LOS, and higher total ICU cost, compared with exsmokers and nonsmokers. Our findings emphasize the essential need for a smoking cessation program.

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P239

Influence of body weight on lung mechanics and respiratory function in ARDS patients

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Introduction Traditionally, ARDS obese patients are ventilated with higher tidal volumes and higher PEEP due to expected increased in pleural pressure. However, data from the literature regarding the influence of body mass on lung mechanics and, particularly, on chest wall elastance are not univocal [1,2]. Failure to account for how the increase in body weight could affect the respiratory function can result in injurious mechanical ventilation and in the onset of VILI. The aim of this study was to evaluate the role of the body weight on respiratory mechanics in ARDS patients.

Methods A group of deeply sedated and paralyzed ARDS patients was divided into three classes according to the body mass index: normal weight (between 18.5 and 24.9 kg/m^2), overweight (between 25.0 and 29.9 kg/m^2) and obese (between 30.0 and 39.9 kg/m^2). They were mechanically ventilated in volume-controlled mode with a tidal volume of 6 to 8 ml/kg according to predicted body weight. Respiratory mechanics and gas exchange were assessed at PEEP levels of 5 and 15 cmH_2O.

Results A total of 101 ARDS patients was enrolled; 44 (43.6%) patients were normal weight, 36 (35.6%) overweight and 21 (20.8%) obese. Lung and chest wall elastance were not different between groups, both at PEEP levels of 5 cmH_2O and 15 cmH_2O ($P = 0.580$ and $P = 0.113$, respectively), and the end-inspiratory transpulmonary pressure was also similar. We did not observe any difference between groups regarding PaO_2/FiO_2 ratio ($P = 0.178$ at PEEP 5 cmH_2O; $P = 0.073$ at PEEP 15 cmH_2O) and $PaCO_2$ ($P = 0.491$ at PEEP 5 cmH_2O; $P = 0.237$ at PEEP 15 cmH_2O).

Conclusion In ARDS obese patients the chest wall elastance and the end-inspiratory transpulmonary pressure are not affected by the body weight, suggesting that normal weight and obese patients present similar risks for lung stress and VILI onset. The severity of hypoxemia was not different between groups.

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P240

Complex approach for diagnosing acute respiratory distress syndrome in nosocomial pneumonia

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Introduction Acute respiratory distress syndrome (ARDS) develops on the basis of nosocomial pneumonia (NP) in 30 to 35% of cases. A complex clinical approach is required for diagnosing it. The aim of this study was to investigate into the role of the PaO_2/FiO_2 ratio (P/F), extravascular lung water index (EVLWI) and surfactant protein D (SPD) as a complex diagnostic tool for ARDS in NP.

Methods The observational study in ICU ventilated septic patients with peritonitis (70%), pancreonecrosis (25%) and mediastinitis (5%) was done in 2010 and 2014. ARDS was diagnosed and staged according to the V.A. Negovsky Research Institute criteria and the Berlin definition. Plasma SPD was measured on ARDS diagnosis (day 0) and days 3 and 5 by the immunoenzyme essay (BioVendor, USA). Patients were treated according to the international guidelines. Data were statistically analyzed by STATISTICA 7.0, ANOVA and presented as median and 25 to 75th percentiles (ng/ml); P <0.05 was considered statistically significant. Areas under the receiver operating curves were calculated.
Results Sixty-five patients (out of 450 screened) were enrolled in the study according to the inclusion/exclusion criteria. Patients were assigned into groups: NP + ARDS (n = 43, 43 ± 4.9 years old, M/F 39/4, mortality 23%) and NP (n = 22, 40 ± 5.1 years old, M/F 20/2, mortality 18%). Groups were comparable in APACHE II and SOFA scores on the baseline. In the NP + ARDS group SPD was higher at all points than in the NP group. Plasma SPD on day 0 >111.2 ng/ml yielded a sensitivity of 68.2% and specificity of 92.3% (AUC 0.85; 95% CI 0.684 to 0.945; P <0.0001) for diagnosing ARDS in NP. P/F ratio on day 0 <280 yielded a sensitivity of 94.1% and specificity of 76.9% (AUC 0.89; 95% CI 0.744 to 0.952; P <0.0001) and EVLWI on day 0 >8.3 ml/kg yielded a sensitivity of 94.1% and specificity of 92.3% (AUC 0.92; 95% CI 0.810 to 0.982; P <0.0001) for the diagnosis of ARDS in NP. A complex ROC analysis (for SPD in the group of patients with P/F <280 and EVLWI >8.3) yielded a much better diagnostic accuracy of SPD: cutoff >93.7 ng/ml, sensitivity 81.0%, specificity 100.0% (AUC 0.96; 95% CI 0.817 to 0.998; P <0.0001).
Conclusion A complex approach (P/F <280, EVLWI >8.3, SPD >93.7) presents as a sensitive and highly specific method for diagnosing ARDS in NP patients.

P241

Effects of a recruitment maneuver on plasma soluble rage in patients with diffuse ARDS: a prospective randomized crossover study

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Introduction The soluble form of the receptor for advanced glycation endproducts (sRAGE) is a promising marker for epithelial dysfunction, but it has not been fully characterized as a biomarker during ARDS. Whether sRAGE could inform on the response to ventilator settings has been poorly investigated, and whether recruitment maneuver (RM) may influence plasma sRAGE remains unknown.
Methods Twenty-four patients with moderate/severe, nonfocal ARDS were enrolled in this prospective monocentric crossover study and randomized into a 'RM-SHAM' group when a 6-hour-long RM sequence preceded a 6-hour-long sham evaluation period, or a 'SHAM-RM' group (inverted sequences). Protective ventilation was applied, and RM consisted of the application of 40 cmH_2O airway pressure for 40 seconds. Arterial blood was sampled for gas analyses and sRAGE measurements, 5 minutes pre RM (or 40-second-long sham period), 5 minutes, 30 minutes, 1 hour, 4 hours and 6 hours after the RM (or 40-second-long sham period).
Results Mean PaO_2/FiO_2, tidal volume, PEEP and plateau pressure were 125 mmHg, 6.8 ml/kg (ideal body weight), 13 and 26 cmH_2O, respectively. Median baseline plasma sRAGE levels were 3,232 pg/ml. RM induced a significant decrease in sRAGE (–1,598 ± 859 pg/ml) in 1 hour (P = 0.043). At 4 and 6 hours post RM, sRAGE levels increased back toward baseline values. Pre-RM sRAGE was associated with RM-induced oxygenation improvement (AUC 0.87). See Figure 1.
Conclusion We report the first kinetics study of plasma sRAGE after RM in ARDS. Our findings could help to design future studies of sRAGE as a marker of response to therapeutic interventions during ARDS.

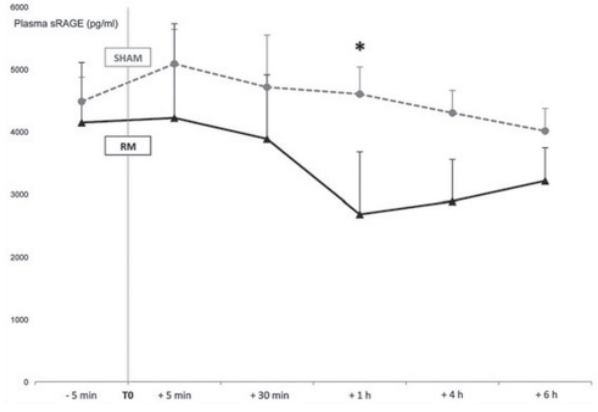


Figure 1 (abstract P241). Evolution of plasma levels of sRAGE (pg/ml) in both randomization sequences.

P242

Oesophageal artefact may significantly affect oesophageal pressure measurement in mechanically ventilated patients

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Introduction Oesophageal pressure is increasingly used to monitor and manage mechanically ventilated patients. Even if the oesophageal balloon catheter is correctly positioned, the measurement can be affected by inappropriate balloon filling and/or oesophageal reaction to balloon inflation. We aimed to assess the oesophageal reaction to oesophageal balloon filling in mechanically ventilated patients.
Methods An oesophageal balloon catheter (NutriVent; Sidam, Mirandola, Italy) was introduced in mid/distal thoracic position in 31 patients under invasive mechanical ventilation for acute respiratory failure. At ambient pressure, the balloon of the NutriVent catheter can be inflated up to 6 ml without generation of recoil pressure. The balloon was progressively inflated in 0.5 ml steps up to 9 ml and end-expiratory values of balloon pressure were used to assemble the balloon pressure–volume curve. The minimum slope section of the curve was graphically detected and inflation volumes corresponding to this part of the curve were considered appropriate. Overdistension of the balloon being excluded by definition in this section of the curve, its slope was attributed to the oesophageal reaction to balloon inflation.
Results Forty-five oesophageal balloon pressure–volume curves were obtained in 31 patients undergoing controlled mechanical ventilation (PEEP 12 ± 5 cmH_2O, FiO_2 0.7 ± 0.2, tidal volume/ideal body weight 8.0 ± 1.6 ml/kg). According to the graphically detected minimum slope section of the curve, the minimum and maximum appropriate balloon volumes were 1.5 ± 0.6 ml and 5.3 ± 0.9 ml, respectively. Between these two volumes, the slope of the curve was 1.1 ± 0.5 cmH_2O/ml, ranging from 0.3 to 3.1 cmH_2O/ml.
Conclusion The oesophageal artefact – that is, the reaction of the oesophageal wall to balloon inflation – may be clinically significant, being on average 1 cmH_2O for each millilitre of volume injected in the catheter, but reaching values as high as 3 cmH_2O/ml. The pressure generated by the oesophageal reaction leads to overestimation of pleural pressure. Therefore, the oesophageal artefact may significantly affect clinical decision-making based on absolute values of oesophageal pressure.

P243

Prone positioning in acute respiratory distress syndrome after abdominal surgery

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Introduction Prone positioning has been used for many years as an alveolar recruitment strategy in acute respiratory distress syndrome (ARDS). Prone positioning in ARDS improves oxygenation and

demonstrated recently its effectiveness on prognosis. Extrapulmonary etiologies of ARDS include abdominal emergencies. In cases of severe hypoxemia in the early postoperative period, intensivists discuss prone positioning based on the risk/benefit ratio.

Methods We conducted a retrospective two-center study of 5 years. The aim was to compare the prevalence of surgical complication potentially related to prone positioning between patients who had at least one prone positioning session and patients that remained in a supine position after abdominal surgery. Patients with ARDS in a context of recent (<7 days) abdominal surgery (except laparoscopy) were included. The primary outcome was the number of patients who had at least one surgical complication potentially related to prone positioning. We defined *a priori* these complications: scar dehiscence, abdominal compartment syndrome, stoma leakage, stoma necrosis, scar necrosis, wound infection, displacing of a drainage system, removal of gastro- or jejunostomy feeding, digestive fistula, evisceration.

Results We identified 43 patients with postoperative ARDS (62 ± 8 years, SAPS II 50 ± 13), among whom 34 (79%) had emergent surgery. Fifteen patients had at least one stoma after surgery. Nineteen patients (44%) had at least one prone positioning session (number of sessions: 2 (1 to 3)). At baseline, prone group patients had minimum PaO_2/FiO_2 ratio lower than the supine group (77 ± 23 vs. 110 ± 46 mmHg, P = 0.005). Plateau pressure was higher in the prone group (28 ± 4 vs. 23 ± 5 cmH_2O, P = 0.002). The first prone positioning session significantly increased the PaO_2/FiO_2 ratio: 106 ± 52 vs. 192 ± 90 mmHg (P = 0.001). Mean duration of the first prone positioning session was 20 ± 10 hours. In the prone group, 11 patients (58%) had at least one surgical complication, in comparison with nine (38%) in the supine group (P = 0.2). These complications resulted in revision surgery for two (10%) patients in the prone group and two (8%) in the supine group (P = 0.8). Mortality in the ICU was respectively 42% and 38% in prone group and supine group (P = 0.8).

Conclusion These preliminary results confirm the effectiveness of prone positioning in terms of oxygenation in ARDS after abdominal surgery without significant increase in surgical complications and no effect on the need for surgical revisions. Hence, if necessary, clinicians should not refrain from proning patients with postabdominal surgery ARDS.

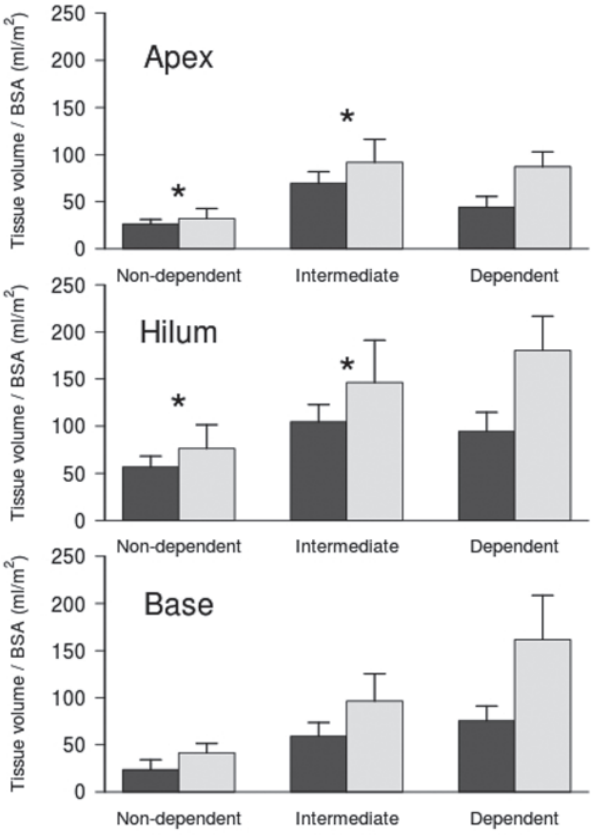


Figure 1 (abstract P244).

P244

Regional distribution of excess tissue mass in ARDS lung

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Introduction ARDS is characterized by edema diffuse to all lung fields. Distribution of excess tissue mass had been studied with CT scan in a few patients on a single slice, comparing with data obtained in healthy controls.

Methods ARDS patients underwent CT scan imaging during their ICU stay at 45 cmH_2O end-inspiratory pressure. After hospital discharge, patients underwent a follow-up CT scan performed at end inspiration. Each lung was divided into three sections along the apex–base axis and into three sections along the sternum–vertebral axis (nine regions per lung). Excess tissue mass in each lung region was defined as the difference in lung tissue (grams) between the CT scan performed during ARDS course and the follow-up CT scan. Results are presented as mean ± SD.

Results We studied eight ARDS patients (55 ± 18 years) with a BMI of 27 ± 6 kg/m². At ICU admission, patients had the following clinical parameters: PaO_2/FiO_2 106 ± 33 with PEEP 15 ± 5 cmH_2O; $PaCO_2$ 43 ± 10 mmHg; pH 7.35 ± 0.05. The average increase in lung weight during ARDS compared with follow-up CT scan was 68 ± 40% (680 ± 320 g). Figure 1 presents the tissue volume during ARDS (white bars) and after ARDS resolution (black bars) and compares the ratio between the two (*P <0.01 vs. dependent region).

Conclusion The excess tissue mass was not different between apex, hilum and base, but was increased in the dependent lung regions at apex and hilum, being uniformly distributed at the lung base.

P245

Functional respiratory imaging of airways in ventilated ARDS patients: revealing the regional relation between PEEP-induced airway opening and airway dilatation

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Introduction ARDS has a wide variability of lung morphological characteristics. Both alveolar collapse and airway narrowing or closing are present, often heterogeneously. Despite advances in ARDS imaging, we have thus far been unable to distinguish regional airway opening from airway dilatation in PEEP-induced lung recruitment. We demonstrate the technique of functional respiratory imaging (FRI) to differentiate these two entities.

Methods Six patients with early-stage ARDS were included in this prospective single-centre cohort trial. The lower infliction point on a pressure–volume curve was considered as the clinically acceptable minimal PEEP value. Subsequently, four distinct PEEP levels were chosen to perform CT scans: at 20 cmH_2O; median value between 1 and 3; clinically acceptable minimal; and 0 cmH_2O. FRI methods as described by De Backer and colleagues [1] were used to evaluate airway opening and airway dilatation.

Results Airway stretching (that is, bronchodilatation) could be quantified and distinguished from airway recruitment with this technique. Higher PEEP pressures not only recruit, but also expand the bronchi. The ratio of dilation/recruitment of bronchi was higher in the upper lobes than in the lower lobes, as illustrated in Figure 1. We were able to phenotype each patient, allowing a prediction on when an increase in PEEP further recruits atelectasis/bronchi or distends certain airway regions.

Conclusion The novel technique of FRI can be used to visualise the airway structures in ARDS and distinguish airway stretching from

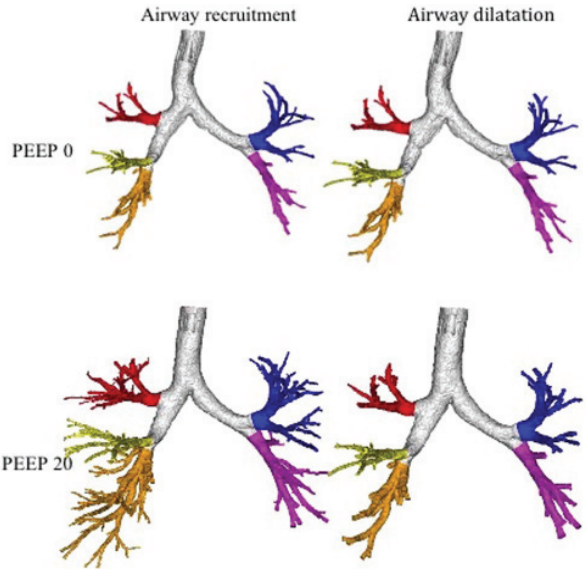


Figure 1 (abstract P245). Bronchodilation and bronchial recruitment split per lobe for one patient.

airway recruitment. This pilot study shows that, in ARDS, the upper lung regions are subject to airway dilation, whereas the lower (atelectatic) lung lobes have more airway opening with higher PEEP levels.

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P246

Efficacy and safety of open lung ventilation in patients with impaired peripheral chemoreflex sensitivity

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Introduction Mechanical ventilation during anesthesia leads to the development of atelectasis, poor oxygenation and postoperative pulmonary complications. Application of PEEP and recruitment maneuver (RM) can significantly reduce the severity of atelectasis and improve lung function. But the application of this strategy often leads to hemodynamic instability, which may be associated with impaired reactivity of the cardiovascular system. The purpose of this study was to evaluate the efficacy and safety of RM in patients with increased sensitivity of peripheral chemoreceptors (SPCR), which reflects the decreasing reactivity of the cardiovascular system.
Methods We conducted a prospective study in 116 patients with high SPCR, evaluated using the breath-holding test. The test was performed by measuring of voluntary breath-holding duration (BHD) after two-thirds of maximal inspiration. The end of breath-hold was determined by a palpation of contraction of the diaphragm. BHD <38 seconds was the marker of high SPCR [1]. All patients received a major abdominal surgery and were randomized into an open lung ventilation group or a PEEP group. The concept of open lung ventilation was performed as follows: PEEP was increased from 4 to 10 cmH_2O for three breaths, from 10 to 15 cmH_2O for three breaths, and from 15 to 20 cmH_2O for 10 breaths [2]. Then PEEP was reduced to 12 cmH_2O. This RM was repeated every hour. In the PEEP group PEEP was maintained at 12 cmH_2O during the whole anesthesia. Hemodynamics, blood gases and dynamic compliance were evaluated.
Results RM improved oxygenation compared with the PEEP group. The mean increase in the oxygenation index at the end of surgery was 31% (from 340 to 445 mmHg, P <0.05), in the PEEP group the increase was less significant and amounted to 12% (from 330 to 370 mmHg, P <0.05). Dynamic compliance increased by 35% in the RM group and did not change in the PEEP group. Hemodynamic changes at RM were more pronounced. So CI on average decreased by 34% (from 3.7 to 2.5 l/minute/m^2) compared with 10% with no RM (P <0.05), and SVR decreased by 19% (from 1,310 to 1,150 dyn × sec^{-1} × cm^{-5}, P <0.05), while in the PEEP group it did not change. No significant differences between groups in the incidence of complications, length of stay in the ICU and in the hospital were noted.
Conclusion RM patients with high SPCR and with reduced reactivity of the cardiovascular system improve lung function, but this is associated with the risk of hemodynamic instability.

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P247

Determinants of energy dissipation in the respiratory system during mechanical ventilation

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Introduction Mechanical ventilation performs at each breath mechanical work on the lung parenchyma. Part of this energy is recovered and part is dissipated into the respiratory system. The purpose of this study is to assess the respective role of three known determinants of energy dissipation: lung opening and closing, strain and lung inhomogeneities [1].
Methods Thirteen female piglets (21 ± 2 kg) were ventilated with a strain (V_T/FRC) greater than 2.5 (V_T ~ 38 ± 3 ml/kg) for 54 hours or until massive lung edema developed. Piglets were divided into five groups characterized by different energy loads obtained varying the respiratory rate: 15 breaths/minute (n = 3), 12 (n = 3), 9 (n = 3), 6 (n = 2) and 3 (n = 2). Every 6 hours two CT scans were performed (end-expiration and end-inspiration) and a static pressure–volume curve was obtained. A total of 51 CT scan couples and 51 corresponding pressure–volume curves was analyzed. The energy dissipated in the lung parenchyma at each breath was determined as the hysteresis area of the pressure–volume curve. CT scans were quantitatively analyzed with dedicated software. Data are presented as median (interquartile range).
Results Piglets ventilated with higher energy loads (RR 15 and 12) developed ventilator-induced lung injury (VILI), while piglets ventilated with lower energy loads (RR 9, 6 and 3) did not. The energy dissipated in the lung parenchyma at each breath was 0.56 J (0.52 to 0.62). Dissipated energy increased with time in piglets that developed VILI, while it remained near-constant in all the other piglets. Recruitability was 6% (3 to 8) of lung parenchyma, strain was 3.1 (2.6 to 3.5) and lung inhomogeneity extent (that is, the percentage of lung parenchyma that is inhomogeneous) was 10% (9 to 11). The energy dissipated in the lung parenchyma was well related to lung recruitability (r^2 = 0.50, P <0.0001), strain (r^2 = 0.57, P <0.0001) and lung inhomogeneity extent (r^2 = 0.42, P <0.0001). Multiple linear regression showed that dissipated energy was independently related to all of the three determinants of energy dissipation: lung opening and closing (P = 0.025), strain (P <0.0001) and lung inhomogeneities (P <0.01).
Conclusion Energy dissipation was largely dependent on strain, obtained with very high tidal volumes, but also lung inhomogeneities and lung opening and closing played a significant role.

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P248

Immune response after prolonged hyperoxic mechanical ventilation

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Introduction Mechanical ventilation and hyperoxia independently promote pulmonary injury and inflammation. However, the time course of the immune response following concurrent exposure is unclear. The

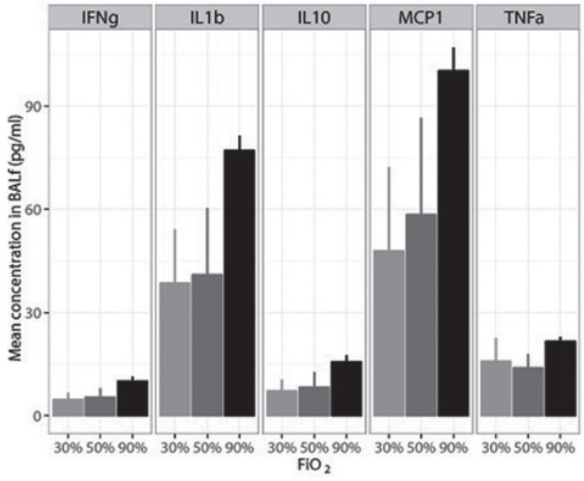


Figure 1 (abstract P248). Inflammatory mediators independent of tidal volumes after 12 hours of MV.

aim of this preclinical study was to study both time-dependent and dose-dependent effects of supplemental oxygen during prolonged ventilatory support on pulmonary inflammation in a well-established murine model of ventilation comparing low and high tidal volumes.
Methods Healthy male C57Bl/6J mice, aged 9 to 10 weeks, were randomly assigned to experimental groups ($n = 8$), in which the applied fractions of oxygen (FiO_2) were 30%, 50% or 90% and tidal volumes were either 7.5 or 15 ml/kg. Anesthetized mice were tracheotomized and ventilated for 8 or 12 hours. Inflammatory cells and mediators were measured in bronchoalveolar lavage fluid (BALf).
Results Mice exposed to higher FiO_2 had significantly higher PaO_2 levels at the end of the experiment. The total number of inflammatory cell in the BALf was not significantly different between the experimental groups ($P = 0.28$), yet an increasing trend in the percentage of neutrophils was observed with increasing FiO_2 ($P = 0.03$). Cytokine and chemokine levels did not differ between FiO_2 groups at 8 hours of ventilation. In mice ventilated for 12 hours, a significantly increasing trend in IFNγ, IL-1β, IL-10, MCP-1 and TNFα (Fig. 1, $P < 0.01$) was measured with increasing FiO_2, whereas IL-6, KC, MIP-2, GM-CSF and VEGF remained virtually unchanged. Differences between the tidal volume groups were small and did not markedly influence the effects of hyperoxia. See Figure 1.
Conclusion Hyperoxia induced a time-dependent and differentiated immune response that was independent of tidal volumes in a model of mechanically ventilated mice. The presence of cytokines and chemokines in the pulmonary compartment was more pronounced with prolonged and severe hyperoxia.

P249

Perioperative assessment of regional ventilation during changing body positions and ventilation conditions by electrical impedance tomography with increased spatial resolution and signal quality

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Introduction Electrical impedance tomography (EIT) is a functional imaging technology allowing one to regionally monitor aeration of the lungs. We used EIT with increased signal quality and spatial resolution to describe and quantify the regional changes in aeration caused by body position, both during spontaneous breathing and mechanical ventilation in pulmonary healthy patients undergoing laparoscopic prostatectomy.
Methods In 40 patients we performed EIT measurements at five points of time (Table 1) with the Swisstom BB2 prototype. Thirty-two electrodes were used to apply weak alternating currents to the thorax and to measure the resulting voltages, from which tomographic images of the changes in regional impedance caused by ventilation were created. We describe the ventilation distribution using a novel EIT lung function parameter called Silent Spaces that provides information about areas that do not receive much or any air during tidal breathing and are divided into nondependent (NSS) and dependent Silent Spaces (DSS) using a reference line that runs perpendicular to the gravity vector right through the centre of ventilation. NSS and DSS are expressed as a percentage of the total lung area.
Results Perioperative changes of NSS and DSS are shown in Table 1 as mean ± SD. Statistically significant differences marked by § when compared with 1 or by * when compared with 3 ($P < 0.05$).
Conclusion We describe for the first time the mapping of Silent Spaces during spontaneous breathing and changing ventilation conditions and body positions in patients with healthy lungs using EIT. This mapping of Silent Spaces might prove useful for developing perioperative protective ventilation strategies.

Table 1 (abstract P249)

	1 (sitting, spontaneous breathing)	2 (supine, spontaneous breathing)	3 (ventilated, supine position)	4 (ventilated, 30° head down position)	5 (ventilated, supine position)
NSS (%)	5.25 ± 2.9	4.12 ± 1.89§	3.05 ± 1.9§	2.8 ± 2.7§	2.67 ± 1.9§
DSS (%)	0.07 ± 0.3	2.29 ± 2.3§	9.23 ± 6.3§	11.5 ± 8.9§*	8.5 ± 5.8§

P250

Structural and functional effects of mechanical ventilation and aging on single rat diaphragm muscle fibers

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Critical Care 2015, **19(Suppl 1):**P250 (doi: 10.1186/cc14330)

Introduction The still unclear mechanisms causing ventilator-induced diaphragm dysfunction (VIDD) are considered intrinsic to the diaphragm muscle fibers. VIDD delays and complicates weaning from mechanical ventilation (MV) and accordingly contributes to prolonged ICU stay by 50%, with older patients being more affected than the young. The main aim of this study was to measure the effects of aging and 5 days of MV on rat diaphragm muscle fiber structure and function. We also aimed to investigate the biological age of the old rats to obtain data useful to design future experimental studies focusing on the effects of age in an ICU setting.
Methods We used a unique ICU rat model, which allows us to maintain the vital parameters stable under deep sedation and MV for long durations (several weeks). Diaphragm fiber cross-sectional area (CSA) and force-generating capacity (specific force = absolute force / CSA) were measured in young (6 months) and old (28 to 32 months) F344/BN hybrid rats in response to 5 days of deep sedation and volume-controlled MV. To investigate the biological age of the old rats, we performed a second set of experiments, comparing muscle fiber CSA and specific force in fast and slow-twitch distal hind limb muscles in three different age groups: young adults (6 months), middle aged (18 months) and old rats (28 months).
Results This study demonstrated an unexpected increase in CSA ($P < 0.001$) of the diaphragm fibers in response to 5 days of MV in both young and old animals. Maximum force decreased 39.8 to 45.2% ($P < 0.001$) in both young and old animals compared with controls, resulting in a dramatic loss of specific force. This increase in CSA and the concomitant decrease in specific force observed in both young and old diaphragm fibers are compatible with an ineffective compensatory hypertrophy in response to the MV. The comparison of the limb muscles

fibers from young, middle aged and old animals confirmed the 28 to 32 month rats to be senescent from a skeletal muscle point of view.
Conclusion These results demonstrate intrinsic changes in diaphragm muscle fibers of significant importance for the prolonged and complicated weaning from MV. Moreover, the increased number of frail diaphragm muscle fibers observed after MV in old age, both controls and mechanically ventilated, offers a further age-related possible mechanism which may be of significant clinical importance. These results also provided useful information to design future experimental studies focused on the effect of age in an ICU setting, pharmacological intervention strategies as well as mechanisms underlying rat strain differences.

P251

Does it make a difference to add automatic EPAP titration to the volume-targeted pressure support mode in noninvasive ventilation of hypercapnic ICU patients?

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Critical Care 2015, **19(Suppl 1):**P251 (doi: 10.1186/cc14331)

Introduction Obese patients are increasing in number in ICUs and more than 90% of them also have sleep apnea syndrome. Variability in upper airway resistance during sleep and awakening periods makes it difficult to set EPAP in these patients. A new mode that automatically titrates EPAP according to upper airway resistance and IPAP according to target tidal volume may be more effective. The aim of this study is to evaluate whether adding automatic EPAP titration to the volume-targeted pressure support mode will provide any therapeutic advantages in hypercapnic ICU patients.
Methods The hypercapnic patients treated with average volume-assured pressure support-automatic EPAP (AVAPS-AE) mode (Group1 (G1)) were compared with those treated with AVAPS mode (Group 2 (G2)). G2 was recruited retrospectively and matched with G1 according to diagnoses, demographic characteristics, arterial blood gas values and daily noninvasive ventilation (NIV) usage times. Trilogy 100® devices and their software Directview® (Philips Respironics) were used to reveal the respiratory data such as pressures, volumes, and daily usage times. For statistical analyses, *t* test, chi-square test and repeated measures of ANOVA were used.
Results Twenty-eight patients were included in G1 and 22 patients in G2. There was no significant difference between the patients' admission parameters and daily NIV usage times. $PaCO_2$ decreased >5 mmHg in 93% of G1 patients and in 60% of G2 patients in the first 6 hours (P = 0.044). A 10 mmHg reduction in $PaCO_2$ occurred in more patients (93% vs. 60%, P = 0.004) and in a shorter time (1.8 ± 1.2 vs. 3 ± 3 days, P = 0.044) in G1. At the time of discharge, $PaCO_2$ levels were <50 mmHg in 79% of G1 and 41% of G2 patients (P = 0.006). Both groups showed similar and significant improvements in PaO_2, $PaCO_2$ and HCO_3^- levels within the first 4 days but only in G1 patients were HCO_3^- levels decreased more rapidly than G2 patients (P = 0.007). Duration of NIV (6 ± 2 vs. 8 ± 3 days, P = 0.002) and the number of mode and pressures changes (0.3 ± 1.8 vs. 2 ± 2 times, P >0.0001) were significantly less in G1. While mean IPAP was similar in both groups, maximum and minimum EPAP titrated automatically in G1 were significantly different from G2. Mean tidal volume and amount of leakage were also significantly higher in G1.
Conclusion These results suggest that the AVAPS-AE mode may provide some advantages in hypercapnic ICU patients such as rapid $PaCO_2$ reduction, less NIV duration and workload.

P252

Retrospective study of patients receiving long-term mechanical ventilation

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Introduction This study analysed the practice of clinicians managing patients requiring long-term mechanical ventilation in the critical care unit (CCU) of the Royal Cornwall Hospital, Truro (RCHT), comparing outcomes of primary tracheostomy (TR) with trial of extubation (TOE).
Methods All 89 inpatients on the CCU who received mechanical ventilation continuously for 7 days or more between October 2012 and December 2013 were initially included. Forty patients who were intubated prior to arrival at RCHT, had incomplete notes, or were extubated during end-of-life care were excluded. Patients were divided into groups by first airway intervention; 31 TOE, 18 TR.
Results A total 52% (16/31) of patients had TOE, required no other airway intervention and survived to discharge from hospital, compared with 72% (13/18) of TR patients. Four patients from each group failed the first intervention and died prior to a second intervention. In total, 8/11 patients who had a second intervention after failed TOE survived to discharge from hospital. One patient had a second TR but died before discharge. This gave an in-hospital mortality rate of 19% for the TOE group and 28% for the TR group. TOE was performed earlier, all 31 on days 7 to 15. TR was performed later; 14/18 on days 7 to 15, and 4/18 on days 17 to 23. Early TR was more successful; 11/11 survived to discharge without a second intervention who had TR on days 7 to 12, compared with 29% (2/7) after day 12. TOE was more successful when performed later; 64% (7/11) survived to discharge without a second airway intervention when TOE was after day 10, 45% (9/20) between days 7 and 10. After first failed TOE, four patients had a successful second TOE; all four survived to discharge resulting in a median CCU stay of 29 days and median hospital stay of 39 days (excluding prior to CCU admission). Seven patients had TR after the first failed TOE, five survived to discharge from the CCU and four to discharge from the hospital. This group had shorter median stays in both the CCU (27 days) and hospital (32 days). Overall, the median duration of time ventilated, in the CCU, and in hospital was shorter for the TOE group; 13, 17 and 24 days respectively, compared with 22, 27.5 and 34 days for the TR group.
Conclusion TOE is more common and is associated with shorter time spent ventilated, in the CCU and in hospital than TR. It is also associated with a lower in-hospital mortality rate. TOE is more successful when performed after day 10; TR is more successful when performed before day 13. After failed TOE, a second TOE is associated with longer time in hospital but a better mortality rate than secondary tracheostomy.

P253

Initial pH and mortality in patients with exacerbations of COPD and pneumonia treated with NIV in a teaching hospital critical care unit

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Introduction Bilevel non-invasive ventilation (NIV) is an established therapy in chronic obstructive pulmonary disease (COPD) but conflicting evidence exists for its use in patients with pneumonia. Initial arterial pH <7.25 is used as a marker of severity and need for admission to critical care (CC) [1]. We examined the impact of pH and condition on outcome in patients with acute respiratory failure (ARF) of mixed aetiology treated with NIV.
Methods Data were collected retrospectively for a 5-year period from 2008 to 2013 using the Metavision electronic patient record. We identified all patients admitted with ARF treated with bilevel NIV. Patients who received continuous positive airway pressure or had a primary surgical problem were excluded. We recorded primary cause of respiratory failure, arterial blood gas values and mortality.
Results A total of 145 patients were identified. Mean age was 64 and 51% were male. The primary diagnosis was pneumonia in 69 patients and exacerbation of COPD in 57. The overall mortality was 19% on CC and 39% at 1 year. In patients with COPD, infective exacerbations had a higher CC mortality (17%) compared with non-infective (0%). However, by 1 year the mortality was 28% in infective and 29% in non-infective. Patients with pneumonia had a higher mortality on CC (25%) and at 1 year (48%). Patients with an initial pH <7.25 were less likely to survive. The mortality at discharge from CC was 16% (pH ≥7.25) and 26% (pH <7.25) but narrowed to 38% and 39% by 1 year. When subdivided, it was found that patients with infective COPD and pH <7.25 had the lowest 1-year mortality (17%) while those with pneumonia and pH <7.25 had the highest mortality (67%).
Conclusion NIV is used in our unit with comparable success rates to published series [2,3]. COPD patients responded well to NIV, while

patients with pneumonia treated with NIV have the highest mortality. A low presenting pH is associated with a higher mortality in patients with pneumonia treated with NIV. However, in COPD patients, pH <7.25 is not associated with higher mortality in CC or at 1 year. Further work defining the precise role of pH as a prognostic indicator is warranted.

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P254

Lung protective ventilation with lower tidal volumes and development of pulmonary complications in critically ill patients without ARDS

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Introduction A large meta-analysis suggests that use of low tidal volumes benefits patients without ARDS [1] but most studies in this meta-analysis included patients receiving ventilation during general anesthesia for surgery. The aim of the present meta-analysis is to determine the association between tidal volume size and development of pulmonary complications in ICU patients.
Methods An individual patient data meta-analysis of studies of ventilation in ICU patients without ARDS. Corresponding authors of retrieved studies provided individual patient data. The primary outcome, pulmonary complications, was a composite of development of ARDS or pneumonia during hospital stay. Secondary outcomes included ICU and hospital length of stay, and in-hospital mortality. Patients were assigned to three groups based on tidal volume size (≤7 ml/kg predicted body weight (PBW), 7 to 10 ml/kg PBW, or ≥10 ml/kg PBW).
Results Seven investigations (2,184 patients) were meta-analyzed. Pulmonary complications occurred in 23%, 28% and 31% respectively in the ≤7 ml/kg PBW, 7 to 10 ml/kg PBW and ≥10 ml/kg PBW group (adjusted RR, 0.72; 95% CI, 0.52 to 0.98; P = 0.042). Occurrence of pulmonary complications was associated with a lower number of ICU-free days and alive at day 28, a lower number of hospital-free days and alive at day 28 and increased in-hospital mortality.
Conclusion Ventilation with low tidal volumes is associated with a lower risk of development of pulmonary complications. Occurrence of pulmonary complications is associated with an increased ICU and hospital length of stay and in-hospital mortality in ICU patients without ARDS.

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P255

Factors associated with survival and hospital discharge amongst critically ill patients undergoing prolonged mechanical ventilation in the North of England Critical Care Network

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Introduction The combination of a global demographic shift and increased survival following critical illness has led to an increasing number of patients requiring prolonged mechanical ventilation (PMV) and longer critical care stay. This is a prospective observational study evaluating the characteristics and speciality-based outcome of critically ill patients undergoing prolonged mechanical ventilation in the North of England Critical Care Network (NoECCN).
Methods A weekly survey was conducted over a 1-year period screening patients older than 16 years of age requiring PMV in all 18 adult critical care units within the NoECCN. Patient data collected included patient demographics, admission diagnosis and speciality, hospital length of stay (LOS) pre and post critical care admission, severity of illness scores, critical care LOS and status at hospital discharge.
Results During the study period 134 patients met the criteria for PMV representing 1% of annual admissions and 6.9% NoECCN bed-days. The majority of patients receiving PMV were medical (50.7%), followed by emergency surgery (20.1%), elective surgery (16.4%) and specialist services such as spinal cord injury (8.2%) and cardiothoracic transplant (4.5%). The commonest admission diagnosis in the medical population was pulmonary infection followed by acute neurological disorders, while 89.4% of surgical patients were admitted to critical care during the perioperative period. At the end of the study period the highest hospital mortality was observed in the nonspecialist surgical population (26.5%). In contrast, the medical population had one of the lowest hospital mortality rates (11.8%), lower than predicted using the intensive care national audit research network illness severity score. Comparable rates of hospital discharge were found in both medical (85%) and nonspecialist surgical patients (88.9%).
Conclusion The results of this study highlight an expanding proportion of NoECCN critical care bed-days occupied by stable patients undergoing PMV. In keeping with published UK data, elevated hospital mortality was observed in the nonspecialist surgical subpopulation. Although the literature suggests the medical cohort of patients has poorer prognosis, within our region all were liberated from mechanical ventilation and over 80% were discharged from hospital.

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P256

Effects of positive end-expiratory pressure on lung ventilation/perfusion matching: a clinical study

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Introduction Positive end-expiratory pressure (PEEP) exerts multiple protective effects in hypoxemic critically ill patients: PEEP can increase end-expiratory lung volume (EELV) and induce recruitment, thus reducing lung strain and opening and closing of alveoli and potentially improving the ventilation/perfusion matching. In particular, estimation of PEEP-induced ventilation/perfusion matching might help identify the optimal PEEP setting, but bedside non-invasive methods are few and complex to be applied in daily clinical practice. Electrical impedance tomography (EIT) is a non-invasive bedside technique that claims to track global and regional changes in perfusion and ventilation over time. In the present study we aimed at verifying the effects of PEEP on ventilation/perfusion matching, as assessed by EIT, in acute respiratory failure patients.
Methods We enrolled 20 intubated critically ill patients undergoing controlled mechanical ventilation, sedated, paralyzed and with PaO_2/FiO_2 ≤300 at PEEP ≥5 cmH_2O. We started EIT monitoring (Pulmovista500®; Dräger Medical GmbH, Lübeck, Germany) and applied two PEEP levels (clinical and clinical + 5 cmH_2O) for 20 minutes each. We collected ventilatory and EIT parameters and, by offline analysis, we calculated the increase of EELV at higher PEEP and the EIT-based indexes of ventilation heterogeneity (VtHetend-insp) and of the regional homogeneity of ventilation/perfusion matching (HA/P).
Results Patients were 62 ± 12 years old, mean PaO_2/FiO_2 was 197 ± 52, lower PEEP level was 7 (7 to 9) cmH_2O, while higher PEEP was 12 (12 to 14) cmH_2O (P <0.001). At higher PEEP, EELV increased (391 (334 to 555) ml vs. PEEP low, considered as baseline, P <0.001); VtHetend-insp was reduced (1.8 (1.5 to 2.4) vs. 2.2 (1.8 to 2.6), P <0.001) and HA/P increased (0.29 ± 0.19 vs. 0.2 ± 0.15, P <0.05). Interestingly, the increase of HA/P was significantly correlated with the decrease of VtHetend-insp (r = –0.48, P <0.05). Moreover, patients with higher potential for improvement of ventilation/perfusion matching (that is, patients with increase of HA/P >16%) had higher baseline VtHetend-insp (2.6 (2.3 to

4.8) vs. 1.9 (1.5 to 2.1), P <0.01) and lower compliance of dependent lung regions (Crsdep, 13 ± 3 ml/cmH_2O vs. 18 ± 6 ml/cmH_2O, P <0.05), as compared with patients with smaller improvement.
Conclusion EIT might represent a feasible, bedside method to estimate PEEP-induced improvement in ventilation/perfusion matching. Assessing regional ventilation and mechanical lung properties might help identify patients who would benefit more from higher PEEP.

P257

18-FDG PET in lung transplantation

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Introduction Lung transplantation is associated with an inflammatory reaction known as primary graft dysfunction. This clinical syndrome occurs within the first 72 hours after transplantation and is characterized by hypoxemia (PaO_2/FiO_2 <300) and bilateral infiltrates not secondary to cardiac dysfunction, viral or bacterial pneumonia and venous anastomotic obstruction.
Methods 18-FDG PET scan was used to study 15 lung transplantation patients. The rate of 18-FDG uptake (Ki) was computed voxel by voxel with the Patlak method. Patients were divided according to the median Ki (27.8 (20.3 to 34.6) ml/minute/ml × 10^4). Data are reported as median and interquartile range.
Results Five patients developed primary graft dysfunction; median Ki in these patients was not different from patients who did not (24.5 (18.2 to 33.6) ml/minute/ml × 10^4 vs. 29.1 (23 to 35.4) ml/minute/ml × 10^4 respectively, P = 0.64). Bilateral lung transplantation patients were characterized by a median Ki of 30.5 (22.9 to 34.5) ml/minute/ml × 10^4, while patients undergoing single-lung transplantation presented a median Ki of 24.4 (21 to 34.1) ml/minute/ml × 10^4 (P = 0.61). Considering single-lung transplantation, graft and native lung had similar Ki: 24.4 (21 to 34.1) ml/minute/ml × 10^4 versus 24.2 (17.7 to 30.1) ml/minute/ml × 10^4 respectively (P = 0.64). When patients were divided according to the median Ki value, higher Ki was associated with higher $PaCO_2$ values (50 (46 to 53) mmHg vs. 37 (34 to 44) mmHg, P = 0.01). See Table 1.

Table 1 (abstract P257)

	Ki <27.8 ml/minute/ml × 10^4 (n = 7)	Ki ≥27.8 ml/minute/ml × 10^4 (n = 8)	P value
PaO_2/FiO_2	280 (261 to 346)	239 (212 to 271)	0.31
pH	7.46 (7.43 to 7.48)	7.41 (7.39 to 7.44)	0.15
$PaCO_2$ (mmHg)	37 (34 to 44)	50 (46 to 53)	0.01
WBCs (10^3 cell/mm^3)	8 (8 to 9)	9 (9 to 16)	0.34
Total lung volume (ml)	1,298 (1,092 to 1,494)	1,516 (1,408 to 1,665)	0.18
Total lung weight (g)	592 (488 to 741)	732 (597 to 774)	0.39
Total lung gas (ml)	706 (551 to 843)	804 (755 to 1,080)	0.15
Not-inflated lung tissue (%)	25 (12 to 30)	23 (17 to 30)	0.95
Poorly inflated lung tissue (%)	34 (42 to 42)	31 (29 to 34)	0.39
Well-inflated lung tissue (%)	36 (27 to 47)	47 (35 to 52)	0.53

Conclusion Patients clinically defined as having primary graft dysfunction did not have an increased rate of 18-FDG uptake. 18-FDG uptake was not different in single-lung versus bilateral transplantation and, in single-lung procedures, the native lung showed elevated inflammatory activity.

P258

Usefulness of extravascular lung water assessment as a predictor of weaning from mechanical ventilation

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Introduction Quantitative measurement of extravascular lung water (EVLW) would be extremely useful for clinical management, both as an index of severity and to guide treatment lung ultrasonography (LU) as a tool to quantify EVLW.
Methods Forty mechanically ventilated patients were examined for 5 successive days after being eligible for weaning; counting B-lines (comets) in both lung fields by LU, peak airway pressure, plateau airway pressure, static compliance and ABG analysis every 6 hours. Patients were divided into two groups according to success of the weaning process: group A (weaned group), and group B (nonweaned group).
Results The median value of LU comets was significantly lower in Group A compared with Group B. There was a significant increase in hypoxic index in Group A compared with Group B. There was no significant difference between both groups as regards PIP, while Pplat showed a significant increase in Group B compared with Group A and Cs showed a significant decrease in Group B.
Conclusion LU is a useful to quantify EVLW; it is a good predictor of weaning.
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P259

Pressure reconstruction method for spontaneous breathing effort monitoring

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Introduction Estimating respiratory mechanics of mechanically ventilated patients is unreliable when patients exhibit spontaneous breathing (SB) efforts on top of ventilator support. This reverse triggering effect [1] results in an M-wave shaped pressure wave. A model-based method to reconstruct the affected airway pressure curve is presented to enable estimation of the true underlying respiratory mechanics of these patients.
Methods Airway pressure and flow data from 72 breaths of a pneumonia patient were used for proof of concept. A pressure wave reconstruction method fills parts of the missing area caused by SB efforts and reverse triggering by connecting the peak pressure and end-inspiration slope (Figure 1). A time-varying elastance model [2] was then used to identify underlying respiratory elastance ($AUCE_{drs}$). The area of the unreconstructed M-wave has less pressure, resulting in a lower overall $AUCE_{drs}$ without reconstruction. The missing area of the airway pressure or $AUCE_{drs}$ is hypothesized to be a surrogate of patient-specific inspiratory to assess the strength of SB efforts. $AUCE_{drs}$ and missing area A_2 are compared with/without reconstruction.
Results Median $AUCE_{drs}$ and breath-specific effort using reconstruction were 24.99 (IQR: 22.90 to 25.98) cmH_2O/l and 3.64 (IQR: 0.00 to 3.87)% versus $AUCE_{drs}$ of 20.87 (IQR: 15.24 to 27.48) cmH_2O/l for unreconstructed M-wave data, indicating significant patient and breath-specific SB effort, and the expected higher elastance (P <0.05).
Conclusion A simple reconstruction method enables the real-time measurement of respiratory system properties of a SB patient and measures the surrogate of the SB effort, that latter of which has clinical use in deciding whether to extubate or re-sedate the patient.
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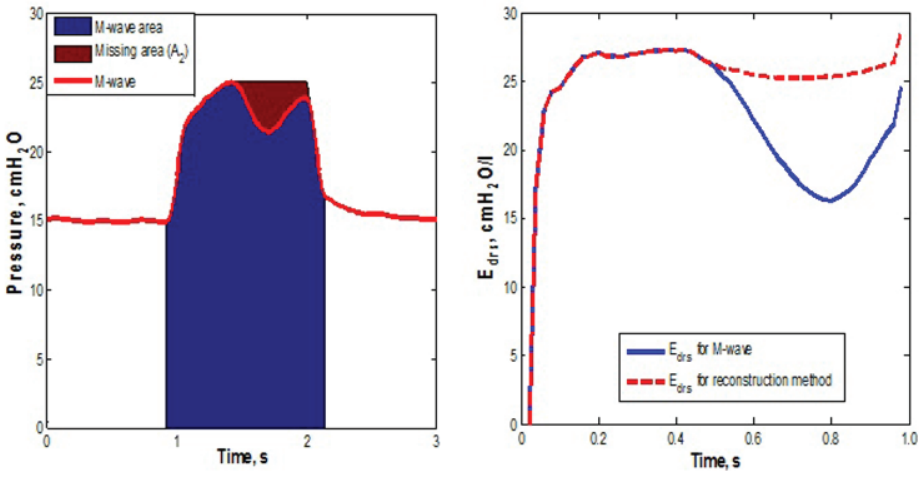


Figure 1 (abstract P259). E_{drs} for M-wave and reconstructed airway pressure at PEEP = 15 cmH_2O.

P260

Breath-to-breath respiratory mechanics variation: how much variation should we expect?

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Introduction Model-based respiratory mechanics can be used to guide mechanical ventilation therapy. However, identified mechanical properties vary breath to breath, leading to potential treatment errors when using model-based care that requires accuracy. This study investigates and quantifies this variability to improve its application in guiding clinical interventions.
Methods Retrospective data from 12 acute respiratory distress syndrome (ARDS) patients were used [1]. Each patient was sedated to prevent spontaneous breathing effort, and ventilated using the volume control mode with a square flow profile. Varied PEEP levels were maintained for 30 minutes before 1 minute of data were collected for analysis. This dataset provides a wide range of respiratory mechanics values, and the clinical protocol detail is in [1]. A clinically proven, single compartment model respiratory system elastance (Ers) is identified from data for every breathing cycle at each PEEP level using a linear regression method. The dynamic elastance (Edynamic = (peak airway pressure – positive end-expiratory pressure) / tidal volume) of the corresponding breathing cycle is calculated for comparison.
Results The coefficient of variation (CV) of identified Ers across all patients was low (<0.005), as expected, as the 30-minute period allows time-dependent alveolar recruitment to fully occur and stabilise. However, even with substantial stabilisation periods, there remains a difference between the minimum and maximum estimated Ers within each 1-minute period of analysed data. The differences were median 2.8% (interquartile range (IQR): 1.5 to 4.6%, 90% range (90R): 0.8 to 13.4) for Ers and 3.6% (IQR: 2.3 to 5.2, 90R: 0.9 to 10.8) for Edynamic, and in extreme cases, can be up to 16%.
Conclusion This study quantified the variability (over short periods) of identified and estimated respiratory mechanics properties used to (potentially) guide ventilation care in sedated patients. It is also important to note that this minimum level of variability occurs even when stabilisation is achieved. Thus, clinically, if this information was to be used to guide ventilation in real time, such as titrating PEEP to minimal elastance, larger errors, at least up to 15% variation in Ers, could be expected, which could well affect care. Such levels thus also begin to define the minimum levels of change necessary to be larger than natural variation.
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P261

Evaluation of a patient-dedicated blood gas analyser

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Introduction Patient-dedicated arterial blood analysers offer the potential to allow close monitoring of critically ill patients without leaving the patient's bedside or net loss of blood for the patient. A new patient-attached blood gas analyser was evaluated in a clinical environment to compare the results against the reference bench-top analyser.
Methods Twenty ICU patients with a range of clinical conditions, including trauma, head injury, post-surgical recovery and sepsis, were included in the study. The new analyser was operated by clinical staff at the Queen Elizabeth Hospital, Birmingham, who each underwent a 90-minute training programme. Patients were monitored using the patient-dedicated analyser (Proxima; Sphere Medical) for up to 3 days. Each time a sample was tested on the patient-dedicated analyser, a concurrent sample was drawn and tested on the hospital's bench-top analyser (Cobas b221; Roche Diagnostics). Samples were assessed using methods described by Bland and Altman for repeated measures. Performance of the novel device was analysed by calculating bias as the mean difference between the new analyser and the comparator device, imprecision as ±1 standard deviation (SD) from the mean and limits of agreement as ±1.96 SD from the mean. Percentage values for bias and precision were calculated from analysis of the percentage difference between the two methods of analysis. Intra-device imprecision for the haematocrit (Hct) sensor was calculated using a pooled variance calculation.
Results Over 275 paired samples were analysed over the following concentration ranges: pH 7.249 to 7.545; pCO_2 3.32 to 11.01 kPa; pO_2 5.59 to 21.80 kPa; Hct 23.6 to 41.4%; K+ 3.3 to 4.79 mM. The imprecision for each sensor was calculated to be: pH –0.00 ± 0.03; pCO_2 –0.48 ± 0.34 kPa; pO_2 –0.85 ± 0.96 kPa; Hct –4.49 ± 3.42%; K+ 0.08 ± 0.15 mM, respectively. The data collected on the new analyser for Hct showed relative imprecision of 3.42%. The pooled SD was calculated to be 1.21% and the mean SD of each of the novel devices used was 1.14%. This indicates that scatter observed on the Hct sensor was largely due to inter-device rather than intra-device factors.
Conclusion The patient-dedicated blood gas analysers demonstrated excellent agreement with the bench-top analyser for pH, pCO_2, pO_2 and K+, while Hct provides a reasonable trend monitor with variable bias. Proxima is well suited to enable staff to more closely manage unstable and critically ill patients. This device may be of significant benefit to patients at risk of iatrogenic anaemia or those being treated in side rooms/isolation rooms.

P262

Tidal volume accuracy during non-invasive ventilation with modern neonatal mechanical ventilators

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Introduction Maintaining the appropriate tidal volume (VT) is important for success of lung protective ventilation. However, in neonates, the presence of airway leaks may increase the errors in the delivery of tiny VT, which raises a concern of ventilator-induced lung injury. This study is to investigate the accuracy of VT delivery during non-invasive ventilation (NIV) with modern neonatal ventilators.
Methods Using a lung simulator for a patient body weight of 3 kg, we measured the actual delivered VT in the lung and compared it with the value displayed on the ventilator in six ventilators. We tested 18 conditions with various combinations of respiratory mechanics (normal, restrictive, obstructive), leak levels (0, 1.0, 1.5 l/minute), and PEEP settings (5, 10 cmH_2O). All conditions were tested in NIV mode. The pressure level was set to achieve VT to the lung at 6 to 7 ml/kg. All other settings were: F_IO_2 0.21, I_{time} 0.6 seconds, f 25/minute, and default rise time. We calculated the mean errors of the ventilator-displayed VT at various levels of airway leak.
Results The VT mean error values are presented in Table 1. When no leak existed, the mean error was less than 5% in all ventilators except one (C3) which showed a mean error of 26%. As the leak level increased, three ventilators (C3, G5, and VN500) showed marked differences between the delivered and displayed VT. In particular, the VN500 could not operate in the large leak condition. The other three ventilators (PB840, PB980, Servo i) showed acceptable VT accuracy across all conditions tested.

Table 1 (abstract P262)

Leak amount (l/minute)	Hamilton C3	Hamilton G5	Servo i	PB840	PB980	VN500
0	26 (15)	4 (6)	3 (2)	2 (7)	–4 (2)	2 (2)
1.0	–9 (5)	9 (5)	–2 (2)	–5 (4)	–2 (4)	20 (5)
1.5	16 (8)	–14 (8)	–2 (2)	–6 (4)	–2 (3)	33 (6)[a]

Data presented as mean (SD), %. [a]Unable to measure in one case.

Conclusion Tidal volume accuracy during neonatal NIV varies greatly among different ventilators and leak conditions. This must be considered in neonatal ventilation management to avoid over-ventilation or underventilation.

P263

Ventilatory response during intentional early rehabilitation in patients with mechanical ventilation

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Introduction Intentional early rehabilitation with mechanical ventilation in ICUs is performed in clinical settings. However, strict indexes for safe rehabilitation have not been fully elucidated. The purpose of this study is to analyze ventilator response (VR) between healthy volunteers and patients with mechanical ventilation.
Methods Sixteen healthy volunteers (Control group) and 13 patients on mechanical ventilation (MV group) were enrolled in this study. Both groups were positioned in a variety of postures (baseline in a supine position, settled back 30°, settled back 60°, and sitting position) and measured with an indirect calorimeter. The instantaneous energy expenditure (EE), tidal volume (TV), respiratory rate (RR) and minute expiratory volume (VE) were non-invasively measured in each posture. The VE was indexed by body weight and the EE was also indexed by the basal energy expenditure (BEE) estimated by the Harris–Benedict formula. VR was defined as the slope in the indexed VE–indexed EE plot with an assumption of those relationship in the linear manner. We examined the correlation between indexed EE and indexed VE in both groups, and the differences of the maximal indexed EE, the maximal indexed MV, and the others between both groups were investigated using the unpaired *t* test. For all the data, significance was accepted at values of $P < 0.05$.
Results There was a significant correlation between the indexed EE and indexed VE in both groups ($R = 0.51$, $P < 0.0001$ in the control group; $R = 0.63$, $P < 0.0001$ in the MV group). The VR was significantly suppressed in the MV group compared with the control group (0.041 ± 0.003/minute/BEE vs. 0.069 ± 0.003/minute/BEE, $P = 0.012$; respectively). Although the indexed VE was comparable in the MV and control groups (0.19 ± 0.07 l/kg vs. 0.17 ± 0.04 l/kg, $P = 0.23$; respectively), the indexed EE was shifted to a higher range in the MV group than in the control group (maximal indexed EE; 2.26 ± 0.68 vs. 1.74 ± 0.20, $P = 0.008$; respectively). The TV was smaller (maximal TV; 985 ± 592 ml vs. 1,410 ± 299 ml, $P = 0.018$; respectively) and the RR was more frequent (maximal RR; 30 ± 8/minute vs. 16 ± 4/minute, $P < 0.0001$; respectively) in the MV group than in the control group.
Conclusion The VR to external stress with mechanical ventilation is more suppressed than in healthy volunteers. The VE in the mechanical ventilation was earned by a higher RR rather than by increased TV. Careful monitoring of VE or RR would be beneficial in early rehabilitation with mechanical ventilation.

P264

Effective capnography training in the ICU using the 'hats and caps' training tool

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Critical Care 2015, **19(Suppl 1):**P264 (doi: 10.1186/cc14344)

Introduction Failure to use or correctly interpret capnography in patients dependent on an artificial airway in ICUs was thought to have contributed to 74% of ICU airway-related deaths in the NAP4 study [1]. However, capnography is only of value if those using it can interpret it correctly, with recommendations for training all ICU staff in capnography [1,2]. A recent UK survey identified that only 48% of ICUs have trained all staff in capnography interpretation (TM Cook, personal communication). In this study, we used a capnography teaching aid ('hats and caps') to educate all ICU staff during a 1-month period, and evaluated its effectiveness.

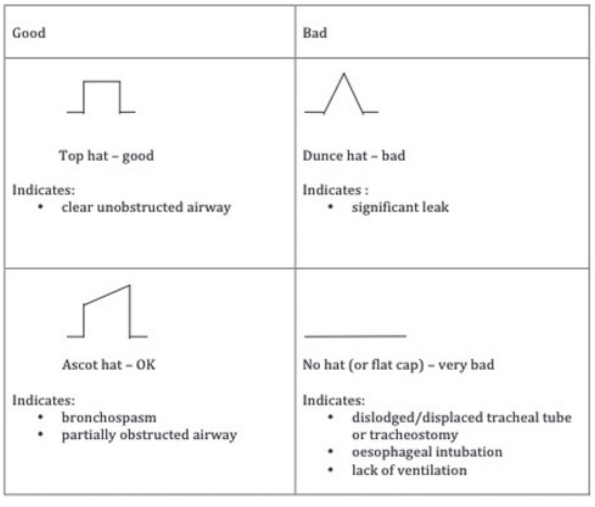


Figure 1 (abstract P264). 'Hats and caps' capnography training guide.

Methods 'Hats and caps' was devised on our ICU [3] and used for the training: this teaches that capnography traces on the left signify the airway is functional, in contrast to the traces on the right which indicate immediate attention is required (Figure 1). This was presented to staff working on the ICU in individual bedside teaching sessions with feedback obtained and evaluated.
Results We delivered teaching sessions to 100% (9/9) of junior doctors, 100% (71/71) of nursing staff and other health professionals. We obtained feedback from 90% (76/84), showing an improvement in understanding of capnography from 73% of respondents to 100%, with 87% reporting that the teaching aid made capnography interpretation much easier. All felt the training would improve patient safety, and 97% felt it would be worthwhile training in other ICUs.
Conclusion Use of 'hats and caps' enabled delivery of short bedside teaching sessions to clinical staff in ICU during everyday work. Feedback shows a marked improvement in confidence around capnography interpretation. It may have value in other ICUs to improve staff understanding of capnography and improve patient safety.
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P265

Comparison of three methods of applying high flow nasal oxygen: *in vitro* study

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Critical Care 2015, **19(Suppl 1):**P265 (doi: 10.1186/cc14345)

Introduction High flow nasal (HNF) requires precise control of the fraction of inspired oxygen (FiO_2) and flow contributed as well as an adequate adjustment of temperature and humidity of the gas provided. There are several equipments for HNF. We evaluated the FiO_2 and flow supplied with three different systems
Methods There have been analyzed: (1) 'Oxygen Therapy' from Dräger Evita-XL®; (2) Fisher & Paykel Airvo® option; and (3) pack of flowmeters Debson®. Measurements were made in the distal part of the circuit that is used in clinical practice. Variables: programmed and measured FiO_2, programmed and measured flow. We used the Oxygen Monitor Ohmeda 5120® and Flow Meter® Fisher-Porter. Before each measurement we checked and/or calibrated each of them. All measurements were performed at room temperature in the ICU of our hospital (23 to 26º).The data were processed using SPSS v.15.0.1, accepting a significance level of 95%.
Results (1) FiO_2 variation –0.001 ± 0.09 (–0.01 to 0.002); FiO_2 percentage variation –0.012 ± 1.88 (–0.27 to 0.25); r^2 = 0.999 and r = 0.998 (P <0.000). Flow variation (l/minute) 5.45 ± 3.23 (4.94 to 5.96); flow percentage variation 19.59 ± 11.63 (17.75 to 21.43); r = 0. 997 and r^2 = 0.994 (P <0.000). (2) FiO_2 variation –0.007 ± 0.26 (–0.011/–0.003); FiO_2 percentage variation –1.4040 ± 4.73 (–2.15 to –0.67); r = 0.996 and r^2 = 0.992 (P <0.000). Flow variation (l/minute) 3.82 ± 3.85 (3.04 to 4.69); flow percentage variation 9.76 ± 8.08 (8.11 to 11.41); r = 0.969 and r^2 = 0.939 (P <0.000). (3) FiO_2 variation –0.005 ± 0.26 (–0001 to 0009); FiO_2 percentage variation –0.72 ± 5.2 (–1.5 to 0.1); r = 0.996 and r^2 = 0.992 (P <0.000). Flow variation (l/minute) 3.91 ± 1.26 (3.69 to 4.13); flow percentage variation 12.77 ± 5.33 (11.84 to 13.7); r = 0.996 and r^2 = 0.992 (P <0.000). See Figure 1.
Conclusion The FiO_2 percentage variation in the Airvo® is higher than the other two devices, with no clinical relevance. The flow percentage variation of Evita XL® is superior to the other two devices; this may have some clinical relevance.

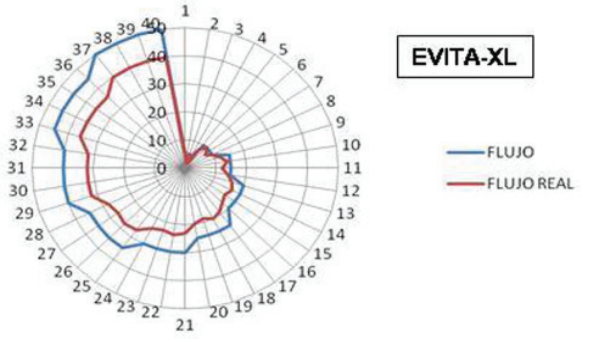


Figure 1 (abstract P265). Programmed and measured flow.

P266

Surface electromyography of respiratory muscles during a CPAP trial for weaning

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Critical Care 2015, **19(Suppl 1):**P266 (doi: 10.1186/cc14346)

Introduction Weaning from mechanical ventilation is an important concern in ICU clinical practice. Surface electromyography (sEMG) [1] is a non-invasive tool to assess activity of different muscles. We describe sEMG patterns of respiratory muscles during a CPAP trial [2] in patients undergoing pressure support ventilation.
Methods Twenty-one adult and clinically stable patients undergoing assisted mechanical ventilation for more than 48 hours were investigated during pressure support (baseline) and during a 2-hour CPAP trial. sEMG of diaphragm (costmar), intercostal and sternocleidal (accessory muscles) was recorded with a dedicated device (Dipha16; Inbiolab, Groningen, the Netherlands) simultaneously with airway waveforms and expressed as the ratio of the signal during baseline. Diaphragmatic electrical activity from a nasogastric tube (EAdi) of 14 of those patients was also measured.
Results The rapid shallow breathing index was lower than 105 in all patients and only one patient failed the trial. We observed that the mean inspiratory value of costmar increased immediately after switch to CPAP but did not significantly vary during the CPAP trial (ANOVA, P = 0.7). On the other hand, the activation of accessory muscles increased significantly during the same period (P = 0.01) and was strongly correlated with respiratory rate (r = 0.41, P <0.001) and inversely with

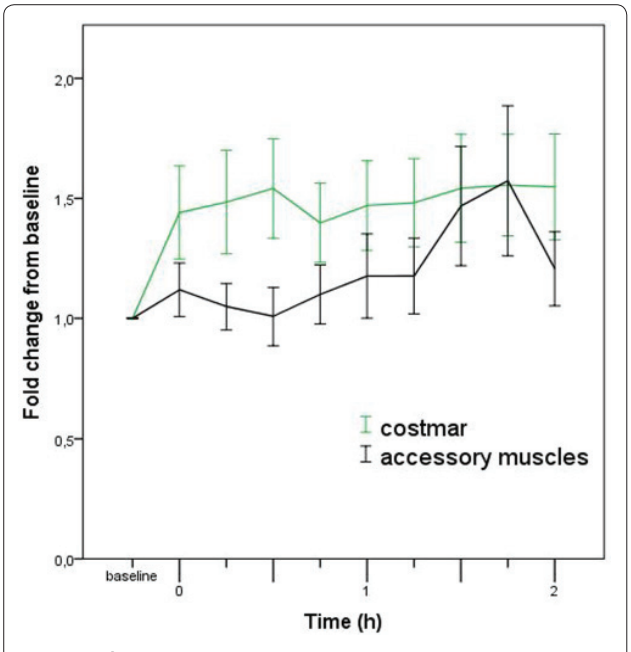


Figure 1 (abstract P266).

tidal volume (r = –0.16, P = 0.02). In patients with EAdi we confirmed a tight correlation between costmar and EAdi (r = 0.62, P <0.001). See Figure 1.

Conclusion sEMG indicated that while diaphragm activation remains constant during the CPAP period, accessory muscles were progressively recruited and particularly in the conditions of increased respiratory rate and lower tidal volumes.

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P267

Ventilator-day reductions not associated with reintubations and further reduced by an early mobilization program

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Critical Care 2015, **19(Suppl 1):**P267 (doi: 10.1186/cc14347)

Introduction Mechanical ventilation is associated with increased risk of pneumonia, barotrauma, VILI, VAP, ARDS and mortality. From 2009 to 2014 in the MICU/SICU of our facility, efforts to reduce ventilator-days included: noninvasive ventilation, sedation reduction, daily sedation vacations and weaning protocols. In 2013, an early mobilization of ventilated patients in the SICU was initiated. Aggressive ventilator-day reduction efforts may be expected to lead to premature extubations and reintubations.

Methods Ventilator-day data were compiled from 2009 to 2014 for MICU and SICU in our facility. Reintubation rates were calculated when intubations were required >1 day after an extubation.

Results Ventilator volume ranged from 639 to 766 distinct patients/year in the MICU and from 555 to 687 for the SICU. Ventilator-day reduction was significant (P <0.01) for the MICU* (7.7 to 5.5, –29%) and the SICU* (5.91 to 5.20, –12%). Reduction patterns differed between the units as the SICU had a distinct reduction (**P = 0.007) between 2012 and 2013 coinciding with implementation of an early mobilization program. Reintubation rates differed between the units and rates did not increase with decreasing mean patient ventilator-days. See Table 1.

Table 1 (abstract P267). Mean ventilator-days/reintubation rates

	2009	2010	2011	2012	2013	2014
MICU mean ventilator-days	7.71	6.81	5.90	5.88	5.50	5.50*
MICU reintubation rates	14.5%	9.8%	9.7%	9.8%	13.9%	8.3%
SICU mean ventilator-days	5.91	5.93	5.68	5.93	4.93**	5.20*
SICU reintubation rates	5.2%	3.0%	4.1%	4.3%	4.7%	7.5%

*, **Significance as described in Results.

Conclusion Initiatives to reduce ventilator-days per patient realized significant reductions from 2009 to 2014 while reintubation rates were unaffected. One component of the bundle, early mobilization, introduced in the SICU in 2013 was associated with an additional reduction in mean ventilator-days.

P268

Open-label randomized control trial between low pressure support and T-piece method for discontinuation from mechanical ventilator and extubation in general surgical ICUs

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Critical Care 2015, **19(Suppl 1):**P268 (doi: 10.1186/cc14348)

Introduction In routine practice for most surgical patients in Thailand, all appropriated patients with planned discontinuation of mechanical ventilator (MV) are routinely changed to T-piece before extubation. However, this method needs to alter the instrument for testing tolerability of the patient. The objective of this study was to compare continuous low pressure support (PSV) and the T-piece method (T) before discontinue mechanical ventilation and extubation in the surgical intensive care unit (SICU).

Methods We performed a prospective open-label randomized control study (non-inferiority trial) in SICU patients who were intubated and used mechanical ventilation, and appropriated discontinuation of the ventilator between June 2011 and November 2013. All patients underwent the same weaning protocol. The appropriated patients for discontinuation of MV were randomized into low pressure support up to 7 cmH_2O and T-piece method. Reintubation within 72 hours, pneumonia after extubation, and hospital mortality were recorded. The statistical significant difference was considered when P <0.05.

Results A total of 520 patients were randomized into two groups: low pressure support group (260 patients) and T-piece group (260 patients). There was no difference in age, gender, body mass index, comorbidity, site of surgery, Charlson Comorbidity Index and Acute Physiologic and Chronic Health II score between groups (P >0.05). Regarding the intention to treat analysis, there were no differences between groups in reintubation rate (PSV 10% vs. T 14.6%; P = 0.109), pneumonia after extubation (PSV 14.2% vs. T 11.9%; P = 0.435) and hospital mortality rate (PSV 3.1% vs. T 3.5%; P = 0.805).

Conclusion The outcomes after discontinuation of the mechanical ventilator between low pressure support and T-piece was not difference in term of reintubation, pneumonia after extubation and hospital mortality.

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P269

Systematic procedures including non-invasive ventilation improve morbidity in sleeve gastrectomy

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Introduction Postoperative morbidity after sleeve gastrectomy is decreasing, but remains significant. Bleeding and surgical fistules remain the leading causes of morbidity and mortality. In several studies in postoperative care of obese patients, non-invasive positive pressure ventilation (NPPV) reduced the risk of lower respiratory tract infection and pneumonia [1], thereby reducing in-hospital morbidity. The aim of study was to describe whether systematic use of NPPV improves morbidity in the postoperative care of sleeve gastrectomy.

Methods A 4-year before–after study was conducted in a 19-bed intermediate care unit of a private hospital. Before period: standard treatment – all patients received oxygen supplementation to achieve SaO_2 above 90%. After period: standard treatment plus NPPV – all patients were submitted to a systematic postoperative protocol: NPPV was provided using an oxygen CIPAP system with 5 cmH_2O. Statistical analysis: complication rates were compared using the chi-square test. P <0.05 was considered statistically significant.

Results A total of 857 patients were included. Inclusion characteristics were similar in the two groups: Before group – noNPPV: 352 patients, 2010 to 2011. Age: 40.58 ± 10.94, BMI: 42.79 ± 5.51, sex ratio F/M: 0.81. After group – NPPV: 504 patients, 2012 to 2013. Age: 40.81 ± 11.24, BMI: 42.92 ± 5.09, sex ratio F/M: 0.77. There is a significant between-group difference in the complication rate: Before group – noNPPV: 10 surgical fistula (2.84%) and six postoperative bleeding (1.70%); After group – NPPV: seven surgical fistula (1.39%) and three postoperative bleeding (0.6%). The overall complication rate fell from 4.54% to 1.98%. The chi-square statistic = 4.58. The number of degrees of freedom is 1. The value returned from the chi-square statistic is P <5%.

Conclusion Systematic use of NPPV significantly improves morbidity in the postoperative care of sleeve gastrectomy.

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P270

Early postoperative pulmonary complications following heart transplantation

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Critical Care 2015, **19(Suppl 1):**P270 (doi: 10.1186/cc14350)

Introduction The aim of this study was to determine the types, incidence, and risk factors for early postoperative pulmonary complications in heart transplantation recipients.
Methods We retrospectively collected data from the records of consecutive heart transplantations from January 2003 to December 2013. A total of 83 patients underwent heart transplantation. Those patients younger than 10 years (n = 9) and the patients who died intraoperatively (n = 1) or during the first postoperative day (n = 1) were not included in the analyses. The data collected for each case were demographic features, duration of mechanical ventilation, respiratory problems that developed during the ICU stay, and early postoperative mortality (<30 days). The respiratory complications that we sought were pleural effusion, pneumonia, pulmonary atelectasis, pulmonary edema, pneumothorax, and acute respiratory failure.
Results Of the 72 patients considered, 52 (72.2%) were male. The mean age at the time of transplantation was 32.1 ± 16.6 years. The mean duration of postoperative mechanical ventilation was 71.8 ± 126.6 hours. The mean length of ICU stay was 13.5 ± 18.0 days. Two patients (2.8%) and one patient (1.4%) required extracorporeal membrane oxygenation support and intra-aortic balloon pump support, respectively, due to low cardiac output or primary graft failure postoperatively. Twenty-five patients (34.7%) developed early postoperative respiratory complications. The most frequent problem was pleural effusion (n = 19, 26.4%) followed by atelectasis (n = 6, 8.3%), acute respiratory distress syndrome (n = 5, 6.9%), pulmonary edema (n = 4, 5.6%), and pneumonia (n = 3, 4.2%). Postoperative duration of mechanical ventilation (44.2 ± 59.2 hours vs. 123.8 ± 190.8 hours, P = 0.005) and the length of ICU stay postoperatively (10.1 ± 5.8 hours vs. 19.8 ± 28.9 hours, P = 0.03) were longer among patients who had respiratory problems. Postoperative length of stay in the hospital (22.3 ± 12.5 days vs. 30.3 ± 38.3 days, P = 0.75) was similar in the two groups. The overall mortality rate was 12.5% (n = 9 patients). The patients who had respiratory problems did not show higher mortality than those who did not have respiratory problems (16.0% vs. 10.6%, P = 0.71).
Conclusion Respiratory complications were relatively common in our cohort of heart transplant recipients. However, these complications were mostly self-limiting and did not result in increased mortality.

P271

Systematic alveolar recruitment after cardiac surgery

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Critical Care 2015, **19(Suppl 1):**P271 (doi: 10.1186/cc14351)

Introduction We designed a pilot study to evaluate the interest of an early systematic acute recruitment maneuver (ARM) in postcardiac surgery hypoxemic patients in order to properly design a larger trial.
Methods This randomized controlled trial included consecutive patients operated on in our institution. Three hours after surgery, hypoxemic patients (PaO_2 <300 mmHg, FIO_2 = 1) were randomly assigned to ARM or control (H0). ARM was performed by applying once a positive end-expiratory pressure of 35 cmH_2O during 45 seconds. Blood gases and hemodynamic variables were collected at H1, H8, H24 and H48. The primary endpoint was the duration of mechanical ventilation (MV). Secondary endpoints were survival rate, ICU length of stay and the occurrence of pneumonia.
Results We included 124 patients, age 67.5 ± 10.6 years, M/F sex ratio 95/29, left ventricle ejection fraction 58.8 ± 10.6%, forced expiratory volume 94 ± 23% of the predicted value, bypass/valve ratio 82/53. The preoperative and postoperative PaO_2/FIO_2 were 401 ± 66 and 204 ± 66 mmHg, respectively (P <0.0001). The hemodynamic and ventilation status as well as the fluid and inotrope supports were comparable in the two groups. At H1, PaO_2/FIO_2 was 367 ± 15 in the recruited group versus 299 ± 15 mmHg in the control group, P = 0.002. At H8 and 24 the difference was not significant. At H48, the PaO_2/FIO_2 was lower in the recruited group (296 ± 10 vs. 343 ± 11 mmHg, P = 0.003) (Figure 1). The duration of mechanical ventilation (invasive + non-invasive) was lower in the recruited group (total 6.4 ± 1.4 vs. 8.4 ± 1.4 hours, P = 0.02). The survival rate, the length of stay in the ICU and the occurrence of pneumonia were similar in the two groups (P >0.2).

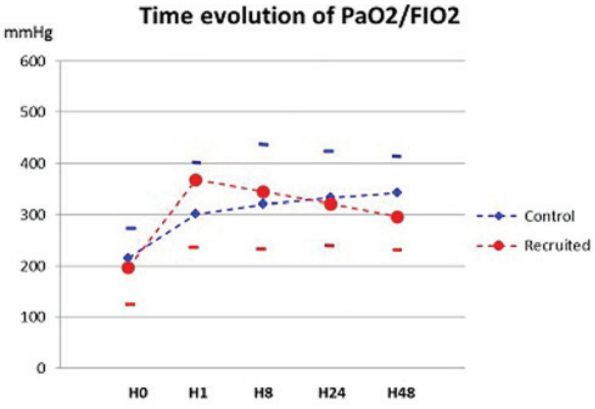


Figure 1 (abstract P271).

Conclusion We can speculate that the inverse evolution of the blood oxygenation between the ARM group versus control may be due to: barotraumatism of normal alveoli during the ARM and/or a higher de-recruitment rate after ARM due to the shorter mechanical ventilation support. This pilot study shows that a unique ARM decreased the duration of MV in cardiac surgery patients but this may have subsequent detrimental effects on blood oxygenation.

P272

Is procalcitonin a valuable marker for identification of postoperative complications after coronary artery bypass graft surgery with cardiopulmonary bypass?

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Critical Care 2015, **19(Suppl 1):**P272 (doi: 10.1186/cc14352)

Introduction The aim of our study was to investigate the value of C-reactive protein (CRP) and procalcitonin (PCT) in identification of the systemic inflammatory response syndrome (SIRS) and other complications in the early postoperative period after cardiac surgery with cardiopulmonary bypass (CPB) [1].
Methods In 93 patients undergoing coronary artery bypass graft surgery with CPB, after Ethical Committee approval in a prospective study, serum PCT and CRP values were collected before operation and daily until postoperative day 5. All patients were divided *post hoc* into patients with SIRS (n = 42) and patients without SIRS (n = 51). Student's t test, the Mann–Whitney U test and receiver operating characteristic (ROC) curves were used.
Results The comparison of serum CRP values in patients with or without SIRS on postoperative day 1 until postoperative day 5 demonstrated an increase in both groups without significant differences (P >0.05). The PCT levels increased more significantly in SIRS patients (5.78 ± 3.21 ng/ml vs. 1.23 ± 0.31 ng/ml) compared with patients without SIRS (P = 0.0001) on postoperative day 1. In patients with postoperative complications (21/93, 22%) (circulatory failure = 10, pneumonia = 2, respiratory insufficiency = 9, sepsis = 0), PCT levels remained elevated until postoperative day 5 (6.11 ± 2.87 ng/ml) but diminished in patients with SIRS (0.96 ± 0.23 ng/ml) (P <0.0001). A PCT threshold value of 2.79 ng/ml was able to discriminate between postoperative complications in patients with or without SIRS with a sensitivity of

82.5% and a specificity of 70% (area under the curve: 0.76 ± 0.05; P <0.01) on postoperative day 1.

Conclusion After cardiac surgery with CPB, PCT values increased significantly in the SIRS group of patients compared with patients without SIRS on postoperative day 1 and remained elevated until postoperative day 5. In the early postoperative period, early rise of PCT values may help to discriminate the development of postoperative complications in patients with or without SIRS.

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P273

Prediction of risk factors related to the development of hepatic dysfunction following open heart surgery

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Critical Care 2015, **19(Suppl 1):**P273 (doi: 10.1186/cc14353)

Introduction Our goal was to investigate the incidence of postoperative jaundice in open heart surgery patients and to determine the risk factors associated with hepatic dysfunction.

Methods A total of 292 patients were included in a prospective study design. Patients undergoing on-pump coronary artery bypass graft surgery (CABG) (n = 154) and valve repair surgery (mitral, mitral and aortic valve and/or tricuspid valve) (n = 138) were included. Postoperative hyperbilirubinemia was defined as occurrence of a plasma total bilirubin concentration of more than 34 µmol/l (2 mg/dl) in any measurement during the postoperative period. All patients were divided into groups with or without hyperbilirubinemia. Liver enzymes were collected on postoperative days 1, 7, 14 and 30. The risk factors including age, cardiopulmonary bypass time, number of blood transfusions, inotropic support, use of intra-aortic balloon pump and ICU stay were evaluated with logistic regression.

Results Postoperative hyperbilirubinemia was observed in 27 of 292 patients (9.3%). The numbers of valves replaced, preoperative total bilirubin concentration, increased cardiopulmonary bypass time, higher number of inotropic support agents, and use of intra-aortic balloon pump correlate with hyperbilirubinemia on postoperative day 7 (P <0.05). Independent risk factors of early postoperative jaundice are; multiple valve replacement surgery, ejection fraction and use of intraaortic balloon pump (R = 0.58, R^2 = 0.33, F = 26.44, P <0.001). The ICU stay was significantly longer in group 2 (11.52 ± 3.76 days) as compared with group 1 (2.79 ± 1.36 days) (P <0.001).

Conclusion Patients undergoing multiple valve replacement procedures are at greater risk for the development of postoperative hyperbilirubinemia and an association with prolonged ICU stay was observed. Other risk factors including ejection fraction, increased cardiopulmonary bypass time and use of intra-aortic balloon pump are also important as they have been reported to increase postoperative complications [1].

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P274

Determinants of gas exchange during extracorporeal CO_2 removal using a novel pump-driven venovenous gas exchange system in a minimally invasive setting

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Critical Care 2015, **19(Suppl 1):**P274 (doi: 10.1186/cc14354)

Introduction Pump-driven venovenous extracorporeal CO_2 removal ($ECCO_2$-R) increasingly takes root in hypercapnic lung failure to minimize ventilation invasiveness or to avoid intubation. A recently developed miniaturized device consisting of a centrifugal pump and a membrane ventilator (iLA Activve®; Novalung, Germany) allows effective decarboxylation via a jugular double lumen cannula. So far no data on gas exchange in this setting exist to date.

Methods We included 10 patients receiving iLA Activve® due to hypercapnic respiratory failure as bridge-to-transplant or obstructive lung disease. Sweep gas flow was increased in steps from 1 to 14 l/minute at constant blood flow (phase 1). Similarly, blood flow was gradually increased at constant sweep gas flow (phase 2). At each step, gas transfer via the membrane as well as arterial blood gas samples were obtained.

Results During phase 1, we observed a significant increase in CO_2 transfer together with a decrease in $PaCO_2$ levels from a median of 66 mmHg (range 46 to 85) to 49 (31 to 65) mmHg from 1 to 14 l/minute sweep gas flow, while arterial oxygenation deteriorated with high sweep gas flow rates. During phase 2, oxygen transfer significantly increased leading to an increase in PaO_2 from 67 (49 to 87) at 0.5 l/minute to 117 (66 to 305) mmHg at 2.0 l/minute. Higher blood flow rates also significantly enhanced decarboxylation. Increasing blood flow to 2.0 l/minute led to negative suction pressures of more than –100 mmHg and signs of hemolysis. See Figure 1.

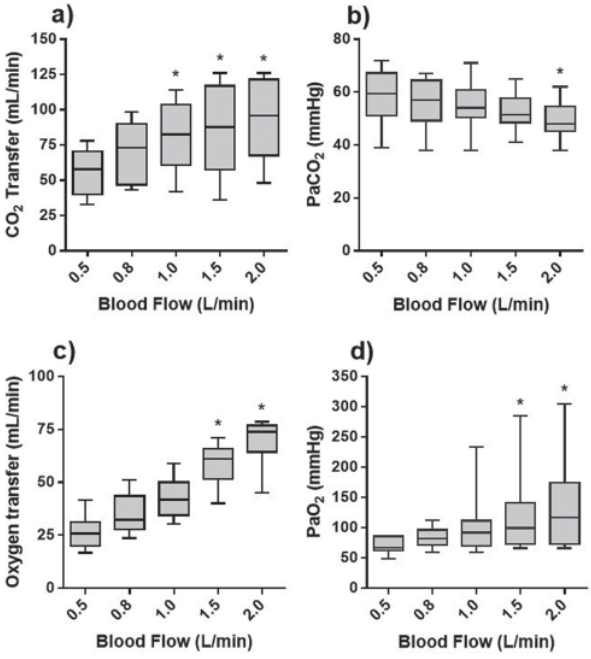


Figure 1 (abstract P274). PaO_2 with increasing blood flow (*P <0.0001).

Conclusion Increasing sweep gas flow results in effective CO_2 removal which can be further reinforced by raising blood flow. The clinically relevant oxygenation effect even in this setting of low invasivity could broaden the range of indications towards hypercapnic lung failure with mild to moderate hypoxia.

P275

Safety and efficacy of extracorporeal CO_2 removal combined with continuous renal replacement therapy in patients presenting both acute respiratory distress syndrome and acute kidney injury

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Introduction Pulmonary overdistension has been observed in 33% of patients with acute respiratory distress syndrome (ARDS) despite low tidal volume (6 ml/kg ideal body weight) ventilation [1]. Tidal volume

(VT) reduction from 6 to 4 ml/kg attenuates overdistension but is associated with hypercarbia [2]. We thought to combine extracorporeal CO_2 removal ($ECCO_2R$) with continuous renal replacement therapy (CRRT) through the insertion of an oxygenator membrane within the hemofiltration circuit in patients presenting both ARDS and acute kidney injury (AKI).

Methods A first set of measurement was performed at 6 ml/kg before and after $ECCO_2R$. Twenty minutes later, VT was reduced to 4 ml/kg for the remainder of the study period (72 hours). Ventilator settings were those of the ARMA trial. The CRRT mode was hemofiltration with 33% of predilution. Ultrafiltration was adjusted to achieve a filtration fraction of 15%. Sweep gas flow was constant at 8 l/minute. The primary endpoint was a 20% reduction of $PaCO_2$ at 20 minutes after initiation of $ECCO_2R$.

Results Eight patients were studied. Age was 69 ± 11 years, SAPS II was 68 ± 9 and SOFA score was 13 ± 4 at inclusion. Blood flow, at the inlet of the oxygenator membrane, was 400 ± 4 ml/minute. CO_2 removal rate was 84 ± 4 ml/minute. Initiating $ECCO_2R$, at 6 ml/kg, induced a mean $PaCO_2$ reduction of 17% (41 ± 5.5 to 33.9 ± 5.6 mmHg, P <0.001). Then, lowering the VT to 4 ml/kg induced a mean $PaCO_2$ increase of 25% (33.9 ± 5.6 to 42.6 ± 8 mmHg) and a mean PaO_2/FIO_2 ratio increase of 8% (176 ± 63 to 190 ± 61). Minute ventilation decrease from 7.4 ± 1.6 to 5 ± 1.2 l/minute. Respiratory system compliance did not vary. No major complications were observed.

Conclusion Combining $ECCO_2R$ and CRRT in patients with ARDS and AKI is safe and feasible through the insertion of an oxygenator membrane within a RRT circuit.

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P276

Interhospital transfer of patients in extracorporeal membrane oxygenation

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Introduction The transfer of patients in extracorporeal membrane oxygenation (ECMO) from a peripheral hospital to a tertiary center represents a high-risk situation of adverse events [1]. The aim of this retrospective study is to determine the feasibility and safety of interhospital transfer for critically ill patients with ECMO support.

Methods We collected data for the ECMO Regional Reference Centre Careggi Hospital activity from September 2009 to June 2014. In this study, 57 transfers were examined. The ECMO service is activated by a telephone call from a peripheral hospital. The team is represented by an intensivist, a heart surgeon, a cardiologist, a perfusionist and an intensive care nurse, all previously trained in the management of patients with ECMO. Medical personnel and the necessary equipment are transported by an ambulance and a van, specially designed and equipped for the transfer of patients with ECMO.

Results In this study, 57 patients transferred from the peripheral hospital to the ECMO center were examined; in all cases the ECMO system was implanted in the peripheral hospital (54 venovenous ECMO and three venoarterious ECMO). On average, trails were 271 km ± 304 (round trip) (minimum 14 km to maximum 939 km). The activation time from the call to the ambulance departure from our hospital was an average of 2 hours 27 minutes 13 seconds ± 1 hour 25 minutes 35 seconds. Transfer duration (from activation to return to the ECMO center) was an average of 8 hours 25 minutes 6 seconds ± 3 hours 27 minutes 58 seconds (minimum 3 hours to maximum 16 hours 55 minutes). The stop time (necessary for evaluation of the patient and for placement of the ECMO system) was an average of 3 hours 53 minutes 40 seconds ± 1 hour 6 minutes 35 seconds (minimum 2 hours 5 minutes to maximum 7 hours 30 minutes). Major complications related to malfunctions of the devices during transport were not recorded; in some cases it was necessary to manage minor complications (circuit cavitation, minor vascula accesses bleeding).

Conclusion Some studies have found several complications during transfer of patients in ECMO [2]. In our experience, there were no complications during the transfer of ECMO patients, even for longer trips. A wide and thorough clinical evaluation and multidisciplinary ECMO team allowed the optimization of clinical parameters before transport and a safely transfer. The start of ECMO treatment at peripheral hospitals and the transfer of patients in ECMO may be a viable option compared with conventional ventilation. Our data suggest that ECMO can be set up safely in peripheral hospitals by a multidisciplinary highly specialized ECMO team [3].

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P277

Microhemorrhages in the corpus callosum after treatment with extracorporeal membrane oxygenation

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Introduction Cerebral microhemorrhages (MH) are diminutive focal bleedings which can be detected best by MRI using susceptibility-weighted imaging sequences (SWI). They can be found in a variety of neurologic diseases. The pattern of distribution can lead to the underlying pathomechanism [1]. Survivors of high-altitude cerebral edema (HACE) showed multiple MH, predominantly in the splenium of the corpus callosum. Mountaineers with a lack of acclimatization to high altitudes tend to suffer from HACE. Hypoxemia in great heights is discussed to be the main trigger of HACE [2]. Acute respiratory distress syndrome (ADRS) is characterized by oxygenation failure in mechanically ventilated patients. The severity is classified by the ratio of arterial oxygen tension to fraction of inspired oxygen [3]. In some patients suffering from severe ARDS, refractory to conventional therapy, venovenous extracorporeal membrane oxygenation therapy is the therapeutic option to ensure oxygenation.

Methods Retrospectively, we examined 20 patients with cerebral MRI (including SWI) who had suffered from severe ARDS and received ECMO therapy. The MRI slides were anonymized and analyzed by two experienced neuroradiologists. Based on the distribution pattern and characteristic, a modified HACE score (mHCS) was surveyed [2].

Results Six of 20 patients (30%) showed multiple MH with emphasis in the splenium of the corpus callosum. Eight patients had sporadic MH in the parenchyma of the brain but not in the corpus callosum. The remaining six patients had no intracerebral alterations. The distribution of MH with involvement of the splenium resembled that seen in HACE survivors.

Conclusion Based on these results, we postulate that hypoxemia is one of the main players in the development of splenium-associated MH, not only in HACE but also in severe ARDS and other diseases accompanied with severe hypoxemia. Further investigations have to examine potential triggers and special circumstances concerning ARDS treatment which lead to MH in this distinctive pattern.

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P278

Differential venous oxygen return: a key factor of differential hypoxia in venoarterial extracorporeal membrane oxygenation

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Introduction Differential hypoxia is a pivotal problem in cardiopulmonary failure patients with femoral venoarterial extracorporeal membrane oxygenation (VA ECMO) support. Although there was some attempt to deliver more oxygenated blood to the upper body, the mechanism of differential hypoxia has not been well investigated.
Methods We used a sheep model of acute respiratory failure that was supported with femoral VA ECMO (from inferior vena cava to femoral artery (IVC-FA)), ECMO from superior vena cava to FA (SVC-FA), ECMO from IVC to carotid artery (IVC-CA) and ECMO adding an additional return cannula to internal jugular vein based on femoral VA ECMO (FA-IJV). Angiography and blood gas analysis were performed.
Results Blood oxygen saturation (SO_2) of IVC (83.6 ± 0.8%) was higher than that of SVC (40.3 ± 1.0%) in sheep with IVC-FA. Oxygen-rich blood was drained back to the ECMO circuit and poorly oxygenated blood in the SVC entered the right atrium (RA). SVC-FA achieved the oxygen-rich blood return from IVC to RA without shifting the arterial cannulation. SO_2 of SVC and pulmonary artery increased (70.4 ± 1.0% and 73.4 ± 1.1%, respectively) subsequently. Compared with IVC-FA, less differences of venous oxygen return and attenuated differential hypoxia were also observed in IVC-CA and FA-IJV. See Figure 1.
Conclusion Differential venous oxygen return is a key factor of differential hypoxia in VA ECMO. We can take advantage of the notion of differential venous oxygen return to choose better cannula configuration in clinical practice.

P279

Successful approach for emergent consent for ECMO research

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Introduction The HELP-ECMO pilot study (Heparin low dose protocol versus standard care in critically ill patients undergoing ECMO; ACTRN12613001324707) is a randomised controlled phase II study evaluating two levels of heparin anticoagulation in patients with no requirement for full anticoagulation. This work is a substudy of the HELP-ECMO trial and describes the consent process of the parent study. At our site, consent for research is often obtained by the research coordinator with little involvement from investigators. However, the nature of the ECMO population required a modified consent approach to be implemented given that ECMO is often inserted emergently. It required a model that would be successful out of hours and could be delivered by any member of the treating team.

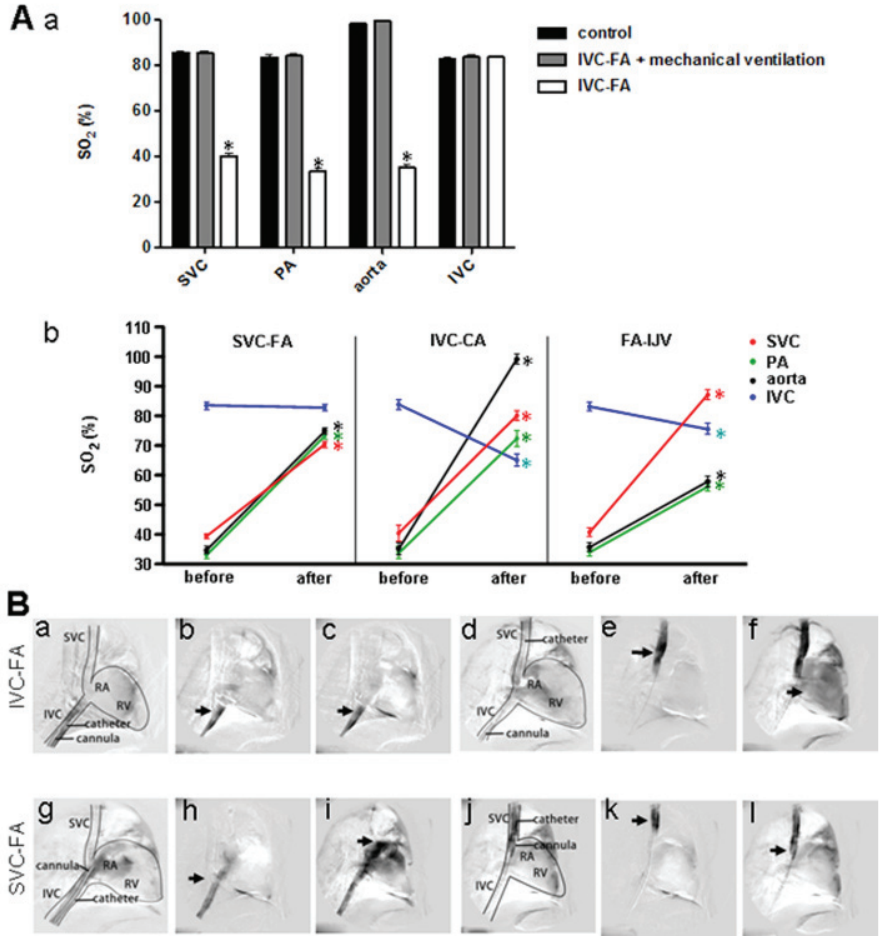


Figure 1 (abstract P278). SO_2 values from blood gas analysis and vena cava angiography.

Methods The HELP-ECMO pilot study is enrolling patients admitted to a large metropolitan ICU who require ECMO. Education on eligibility criteria and study processes was given to all ICU senior medical staff. Consent must be performed prior to the commencement of anticoagulation, often only a short time after ECMO cannulation. To facilitate recruitment at all hours, a HELP-ECMO study box is located in the ICU. Within the box is an instruction page outlining the screening, consent and randomisation process, as well as administrative tasks. Plain language statements, randomisation envelopes and consent documentation stickers are provided. A consent script is provided to ensure consistency across consenting personnel. The process is reviewed by the research coordinator the following day to confirm local governance compliance.
Results From April to December 2014, 30 patients were screened. Fourteen met the eligibility criteria and were approached for consent. Twelve patients were enrolled and randomised to receive either standard anticoagulation or low-dose heparin as per the study protocol. Consent was provided by the person responsible for 10 patients. One patient was competent to consent for themselves and one was enrolled under legislation allowing enrolment into research in the absence of a person responsible. There were two refusals. Seventy-one per cent of participants were approached out of hours. Eighty-six per cent were consented by clinicians. Twenty-one per cent of patients were consented by a non-investigator.
Conclusion The model of consent described has proven to be successful in this challenging patient population. The ability of all staff to perform consent for the study has been a significant factor in the success of the pilot. The review of study processes by research coordinators has supported this model.

P280

Extracorporeal membrane oxygenator and ventricular assist device activity of a tertiary cardiothoracic centre: survival rates and length of ITU stay

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Introduction Harefield Hospital accepts patients as a tertiary centre for end-stage heart and respiratory failure for the south of England. Interventions include VA-ECMO, VV-ECMO as a bridge to lung transplantation, left ventricular assist devices (LVAD) as a bridge for heart transplantation, right ventricular assist devices (RVAD) and BIVADs. The aim of this review was to identify the total number of such patients, analyse the individual length of ITU stay and calculate survival and mortality rates for each intervention.
Methods Patients consisted of six groups: Group 1: VA ECMO, Group 2: VV-ECMO, Group 3: LVAD, Group 4: RVAD, Group 5: BIVAD, Group 6: combination of devices. Data were extracted from the Perfusion Department records and the intensive care dataset from 2011 to 2013. Data included length of ITU stay, outcome, indication for device insertion and device-related major complications.
Results Forty patients were identified. Twenty-nine were male and 11 female. Group 1 included 22 patients, Group 2: two patients, Group 3: four patients, Group 4: four patients, Group 5: zero, Group 6: eight patients treated with various combinations of ECMO or ventricular assist devices. ITU stay varied from 1 day to a maximum of 6 months intermittently for one patient. Duration of ITU stay for all 40 patients was 1,052 days with an average of 26.3 days per patient. Sixteen patients survived and were discharged to the Transplant Unit. Twenty-four patients died, putting the survival rate at 40% for this group.
Conclusion This review demonstrates that the majority of these patients occupied intensive care beds for a prolonged period of time and despite the use of advanced support devices survival rates were significantly lower than mortality rates.

P281

In-hospital and long-term mortality after venoarterial ECMO for refractory cardiogenic shock

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Introduction Venoarterial (VA) ECMO is used for mechanical support in patients with cardiogenic shock (CS) unresponsive to medical therapy. Long-term survival and quality of life after hospital discharge have not yet been well analyzed.
Methods We performed a retrospective observational study of patients admitted to the ICU for refractory CS from January 2010 to November 2014. Patients with postcardiotomy and/or post-transplant CS were excluded. Demographic, clinical and biochemical variables were collected. Continuous variables are presented as mean (standard deviation) and categorical variables as percentage. Long-term outcome and quality of life were assessed during scheduled follow-up evaluations or telephonic interviews.
Results We analyzed 23 consecutive patients undergoing VA ECMO for refractory CS. Etiologies of cardiac collapse were: 11 acute myocarditis, five acute myocardial infarctions and seven acute decompensation of chronic cardiomyopathies (CCM). Thirteen patients died during the hospital stay and 10 survived. The main cause of ICU death was progressive multiple organ dysfunction (12/13). Baseline variables are presented in Table 1. All patients discharged from the hospital are still alive at follow-up (median 27 months, range 4 to 56) with a median NYHA class of 1 (range 1 to 2). All patients except one returned to an active style of life. Multivariate analysis (Cox) revealed pre-ECMO SOFA score (HR = 2.18, 95% CI = 1.016 to 4.6) and history of CCM (HR = 19, 95% CI = 2 to 178) and pre-ECMO lactate (HR = 1.2, 95% CI = 1.02 to 1.4) as independent risk factors for hospital mortality.

Table 1 (abstract P281)

	Alive	Dead	*P* value
Age (years)	30 ± 18	43 ± 14	0.012
CCM	0 (0%)	7 (100%)	0.014
SOFA	8 ± 1.4	10 ± 1.9	0.002
Creatinine (mg/dl)	1.1 ± 0.3	2.2 ± 0.7	0.001
Bilirubin (mg/dl)	1 ± 0.4	2 ± 1.8	0.09
Lactate (mmol/l)	5 ± 2.1	8 ± 5.3	0.021
Platelets (10^3/μl)	257 ± 79	162 ± 99	0.03

Conclusion VA-ECMO is an effective treatment tool for refractory CS in patients with acute life-threatening heart failure. Patients affected by acute decompensation of CCM had poorer outcomes characterized by multiple organ dysfunction, as already known in the literature.

P282

Characteristics of trauma patients with creatine kinase elevation

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Critical Care 2015, **19(Suppl 1):**P282 (doi: 10.1186/cc14362)

Introduction Rhabdomyolysis is a condition that results in the release of mainly creatine kinase (CK) and myoglobin from the breakdown of myocytes. Myoglobin has been known to cause renal failure (RF) and the CK level is routinely used as an indicator. A CK level >5,000 U/l was found to be associated with the risk of RF [1]. However, data are lacking on the level of CK to predict RF, especially in general trauma patients. The purpose of this study was to determine the initial CK level that predicts markedly elevated CK and the characteristics of trauma patients with elevated CK.

Methods Data from the Songklanagarind Hospital trauma registry were reviewed over 1 year (January 2013 to December 2013). Patients with at least two records of CK and creatinine (Cr) levels were included. Creatine kinase levels were analyzed during the first 3 days of hospital admission. RF was defined as a Cr increment >0.3 mg/dl within 48 hours.
Results Of the 1,491 patients admitted to the trauma service, 47 patients had CK levels drawn twice. These patients had a mean age of 32 years and a median Injury Severity Score (ISS) of 14. The predominant mechanism of injury was motorcycle crash. Only three patients developed RF. The median CK during the first 3 days after admission was 3,088 (IQR 1,327, 6,072) U/l. The CK peaked at 11 hours after admission at a mean value of 16,114.167 (SD 34,010.80) U/l. There were no significant differences in demographic data, ISS scores and fluid balance between the groups of CK level over or below 5,000 U/l. A mean positive fluid balance observed; however, initial CK was significantly different between the two groups. None of the patients with initial CK of <900 U/l had a peak of CK >5,000 U/l.
Conclusion Trauma patients had varying levels of elevated CK. Initial CK shows a promising result as a predictor of high peak CK levels. A larger sample size is needed to demonstrate the predictors of RF in trauma patients with elevated CK levels.
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P283

Rhabdomyolysis: early prognostication of renal failure and other adverse outcomes

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Introduction The clinical diagnosis of rhabdomyolysis is confirmed by creatine kinase (CK) levels >1,000 IU/l [1]. A local therapeutic protocol triggers aggressive renoprotective treatment in all patients with CK >2,000 IU/l. To evaluate local practice and refine CK thresholds for the instigation of renoprotective treatment, we studied the correlation between CK time trends and adverse outcomes such as acute kidney injury (AKI), the need for emergency renal replacement therapy (RRT) and mortality. We also evaluated the McMahon Score, a risk prediction model based on demographic, clinical, and laboratory variables available on admission [2].
Methods A retrospective observational study of adults with confirmed rhabdomyolysis admitted to the Neurosciences Critical Care Unit between 2002 and 2012. Data collection included APACHE score, daily CK (with PEAK CK defined as the maximum CK recorded throughout ICU stay), creatinine, calcium, phosphate and bicarbonate levels, AKI, RRT, ICU length of stay and mortality.
Results A total of 232 patients met the inclusion criteria. Rhabdomyolysis was associated with trauma (76%), medical (15%) and surgical (9%) admission diagnoses. Forty-five (19%) patients developed AKI, with 29 (12.5%) requiring RRT. Mortality was significantly higher in patients who developed AKI (62% vs. 18%, P <0.001). Average CK on admission was 5,009 IU/l (SD 12,403 IU/l). CK values remained greater than 2,000 IU/l for an average of 3.3 days (range 1 to 10 days). Although PEAK CK was greater in patients requiring RRT compared with those that did not (PEAK CK: 32,354 IU/l vs. 7,353 IU/l, P = 0.001), receiver operator characteristic curves revealed that a threshold for PEAK CK >5,000 IU/l is only 55% specific and 83% sensitive for the prediction of need for RRT. CK peaks on the day of admission in 46% of patients, on day 2 in 37%, and on day 3 or later in 17% of cases. A McMahon Score >6 calculated on admission is 68% specific and 86% sensitive for RRT.
Conclusion Although higher CK levels are associated with adverse outcomes, instigation of renoprotective treatment should not be based solely on CK levels. A McMahon Score >6 on admission allows for a more sensitive, specific and timely identification of patients at risk of renal failure requiring RRT.
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P284

Risk factors for acute kidney injury in patients with complicated intra-abdominal infection

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Introduction AKI has been poorly studied in surgical septic patients. The aim of our study was to determine the factors related to AKI in surgical septic patients with complicated intra-abdominal infection (CIAI) and mortality associated with AKI in this setting.
Methods An observational study was performed of all adult patients with CIAI requiring surgery and ICU admission from June 2011 to June 2013. We recorded demographic data, SAPS II, SOFA score at admission, presence of septic shock, history of pre-existing comorbidities, angiotensin-converting enzyme inhibitor (ACEI), angiotensin receptor blocker (ARB), NSAIDs, statins or diuretics consumption, baseline creatinine and at admission, and standard biomarkers. Factors associated with developing AKI and renal replacement therapy (RRT) were studied using a multivariate analysis. Association between mortality and AKI and RRT need was also analyzed.
Results A total of 114 patients were included, with a mean SAPS II of 42.14. Sixty-seven patients (58.8%) developed AKI and 33 (28.9%) required RRT. Development of AKI (R^2 = 0.498; P <0.0001; AUC = 0.926) was independently associated with SOFA (OR = 1.57; 95% CI = 1.29, 2.02) and creatinine at admission (OR for 0.1 units = 1.56; 95% CI = 1.30, 1.99). RRT need (R^2 = 0.382; P <0.0001; AUC = 0.892) was independently associated with arterial hypertension (HTN) (OR = 4.90; 95% CI = 1.50, 15.97) and SOFA score (OR = 1.71). In another model with more predictive capacity (R^2 = 0.433; P <0.0001; AUC = 0.918) the number of previous medications (OR = 3.73; 95% CI = 1.92, 8.38) and SOFA score (OR = 1.86; 95% CI = 1.47, 2.54) were related to RRT need. Both AKI and RRT need were related to ICU (RR = 8.41, 95% CI = 1.14, 62.5; and RR = 8, 95% CI = 2.40, 27.85 respectively) and 28-day mortality (RR = 2.8, 95% CI = 1.00, 7.86; and RR = 4.65, 95% CI =1.99, 10.40 respectively).
Conclusion Severe AKI with RRT need is highly associated with previous HTN. The number of previous medications is related to severe AKI too. HTN has been described as a risk factor for developing AKI in critically ill patients [1]. ACEI and ARB use has been associated with AKI development in septic patients [2]. To our knowledge, this is the first study that investigates risk factors associated with AKI in surgical septic patients with CIAI.
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P285

Early detection of acute kidney injury during the first week of the ICU

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Introduction Acute kidney injury (AKI) is associated with increased morbidity and mortality in critically ill patients [1]. Early detection and treatment may improve outcome.
Methods A retrospective analysis of prospectively collected data from 2,158 patients without end-stage renal disease from the EPaNIC trial [2]. For early detection of AKI, defined according to the creatinine-based KDIGO guidelines [3], three multivariate logistic regression models (LR) were developed using data available at baseline (LR_B), upon ICU admission (LR_BA), and at the end of the first day in the ICU (LR_BAD1). In a subpopulation (n = 580) where plasma neutrophil gelatinase-associated lipocalin (pNGAL), an early biomarker of AKI, was measured at ICU admission, the value of adding pNGAL to LR_BA and LR_BAD1 was assessed. The models were evaluated via bootstrapping, by comparing receiver operator characteristic (ROC) and decision curves.

Table 1 (abstract P285). Area under ROC curves for the different models

LR_B (*n* = 2,158)	LR_BA (*n* = 2,067)	LR_BAD1 (*n* = 1,808)	pNGAL on subpopulation with pNGAL (*n* = 528)	LR_BA on subpopulation with pNGAL (*n* = 528)	LR_BA + pNGAL on subpopulation with pNGAL (*n* = 528)
0.73	0.76	0.82	0.64	0.70	0.76

Results Table 1 presents the performance of the models and admission pNGAL. Performance improved when predictions were made at a later time point, and was highest for LR_BAD1. Similar results were obtained in subgroups of septic and cardiac surgery patients. As an independent predictor, pNGAL alone did not perform better than a model using routine clinical data available upon admission. However, when combining pNGAL with LR_BA, predictive performance improved. The performance of LR_BAD1 was not improved by including pNGAL.
Conclusion This study shows the potential of data-driven models based on routinely collected patient information for early detection of AKI during the first week of ICU stay. Although adding admission pNGAL to admission data improved early detection of AKI, this added value is lost upon inclusion of data from the first day of ICU.
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P286

Is acute kidney injury in the early phase of sepsis a sign of metabolic downregulation in tubular epithelial cells?

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Critical Care 2015, **19(Suppl 1):**P286 (doi: 10.1186/cc14366)

Introduction This study tested the hypothesis that the cellular response in the kidney to sepsis is characterized by early activation of AMP activated protein kinase (AMPK), and that such activation is temporally associated with downregulation of the epithelial sodium channel (B-ENaC).
Methods Fifteen C57BL/6 wildtype (WT) mice were subjected to cecal ligation and puncture (CLP), and sacrificed at 2, 6, 18, 24, or 48 hours. In addition, we pretreated three WT and three AMPK Beta 1 knockout mice with the AMPK activator AICAR (100 mg/kg intraperitoneal, 24 hours before CLP), and sacrificed 24 hours after CLP. Blood and tissue samples were collected for all animals. AMPK activation (pThr172), B-ENaC, and mitophagy (LC3 II/I) were examined by western blot of kidney lysates. Plasma creatinine (Scr) was assessed using ELISA.
Results The acute response to sepsis was characterized by early activation of AMPK which increased from 6 to 18 hours, peaked at 24 hours, and decreased by 48 hours (Figure 1A). This activation was associated with a consistent decrease in B-ENaC expression. In AICAR pretreated animals, AMPK was only activated in WT mice, which was associated with a decrease in the expression of B-ENaC as compared with AMPK KO mice (Figure 1B).
Conclusion AMPK was activated early after induction of sepsis, and was associated with a consistent decrease in Beta-ENaC expression in the apical membrane of tubular epithelial cells. In addition, absence of AMPK activation in KO animals was associated with increased expression of Beta-ENaC at 24 hours after CLP. These data support the hypothesis that early activation of AMPK decreases energy consumption through ion channel downregulation.

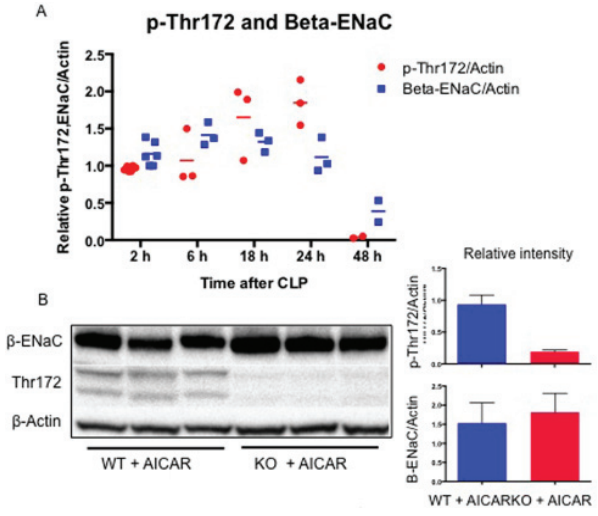


Figure 1 (abstract P286). (A) AMPK activation (p-Thr172) and Beta-ENAC expression during early CLP. **(B)** Difference in Beta-ENAC expression between AICAR pretreated WT versus KO at 24 hours after CLP.

P287

Urinary TIMP-2 and IGFBP7 elevate early in critically ill postoperative patients that develop AKI

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Introduction Little is known about temporal changes in [TIMP-2·IGFBP7] relative to injury in patients who develop AKI. In this analysis, we examined [TIMP-2·IGFBP7] in serial urine collections from the subset of Sapphire patients who were admitted to the ICU after major surgery.
Methods We stratified 238 Sapphire patients into three groups by their maximum AKI stage within 48 hours of the start of surgery using KDIGO criteria (No AKI, KDIGO 1, and KDIGO 2 to 3). Median TIMP-2·IGFBP7 values were calculated from all samples collected at 12 (±6)-hour intervals for 4 days following the start of surgery.

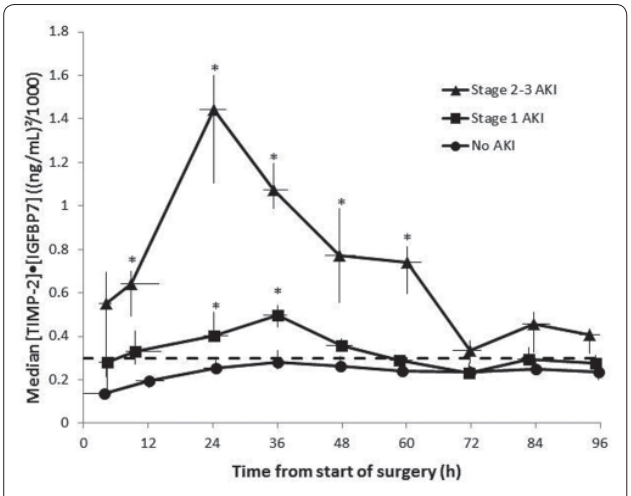


Figure 1 (abstract P287).

Results There were 101 patients without AKI, 95 patients with KDIGO 1 AKI, and 42 patients with KDIGO 2 to 3 AKI within 48 hours of the start of surgery. In patients without AKI, median TIMP-2·IGFBP7 values were less than 0.3 $(ng/ml)^2/1,000$ (dashed line in Figure 1) for all time points. In patients with KDIGO 1 AKI, median [TIMP-2·IGFBP7] significantly exceeded this cutoff at 24 and 36 hours following the start of surgery (*one-sided P <0.025). Median [TIMP-2·IGFBP7] increased earlier in KDIGO 2 to 3 AKI patients, remaining significantly elevated relative to the cutoff from 12 to 60 hours after the start of surgery. The highest median [TIMP-2·IGFBP7] was observed at 24 hours for KDIGO 2 to 3 AKI patients and was nearly five times the 0.3 $(ng/ml)^2/1,000$ cutoff.
Conclusion Urinary [TIMP-2·IGFBP7] was significantly elevated as early as 12 to 24 hours from the start of surgery in patients who developed AKI within 48 hours. Monitoring of these biomarkers in the immediate postsurgical period might enable improved management of patients at risk for AKI.

P288

Urinary TIMP2 and IGFBP7 as early biomarkers of acute kidney injury in septic and nonseptic critically ill patients

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Introduction Sepsis and acute kidney injury (AKI) have a high prevalence in the ICU population. The aim of this study is to describe the composite of tissue inhibitor of metalloproteinases-2 (TIMP2) and insulin-like growth factor-binding protein-7 (IGFBP7) as novel urinary renal biomarkers in both septic and nonseptic patients.
Methods We conducted a prospective, observational study in two university hospitals. Patients were admitted in ICU either from the emergency department or after undergoing an acute surgery at hospital admission. Two months prior to the admission, recruited patients had not been admitted to hospital. We collected epidemiological, clinical and laboratory data at admission, 24 and 48 hours. TIMP2*IGFBP7 was analysed in urine samples by a point-of-care device (Nephrocheck®; Astute Medical).
Results The sample included 98 patients (65 men) with mean age 55 ± 17.3 years, length of ICU stay 11.1 ± 14.6 days. In total, 41.4% had sepsis at ICU admission; 59.2% were diagnosed of sepsis within the first 48 hours of stay. We stratified patients based on the presence of AKI as per the AKIN KDIGO definition, as well as their worst level of TIMP2*IGFBP7 during their first 2-day stay. Values of mean and 25th to 75th percentile for the worst value of TIMP2*IGFBP7 were 0.24 (0.11 to 0.46), 0.50 (0.28 to 1.24), 0.94 (0.34 to 3.28) and 3.34 (1.47 to 6.22) for no AKI, AKIN I, II and II respectively (P <0.0001). The worst values for no AKI/no sepsis, no AKI/sepsis, AKI/no sepsis and AKI/sepsis were 0.21 (0.10 to 0.4), 0.32 (0.15 to 0.63), 1.05 (0.41 to 2.31) and 0.98 (0.36 to 3.94) respectively, with P <0.05 for AKI and P = NS for sepsis. The AUC ROC curve for prediction of AKI of the worst value was 0.80 with sensitivity of 73.5% and specificity of 71.4% (P <0.0001). In contrast to the Sapphire study, in our population cutoff values of 0.4 and 0.8 $(ng/ml)^2/1,000$ predict AKI and AKIN ≥II respectively, regardless of the presence of sepsis. See Figure 1.
Conclusion TIMP-2 and IGFBP-7 can predict AKI in both septic and nonseptic critically ill patients. Further pragmatic randomised controlled trials are needed to prove their role on clinical basis.
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P289

Single point measurement of cystatin C has similar performance as serum creatinine for assessment of kidney function in critically ill patients

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Critical Care 2015, **19(Suppl 1):**P289 (doi: 10.1186/cc14369)

Introduction The gold standard for routine evaluation of kidney function is measurement of serum creatinine concentration (Scr). In ICU patients, muscle loss and dilution leads to decreased Scr. Scr is distributed in total body water, resulting in delay of Scr changes when the glomerular filtration rate (GFR) changes (lag time). Cystatin C (CysC) is a protein produced by all cells with a nucleus and therefore less affected by muscle mass. Also, the lag time may be shorter as the volume of distribution is only extracellular fluid. The objective of this study was to evaluate whether single point measurement of CysC is more adequate than Scr for monitoring of kidney function in ICU patients.
Methods Data were collected in two prospective single-center studies on a convenience sample of ICU patients. During the 24-hour study period, we measured CysC, Scr, and urinary inulin clearance (Cinu) as a

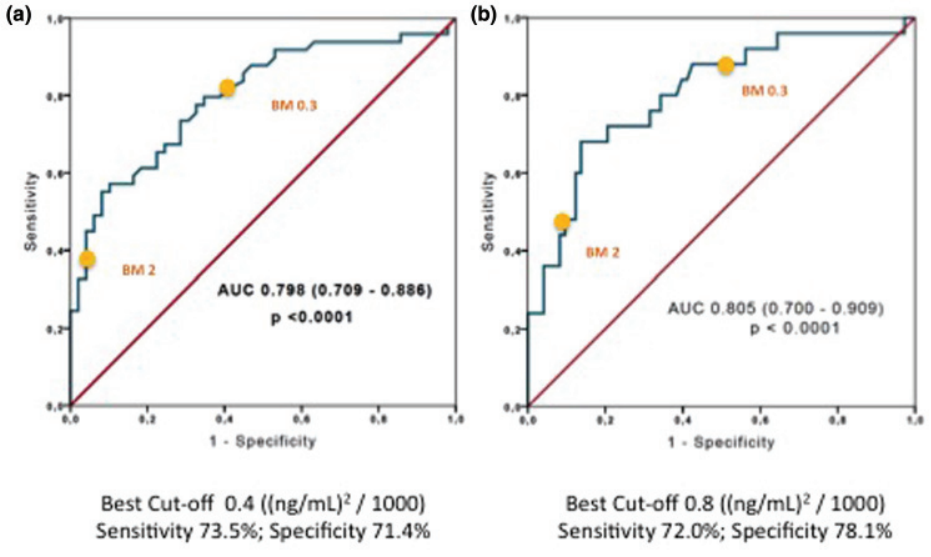


Figure 1 (abstract P288). ROC curve and area under the curve (AUC) for the worst [TIMP2]*[IGFBP7] value within the first 48 hours of ICU admission to predict **(a)** AKI and **(b)** AKIN KDIGO ≥2.

gold standard for assessment of GFR. We compared Scr and CysC, with Cinu. Also, we assessed Cinu in patients who had CysC and Scr within the normal sex and age corrected limits. Finally, we determined the ability of CysC and Scr to detect normal range and decreased GFR (80 to 120 ml/minute/1.73m^2 resp. <60).

Results We included 68 patients, with median age 58 years (IQR 29 years), length of stay in the hospital before study 11 days (IQR 16), and APACHE II score 19 (IQR 9). Scr was 1.12 (IQR 1.55), CysC 0.64 (IQR 0.73), and Cinu 80 ml/minute/1.73 m^2 (IQR 82). Cinu was markedly decreased in patients with Scr in normal range (n = 12) compared with patients with CysC in normal range (n = 22) (55 ml/minute/1.73 m^2 (IQR 57.4) vs. 100 (IQR 42.2), P <0.001). Patients with normal range Scr had similar proportion of patients with Cinu in the normal range compared with normal range CysC patients (33.3% vs. 45.5%, P = 0.23). ROC analysis showed that Scr and CysC had similar performance for detection of normal range Cinu (AUC: 0.66; 95% CI = 0.53 to 0.77 vs. 0.77; 95% CI = 0.65 to 0.87; P = 0.118), and decreased Cinu (AUC: 0.86; 95% CI = 0.76 to 0.97 vs. 0.94; 95% CI = 0.88 to 1; P = 0.113).

Conclusion Single point measurement of Scr and CysC has similar performance for detection of normal and decreased GFR in this cohort of ICU patients. Performance was weak for detection of normal GFR, but both biomarkers had moderate good performance for detection of decreased GFR.

P290

Early prediction of acute kidney injury after transcatheter aortic valve implantation with urinary G1 cell cycle arrest biomarkers

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Introduction Acute kidney injury (AKI) is a common complication following transcatheter aortic valve implantation (TAVI) and has been shown to increase mortality. The concentration of the G1 cell cycle arrest proteins TIMP-2 and IGFBP7 in the urine have recently been suggested as sensitive biomarkers for early detection of AKI in critically ill patients. Whether postoperatively elevated levels of urinary [TIMP-2][IGFBP7] (UTI) predict the development of an AKI in patients undergoing TAVI is currently unknown.

Methods In a prospective cohort study, 40 patients undergoing TAVI, either trans-apical (TA) or trans-aortic (TAo), were enrolled. Serial measurements of UTI were performed every 12 hours in the postoperative course. Results were calculated for their multiplication and presented as arbitrary values. Urinary output and serum creatinine were recorded simultaneously. The primary clinical endpoint was the occurrence of AKI according to the AKI Network.

Results Mean age was 81 ± 5.6 years (16 male, 40.0%). Thirty-five patients underwent TA-TAVI and five patients TAo-TAVI. AKI developed in 17 patients (42.5%); seven patients (17.5%) suffered from AKI 3 and required renal replacement therapy (RRT). Mean maximum value of UTI within 24 hours after TAVI was significantly higher in patients with AKI compared with patients without renal impairment (2.19 ± 3.11 vs. 0.67 ± 0.816, P = 0.037) and higher in patients with AKI 3 compared with patients with AKI 2 (4.73 ± 3.58 vs. 0.59 ± 0.71, P = 0.022). In contrast, preoperative creatinine (AKI (mg/dl) 1.22 ± 0.41 vs. no AKI 1.30 ± 0.59; AKI 3 1.32 ± 0.49 vs. AKI 2 1.26 ± 0.53, P = NS) and early postoperative serum creatinine levels (maximum within 24 hours after TAVI: AKI 1.41 ± 0.50 vs. no AKI 1.34 ± 0.60; AKI 3 1.69 ± 0.56 vs. AKI 2 1.32 ± 0.54, P = NS) did not show any association with the development of AKI. ROC analyses revealed a very good predictive value of early UTI levels for the development of AKI 3 within the next 72 hours after TAVI with a sensitivity of 100% and a specificity of 80% for a cutoff value of 0.815 (AUC = 0.919, 95% CI = 0.824 to 1.0, SE 0.048, P = 0.001).

Conclusion Early elevation of urinary [TIMP-2][IGFBP7] after TAVI is associated with the development of postoperative AKI. These biomarkers have an excellent diagnostic accuracy in the prediction of severe AKI requiring RRT that is superior to that of serum creatinine. Further studies are necessary to prove whether UTI-guided therapy of patients with AKI can reduce morbidity and mortality.

P291

Association between urinary TIMP-2 and IGFBP7 as early biomarkers of AKI and oliguria during liver surgery: a prospective pilot study

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Introduction Patients undergoing elective liver surgery have an increased risk for developing AKI [1]. This study was intended to assess [TIMP-2]*[IGFBP7] and its possible association with urine output (UO) in this population. Secondly we sought to compare [TIMP-2]*[IGFBP7] with serum creatinine concentration (Scr).

Methods A prospective single-center pilot study performed on 12 patients undergoing elective liver surgery. Serial urine samples were analyzed for [TIMP-2]*[IGFBP7] measured with the Nephrocheck device (Astute Medical, San Diego, CA, USA). Serial Scr was analyzed, UO, blood losses, and mean arterial pressure (MAP) were recorded. Fluid management was standardized, oliguria defined as a UO <0.5 ml/kg/hour. [TIMP-2]*[IGFBP7] values of >0.3 identify patients at high risk and >2 at highest risk for AKI [2].

Results Males comprised 66.7%, median age was 72 years. Median surgical time was 195 minutes. Peroperative median MAP was 71 mmHg (IQR 69; 77). Baseline median GFR was normal in eight patients and decreased in four patients (eGFR >90 and 66.5 ml/minute/1.73 m^2 respectively). Median baseline Scr was 0.75 mg/dl (IQR 0.61; 1.10), 0.74 mg/dl (IQR 0.64; 1.04) at ICU admission and 0.74 mg/dl (0.64; 1.04) on day 1 postoperatively. No difference in Scr and eGFR was seen between these time points (P = 0.457 and P = 0.517 respectively; repeated-measures ANOVA). Median peroperative and postoperative UO was 0.18 ml/kg/hour (IQR 0.13; 0.23) and 0.93 ml/kg/hour (IQR 0.79; 1.49) respectively. Median baseline [TIMP-2]*[IGFBP7] was 0.10 (IQR 0.04; 0.34), 2.02 (1.44; 6.23) during surgery, 0.61 (IQR 0.27; 1.22) at ICU admission and 0.74 (0.67; 0.97) on day 1 postoperatively. [TIMP-2]*[IGFBP7] differed at these time points (P <0.0001; repeated-measures ANOVA). Peroperative oliguria was associated with increased [TIMP-2]*[IGFBP7] (P = 0.018, chi-squared test).

Conclusion This pilot study demonstrated the association between [TIMP-2]*[IGFBP7] increase and oliguria and may therefore indicate kidney damage during liver surgery. As Scr could not differentiate for these changes, patients did not meet the classical biomarker criteria for AKI.

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P292

Continuous infusion of low-dose iohexol confirms 1-hour creatinine clearance is more accurate in acute kidney injury than 4-hour creatinine clearance: preliminary data

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Introduction There is currently no accurate method of measuring the glomerular filtration rate (GFR) during acute kidney injury (AKI). Four-hour creatinine clearance (4-CrCl) is often used. We have previously validated a method of measuring the GFR using a continuous infusion of low-dose iohexol (CILDI) in patients with stable renal function (GFR from normal to <30 ml/minute/1.73 m^2). Steady state was achieved in <10 hours in all subjects and we calculate that variations >10.3% suggest an AKI. In this study we compare GFR measured by CILDI with 4-CrCl and 1-hour creatinine clearance (1-CrCl).

Methods Critically ill patients with evolving AKI and patients following nephrectomy were recruited. Demographics were compared using the t test. CIDLI was connected for up to 72 hours. Plasma and renal iohexol and creatinine concentrations were measured by tandem mass spectrometry four times daily. Iohexol renal clearance (IRC) and

1-CrCl and 4-CrCl were calculated and compared using Bland–Altman analysis.
Results Baseline estimated GFR was similar in the postnephrectomy (88 ± 28) to the evolving AKI group (92 ± 23), $P = 0.70$. The evolving AKI group had a higher APACHE score (17.8 ± 5.1 vs. 10.6 ± 3.9; $P < 0.001$). When 1-CrCl was compared with IRC, a bias of 0.8% (SD 26%, limits of agreement –52 to 50%; Pearson's $r = 0.90$) was observed in the evolving AKI group, whereas bias was –3.3% (SD 16, limits of agreement –35 to 29%; Pearson's $r = 0.95$) in the postnephrectomy group. When 4-CrCl was compared with IRC, bias was 5.1% (SD 54, limits of agreement –102 to 112%, Pearson's $r = 0.45$) in the established AKI group and bias was –4.5% (SD 38, limits of agreement –79 to 70%; Pearson's $r = 0.78$) in the postnephrectomy group.
Conclusion Our data suggest that 4-CrCl is not as accurate and precise as 1-CrCl in patients with AKI and following nephrectomy. IRC appears to be more accurate and precise in patients with a predicted AKI risk and outcome (post nephrectomy) than in patients with evolving AKI. We hypothesise that IRC will be useful alternative to creatinine-based measures of AKI.

P293

Does cardiopulmonary bypass increase the risk of postoperative acute kidney injury after coronary artery bypass grafting?

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Introduction Acute kidney injury (AKI) following coronary artery bypass grafting (CABG) results in significant morbidity, mortality and prolonged stay on the cardiothoracic ICU. We sought to determine the incidence of AKI in our cardiothoracic centre, hypothesizing a higher occurrence in patients undergoing CABG using cardiopulmonary bypass (ONCAB) compared with off-pump (OPCAB) surgery [1].
Methods Retrospective data from all nondialysed patients undergoing isolated CABG at our institution were collected for the year 2013. Propensity scoring using the software platform MatchIt® was used to match subjects from ONCAB and OPCAB groups with regard to preoperative variables: logistic EuroSCORE, creatinine clearance (CrCl), gender and operative urgency. Postoperative AKI was defined as a rise of 50% or more in baseline serum creatinine [2]. Chi-square analysis was used to determine statistically significant differences.
Results From 500 cases (369 OPCAB, 131 ONCAB), 262 subjects were included in the final analysis, with 131 in each group. There was a higher incidence of AKI and renal replacement therapy (RRT) in the ONCAB group, although this was not significantly greater than in the OPCAB group (Table 1). The mortality rate was identical with three deaths in each group. The average length of ICU stay for the OPCAB group was 1.96 days versus 2.49 days for the ONCAB group.

Table 1 (abstract P293)

	OPCAB	ONCAB	*P* value
AKI	14 (10.69%)	19 (14.50%)	0.35
RRT	6 (4.58%)	9 (6.87%)	0.43

Conclusion Our study is limited by its size and the use of logistic EuroSCORE as a composite measure of risk factors. However, it has demonstrated that in our predominantly off-pump cardiac unit, OPCAB conferred no statistically significant advantage over ONCAB with regard to postoperative AKI. Studies to date have standardised patient-specific variables, but not the conduct of the procedure itself; for example, minimising renal hypoperfusion during OPCAB. This may be a reason for the lack of clear superiority in the continuing debate over choice of CABG procedure and reducing the risk of AKI.
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P294

Impact of kidney injury on fluid overload and impaired oxygenation

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Introduction Severity of acute kidney injury (AKI) and fluid overload (FO) are not incorporated into current severity of illness measures and are invisible to the practitioner. The causal relationship and timing between AKI and FO and oxygenation is not clear. The Fluid Overload Kidney Injury Score (FOKIS) is a daily score incorporating subscores for AKI (pRIFLE (creatinine (Cr) and urine output (UOP))), FO (total fluid (in – out) / ICU admission weight) >15% in five percentile increments, and exposure to nephrotoxic medications. We previously reported that FOKIS outperforms PRISM in mortality prediction in our pediatric intensive care unit (PICU). We hypothesized that patients with AKI on admission to the PICU developed worse fluid overload and in turn worse oxygenation.
Methods We prospectively calculated daily FOKIS scores and subscores (Cr, UOP, FO) in PICU patients. We excluded patients with <7 day stays in order to properly explore the association between timing of AKI and FO and oxygenation by oxygenation index (OI).
Results Over 18 months, there were 2,830 patients, 436 patients with PICU stay >7 days, 361 patients had complete data for all 7 days. Mortality was 4.5% overall and 11% cohort. A total of 246 patients (68%) had AKI (by FOKISCr or FOKISuop); 205 patients (57%) on day 1, 85 patients (24%) on day 3. Admission or day 3 AKI by either FOKIS subscore (FOKISCr or FOKISuop) did not predict maxFO or mortality. Increasing total FOKIS score was associated with increasing mortality and increasing OI (Table 1). FOKIS, controlled for PRISM, was an independent predictor of OI ($P = 0.03$).

Table 1 (abstract P294)

FOKIS	0	<4	4 to 7	>7	*P* value
maxOI, median (IQR)	7.4 (5.9 to 16.4)	11.1 (6.2 to 23.6)	16.4 (7.3 to 29.6)	14.2 (10 to 38.7)	0.03
Mortality, %	3.6	7.7	13	38	<0.001

Conclusion In PICU patients, admission or day 3 AKI alone did not predict maxFO. A composite score that includes both AKI and FO parameters correlated with OI and discriminated survivors from nonsurvivors. FO seems to result from combination of increased fluid exposure with underlying AKI but cannot fully be explained by oliguria in pediatric patients.

P295

Acute kidney injury biomarkers offer the opportunity to reduce exposure to nephrotoxic drugs

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Introduction Tissue inhibitor of metalloproteinase-2 (TIMP-2) and insulin-like growth factor binding protein 7 (IGFBP7) are specific urinary biomarkers which can predict acute kidney injury (AKI) in critically ill patients within 12 hours [1]. A [TIMP-2]·[IGFBP7] result >0.3 $(ng/ml)^2/1{,}000$ is associated with seven times the risk of AKI compared with a test result ≤0.3 [2]. The aim of our study was to explore the use of potentially nephrotoxic medications within the window between a positive biomarker test and the diagnosis of AKI stage 2 or 3.
Methods We identified all patients enrolled into the Sapphire study [1] who received at least one potentially nephrotoxic drug on the day of AKI (defined by stage 2 or 3 as per KDIGO classification). We subsequently

determined the proportion of patients who had a [TIMP-2]·[IGFBP7] result >0.3 $(ng/ml)^2$/1,000 before meeting the criteria for AKI.
Results Of 184 patients who developed AKI, 58% received one or more potentially nephrotoxic drug on the day of AKI. Eighty-nine percent of these patients had a positive biomarker test ≥12 hours earlier. In 41% of patients receiving one or more nephrotoxic drug on the day of AKI, at least one nephrotoxic medication was stopped within 1 day of AKI, and in 24% of patients all nephrotoxic drugs were stopped within 1 day of AKI, which implies that these medications were not absolutely necessary.
Conclusion Nephrotoxic medications are commonly used in patients who develop moderate or severe AKI. The [TIMP-2]·[IGFBP7] test could have identified many of these patients earlier and would have offered an opportunity to reduce exposure to non-essential nephrotoxic drugs.
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P296

Retrospective analysis of the efficacy of radio-contrast-induced nephropathy prophylaxis

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Introduction This study investigated renal outcomes following radio-contrast (RC) administration in patients from two intensive care units (ITUs), where one gave RC-induced nephropathy (RCIN) prophylaxis, while the other did not. Acute kidney injury (AKI) during critical illness increases morbidity and mortality. ITU patients, who already suffer a variety of renal insults, often require RC, increasing their risk of developing AKI, and requiring renal replacement therapy (RRT). Evidence suggests that hydration alone is inadequate for the prevention of RCIN in ITU patients, and is contraindicated in some disease states [1]. The European Society of Intensive Care Medicine (ESICM) provides recommendations for prophylaxis [2]. The current study aimed to establish the efficacy of the ESICM recommended prophylaxis.
Methods Retrospective data from 140 Maidstone (M) ITU patients (men 101, women 39, mean age 63.5, mean APACHE 15.3) and 73 Tunbridge Wells (T) ITU patients (men 41, women 32, mean age 60.2, mean APACHE 20.2) admitted between 22 September 2011 and 22 September 2013, who underwent RC-enhanced CT, were collected. Patients on MITU received ESICM-recommended RCIN prophylaxis: 200 mg aminophylline i.v. over 30 minutes prior to RC, 1.26% sodium bicarbonate 3 ml/kg/hour for 1 hour prior to RC and 1 ml/kg/hour for 6 hours post RC. TITU patients received standard critical care alone. Exclusion criteria were: those undergoing RRT prior to CT, >1 CT in 48 hours, no creatinine (Cr) data available post scan. The Cr prior to CT (baseline), at 24, 48 and 72 hours post CT scan were identified. The RIFLE criteria was used to classify the changes of Cr from baseline into low risk (% change >1.25), risk (% change >1.5), injury (% change >2) or failure (% change >3, or Cr>355 and increase of >44).
Results The total number of patients developing renal injury falling into any RIFLE category for MITU at 24, 28 and 72 hours was eight (0.06%), 12 (0.09%) and 14 (0.1%), while for TITU it was five (0.07%), six (0.08%), and four (0.05%) respectively. A repeated-measures ANOVA revealed no significant differences in outcomes between the two groups overall ($F = 2.35$, $P = 0.127$) or at each time point ($F = 1.93$, $P = 0.123$).
Conclusion While RCIN is a recognised problem within the critical care population, there is little clear evidence for any prophylactic strategy to reduce this risk. This study suggests that a RCIN prophylaxis protocol based on the ESICM recommendations has no effect on the incidence of RCIN. However, further studies are needed.
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P297

Base deficit and SOFA score are predictive factors of early acute kidney injury in oncologic surgical patients

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Introduction Patients who undergo major oncology surgery are under high risk to develop postoperative acute kidney injury (AKI), mainly due to inflammatory and ischemic insults. This complication results in worse outcomes. The aim of this study is to identify predictive factors of AKI in this population.
Methods We performed an observational study in 285 consecutive patients admitted to a surgical ICU after major abdominal oncology surgery. Baseline characteristics, laboratorial, clinical and intraoperative data, such as type of fluids, blood transfusion, bleeding and use of vasopressor, were collected at ICU admission. Early acute kidney injury was defined according to the Acute Kidney Injury Network classification at 48 hours of ICU admission. Logistic regression model was performed using AKI as the outcome.
Results There were 76 (26.7%) patients who developed AKI within the first 48 hours after ICU admission. In a univariate analysis, patients with AKI were more likely to be male, had higher Sequential Organ Failure Assessment (SOFA) score, higher baseline serum creatinine and urea levels, higher serum lactate levels and had more metabolic academia at admission. These patients also had a higher 24-hour Simplified Acute Physiology III score and higher length of mechanical ventilation as compared with non-AKI patients. There were no differences between patients regarding intraoperative vasopressors, type and amount of fluids, diuresis and blood transfusion. In a multivariate analysis we identified admission base deficit (BD) (OR = 1.13, 95% CI = 1.02 to 1.24, $P = 0.017$) and SOFA score (OR = 1.35, 95% CI = 1.2 to 1.51, $P < 0.001$) as independent predictive factors of early AKI.
Conclusion Both SOFA score and BD may be used to predict AKI in surgical oncology patients at ICU admission. These variables allow physicians to recognize early patients who might be under risk, and anticipate measures to avoid further renal impairment.
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P298

Predictors of renal recovery in critically ill patients with AKI: observations from the ongoing FBI clinical trial

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Introduction The predictive value of NGAL for renal recovery is not established.
Methods Data from the first 19 patients were assessed during a multicentre low molecular weight heparin trial (FBI, EudraCT Number: 2012-004368-23). Critically ill patients with AKI are randomly assigned into either a treatment arm (1 mg/kg enoxaparin) or a control arm (40 mg enoxaparin) upon commencement of CRRT. The primary outcome is the occurrence of venous thromboembolism. NGAL was measured at baseline and during CRRT-free intervals.
Results Patients were comparable at baseline with respects to demographics, APACHE II, creatinine, NGAL, start of dialysis, and the duration of dialysis. The main cause of AKI was sepsis (42%). In 63% of the patients, the reason for starting dialysis was a combination of anuria and electrolyte disturbances. Twenty-six percent of patients were dialysis dependent after the first CRRT-free interval. Plasma NGAL levels were higher in nonrenal recovery patients (1,074 (±694) ng/ml) compared with renal recovery patients (296 (±197) ng/ml; $P = 0.01$). Urine NGAL levels were higher in nonrenal recovery patients (3,885

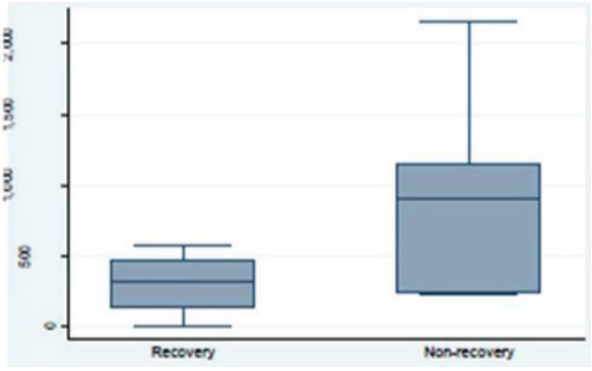


Figure 1 (abstract P298). Plasma neutrophil gelatinase-associated lipocalin concentration by recovery.

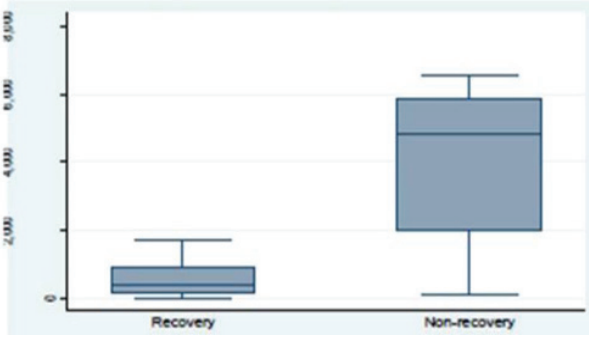


Figure 2 (abstract P298). Urine neutrophil gelatinase-associated lipocalin concentration by recovery.

(±2,722) ng/ml) compared with renal recovery patients (597 (±565) ng/ml; $P = 0.006$). See Figures 1 and 2. Inflammatory parameters (WBCs, CRP, and procalcitonin) did not differ significantly between the groups.
Conclusion NGAL may be able to predict renal recovery, and allow proper utilization of resources.

P299

Comparison of two strategies for initiating renal replacement therapy in the ICU: study protocol plan for a multicenter, randomized, controlled trial from the AKIKI research group

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Introduction There is currently no validated strategy for the timing of renal replacement therapy (RRT) for acute kidney injury (AKI) in the ICU when short-term life-threatening metabolic abnormalities are absent. No adequately powered prospective randomized study has to date addressed this issue. As a result, significant practice heterogeneity exists and may expose patients either to unnecessary hazardous procedures or to undue delay in RRT.
Methods This is a multicenter, prospective, randomized, open-label parallel-group clinical trial that compares the effect of two RRT initiation strategies on overall survival of critically ill patients receiving intravenous catecholamines and/or invasive mechanical ventilation and presenting with RIFLE F stage of AKI. In the early strategy, RRT is initiated immediately. In the delayed strategy, clinical and metabolic conditions are closely monitored and RRT is initiated only when one or more events (severity criteria) occur, including: oliguria or anuria for more than 72 hours after randomization, serum urea concentration >40 mmol/l, serum potassium concentration >6 mmol/l, serum potassium concentration >5.5 mmol/l persisting despite medical treatment, arterial blood pH <7.15 in a context of pure metabolic acidosis ($PaCO_2$ <35 mmHg) or in a context of mixed acidosis with a $PaCO_2$ >50 mmHg without possibility of increasing alveolar ventilation, acute pulmonary edema due to fluid overload despite diuretic therapy leading to severe hypoxemia requiring oxygen flow rate >5 l/minute to maintain SpO_2 >95% or FiO_2 >50% under invasive or non-invasive mechanical ventilation. The primary endpoint is overall survival, measured from randomization (D0) until death, regardless of the cause. The minimum follow-up duration for each patient will be 60 days. To demonstrate a 14% decrease in mortality, a total of 546 subjects (273 per group) should be randomized.
Results Enrollment is ongoing. After the first interim analysis, the DSMB recommended to continue the study. On 5 December 2014, 318 patients were included in the trial.
Conclusion The AKIKI study will be one of the very few large randomized controlled trials evaluating mortality according to the timing of RRT in critically ill patients with RIFLE F stage of AKI. Results should help clinicians better decide when to initiate RRT.

P300

Micronutrient loss in renal replacement therapy for acute kidney injury

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Introduction The prevalence of malnutrition in acute kidney injury (AKI) is high. Patients with AKI may require renal replacement therapy (RRT), which could result in loss of water-soluble micronutrients. Little is known about these losses in RRT and whether they differ between types of RRT. This study aims to quantify micronutrient losses during RRT in patients with AKI and to compare them in three different RRT modalities: continuous venovenous haemofiltration (CVVH), intermittent haemodialysis (IHD) and sustained low-efficiency diafiltration (SLEDf).
Methods A prospective observational study is being conducted at NUH. Thirty-three adult patients with AKI requiring RRT (13 IHD, 10 SLEDf, 10 CVVH) have been recruited. Samples of blood and RRT effluent were obtained at baseline, mid and end-session from each participant during their first RRT treatment. Samples were processed and stored at –80°C for subsequent analysis of amino acids by high-performance liquid chromatography and trace elements by inductively coupled mass spectrometry after derivatization from physiological fluids. Micronutrient losses were calculated by multiplying mass-corrected concentrations by total volume of RRT effluent, adjusted for baseline plasma concentrations and RRT dose. Data were analysed by restricted maximum likelihood estimating equations.
Results The total baseline plasma concentration of all standard amino acids was similar between IHD versus SLEDf groups (1,812 ± 517 vs. 2,675 ± 527 µmol/l, respectively) but were higher in the CVVH group (3,194 ± 564 µmol/l). RRT reduced the plasma concentration of amino acids in the SLEDf group (to 1,732 ± 529 µmol/l; $P = 0.02$), but had no effect in the IHD or CVVH groups (IHD; 1,853 ± 523, CVVH; 2,845 ± 512 µmol/l). The average, unadjusted loss of amino acids was significantly influenced by mode of RRT (IHD, 5.13 ± 3.1 vs. SLEDf, 8.21 ± 4.07 vs. CVVH, 18.69 ± 3.04 g; $P < 0.01$). The total baseline plasma concentration of trace elements was similar in the IHD, SLEDf and CVVH groups (3,797 ± 827, 3,667 ± 791, 3,642 ± 481 µg/l, respectively). By the end of the RRT session, the plasma concentration of trace elements had reduced (IHD, to 3,103 ± 827; SLEDf, to 2,805 ± 797; CVVH, to 3,433 ± 481 µg/l; $P = 0.01$). By the end of each RRT session, total losses of trace elements were estimated at IHD, 5,051 ± 2,312; SLEDf, 8,751 ± 2,421; CVVH, 11,258 ± 2,547 µg/l; $P = 0.02$ for treatment.
Conclusion Micronutrients are lost during RRT in AKI. The degree of micronutrient loss is influenced by the type of RRT used.

P301

Super high-flux CVVHD using regional citrate anticoagulation: long-term stability of middle molecule clearance

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Introduction Conventional membranes used for CRRT have a limited middle molecule clearance. New membranes called super high-flux (SHF) or high cutoff membranes have been investigated. The loss of albumin with hemofiltration is a major drawback, but these membranes can be used in CVVHD with regional citrate anticoagulation (Ci-Ca® CVVHD), which may limit albumin loss, and contribute to a prolonged filter patency and an improved and stable middle molecule clearance. We evaluated saturation coefficients (SC), plasma clearances (PCL) and serum levels of eight small and middle molecules during 72 hours of Ci-Ca® CVVHD with a SHF membrane (Ultraflux®EMiC®2).
Methods After approval of the local committee of medical ethics and written informed consent we enrolled patients on a surgical ICU with AKI RIFLE-F who were treated with a Ci-Ca® CVVHD with a SHF membrane for 72 hours. We measured urea (0.006 kDa), creatinine (0.113 kDa), osteocalcin (5.8 kDa), B2MG (12 kDa), myoglobin (17.2 kDa), FreeLightChains (FLC) kappa (25 kDa) and lambda (50 kDa) and albumin (66 kDa) at 0 hours, 1 hour, 6 hours, 12 hours, 24 hours, 48 hours, and 72 hours. PCL, SC and serum levels during 72 hours were compared, using the Wilcoxon signed-rank test with $P < 0.05$.
Results Four females and 10 males (mean age 68.1 ±15.1 years; mean APACHE II score 13.7 ± 14.7; mean SAPS II 38.7 ± 12.7) were included. The SC and the PCL (ml/minute) of small solutes like creatinine at 1 hour (1.0 ± 0.0/23.72 ± 1.04) and 72 hours (0.95 ± 0.16/22.19 ± 3.99) were not statistically significantly different ($P = 0.5$/$P = 0.42$), the PCL was slightly reduced by 6%. The creatinine serum level was reduced by 42%. The SC and PCL of B2MG from 1 hour (0.61 ± 0.09/14.49 ± 2.5) to 72 hours (0.48 ± 0.13/11.6 ± 2.96) were significantly decreased ($P = 0.0024$/$P = 0.0061$). The reduction was 23% only; the overall clearance still was high. There was almost no reduction in SC or PCL for FLC kappa from 1 hour (0.176 ± 0.047/4.14 ± 1.08) to 72 hours (0.164 ± 0.078/3.854 ± 1.87), not reaching statistical significance ($P = 0.94$/$P = 0.81$). The serum levels of B2MG and FLC kappa were decreased by 39% and 23%. The SC of albumin was low (1 hour: 0.0009 ± 0.0004) and clearance decreased rapidly within the first 6 hours from 0.021 ± 0.01 to 0.011 ± 0.009. Serum levels of albumin did not decrease (1 hour: 2.64 ± 0.51; 72 hours: 2.63 ± 0.25).
Conclusion This study shows high middle molecular clearances using a SHF membrane with Ci-Ca® CVVHD for 72 hours with no loss of albumin. This set-up may improve blood purification in critically ill patients with acute kidney injury.

P302

Citrate anticoagulation for continuous venovenous haemodiafiltration: the impact of a novel protocol on patients receiving therapy in one regional hospital

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Introduction Citrate has been used to anticoagulate extracorporeal haemofiltration circuits since the 1960s, and has been used as the first-line anticoagulant for continuous venovenous haemodiafiltration (CVVHDF) at Conquest Hospital since 2009. Benefits of citrate demonstrated in clinical trials include increased filter life and increased bicarbonate formation from metabolism of the citrate complex; citrate also lacks the increased bleeding risk associated with unfractionated heparin use. One of the main issues with new renal replacement therapies is the development of ideal dialysate fluids. During the initial period of citrate use at Conquest, hyponatraemia was identified as an issue, with off-license supplementation of dialysate fluid with sodium bicarbonate often necessary to prevent this. New protocols were therefore developed, designed to maximise the filtration dose and maintain normal electrolyte balance.
Methods A comparison of patients receiving CVVHDF on the 11-bed critical care unit at Conquest Hospital, Hastings was undertaken, before and after the implementation of new CVVHDF protocols. All patients receiving CVVHDF were identified from the electronic patient record system between March 2012 to 2013 and September 2013 to 2014. Patient demographics, the duration of CVVHDF and sodium bicarbonate supplementation were analysed between the groups to assess the impact of the new protocols.
Results Sixty-four patients received CVVHDF in 2012 to 2013, 61 receiving citrate and three receiving unfractionated heparin due to fulminant liver failure. Forty-seven patients received CVVHDF in 2013 to 2014, two receiving no anticoagulation due to severe coagulopathy and one receiving unfractionated heparin. The two patient cohorts assessed were similar in age (median 65.5 for March 2012 to 2013 cohort vs. 66 for September 2013 to 2014 cohort), gender mix (64% male vs. 57% male) and severity of illness as assessed by APACHE II score (23 vs. 24). Mean duration of CVVHDF was also similar (71.5 hours vs. 75 hours). A total 30/64 of 2012 to 2013 patients did not require a filter change prior to completion of RRT, compared with 23/47 of 2013 to 2014 patients. Sodium bicarbonate was added to the dialysate fluid in 29/64 2012 to 2013 patients, compared with just 2/47 2013 to 2014 patients.
Conclusion Changing protocols resulted in a significant reduction in off-license addition of sodium bicarbonate to dialysate bags without impacting on filter life, thus reducing nursing workload and removing a potential source of adverse events in this high-risk group of patients.

P303

Descriptive study of the haematological management of adult patients with severe respiratory failure receiving venovenous extracorporeal membrane oxygenation

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Introduction Venovenous extracorporeal membrane oxygenation (VV-ECMO) is a novel therapy for severe respiratory failure (SRF). Its introduction has reduced mortality; however, patients require substantial blood product support and between 10 and 20% of cases develop a life-threatening haemorrhage.
Methods We contacted 336 practitioners at 135 centres, examining their haematological management.
Results In total 25% of practitioners contacted responded; 85% were attending physicians, predominantly based in North America and Europe, 41 and 32% respectively. Ninety-six per cent of units used a polymethylpentene membrane oxygenator and all used a centrifugal pump. Thirty-four per cent of responders managed <10 cases a year and 60% worked in units handling <20 annually, 6% saw >50 patients. One centre did not use unfractionated heparin. Monitoring of anticoagulation varied; 52% used the APTT, 43% the ACT and 5% the APTTr. Sixty per cent did not routinely measure antithrombin. Scenario 1 was based on a patient with H1N1. Practitioners targeted a haemoglobin (Hb) of 80 to 100 g/l; however, 20% targeted a Hb outside this range; 38% favouring a transfusion threshold of <80 g/l when the patient was improving compared with 32% when the patient had just started on ECMO. Seventeen per cent of practitioners transfused platelets when the count was $<30 \times 10^9$/l whilst 21% maintained the platelet count $>100 \times 10^9$/l. Scenario 2 described a patient with SRF secondary to a hospital-acquired pneumonia. The patient developed a haemothorax, with persistent blood loss of 200 ml/hour. Practitioners targeted a higher haemoglobin concentration of 100 g/l and targeted a higher platelet count of $>100 \times 10^9$/l when compared with the patient in scenario 1, neither of these differences was statistically significant. Seventy-one per cent stated they would manage the patient off anticoagulation. There was no agreement as to the length of time off anticoagulation; 26% restarted anticoagulation in <12 hours, compared with 22% who advised no anticoagulation for >5 days. Scenario 3 examined the management of an incidental intracranial haemorrhage. There was a lack of consensus regarding the duration off anticoagulation; 14% of responders held anticoagulation for less than

12 hours whilst 37% held anticoagulation for >5 days and tranexamic was considered useful by 25%.
Conclusion There was wide variation in the use of blood products and the intensity of anticoagulation. This is not surprising given the current lack of evidence. Further work is required to provide a standardised approach.

P304

Comparison between nafamostat mesilate and unfractionated heparin as anticoagulant during continuous renal replacement therapy

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Introduction For continuous renal replacement therapy (CRRT), continuous administration of anticoagulant would be necessary to prevent the circuit clotting. Nafamostat mesilate (NM) is commonly used as its anticoagulant in Japan, although unfractionated heparin (UFH) is the most frequently used anticoagulant internationally. There is little study to compare the risk and benefit of NM with UFH as an anticoagulant during CRRT.
Methods We conducted a single-center retrospective observational study to compare NM with UFH as anticoagulant during CRRT. We screened subsequent critically ill patients requiring CRRT in our ICU from January 2011 to December 2013. We excluded patients who required any other extracorporeal circuit including extracorporeal membrane oxygenation, who used both NM and UFH simultaneously, or who were administered any other anticoagulant including gabexate mesilate or urokinase. The primary outcome of this analysis was filter life, and the secondary outcome was the incidence of bleeding complications during CRRT. As an initial dose, NM and UFH were given pre filter at 15 to 25 mg/hour and 1,500 to 3,000 IU/hour, respectively. The dose of both drugs was adjusted to maintain activated clotting time at post filter between 150 and 200 seconds. Filter life was assessed using the Kaplan–Meier method and the incident of bleeding complications was compared using the chi-square test. P <0.05 was considered to be statically significant.
Results We included 101 patients in this study. Among them, 76 patients were with NM and 25 patients were with UFH. They used 239 filters in total; 173 with NM, 66 with UFH. There were significantly more post-surgical patients in the NM group (P = 0.001). There was no difference in age, APACHE II score, days from ICU admission to commencement of CRRT, length of ICU stay and mortality between two groups. There was no difference in median number of filters used by one patient (NM vs. heparin; median of 1.5 (IQR) vs. 2 (IQR), P = 0.27). Filter life in the UFH group was significantly longer than those in the NM group (NM vs. UFH; median of 24 hours vs. 36 hours; P = 0.01). The incidence of bleeding complications was not significantly different between two groups (P = 0.15).
Conclusion In our retrospective analysis with 101 patients, filter life with UFH was significantly longer than those with NM. The incidence of bleeding complications was not significantly differed between patients with NM and UFH.

P305

Long-term renal and survival outcomes in acute kidney injury patients receiving renal replacement therapy in intensive care

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Introduction Acute kidney injury (AKI) affects 40% of critically ill patients, with UK data reporting 5% needing renal replacement therapy (RRT). Hospital mortality is reported as being up to 60%. We sought to evaluate renal and long-term patient survival outcomes in AKI patients receiving RRT on our ICU.
Methods Data were collected from our computerised information system on all AKI patients receiving RRT on our ICU, between October 2008 and October 2013. This included demographics, APACHE II and SOFA scores, modality and dose of RRT and ICU length of stay (LOS). Renal and patient survival at ICU discharge was collected, in addition to outcome data at 28 and 90 days and 12 months. Data were examined using Cox proportional hazard multivariate analysis, with Stata 10.1.
Results A total of 620 patients with AKI received RRT on our ICU between October 2008 and October 2013. Sixty-one per cent were males. Median age was 65 years (IQR 54 to 74). Median APACHE II score was 23 (IQR 18 to 27). Median SOFA score was 11 (IQR 8 to 13). Fifty-five per cent were mechanically ventilated. A total of 96.7% received CVVH as the principal RRT modality. Twenty-one per cent received a period of high-volume haemofiltration (HVHF) (80 ml/kg/hour), median LOS was 6 days (IQR 3 to 14). In total, 331 (53.4%) patients recovered their renal function at ICU discharge, whilst 237 (38.2%), 220 (35.4%), and 220 (35.4%) patients did not at 28 and 90 days and 12 months respectively. A total of 414 (66.7%) patients survived to ICU discharge, with 368 (59.3%), 341 (55%) and 308 (49.6%) patients being alive at 28 and 90 days and 12 months respectively. Overall patient survival at the end of follow-up was 43%. Adjusting for age and sex; APACHE II score, SOFA score and use of HVHF were associated with worse patient survival at ICU discharge (HR: 1.07, 95% CI: 1.03 to 1.11, P <0.001, HR: 1.11, 95% CI: 1.03 to 1.19, P = 0.006 and HR: 2.27, 95% CI: 1.4 to 3.66, P = 0.001, respectively). Adjusting for age and sex; APACHE II score and use of HVHF were associated with worse renal recovery at ICU discharge (HR: 1.06, 95% CI: 1.03 to 1.09, P <0.001 and HR: 1.55, 95% CI: 1.03 to 2.3, P = 0.032 respectively). SOFA score did not appear to significantly impact renal recovery (HR: 0.99, 95% CI: 0.94 to 1.04, P = 0.81).
Conclusion Results from our cohort suggest that, in patients with AKI presenting to ICU for RRT, long-term patient survival is significantly impaired. Renal outcomes are poor with 35% being either dialysis dependent or having severe chronic kidney disease (eGFR <15 ml/minute), at 1 year from ICU discharge. Our data do not suggest a benefit of using HVHF in AKI patients presenting to ICU for RRT.

P306

Plasma antioxidant capacity in critical traumatized patients: severity and anatomical location

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Introduction Oxidative stress (OS) has been invoked as a relevant factor in the evolution and outcome of critical care patients. Indeed, antioxidant therapies have been used in critical care patients, but with controversial results. This may be explained by assuming OS as a homeostatically regulated parameter and both its excess and its deficit influencing severity progression. Nonetheless, antioxidant agents could mask an OS signaling role, blocking otherwise physiological responses aimed at recovery of homeostasis. We have evaluated plasma total antioxidant capacity (TAC) in traumatized patients in the emergency department (ED) and we determined its potential relationship with severity and trauma location.
Methods In a prospective observational study of ED polytraumatized patients (n = 23, mean Acute Physiology and Chronic Health Evaluation II (APACHE II) score of 11 ± 6) we measured (in the first 24 hours) plasma TAC by the ferric reducing activity/antioxidant power (FRAP). For control subjects, we used age-matched and gender-matched volunteers (n = 32). We also evaluated the contribution of antioxidant molecules (uric acid, bilirubin, and albumin) to these values.
Results Polytraumatized patients show differences in TAC with reference to control subjects. ED polytraumatized patients show high FRAP values. We found that FRAP values were inversely correlated with APACHE II score (r = –0.266, P <0.01) suggesting that, in trauma patients, increased antioxidant response, as measured by FRAP assay, could be a pathophysiological response to stress. Albumin and uric acid concentrations reproduced the FRAP trend with severity.
Conclusion FRAP values in trauma ED patients are independently influenced by age (β = 0.271, P <0.021), APACHE II score (β = –0.356,

P <0.002) and head trauma (β = –0.219, *P* <0.045). These results accentuate the influence of trauma location and severity in TAC changes. TAC response in ED patients reinforces the need for an adequate tailoring of treatments aimed at their recovery, such as antioxidant therapies.

P307

Hypothermia as a predictor for mortality in trauma patients

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Introduction Previous studies reported hypothermia as an independent predictor for mortality. However, different cutoff points were used in these studies and external validation has never been applied. The aim of this study was to quantify the net effect of hypothermia on admission to the ICU on the 28-day mortality and to test the predictors from the developed model in another level 1 trauma center with a comparable patient population to validate the model.
Methods A retrospective cohort study was performed in adult trauma patients admitted to a level 1 trauma center and who were transferred to the ICU between 2007 and 2012. Different cutoff points for hypothermia were compared to find the best definition for hypothermia. Logistic regression analysis was performed to quantify the net effect of hypothermia on admission to the ICU on 28-day mortality and to develop a model with predictors. The developed model was externally validated in data from another level 1 trauma center with a comparable patient population.
Results In total, 722 trauma patients were included, of which 300 patients were hypothermic. The mortality in the hypothermia group was significantly higher than in normotherm patients (OR = 3.73, 95% CI = 2.02 to 7.13, *P* <0.001). A cutoff point of 36°C was observed as the best threshold for hypothermia (sensitivity 74%, specificity 56%). Besides hypothermia, other predictors found for 28-day mortality were APACHE II score corrected for temperature, minimum thrombocytes in first 24 hours and urea and included in the final model with an AUC of 0.89 (95% CI = 0.85 to 0.92). External validation of the model was associated with a predicted probability of an AUC of 0.64 (95% CI = 0.51 to 0.77).
Conclusion Hypothermia, defined as <36°C, is associated with an increased 28-day mortality. The discriminative ability of the developed model for predicting mortality in a new patient population is moderate.

P308

Near-infrared spectroscopy to assess tissue oxygenation in patients with polytrauma: relationship with outcome

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Introduction We evaluated tissue oxygenation by means of near-infrared spectroscopy (NIRS) and explored its relationship with outcome in polytrauma patients.
Methods A prospective observational study; 37 polytrauma patients underwent NIRS monitoring (thenar eminence) every day during their stay in the ICU. A VOT was performed with a 40% tissue oxygen saturation (StO_2) target. Healthy volunteers (*n* = 27) were studied as controls.
Results StO_2 increased over the first 7 days only in hospital survivors (*n* = 29), who showed higher values as compared with healthy volunteers at days 5 and 7 (Figure 1). StO_2 downslope and upslope tended to be lower in H-nonsurvivors (*n* = 8) (*P* <0.05 at days 2 and 4) as compared with H-survivors. Tissue hemoglobin index was lower in H-no survivors over the first 7 days and tended to normalize only in H-survivors (*P* >0.05 vs. healthy at day 7). Five patients were discharged from the ICU but did not survive until H-discharge. At discharge from the ICU, these patients were similar to H-survivors in SOFA score, heart rate, mean arterial pressure and lactate, but showed lower StO_2 downslope (–13 (–16.5, –11.7)%/minute vs. –8.6 (–11.7, –6.5)%/minute, *P* = 0.01).

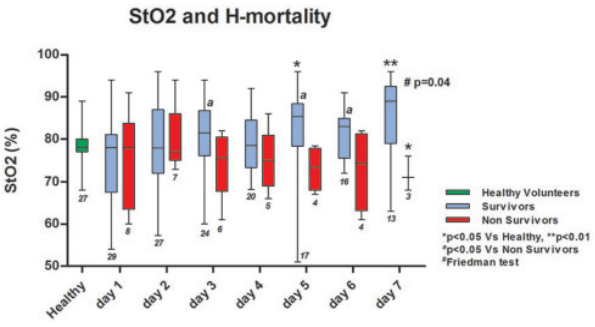


Figure 1 (abstract P308).

Conclusion An increase in StO_2 and lower tissue oxygen extraction rates were associated with H-survival in polytrauma patients.

P309

Features and treatment of surviving casualties in the Kunshan 'August 2' Explosion Accident: 40 case reports and literature review

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Introduction The aim was to analyze the injury features and treatment strategies of surviving casualties in the explosion accident on 2 August 2014 in Kunshan city (Kunshan 'August 2' Explosion Accident).
Methods We retrospectively studied 40 cases of surviving casualties in the Kunshan 'August 2' Explosion Accident, and systemically reviewed the relevant literature.
Results A total of 40 cases were admitted to our hospital within 6.3 ± 0.8 hours after the explosion accident on 2 August 2014 in Kunshan city, including 28 males and 12 females. The major injury types included burn injury, inhalation injury, blast injury (lung, eye, eardrum, and so forth), traumatic brain injury and bone fractures. All cases suffered from burn injury caused by the explosion. The mean burned area in the surviving casualties accounted for 92 ± 14% total body surface area (TBSA) and those with third-degree burns for 77 ± 19% TBSA. Additionally, incidence rate of inhalation injuries was 97.5%. There were 34 cases complicated by multiple organ dysfunction syndrome, which accounted for 85.0%. The common organ dysfunction of surviving casualties included the lungs, circulation, liver, gastrointestinal tract, kidney, brain, and coagulation. During hospitalization, the most common infectious site in surviving casualties was a burn wound, followed by blood and lung. The most common infectious strain of bacteria was Gram-negative bacteria, which accounted for 91.3%. Further analysis showed that *Proteus mirabilis* ranked first in occurrence, followed by *Acinetobacter baumannii* and *Pesudomonas aeruginosa*, and *Klebsiella pneumonia* and *Enterobacter cloacae* ranked fourth and fifth. After intensive treatment, the mean 28-day mortality was 20.0% and 90-day mortality was 62.5%, mainly due to septic shock and multiple organ dysfunction syndrome.
Conclusion During the Kunshan 'August 2' Explosion Accident, burn injury was the leading cause of injuries. Most surviving casualties are accompanied by multiple organ dysfunction syndrome and infection.

P310

Duration of mechanical ventilation in trauma patients: risk factor for VAP?

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Introduction In the literature, duration of mechanical ventilation (DMV) is often considered an important risk factor (RF) [1] for VAP [2] in critical patients; generally the whole duration of MV is taken into

account, including days before and after infection onset. We tried to assess whether, counting only MV days prior to VAP development (MVp), something would change.

Methods We considered, in a 10-year period, data prospectively collected in our database (4D solution, V11) on trauma patients admitted to the ICU directly from the emergency department. Inclusion criteria were: age ≥16 years, ICU length of stay (ICUlos) ≥4 days, DMV ≥48 hours; we excluded patients who received antibiotics before VAP (or during the whole stay, for patients without VAP) and with incomplete data. Data were: age, sex, prehospital GCS <9, prehospital intubation (preHTI), admission base excess (BE), Injury Severity Score (ISS), surgery, massive transfusion, feeding, antacids, nursing, DMV, ICUlos and MVp. MVp was calculated as the difference between the first day of VAP and the first day of MV in patients who developed VAP (vapY) and whole DMV in patients that did not (vapN). We only considered the first infectious episode. The outcome was VAP onset. Group comparison was made with Fisher's exact test and Student's *t* test. Significant variables were evaluated in a logistic regression (LR) model; the Hosmer–Lemeshow test (HL) was used as the post-estimation test. Odds ratio (OR) and 95% confidence interval (95% CI) were calculated. Statistical significance for $P < 0.05$. We used Stata/IC 10.1 for analysis.

Results A total of 541 patients met the inclusion criteria, 378 (69.9%) developed VAP. MVp does not seem to be a RF for VAP because they are longer in vapN than in vapY (mean MVp 5.5 vs. 4.41, $P = 0.001$). PreHTI (vapY/N: 49.74%/38.65%; OR: 1.57; 95% CI: 1.08 to 2.28), ISS (mean vapY/N: 28.4/25.55; $P = 0.0018$), BE (mean vapY/N: −3.76/−3.04; $P = 0.03$) were significantly different between the two groups. In LR only preHTI (OR: 1.47; 95% CI: 1.01 to 2.15) and ISS (OR: 1.03; 95% CI: 1.01 to 1.05) are RF for VAP (HL: $P = 0.133$).

Conclusion In our study MVp are not a RF for VAP in trauma patients, although the whole DMV is longer in patients with VAP (mean DMV vapY/N: 13.57/6.09; $P = 0.0001$). Further studies could confirm whether the whole DMV in trauma patients with VAP is a consequence of infection.

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P311

In-depth study of road accidents in Florence: understanding the biomechanical effects in major trauma involving vulnerable road users

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Introduction Road accidents are the leading cause of death for young people, 50% being represented by vulnerable road users (VRU) (pedestrians, cyclists). In-depth accident studies assess the consequences of lack of use of safety devices and the need to develop new ones. Since 2009 a permanent team (physicians and engineers) has performed in-depth studies on road trauma admitted to our ICU [1].

Methods The team studied 52 VRU crashes that occurred in an urban area. The clinical data included an injury assessment using total body CT scan, Injury Severity Score (ISS), Abbreviated Injury Score (AIS), ICU and hospital length of stay and outcome score. Engineers collect data onsite with the partnership of the police, and assess the dynamics of the vehicles with the most advanced reconstruction techniques. Medical and engineering data were cross-matched during the correlation process. Injuries suffered by each person were related to specific impact objects.

Results The average ISS is 21.5 (SD 10.9). Cars are the most involved in serious urban VRU crashes. Car-to-pedestrian crashes are the most frequent (50%). The impact speed is always over 40 km/hour (Table 1). The head and face are the most frequently injured part (48% of the 571 injuries collected), followed by lower extremities (15%). In terms of maximum AIS (MAIS), the head is the most severely injured region with 42% of MAIS 3+ (Figure 1).

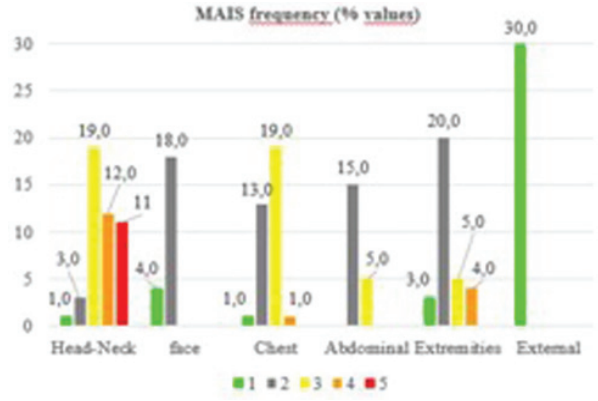


Figure 1 (abstract P311). Frequency of lesions.

Table 1 (abstract P311). Accident dynamics: medium speed (km/hour)

Dynamic	*N* injured	Speed (SD)
Car vs. pedestrian	29	41.1 (13.9)
Motorcycle vs. pedestrian	7	40.6 (4.3)
Car vs. cyclist	10	40.7 (15.9)
Other	6	49.0 (5.4)

Conclusion The head is still the most frequently and severely injured region. The severity of injuries increases in the most rigid part of the car. Improving VRUs' safety devices (active and passive) to reduce impact speed and severity of the primary impact has to be the next step.

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P312

Missed fractures in severely injured patients

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Introduction The purpose of this study is to analyze anatomic distributions, diagnostic methods, and prognosis of missed fractures in patients with severe injury.

Methods A review of single-institutional medical records between January 2001 and May 2012 identified 58 patients with 62 delayed diagnoses of fractures among 4,643 severely injured patients older than 20 years with Injury Severity Scores higher than 16. We evaluated combined injuries, location of fractures, diagnostic methods, and reasons for missed diagnosis at initial examination.

Results Among 62 missed fractures, there were eight cases of spine fracture, 10 cases of peri-shoulder joint fracture, eight cases of upper extremity fracture, 10 cases of pelvis of acetabulum fracture, and 26 cases of lower extremity fracture. Head injury was the most common concomitant injury (23 cases). Initially missed fractures were most commonly discovered by official reading by radiologists. The most common reasons for misdiagnosis were the use of improper radiologic study and missed-reading of proper radiologic studies.

Conclusion In order to prevent misdiagnosis of fractures in patients with severe injury, meticulous physical examination with suspicion of fractures should come first. In addition, obtaining proper radiologic study and thorough evaluation of radiologic images are important to decreasing the rates of missed fracture diagnoses. In addition, thorough surveillance for ipsilateral fractures is important in extremities with identified fractures.

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P313

Endogenous microparticles drive the proinflammatory host immune response in severely injured trauma patients

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Introduction Severe trauma affects the immune system, which in its turn is associated with poor outcome. The mediators driving the immune responses in trauma are largely unknown. The aim of this study was to investigate the role of endogenous microparticles (MPs) in mediating the immune response following severe trauma.
Methods A prospective, observational substudy of the Acute Coagulopathy and Inflammation in Trauma (ACIT) II study was performed at our academic level 1 trauma center. Adult multiple trauma patients with an Injury Severity Score of 15 or higher were included between May 2012 and June 2013. *Ex vivo* whole blood stimulation with lipopolysaccharide was performed on aseptically collected patient plasma containing MPs and in plasma depleted of MPs. Flow cytometry and transmission electronic microscopy were performed on plasma samples to investigate the numbers and cellular origin of MPs. Healthy individuals served as a control group.
Results Ten trauma patients and 10 healthy individuals were included. Trauma patients were significantly injured with a median ISS of 19 (17 to 45). On admission to the hospital, the host response to bacterial stimulation was blunted in trauma patients compared with healthy individuals, as reflected by decreased production of IL-6, IL-10 and TNFα (P <0.001). In trauma patients, MP-positive plasma was associated with a significantly higher synthesis of IL-6 and TNFα compared with plasma depleted from MPs (P = 0.047 and 0.002 respectively). Compared with healthy individuals the number of circulating MPs was significantly decreased in trauma patients (P = 0.009). Most MPs originated from platelets. Multiple cellular protrusions, which result in MP formation, were observed in plasma from trauma patients, but not in healthy controls.
Conclusion On admission, trauma patients have a reduced immune response towards endotoxin challenge which is, at least in part, mediated by MPs, which circulate in low numbers and in early stages. Most MPs originate from platelets, which indicates that these cells may be the most important source of MPs involved in initiating an inflammatory host response post injury.

P314

DNA and sRAGE circulation in the early phase after polytrauma

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Introduction Various DAMPS, alarmins are released after trauma. The soluble receptor for advanced glycation endproducts (sRAGE) was reported to be associated with acute renal failure and duration of ventilation [1]. Cell-free DNA (cfDNA) has been associated with prognosis in trauma patients [2]. We studied the kinetics of these two biomarkers over the first 5 days, in a cohort of severely ill trauma patients.
Methods Patients who had sustained serious traumatic injury, within 24 hours of trauma, were recruited in a level I trauma center. We collected ISS, baseline demographic characteristics, resuscitation information and daily organ dysfunction (MOD) scores, over 10 days. Blood samples were collected within 24 hours of trauma (day 0) and on days 1, 3 and 5. sRAGE was measured by ELISA and cfDNA was measured by UV absorbance after plasma isolation.

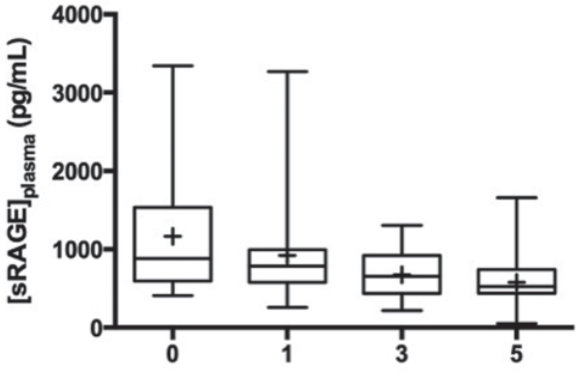


Figure 1 (abstract P314). sRAGE kinetics (days).

Results Median ISS was 39 and mortality was 21% (8/38). During the first 5 days after trauma, the median concentration of sRAGE (Figure 1) decreased significantly over time (P <0.0001) while median levels of DNA did not (P = 0.73), and remained elevated compared with normal control. No correlation was found with ISS. Patients initially in shock had lower levels of sRAGE or cfDNA (P <0.05) and had received more fluid (10.6 l vs. 5.25 l) or blood (6 l vs. 0.5 l). Day 3 and day 5 sRAGE levels were inversely correlated with PRBC received. Medians of sRAGE on days 0 (1,301 vs. 730 pg/ml) and day 1 (925 vs. 760 pg/ml) were significantly higher in nonsurvivors (P <0.01). Finally, day 0 sRAGE was correlated with the maximal (r = 0.44; P = 0.007) and the cumulative renal failure component of the MODS, over the 10 days (r = 0.48; P = 0.005).
Conclusion DNA and sRAGE kinetics differ following trauma. Early elevation of sRAGE predicts mortality in univariate analysis and correlates with subsequent renal failure.
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P315

Clinical decision rule for cervical magnetic resonance imaging in suspected cervical spinal cord injury without bony injury is useful in predicting severity of cervical stenosis

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Introduction Cervical spinal cord injury (CCI) without bony injury (CCIWOBI) is more frequent among Asian than among Caucasian populations and shows various extents of severity. Cervical magnetic resonance imaging (MRI) is useful for detecting intramedullary lesions, ligament injuries and intervertebral disk hernias, but some patients with mild CCIWOBI do not show clinically significant abnormalities on MRI. To date, the cost–benefit ratio of performing MRI in addition to computed tomography (CT) is unclear. We have developed a clinical decision rule for cervical MRI (MR-CDR), indicating MRI for patients >70 years old with ossification of the posterior longitudinal ligament on CT or injury in a ground-level fall or a fall down stairs. The objective of the present study was to prospectively validate this MR-CDR for cervical MRI in patients with suspected mild CCIWOBI.
Methods We have been conducting a prospective observational study in two institutions in Japan since September 2012, enrolling patients with CCIWOBI among head or neck trauma patients >16 years old brought in by ambulance. We collect data about patient characteristics, injury profiles, neurological findings, results of radiological examinations, and medical courses. We then analyze the sensitivity and specificity of MR-CDR for detecting intramedullary lesions on MRI and conduct further analysis.

Results During the study period, 63 patients were brought in with CCIWOBI. Mean age was 60.6 years (standard deviation, 17.9 years) and 76% were male. Forty-five patients presented with mild symptoms (Frankel Grade D). Cervical MRI was performed for 23 patients. Sensitivity and specificity of MR-CDR in detecting intramedullary lesions on T2-weighted imaging among cases of suspected mild CCIWOBI were 85.7% (95% confidence interval (CI), 60.1 to 96.0%) and 33.3% (95% CI, 12.1 to 35.4%). Further analysis showed a significant difference in minimal spinal canal diameter as measured on sagittal T2-weighted imaging between the MR-CDR-positive and MR-CDR-negative groups (5.0 mm vs. 8.3 mm, $P = 0.0003$). One patient underwent surgery during hospitalization and no patients experienced exacerbated neurological findings. No significant differences were evident between groups in discharge status, duration of hospitalization, or neurological findings at discharge.
Conclusion MR-CDR was not validated for predicting the existence of intramedullary lesions on cervical MRI. MR-CDR is useful in predicting the severity of cervical stenosis.

P316

Accuracy of targeted wire-guided tube thoracostomy in comparison with classical surgical chest tube placement: a clinical study

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Introduction Chest tube malfunction, after the tube thoracostomy, is often the result of an inappropriate chest tube tip position. The aim of this study was to analyze the precision of chest tube placement using the targeted wire guide technique (TWG technique) with a curve dilator and to compare it with the classical surgical technique (CS technique).
Methods In this clinical study 80 patients with an indication for thoracic drainage due to pneumothorax or pleural effusion were included. The experimental group contained 39 patients whose chest tube was placed using the TWG technique. The control group contained 41 patients whose chest tube was placed using the CS technique.
Results The comparison of the outcomes of the two techniques applied suggests that the TWG technique was significantly more successful, irrespective of patient diagnosis (TWG vs. CS in all patients, 78.4% vs. 36.6%, $P < 0.001$). See Table 1.

Table 1 (abstract P316)

Diagnosis	*N*	CS technique (% of success)	TWG technique (% of success)	*P* value
Pleural effusion	47	37.5	78.2	0.005
Pneumothorax	31	35.3	78.6	0.029
Total	78	36.6	78.4	<0.001

Conclusion Using a curved dilator and the TWG technique for the thoracic drainage procedure we found statistically significant advantage to the TWG technique in comparison with the CS technique regarding precise chest tube placement within the pleural cavity.
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P317

Evaluating trauma care: comparison of early versus late tracheostomy ICU data outcome on injured patients

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Introduction In the surgical ICU, bedside tracheostomy (T) is one of the most frequently applied surgical techniques for multi-injured patients mainly with TBI [1]. The optimum surgical time decision for T still remains a contradiction in trauma. This retrospective study was designed to register all trauma patients who underwent T, during 60 months of observation (2009 to 2013), in order to identify factors associated with their ICU outcome on the basis of the T day (A <10th day >B) after tracheal intubation.
Methods Seventy-eight injured patients in the SICU underwent T, from a total of 403 issues; 58 male and 20 female, with mean age 59.3 and 74.7 years respectively. The total length of ICU stay recorded was 2,098 days, nursing time 26.55 (4/93), whereas the T time was adjusted between the 6th and 16th day (mean 11th). Mean ISS score was 22.59 (9 to 50). Classification according to trauma type was TBI ($n = 44$) followed by thoracic trauma. Thirty-one male survivors were discharged from the ICU, to the ward. The mortality rate amounts to 47 cases due to infectious/non-infectious nosocomial complications and multiorgan dysfunction syndrome. Clinical ISS, the type of injury, ICU length of stay (LOS), T day, demographic (gender, age) data and ICU outcome were registered. Statistical analysis was performed with GraphPad 5.0.
Results There is positive significant correlation between T day and LOS of injured patients ($P < 0.001$, Spearman coefficient = 0.1672). Statistical analysis by Mann–Whitney test, between groups A and B, showed significant differences in ICU LOS ($P < 0.001$); no significant differences ($P < 0.05$) were found for age, ISS and outcome (Table 1).
Conclusion The optimum and early time point of tracheostomy seems to be directly related with LOS in the ICU, independently of the rate of ISS, patient's age and outcome. These results could account for ICU cost-effectiveness, as diminished LOS decreased the overall cost.
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P318

Factors related to sepsis and outcome in multiple trauma patients

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Introduction The outcome of multiple trauma patients is related to a number of diagnostic and therapeutic interventions during hospitalization. ICU patients with severe trauma are susceptible to sepsis leading to poor outcome. Factors associated with the occurrence of sepsis and the outcome of these patients were investigated.
Methods We studied retrospectively all trauma patients admitted to the A' ICU of KAT General Hospital in Athens during the last 3 years and were treated for more than 5 days. Age, gender, the type of injury, the severity of injury (Injury Severity Score), the length of ICU stay, severe sepsis, coexisting diseases, the outcome and the cause of death were recorded. Logistic regression and chi-square tests were used for statistical analysis.

Table 1 (abstract P317). SICU data

					Outcome	
ICU data	ISS	Age	ICU LOS (days)	Tracheostomy day	Survival	Mortality
A <10	16 ± 87 (16/45)	66 ± 94 (28/87)	602 17.2 ± 21.5 (4/47)	5.5 ± 6.5 (1/10)	*n* = 13 (43.3%)	*n* = 17 (57.7%)
B >10	16 ± 25 (9/50)	64 ± 87 (23/93)	1,496 25 ± 34 (9/95)	15 ± 26 (11/23)	*n* = 18 (40%)	*n* = 27 (60%)
t test	NS	NS	<0.001	<0.001	NS	NS

Data presented as median ± IQR.

Results A total of 106 multiple trauma patients, 85 men and 21 women, met the inclusion criteria. Depending on their age, patients were divided into two groups: <60 years old and >60 years old. In both groups, gender, the type and severity of injuries and the length of ICU stay were not associated with outcome. The length of ICU stay was correlated with severe sepsis and coexisting diseases (P <0.01) in both groups. Mortality was not different in the two groups. The presence of at least one coexisting disease was significantly associated with mortality (P <0.007). Sepsis was significant cause of death in trauma patients >60 years (P <0.05).
Conclusion In multiple trauma patients, the length of ICU stay and comorbidities influence the occurrence of severe sepsis, comorbidities increase mortality, and sepsis is the leading cause of death in trauma patients >60 years old.
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P319

Ventilator-associated pneumonia in a trauma ICU

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Critical Care 2015, **19(Suppl 1):**P319 (doi: 10.1186/cc14399)

Introduction Ventilator-associated pneumonia (VAP) is associated with increased length of ventilation, ICU stay, mortality, cost and antibiotic burden [1]. There is a large variation in reported rates of VAP, partly as a result of inconsistencies in definition [2]. We explored a more pragmatic definition to describe the VAP rate, antibiotic burden and outcome of VAP in a 44-bed adult critical care unit in a level 1 trauma centre.
Methods A retrospective review of all adult patients admitted to the ICU at The Royal London Hospital over a 6-month period (February to August 2014). The diagnosis of VAP was based on the Clinical Pulmonary Infection Score. Patients were identified with VAP if they were started on antibiotics for chest sepsis 48 hours after start of mechanical ventilation. Demographic, clinical, microbiological and radiological data were collected to identify risk factors, and compare VAP and non-VAP groups. Chi-squared and ANOVA tests were performed using the SOFA statistics package.
Results A total of 535 mechanically ventilated patients were admitted in the study period, with 281 ventilated for more than 48 hours. The incidence of VAP was 11% in all ventilated patients and 19.6% in those ventilated more than 48 hours. VAP rates were 31% in polytrauma, 25% in neurotrauma and 18% in the neuromedical/surgical cohort. Early and late onset VAP were equal in number. Patients with VAP spent longer on mechanical ventilation (9 ± 9 in no VAP vs. 18 ± 18 days in VAP patients; P <0.001), and had longer ICU and hospital LOS (11 ± 10 vs. 22 ± 20 days; P <0.001). However, APACHE II scores and hospital mortality were unaffected (VAP 33.3% vs. no VAP 37.6%; P = 0.173). Despite rising inflammatory markers and secretion load, many patients did not exhibit oxygenation deficits. Sputum microbiology showed *S. aureus*, *H. Influenza*, Klebsiella and Enterobacter as predominant pathogens with low rates of Pseudomonas, Acinectobacter and other resistant organisms. Average length of antibiotic use was 6 (3 to 18) days.
Conclusion Chest sepsis after 48 hours of mechanical ventilation commonly complicates neurocritical illness and polytrauma requiring significant ICU resources and antibiotic burden. However, it does not affect mortality. Further research should focus on pathophysiology and new preventative measures to reduce VAP in the at-risk population.
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P320

Normobaric oxygen paradox and erythropoietin production in critically ill patients: a prospective observational study

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Introduction The normobaric oxygen paradox (NOP) postulates that a period of normobaric hyperoxia followed by a rapid return to normoxia will create a condition of relative hypoxia, which acts in turn as a stimulus for erythropoietin (EPO) production [1]. Variations in GSH and oxygen free radical (ROS) levels may be involved in this process. We tested the NOP in critically ill patients.
Methods A prospective observational study on 38 mechanically ventilated (FiO_2 <50%) patients with no active bleeding, no blood transfusion needed, and no kidney failure. Eighteen patients underwent a 2-hour period of normobaric hyperoxia (FiO_2 = 100%), 20 patients were evaluated as controls (no FiO_2 variations). EPO was assayed at baseline (t0), 24 hours (D1) and 48 hours (D2). Serum GSH and ROS were assayed at t0 (baseline), t1 (2-hour FiO_2 100%) and t2 (2-hour return to normoxia) in 12 patients in the hyperoxia group.
Results EPO tended to increase in the hyperoxia group over time (P = 0.05), while it remained stable in the control group (P = 0.53) (Figure 1). ROS levels increased at t1 and decreased at t2, GSH tended to decrease at t1 and increased at t2 in the hyperoxia group.
Conclusion Relative hypoxia after a transient period of normobaric hyperoxia induces an increase in GSH levels, thus enhancing ROS scavenging. This may act as a stimulus for EPO production.
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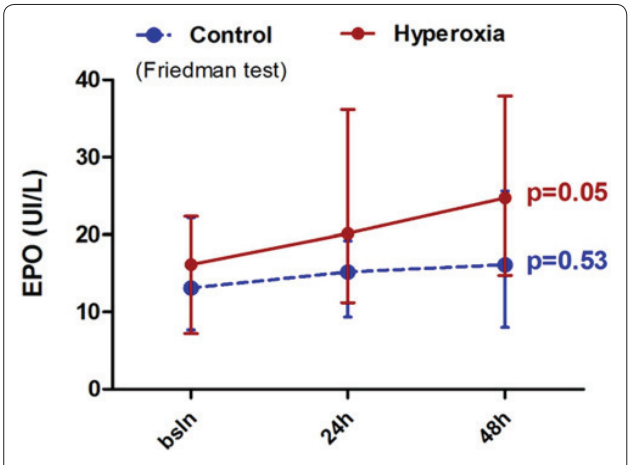


Figure 1 (abstract P320).

P321

Comparison of the PATHFAST D-dimer assay with two POC D-dimer assays

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Introduction The early exclusion of PE is a major precondition for goal-oriented diagnostic and therapeutic measures. The aim of the study was to evaluate the new point-of-care assay PATHFAST D-dimer in comparison with VIDAS D-Dimer Exclusion and STRATUS CS D-dimer.
Methods A total of 272 patients with symptoms of PE and VTE were included. The diagnoses of VTE and PE were established by duplex ultrasound, venography and spiral CT. D-dimer values were determined in the patients and in plasma samples obtained from 102 healthy individuals who served as the control group.
Results Mean D-dimer concentration of the control group and of the patient group with PE was 0.28 (95% CI: 0.25 to 0.31) mg/l and 1.45 (95% CI: 1.23 to 1.72) mg/l, respectively. Receiver operator characteristics analysis revealed an optimized cutoff value of 0.466 mg/l for the PATHFAST D-dimer assay (AUC = 0.975 (95% CI: 0.938 to 0.993); sensitivity: 95% (95% CI: 86 to 99%); specificity: 89% (95% CI: 82 to 95%)). Therefore we used a rounded up cutoff value of 0.5 mg/l to examine the diagnostic accuracy of PATHFAST D-dimer to exclude PE. The correlation between PATHFAST and VIDAS results was particularly close for concentrations at or around the critical cutoff value of

0.5 mg/l. The correlation between PATHFAST and STRATUS results was particularly close in the patient group with VTE (r = 0.9694), whereas slightly lower results were obtained with STRATUS in the control group. With the widely used cutoff value 0.5 mg/l, PATHFAST demonstrated suitable sensitivity but not STRATUS. ROC analysis indicated that optimal cutoff values could be set at either 0.5 or 0.6 mg/l and at 0.3 or 0.4 mg/l for PATHFAST and STRATUS, respectively.

Conclusion By use of the PATHFAST D-dimer assay only six of diagnoses were missed at the time of first presentation compared with 10 diagnoses missed by the VIDAS D-dimer Exclusion assay, yielding higher sensitivity of the PATHFAST D-dimer assay compared with the VIDAS assay (90% vs. 83%). The STRATUS assays showed comparable performance and appeared to be suitable for the exclusion of VTE in the emergency room setting, whereas PATHFAST demonstrated superior sensitivity. Moreover, the PATHFAST analyzer allows simultaneous determination of D-dimer and cardiac troponin I within 16 minutes from whole blood samples. Therefore, this method might be useful at the point of care for early diagnostic assessment of patients with symptoms of PE or chest pain admitted to the ER or to the chest pain unit.

P322

Using rivaroxoban in patients with venous thromboembolism

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Introduction A prospective study was conducted in patients for treatment of venous thromboembolism (VTE) to compare the effect of enoxaparin and rivaroxaban using the method of low-frequency piezoelectric thromboelastography (LPTEG) for checking coagulation activation markers.

Methods A total of 60 patients entered the Odessa Clinical Regional Hospital for treatment venous thromboembolism. Patients were divided into two groups. The first group (n = 30) were receiving enoxaparin in dosage 1.5 mg/kg subcutaneously per day. The second group (n = 30) were receiving rivaroxaban orally 15 mg/day. For checking the coagulation state we were using such indicators of LPTEG as constant thrombin activity (CTA), intensity of coagulation drive (ICD) and gel point (GP). We performed LPTEG three times per day: 4, 12 and 24 hours after taking the drug to check for changes in the coagulation state in both groups of patients.

Results The peak action of enoxaparin and rivaroxaban was observed at 4 hours post administration. LPTEG indicators that determine the coagulation state after 4 hours in the first group: CTA was decreased by 72.12% (P <0.05), ICD was decreased by 68.44% (P <0.05), GP was increased by 17.9%; in the second group: CTA was decreased by 76.24% (P <0.05), ICD was decreased by 74.52% (P <0.05), GP was increased by 23.34%. After 12 hours, CTA in the first group decreased by 22.41%, ICD decreased by 5.3%, GP increased by 8.12%, indicating reduction of hypocoagulation effect; in the second group, CTA decreased by 39.35% (P <0.05), ICD decreased by 40.24% (P <0.05), GP increased by 18.25%. After 24 hours in the first group LPTEG indicators returned to the original value, and in the second group of patients CTA was decreased by 15.14%, ICD was decreased by 6.62%, GP increased by 14.22%.

Conclusion Using LPTEG showed the hypocoagulation effect of continuous rivaroxaban 24 hours after oral administration compared with enoxaparin, which retains less hypocoagulation effect 12 hours after administration. LPTEG indicators in the second group were bigger than in the first group after 12 hours: CTA 43.07%, ICD 69.72%, GP 54.12%.

P323

Is delaying pharmacological thromboprophylaxis associated with thromboembolic complications?

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Critical Care 2015, **19(Suppl 1):**P323 (doi: 10.1186/cc14403)

Introduction Thromboembolic complications (TEC) are very common and lethal in patients suffering from traumatic injury [1]. The trauma clinical guidelines recommend the administration of pharmacological thromboprophylaxis (PTP) to reduce the risk of developing TEC [2]. However, it is unknown whether delayed PTP initiation increases risk of TEC. We hypothesize that delayed PTP initiation is associated with increased TEC rates.

Methods A retrospective chart review (2010 to 2013) was conducted on adult trauma patients that were admitted into a level 1 trauma centre in Toronto. Demographics, date of PTP initiation, date of TEC diagnosis (CT-PE/US Doppler), injury type and severity were collected. A comparison between early and late PTP initiation has been made with regards to TEC development. Student's t test, univariate and multivariate logistic regression analyses were performed.

Results A total of 1,312 patients received PTP, 821 (62.5%) initiated early PTP (within 48 hours) while 491 (37.5%) initiated after 48 hours. The group that initiated early prophylaxis was younger (mean: 46 vs. 55, P <0.0005), had lower ISS (mean: 17 vs. 24, P <0.0005), shorter length of stay (LOS) (mean: 11 vs. 23, P <0.0005), more pelvic fractures (19% vs. 13%, P = 0.0058), more head injury (AIS Head ≥3, P <0.0005), less blunt trauma (85% vs. 95%, P <0.0005), lower incidence of TEC (5.3% (44) vs. 8.5% (42), P = 0.023), and lower mortality rate (1.5% vs. 7.5%). Univariate analysis showed LOS (P <0.0005), ISS (P <0.0005), time to PTP initiation (P = 0.0018) and blunt MOI (P = 0.0099) significantly associated with TEC events. Multivariate analysis, however, showed TEC events correlated only to LOS (P = 0.0001). Stepwise multiple logistic regression confirmed LOS as independently associated with TEC events (95% CI = 0.003, 0.006, P <0.0005).

Conclusion Mortality rates in patients with delayed PTP are higher. Our study shows LOS as the only independent predictor for TEC. However, this might not necessarily reflect causation. Delayed PTP appears not to be an independent predictor to TEC events in trauma patients, which favours current clinical trends when it comes to contraindicating early PTP initiation.

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P324

Impact of introducing guidelines for thrombolysis of submassive pulmonary embolism at a large UK teaching hospital

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Introduction Pulmonary embolism (PE) is a significant cause of death with 10% of patients dying within 3 months [1]. Multiple studies now advocate the use of thrombolysis (TPA) in both massive and submassive PE [1,2]. This audit assessed the impact of introducing a guideline allowing for thrombolysis of submassive and massive PE at a large UK teaching hospital.

Methods Retrospective data collection using notes and imaging to risk-stratify patients. First audit ran from January to June 2012. New guidance was introduced in March 2013 (Figure 1) after which a second cycle ran for a further 6 months.

Results Re-audit revealed 46 patients with radiological evidence of massive or submassive PE on CTPA (32% of all PEs). Ten patients had clinical features of submassive PE and nine presented as massive PE. Previous guidelines suggested consideration of TPA in only seven patients in 6 months. TPA was given to two patients; however, six patients had no contraindications to treatment (Table 1). Limitations to TPA administration were late recognition of submassive PE and inadequate knowledge of changes to guidelines.

Conclusion Delivering a service that offers TPA to patients with submassive PE significantly increases the need to consider this therapy. Introducing this service is only effective if doctors initially assessing these patients are aware of recent changes to guidelines for PE.

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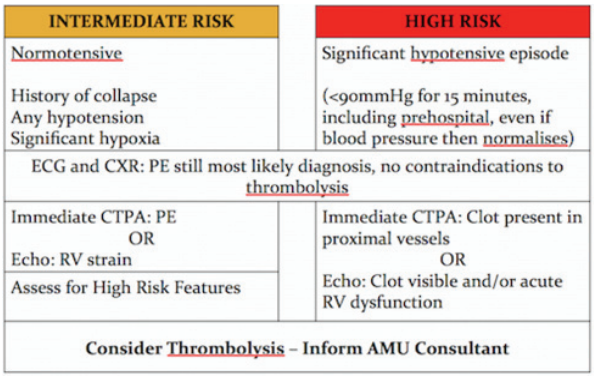


Figure 1 (abstract P324). New local guidelines.

Table 1 (abstract P324). TPA decisions

	Total	High risk	Intermediate risk
Considered TPA and given	2	2	0
Considered TPA but contraindications	1	1	0
Considered TPA and not given on balance	3	0	3
Considered TPA and not given but fit criteria	**3**	**2**	**1**
Not considered TPA but contraindicated anyway	4	1	3
Not considered TPA and on balance would not be given	5	1	4
Not considered TPA but fit criteria	**1**	**0**	**1**

P325

Examining venous thromboembolic disease in postoperative neurosurgical and trauma patients in the ICU

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Introduction Despite preventive anticoagulation therapy measures, venous thromboembolic disease is a major cause of morbidity and mortality among patients hospitalized in ICUs. In fact, pulmonary embolism is not only the most serious manifestation of the disease, but also one of the primary causes of sudden death. The aim of this study is to investigate the frequency of thromboembolism and pulmonary embolism in ICU hospitalized trauma and neurosurgical patients.
Methods One hundred ICU patients, 51 postoperative neurosurgical and 49 trauma, were included in the study. Patients' demographic data as well as medical history, temperature, white blood cells and platelets counts were recorded on admission, the day of thrombosis diagnosis and the final outcome of their treatment. Statistics were performed with SPSS-19. P <0.05 was considered significant.
Results Thirty-eight out of 100 patients presented thrombosis, 14 trauma and 24 neurosurgical. We examined the correlation of thrombosis development during hospitalization with diagnosis, treatment allocated time and overall patient outcome. It was found that neurosurgical patients developed thrombosis more frequently than trauma patients (P <0.05). In relation to diagnosis, thrombosis was prevalent among patients with brain lesions (P = 0.018). Regarding the type of thrombosis, pulmonary embolism was also commonly apparent among individuals with brain lesion (P = 0.020). In addition, there was a statistically significant correlation in thrombosis occurrence between hospitalization day (P <0.01) and patients' outcome on discharge (P <0.001). The type of thrombosis was directly associated with poor outcome, especially one that resulted from central catheters (P <0.001) and pulmonary embolism (P <0.001). However, no correlations were found with temperature, white blood cells and platelet counts on admission (P > 0.05).
Conclusion Thrombosis affects the ICU patient's final outcome. The type of thrombosis contributes to a poor outcome and mainly the occurrence of pulmonary embolism significantly increases the mortality rate.

P326

Incidence and outcome of asymptomatic deep vein thrombosis in critically ill patients: a prospective cohort study

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Introduction Asymptomatic deep vein thrombosis (DVT) including catheter-related thrombosis (CRT) is an increasingly recognized disease entity in critically ill patients. However, the reported rate and outcome of DVT vary widely depending on study design, patient background and detecting method. The objective of this study is to evaluate the incidence and outcome of DVT in adult critically ill patients.
Methods This study is a prospective cohort study of patients admitted to a medical and surgical ICU from 1 July 2014 to 15 October 2014. All consecutive patients over 18 years of age and with expected ICU stay over 72 hours were included. Patients who had previous history of DVTs were excluded. We examined internal jugular vein, subclavian vein, axillary vein, brachial vein, femoral vein, superficial femoral vein, and popliteal vein, on ICU admission and within 48 hours after ICU discharge. The DVT was diagnosed using compression ultrasonography with color Doppler. Images were interpreted by two independent investigators trained in ultrasonography. All patients received intermittent pneumatic compression and unfractionated heparin twice daily during their IUC stay. Once the DVT was detected, therapeutic anticoagulation was initiated. Contrast-enhanced CT was performed when the patients were suspected to have pulmonary embolism. The primary outcome was the incidence of DVT during the ICU stay. Patients were followed until their hospital discharge.
Results A total of 51 patients were included. The median age and BMI were 73 years and 23 kg/m^2, respectively; 31% were female and 69% were surgical critical care patients. The median APACHE II and SOFA scores were 20 and 8, respectively. Risk factors associated with DVT were presence of central venous catheter 63%, malignancy 9% and hemodialysis 14%. The rate of DVT was 18.6% and the rate of CRT was 13.7%. All of these were asymptomatic and seen in neck and upper extremities. There was no DVT-associated adverse event (pulmonary embolism, bleeding) during hospital stay. The 28-day all-cause mortality rate was 3.4%.
Conclusion While incidence of asymptomatic DVT is relatively high in adult critically ill patients, they were found only in the neck and upper extremities without any adverse event. Further research is needed to evaluate the clinical significance of this type of DVT.

P327

Computed tomographic pulmonary angiographic findings to predict adverse outcomes in acute pulmonary embolism

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Introduction Computed tomographic pulmonary angiography (CTPA) has been used as a standard tool for diagnosing an acute pulmonary embolism (APE). The right ventricular (RV) strain signs may be used to predict adverse outcomes. However, the results are still controversial. The primary objective of our study was to evaluate the relationship between the RV strain signs and respiratory failure requiring mechanical ventilation or death in APE. The secondary objective was to identify clinical factors which related to those outcomes.

Methods CTPA and the medical records of patients with suspected APE on admission from June 2011 to March 2013 were reviewed. RV dysfunction signs included right ventricular to left ventricular (RV/LV) diameter ratio, interventricular septal shift, main pulmonary artery to ascending aorta (mPA/AA) diameter ratio, IVC contrast reflux, SVC diameter, IVC diameter, PA diameter and azygos vein diameter. Clinical factors included cardiovascular, respiratory parameter and also time to diagnosis and treatment.
Results There were total of 36 cases with suspected APE on admission. Ten patients required mechanical ventilation (27.8%) and seven patients died (19.4%). Interventricular septal (IVS) shift was a significant risk factor of in-hospital death (85.7% vs. 27.6%, P = 0.008) and respiratory failure (70% vs. 26.9%, P = 0.026). The sensitivity, specificity, positive predictive and negative predictive values of IVS shift to predict in-hospital death were 85.7%, 70%, 42.8% and 95.5%, respectively. The sensitivity, specificity, positive predictive and negative predictive values of IVS shift to predict respiratory failure were 70%, 73.1%, 50% and 86.4%, respectively. The ratios of RV to LV diameter and the ratio of main pulmonary artery to ascending aorta diameter tended to be higher in the nonsurvivor group. The clinical factor that predicted mortality was the PaO_2 to FiO_2 ratio (P/F ratio). Mean P/F ratio in survivor and nonsurvivor groups was 246.1 ± 94.1 vs. 132.2 ± 78.1, respectively (P = 0.011). P/F ratio ≤150 was the best predictor of mortality (66.7% vs. 8.7%, P = 0.008).
Conclusion The IVS shifting from CTPA and P/F ratio ≤150 helps predict poor outcomes in APE.
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P328

Mean platelet volume and mean platelet volume/platelet count ratio in risk stratification of pulmonary embolism

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Introduction Recently, mean platelet volume (MPV) was reported to predict early death in acute pulmonary embolism (PE). The aim of this study was to investigate the role of MPV and MPV/platelet count ratio (MPV/P) in risk stratification of patients with acute PE.
Methods We retrospectively reviewed the medical records of patients with acute PE admitted to the emergency department. In addition to the clinical evaluation, platelet count and MPV were measured on admission.
Results One hundred and fifty-two patients were included. Patients with right ventricular (RV) dysfunction had significantly higher MPV levels and MPV/P than patients without RV dysfunction. Receiver operating characteristic analysis revealed that a MPV cutoff of 7.85 fl provided 53.3% sensitivity and 68.5% specificity, and a MPV/P cutoff of 0.0339 fl/(10^9/l) provided 69.6% sensitivity and 65% specificity for prediction of RV dysfunction. There was a positive correlation between MPV and systolic pulmonary artery pressure (SPAP) and between MPV and RV diameter. There was a positive correlation between MPV/P and SPAP and between MPV/P and RV diameter. The low-risk PE group had lower MPV and MPV/P than the massive PE and submassive PE groups.
Conclusion MPV and MPV/P are associated with RV dysfunction and clinical severity in acute PE. Low MPV and MPV/P levels may be an indicator of low risk in patients with acute PE.

P329

Progression to end-stage renal disease is reduced with eculizumab in patients with atypical haemolytic uraemic syndrome

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Introduction Atypical haemolytic uraemic syndrome (aHUS) is associated with severe kidney damage; almost one-half of adults with aHUS progress to end-stage renal disease (ESRD) after the first episode [1]. Two prospective clinical trials have assessed the efficacy of eculizumab (Ecu) in patients with aHUS [2]. We now evaluate data on progression to ESRD before and during Ecu treatment.

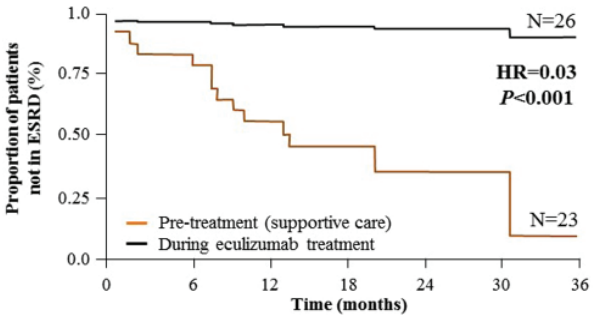


Figure 1 (abstract P329). Kaplan–Meier analysis of ESRD progression for SC and Ecu treatment for all patients.

Methods Patients with chronic kidney disease (CKD) stage 1 to 4 were analysed for progression to an ESRD event (two consecutive glomerular filtration rate measurements <15 ml/minute/1.73m² (CKD stage 5)). ESRD incidence rate ratios during supportive care (SC) and Ecu treatment phases were calculated using a negative binomial regression analysis. Kaplan–Meier analyses were calculated for all patients and stratified by CKD stages 2 to 4 at baseline. Hazard ratios (HR) were calculated from Cox proportional hazard models.
Results The SC and Ecu treatment phases included 32 and 33 patients, respectively. With SC, during a median (range) of 211 (7 to 745) days, 13 (41%) patients had a total of 16 ESRD events. On Ecu treatment, during a median (range) of 924 (73 to 1,254) days, three (9%) patients had a total of five ESRD events. The ESRD event rate was 92% lower during Ecu treatment versus the SC phase (0.36 vs. 0.07; P = 0.001); the incidence rate ratio was 0.08 (95% CI = 0.02 to 0.37; P = 0.001). HR for progression to ESRD for patients on Ecu versus SC was 0.03 (95% CI <0.01 to 0.34), a 97% reduction (Figure 1). Stratification by baseline CKD stage showed no patients with CKD stage 2 or 3 at baseline progressed to ESRD over 3 years of Ecu treatment.
Conclusion Ecu treatment reduces the number of ESRD events and the rate of progression to ESRD; thus initiation of Ecu early after aHUS diagnosis may prevent cumulative kidney damage and progression to ESRD.
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P330

Early initiation of eculizumab treatment in patients with atypical haemolytic uraemic syndrome improves long-term outcomes: a pooled analysis of clinical trials

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Introduction Atypical haemolytic uraemic syndrome (aHUS) is a severe, life-threatening disease requiring rapid treatment to inhibit complement-mediated thrombotic microangiopathy (TMA) and avoid irreversible organ damage. Four prospective clinical trials have reported the safety and efficacy of eculizumab (Ecu) in the treatment of aHUS [1,2]. We report data from a pooled analysis of these trials on renal function in patients starting Ecu within ≤7 days or >7 days after the current aHUS manifestation.
Methods Data from four phase 2, open-label, single-arm trials including both paediatric and adult patients with aHUS were pooled. Patients with a documented date of onset of current TMA manifestation and a baseline estimated glomerular filtration rate (eGFR) of <90 ml/

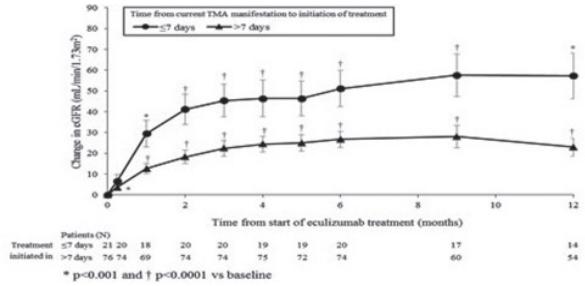


Figure 1 (abstract P330). Mean change in eGFR from baseline over 1 year (standard error).

minute/1.73 m^2 were included. Changes from baseline in eGFR were analysed at study visits using a one-sample *t* test.
Results Data from 97 patients were analysed: median (range) age at enrolment was 29 (0 to 80) years; 62% of patients were females; median (range) duration of current manifestation to start of Ecu treatment was 23 (1 to 1,447) days; median (range) baseline eGFR was 15.9 (5.6 to 76.1) ml/minute/1.73 m^2. Ecu treatment was started in 21 patients in ≤7 days and 76 patients in >7 days after presentation with TMA. Median eGFR was 11 ml/minute/1.73 m^2 for the patients started within 7 days and 16 ml/minute/1.73 m^2 for those initiating >7 days. The mean change from baseline in eGFR for patients starting Ecu in ≤7 days and in >7 days after presentation with TMA were 57 and 23 ml/minute/1.73 m^2 at 1 year, respectively (Figure 1).
Conclusion This pooled analysis indicates that patients treated with Ecu within 7 days of a TMA manifestation had a greater improvement in eGFR over time than patients in whom treatment was delayed. These data show the importance of rapid diagnosis and treatment of aHUS for recovery of renal function.
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P331

Evaluation of the quotient of the venoarterial carbon dioxide gradient and the arteriovenous oxygen content difference as a transfusion trigger parameter in hemodynamically stable patients with significant anemia

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Introduction Hemoglobin as the main trigger parameter for blood transfusion usually gives diminutive information about oxygen delivery and consumption. Although central venous oxygen saturation ($ScvO_2$) is an alternative parameter, its changes are unable to detect regional hypoxia. Our aim was to evaluate the quotient of the central venous-to-arterial carbon dioxide gradient (δPCO_2) and the arteriovenous oxygen content difference ($Ca\text{-}cvO_2$) as a valid transfusion trigger parameter in hemodynamically stable anemic patients to reduce the amount of potentially counterproductive erythrocyte transfusions [1].
Methods Forty-five postoperative patients admitted to our cardiac ICU were enrolled between January 2013 and September 2014. Three groups were defined according to the trend of blood loss over the surgical drains in the first 24 postoperative hours. Mild blood loss was defined as 500 to 1,000 ml/24 hours, moderate (1,000 to 1,500/24 hours) and severe (>1,500 ml/24 hours). In addition to the δPCO_2 the following parameters were monitored: CI, CO, SVR, serum lactate, $ScvO_2$ and hemoglobin. $Ca\text{-}cvO_2$ was calculated and the $\delta PCO_2/Ca\text{-}cvO_2$ quotient was assessed for a total of 400 paired blood samples. All enrolled patients were hemodynamically stable. A retrospective analysis of this data was performed.
Results $\delta PCO_2/Ca\text{-}cvO_2$ showed significant correlation with the moderate and severe blood loss groups (P <0.01), while no significant correlation was detected in the mild blood loss group. The abnormality of the $\delta PCO_2/Ca\text{-}cvO_2$ was easy detectable and reflected intracapillary hemoglobin capacity decline and significantly improved after erythrocyte transfusions (P <0.005).
Conclusion Blood transfusions carry risks of adverse effects and should be carried out responsibly. Our findings suggest an additive and easy detectable transfusion trigger parameter ($\delta PCO_2/Ca\text{-}cvO_2$) providing physiological information on anemia-related altered oxygen extraction conditions and hence the indication for erythrocyte transfusions. However, additional studies are warranted to confirm these findings.
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P332

Red blood cell transfusion in patients with traumatic brain injury: a systematic review

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Introduction We aimed to evaluate the frequency of red blood cell (RBC) transfusion in patients with traumatic brain injury (TBI) as well as determinants and outcomes associated with RBC transfusion in this population.
Methods We conducted a systematic review of cohort studies and trials of patients with TBI. We searched Medline, Embase, The Cochrane Library and BIOSIS databases from their inception up to 30 June 2014. We selected cohort studies and RCTs of adult patients with TBI reporting data on RBC transfusions. We extracted data related to demographics, baseline characteristics, blood product use and any relevant clinical patient-oriented outcome. Cumulative incidences of transfusion were pooled through random effect models with a DerSimonian approach, after a Freeman–Tukey transformation to stabilize variances. To evaluate the association between RBC transfusion and potential determinants as well as outcomes, we pooled risk ratios or mean differences with random effect models and the Mantel–Haenszel method. Sensitivity and subgroup analysis were planned *a priori*.
Results We identified 21 eligible studies (16,951 patients). After pooling data from the 20 included cohort studies (16,884 patients), at least around 33% (95% CI: 27 to 39; I^2: 97.8%) of patients with TBI in published reports received transfusions at some point during their hospital stay. In a *post hoc* analysis of one RCT comparing transfusion strategies, 82% of patients were transfused RBCs. Thresholds for transfusion were rarely available and varied from 6 to 10 g/dl. From raw data, Glasgow Coma Scale scores were lower in patients who were transfused than those who were not (three cohort studies; n = 1,371; mean difference of 1.38 points (95% CI: 0.86 to 1.89); I^2 = 12%). Mortality was not significantly different among transfused and nontransfused patients both in univariate and multivariate analyses. Hospital length of stay was longer among patients who were transfused (three studies; n = 455; mean difference 9.58 days (95% CI: 3.94 to 15.22); I^2 = 74%). Due to the observational nature of included studies, results should be considered cautiously due to the high risk of confounding.
Conclusion RBC transfusion is frequent in patients with TBI, but practices varied widely in cohort studies in this population. The paucity of data precludes definitive conclusions and highlights the lack of clinical evidence guiding transfusion strategies in TBI.

P334

Red blood cell transfusion is associated with an increased mortality in critically ill surgical patients

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Introduction The aim of this study is to explore the association between red blood cell transfusion (RBCT) and mortality in Thai critically ill surgical patients.

Methods This study was a part of the multicenter, prospective, observational study performed in nine surgical intensive care units (SICUs) across the nation between April 2011 and November 2012 [1]. This study included adult patients admitted to the SICUs after surgery. Patients were categorized into transfusion and no transfusion groups according to whether or not they received RBCT at any time during SICU stay. Demographic data, clinical outcomes as well as SICU and hospital length of stay (LOS) and SICU and hospital mortality were collected. Patients were followed for up to 28 days or until discharge from the SICUs. The primary endpoint was hospital mortality. Data were compared between groups and logistic regression analysis was performed to determine whether RBCT was an independent risk factor of hospital mortality. In addition, patients were matched between groups based on the propensity score of the requirement of RBCT and were then compared.
Results Overall, 968 of 2,374 (40.8%) patients received RBCT. Transfused patients, when compared with those without RBCT, had more frequency of admission after emergency surgery, higher APACHE II score, higher SOFA score, higher number of organ dysfunctions and lower hemoglobin level at admission. When compared with patients without RBCT, those with RBCT had more frequency of all adverse events including infection, AKI, ALI/ARDS and MI, and longer SICU and hospital LOS. Both SICU and hospital mortality were also higher in the transfusion group compared with the no transfusion group (9.4% vs. 1.6% and 13.7% vs. 3.6%, both P <0.001, respectively). The logistic regression analysis showed that RBCT was an independent risk factor of hospital mortality with odds ratio of 1.60 (95% CI 1.05 to 2.45). In the propensity-score matched cohort of 852 patients, when compared with patients without RBCT, transfused patients had more frequency of adverse events including infection and AKI, longer SICU and hospital LOS and higher hospital mortality (7.5% vs. 4.0%, P = 0.027).
Conclusion This study showed that RBCT was associated with increased morbidity and mortality in critically ill surgical patients. These results supported the restrictive strategy of RBCT suggested by more recent studies.
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P335

Effect of the haemoglobin level on neurologic outcome in patients with severe traumatic brain injury

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Introduction Anaemia in patients with severe traumatic brain injury (TBI) may worsen neurologic outcome. The aim of this study was to determine the association of haemoglobin level (Hb) with neurologic outcome and to determine a transfusion threshold which may be used in future transfusion trials aimed at improving neurologic outcome in TBI patients.
Methods A substudy of the prospective multicentre Activation of Coagulation and Inflammation in Trauma (ACIT) II study was performed on subjects recruited between January 2008 and December 2014. All adult trauma patients admitted to a level 1 trauma centre with severe traumatic brain injury (AIS head ≥3), ICU admission and available Hb levels on admission were selected for analysis. The primary outcome was the cognitive functioning of patients as determined by an estimated Glasgow Outcome Scale (GOS) on discharge. Anaemia was defined as a Hb level of ≤9 g/dl (severe anaemia) or ≤10 g/dl (moderate anaemia) within the first 24 hours post injury. Multivariate logistic regression models were used to determine the association between anaemia and neurologic outcome. The receiver operating characteristic curve and the Youden Index were used to determine an optimal transfusion threshold.
Results Of a total of 261 TBI patients, 61 patients (23%) fell below the threshold for severe anaemia and 101 patients (39%) had moderate anaemia within the first 24 hours. In a model adjusted for all relevant confounders, a Hb level of ≤9 g/dl was associated with a poor neurologic outcome (OR = 2.572, 95% CI = 1.058 to 6.250), whereas an Hb level of ≤10 g/dl was not. A Hb level of ≤10.3 g/dl had a sensitivity of 82% and a specificity of 62% to predict poor neurologic outcome in TBI patients.
Conclusion In TBI patients a Hb level of ≤9 g/dl is associated with poor neurologic outcome. A transfusion threshold of ≤10.3 g/dl may be a reasonable target to be tested in future transfusion trials aimed at improving neurologic outcome of TBI patients.
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P336

Microparticles from red blood cell transfusion products induce a strong inflammatory host response

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Introduction Red blood cell (RBC) transfusion is associated with increased morbidity and mortality in the critically ill. Adverse effects of transfusion may be mediated by red blood cell storage lesion. In this study, we hypothesized that MPs from stored RBC bags would induce a more pronounced host response than MPs from fresh RBC bags and that this response is dose dependent.
Methods MPs were isolated by high-speed centrifugation from red blood cell transfusion bags stored for 2 to 7 (fresh) or 25 to 35 (stored) days. Whole blood from healthy volunteers was incubated with supernatant from the bags either containing MPs or depleted from MPs (n = 12 bags per group). Controls were incubated with PBS as a negative and LPS (10 ng/ml) as a positive control. Cytokines in supernatant were measured by ELISA. Data are expressed as medians and interquartile ranges.
Results Supernatant from blood bags containing MPs strongly induced production of all cytokines compared with supernatant without MPs, a reaction which equaled that of LPS stimulation. MPs from stored RBC bags induced higher production of TNF (868 (263 to 1,625) vs. 2,596 (407 to 3,040) pg/ml, P = 0.049), IL-6 (1,088 (234 to 3,716) vs. 6,952 (1,507 to 21,990), P = 0.042) and IL-8 (1,333 (535 to 3,569) vs. 5,562 (833 to 13,904), P = 0.081) compared with MPs from fresh RBC bags. There was no difference in IL-10 responses between groups (8.0 (3.9 to 32.1) vs. 3.9 (3.9 to 22.2), P = 0.390). The host response was dose dependent both for fresh and stored MPs. In addition, the same amount of older MPs induced a stronger host response compared with fresh MPs.
Conclusion MPs from RBC transfusion bags induce a strong proinflammatory response, which is largely negated when MPs are removed. This MP-mediated response depends both on the amount of MPs as well as on alterations in MPs as a result of storage.

P337

Improving blood transfusion safety in a low-resource setting: an audit of 1,163 transfusion requests

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Introduction Sub-Saharan Africa suffers from more acute life-threatening indications for blood transfusion compared with high-income countries [1]. The commonest 'systems failure' contributing to perioperative death in low-resource settings is the timely availability of correctly cross-matched blood products [2]. Often this is not the result of an absolute shortage of blood products, but failure in the chain of supply and distribution. We audited an early step in this chain, the quality of blood requests, at the University Teaching Hospital (UTH) in Lusaka, Zambia. UTH does not have a formal blood request form, and only the cancer diseases hospital (CDH) has a blood request form developed by the blood bank.

Methods We performed a 1-day retrospective review in June of blood request forms submitted to the cross-match laboratory, followed by a 14-day prospective review in September 2014. Group and save requests were excluded. Each form was audited against the American Association of Blood Banks (AABB) minimum standards for content of a blood request form. Analysis was performed with Fisher's exact test for nominal data and *t* test for continuous data.
Results A total of 1,163 blood requests were reviewed, 51 from CDH and 1,112 from other wards. Eighteen forms from CDH (35%) and 22 from other wards (2%) met all minimum AABB standards (P <0.0001). The mean number of standards met on the requests from CDH and the rest were 11.25 (SD 0.93) and 8.87 (SD 1.75) respectively (P <0.0001). Considering all blood requests, the standards met in order from least to most were: signature of requesting doctor (36%), urgency of request (43%), hospital number (59%), indication for transfusion (62%), type of product requested (72%), requesting doctor's name (78%), age or date of birth of patient (84%), gender of patient (89%), quantity of products requested (90%), date form was completed (90%), patient's ward (95%), and patient's full name (100%).
Conclusion The audit revealed an important system failure impacting on efficacy and safety of transfusion practice at UTH. Full patient identifiers, as well as vital information such as the indication and urgency, were rarely filled in, which are crucial for the blood bank to prioritise the release of blood products. The audit shows that practice may be significantly improved by a cheap intervention such as a standardised blood request form meeting international standards.
Acknowledgements UK aid, THET.
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P338

Inadequate monitoring risks safety of blood transfusion in rural Zambia

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Introduction In Zambia, supply of blood is insufficient to meet clinical need, on a national level. Paradoxically, blood is also more often transfused unnecessarily in this setting. The Zambian National Blood Transfusion Service is currently scaling up voluntary blood donation and supply systems, and requires hospitals to improve blood transfusion safety. At a rural district hospital in Zambia, we audited practice and surveyed knowledge amongst staff using standards established in national guidelines.
Methods A retrospective audit over 2 months of all blood transfusion forms at St Francis Hospital, Eastern Province, Zambia. Respective patients' notes were reviewed for: record of observations during transfusion; patient demographics; and length of stay. We surveyed nurses' attitudes, confidence and knowledge in relation to blood transfusion standards.
Results In May and June 2014, 457 requests were made for blood, of which 157 (34%) received blood transfusion, of which 108 (69%) had records of observations available. The audit demonstrated that requests were mostly complete (90%), but urgency was indicated in only 32%. The matching of blood to patient by more than one nurse was recorded amongst 66% of cases. Only 2% of transfusions met minimal requirements for transfusion reaction monitoring. Of nurses surveyed (n = 20), most were experienced in their post (mean 7.3 years, range 2 weeks to 20 years). Nurses rated themselves as highly confident in handling blood transfusions and identifying and dealing with transfusion reactions. However, 90% believed they could identify all transfusion reactions by measuring temperature alone, and 25% would measure temperature only as a parameter to monitor the transfusion, even in ideal settings. Most knew to check observations before, 15 minutes after the start of transfusion and then hourly thereafter (88%); but only 10% would check at the start, at completion and 4 hours after completing transfusion. The most frequently reported reason for not doing observations was time pressure on the ward (85%).
Conclusion In this setting, current practice is evidently inadequate to identify and prevent blood transfusion reactions. The survey revealed high confidence but patchy knowledge amongst nurses of the requirements for safe blood transfusion. Better timing to transfuse at times when nursing staff numbers are higher, alongside compulsory training, may together represent potential low-cost interventions to improve blood transfusion safety.

P339

Effects of iron deficiency on transfusion requirements in critically ill patients: a preliminary observational study

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Introduction Critically ill patients often need blood transfusion, but no reliable predictors of transfusion requirements are available at ICU admission. We hypothesized that ICU patients admitted with iron deficiency may be at higher risk for developing anemia, requiring blood transfusion. The aims of this study were to determine the frequency of iron deficiency in ICU patients at admission and to investigate its relationship with transfusion requirements in ICU patients.
Methods Eighty-five patients admitted to the general ICU were enrolled in the prospective observational study. We studied 58 patients, after excluding those transfused on or before ICU admission. The patients' age, gender, APACHE II score, diagnosis, severity score, presence of sepsis, ICU complications, ICU treatments, and transfusion-free interval were recorded. Iron deficiency was assessed on the basis of several parameters, including hemoglobin, hematocrit, levels of serum iron, iron-binding capacity, transferrin saturation, levels of ferritin, soluble transferrin receptor, hepcidin, C-reactive protein, and peripheral blood smear.
Results The mean age was 43.5 ± 5.7 years. Of 58 patients (38 male/20 female), 25 (43.1%) had iron deficiency with outcomes of blood samples used at ICU admission. The overall transfusion rate was 32.8%, being higher in iron-deficiency patients than in normal iron profile patients (42.3 vs. 14.9%, P = 0.001). After adjusting for severity of illness and hemoglobin level, iron-deficiency patients remained significantly associated with transfusion, with a hazard ratio of 4.2 (95% CI, 1.3 to 12.9; P = 0.001).
Conclusion Iron deficiency is common at ICU admission and is associated with higher transfusion requirements. These findings have important implications for transfusion practices in ICU patients.

P340

Value of thromboelastography in managing hypercoagulopathy in intensive care

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Introduction This aim of this analysis is to explore the use of thromboelastography (TEG) in the management of hypercoagulation in the ICU. TEG allows the assessment of whole blood coagulation and fibrinolysis and hence can identify patients who are hypercoagulable.
Methods A prospective audit of TEG tests performed on patients being treated on a general surgical and medical ICU was conducted over a 2-month period.
Results Twenty-one out of 78 patients (26.9%) had one or more TEG criteria consistent with hypercoagulopathy. Admission diagnoses included trauma (37%), haemorrhage (23%), postoperative (23%) and sepsis (14.3%). Sixty-two per cent of patients with a primary diagnosis of trauma were in a hypercoaguable state. Hypercoagulopathy was suggested by an abnormally short R time in 16 patients (76%), an abnormal alpha angle in 17 cases (81%), a maximum amplitude >74 mm in nine cases (43%) and a high LY30 in one case. Procoagulant treatment was given to seven patients and five patients had received no coagulation modification prior to testing (Figure 1). Eight patients were receiving prophylactic anticoagulation and only one was receiving treatment-dose anticoagulation. A change in management

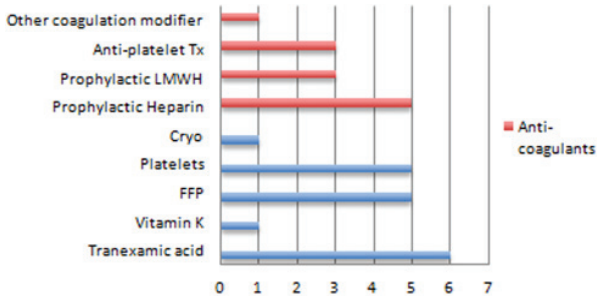


Figure 1 (abstract P340). Coagulation modification prior to TEG analysis in hypercoagulable patients.

as a result of performing TEG was documented in 14 of these 21 patients. No further blood products were administered in all cases and anticoagulation was commenced or increased in four cases.

Conclusion Hypercoagulopathy was present in 27% of patients. One-third of these patients had recently received prothrombotic therapy indicating a possible iatrogenic aetiology. TEG analysis resulted in cessation of prothrombotic drug and blood product administration in all cases. Further research is required to determine whether titrated anticoagulation treatment to normalise the TEG profile in these patients would be beneficial.

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P341

Thromboelastography may detect hypercoagulation in early sepsis and improve anticoagulation during extracorporeal treatments

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Introduction During early sepsis, activation of the inflammatory response and coagulation occurs. Extracorporeal therapies are used to adsorb mediators, but the coagulation of filters is a drawback [1,2]. The aim of this study is to evaluate whether thromboelastography (TEG) may detect hypercoagulation and may improve anticoagulation during extracorporeal treatments.

Methods Twenty-four patients with early severe sepsis had a TEG monitoring at basal time (T0) and during three different extracorporeal treatments (T1): coupled plasma filtration (CPFA) with heparin infusion (Group A), CPFA with citrate infusion (Group B) and RRT with oXiris filter – heparin coated – and no heparin infusion (Group C). ANOVA test was used for the statistical analysis.

Results Table 1 presents the TEG values in early septic patients at T0. At T1, angle and MA decreased and *r* increased in Group A at difference with Group B and Group C (P <0.01). In group C, LY 30 was higher than in Group A and B (P <0.01).

Table 1 (abstract P341)

	Control	Sepsis
r	8 ± 2	6 ± 3
k	4 ± 2	1.7 ± 0.5*
Angle	47 ± 15	67 ± 7*
MA	55 ± 8	72 ± 5*
LYS 30	1.8 ± 1	0.95 ± 0.9

*P <0.01.

Conclusion In early sepsis, TEG monitoring may detect hypercoagulability. CPFA with heparin, but not CPFA with citrate and oXiris, is able to reverse hypercoagulability. OXiris may induce fibrinolysis. TEG detects alterations of coagulation during early sepsis and extracorporeal treatments.

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P342

In trauma, when used in the emergency department, do viscoelastic hemostatic tests decrease mortality? A systematic review

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Introduction This systematic review done in March and updated in November 2014 has been conducted in accordance with the STARD, PRISMA and STROBE recommendations. Retrospective and prospective studies with a comparison group published in English were kept.

Methods Two reviewers (JC and ÉN) and two librarians (MC and DR) independently conducted a systematic review and identified abstracts. Full texts were read by two authors (ÉN and ÉP), and data were extracted. The following databases were searched: Cochrane CENTRAL, Medline, Embase, LILACS, Web of Science, Science.gov, SciFinder Scholar, WorldCat, the Transf Evid Lib Database, and proceedings of the congresses of the International Society on Thrombosis and Haemostasis and the American Society of Hematology.

Results We initially kept 2,870 references. In total, 453 articles had mortality in their keywords. After reading the abstracts, 37 papers were analysed, and three articles evaluating mortality in two groups of patients (using and not using a VHT) were identified. Among these three studies, only one had raw data available. We did not succeed in getting this information from the two other authors. We asked the main authors of the 37 selected papers, and renowned authors in the field, if they had studies with new data that could be included in our review. The answers were negative. The three studies were: Johansson and Stensballe, total 832 cases, 121 traumas, raw data unavailable for trauma [1]; Messenger and colleagues, prospective study, 50 cases, mortality similar, raw data unavailable [2]; and Kashuk and colleagues, prospective study, 68 cases, mortality 59% control group, 28% VHT group [3].

Conclusion With the studies available as of the end of 2014, it is impossible to conclude whether the use of a VHT in the emergency department decreases mortality. Other studies are needed.

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P343

Role of thromboelastography in the management of haemorrhage: an observational analysis

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Introduction The aim of this analysis is to explore and evaluate the role of thromboelastography (TEG) in aiding the management of patients admitted with haemorrhage to the ICU. TEG has been shown to rationalise and reduce transfusion requirements [1] but the precise role of TEG in the assessment and management of haemostasis in the bleeding patient is uncertain and has not been previously demonstrated.

Methods A prospective audit of TEG analyses performed on patients in the general medical and surgical ICU was recorded over a 2-month period. Operators documented the reason for admission, demographic data, indication for TEG, laboratory results, blood gas analysis, TEG results, diagnosis and subsequent action from the TEG result. Only patients who had been admitted with haemorrhage were included in this analysis.

Results Seventy-eight audit sheets were completed, of which 31 identified haemorrhage as the reason for admission. The mean age was 59.3 (range 21 to 90) and the mean APACHE II score was 18.23 (range 11 to 37). The main indications for TEG analysis included coagulopathy (64%) and ongoing haemorrhage (45%). As a result of performing TEG analysis, 23 (74%) patients had a documented change in their management. Ten patients did not require any further administration of blood products, which they would have received based on conventional laboratory results. The information gained from TEG also resulted in the omission of anticoagulation in three patients, and with a further two patients anticoagulation increased.
Conclusion TEG aids prompt rationalisation of blood products and titration of anticoagulation in the bleeding patient. TEG identifies a number of patients who required administration of platelets and other procoagulants which would not have been identified by conventional methods. Several patients would have also received inappropriate transfusions which has both cost and resource implications, alongside the potential adverse effects on patients. We recognise that further research is needed to clarify the overall efficacy of TEG in the bleeding patient.
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P344

Utilisation review of thromboelastography in intensive care

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Critical Care 2015, **19(Suppl 1):**P344 (doi: 10.1186/cc14424)

Introduction This review aims to assess the value of thromboelastography (TEG) on the general ICU, which has not been previously demonstrated. TEG is a near-patient assessment of whole blood coagulation and fibrinolysis, which reduces transfusion requirements during cardiothoracic surgery and liver transplantation.
Methods A prospective audit of TEG tests performed on patients being treated on a general ICU was conducted over 2 months.
Results A total of 332 TEG tests were performed with a failure rate of 29.8%. Seventy-eight audit sheets were collected. Mean patient age was 68.9 years and mean APACHE II score was 18.1. Admissions included trauma (33.0%), perioperative (43.6%), haemorrhage (42.3%) and sepsis (21%). Standard tests of coagulation demonstrated 22 deficits in coagulation which were not identified as functionally significant with TEG. Of these, 20 had abnormal clotting factor activity as measured by the INR/APTTr and 13 patients were thrombocytopenic. In total, 52.6% documented that the TEG result changed the management of the patient. In 46.8% of these cases no further blood products were required. In 41% there was no documentation. See Table 1 and Figure 1.

Table 1 (abstract P344). Summary of concordance with standard tests versus TEG analysis

	Both abnormal	TEG normal/ standard abnormal	Standard normal/ TEG abnormal
Clot factor deficit	9 (11.5)	20 (25.6)	3 (3.8)
Platelet deficit	11 (14.1)	13 (16.6)	2 (2.6)
Fibrinogen deficit	5 (6.4)	4 (5.1)	5 (6.4)

Data presented as *n* (%).

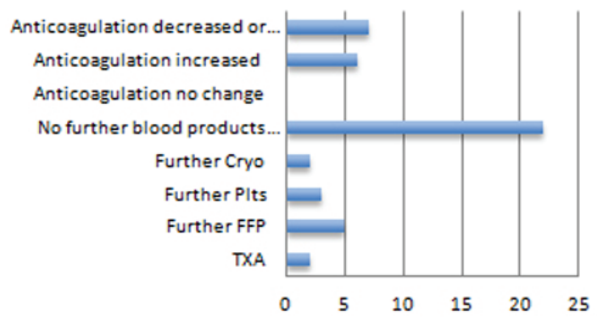


Figure 1 (abstract P344). Change in management due to TEG results.

Conclusion TEG analysis suggested that 22 patients who were identified as coagulopathic with traditional measures of coagulation did not have a functional deficiency. Over one-half of TEG studies resulted in a change in management and in 46.8% no further transfusions were required. There was a high technical failure rate and a low audit return rate, which may indicate the need for further training.
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P345

Decreased coagulation kinetics is associated with high blood loss in patients with end-stage liver disease undergoing liver transplantation

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Introduction Our aim was to assess hemostasis, using ROTEM, in patients with end-stage liver disease (ESLD) undergoing liver transplantation (LT) and to develop a predictive model for patients prone to high intraoperative blood loss.
Methods We retrospectively analyzed 122 patients who underwent LT between January and December 2013 in a single national center. Patients with acute liver failure or incomplete data were excluded. Demographic data, severity of liver disease assessed by MELD score (model for ESLD), presence of portal vein thrombosis, and laboratory data were recorded preoperatively. We performed concomitant ROTEM assay and standard coagulation tests (prothrombin time (PT), International Normalized Ratio (INR), fibrinogen) 1 hour before surgery and 15 minutes after the neohepatic phase. Intraoperative blood loss was recorded. High blood loss was defined as loss of one blood volume during surgery. Correlation between recorded data standard ROTEM parameters and derived thrombodynamic ROTEM parameters (potential index (TPI), maximum velocity of clot formation (MaxV), time to MaxV (MaxVt), AUC) were analyzed using SPSS 19.0.
Results After applying exclusion criteria, 72 patients were analyzed with mean age of 54.5 years (SD 11.6) and a median MELD score of 17.4 (7 to 34). Preoperative MCE correlated with age (P = 0.044, 95% CI (–7.50, –0.12)) and MELD score (P = 0.009, 95% CI (–37.21, –6.69)), but not with PT (P = 0.557) or INR (P = 0.623). MaxV correlated with fibrinogen level (P = 0.005, 95% CI (0.01, 0.05)) and AUC correlated with age (P = 0.034, 95% CI (–257.74, –11.91)) and MELD score (P = 0.01, 95% CI (–1,233.14, –215.33)). Patients with portal vein thrombosis had an increase in InTEM CFT (P = 0.002, 95% CI (77.98, 317.97)) and MaxVt (P = 0.03, 95% CI (5.53, 105.63)). No correlation was found between preoperative ROTEM parameters and intraoperative blood loss. We calculated ΔMaxV, ΔMaxVt and ΔAUC as the mathematical difference between preoperative and intraoperative MaxV, MaxVt and AUC. High blood loss correlated with ΔAUC (P = 0.005, 95% CI (15.69, 61.03)), ΔMaxV (P = 9=0.002, 95% CI (–20,413, 6,392)) and ΔMaxVt (P = 0.008, 95% CI (15.69, 61.07)).
Conclusion MELD score correlated with a decrease in MaxV and AUC on preoperative ROTEM but not with INR. Patients with portal vein thrombosis have increased InTEM CFT and MaxVt. High blood loss was associated with a decrease in thrombodynamic parameters, but no correlations were found between blood loss and standard ROTEM parameters.

P346

Evaluation of fixed dose four-factor prothrombin complex concentrate for warfarin reversal at a level 1 trauma center

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Introduction FDA-approved dosing of four-factor prothrombin complex concentrate (4F-PCC) in the USA is based on an INR and weight; however, there are data suggesting that a fixed dose of 4F-PCC may be sufficient for INR reversal and hemostasis [1,2]. The objective of this study was to assess the efficacy and safety of a fixed dose of 1,500 units of 4F-PCC. Historically, warfarin reversal included a combination of factor IX complex, vitamin K, and fresh frozen plasma (FFP). Using a fixed dose of 4F-PCC may also provide significant cost savings when compared with traditional dosing.
Methods This retrospective chart review compared 26 admitted adults who received a fixed dose of 1,500 units 4F-PCC with 26 patients who received a combination of factor IX complex and vitamin K, with or without FFP, for warfarin reversal from 1 January 2012 to 1 November 2014. Primary outcomes included reversal to an INR of <2 and reversal to an INR of <1.6. Secondary outcomes included ICU and hospital length of stay (LOS), change in INR, INR nadir, potential cost savings from 4F-PCC versus traditional dosing, and major adverse effects.
Results The INR was reduced to <2 in 100% of patients in the 4F-PCC group versus 84.6% of patients in the factor IX group (P <0.05). The INR was reduced to <1.6 in 90.8% of patients in the 4F-PCC group versus 50% in the factor IX group (P <0.05). Mean pre-reversal INRs were 3.5 and 4 and ranged from 1.1 to 10 and from 1.3 to 10 in the 4F-PCC and factor IX group respectively (P = 0.29). On average, a medication cost savings of US$802.63 dollars per patient was calculated from using a fixed 1,500 unit dose over traditional dosing of 4F-PCC. There was a trend toward a shorter mean ICU LOS in the PCC group when compared with the factor IX group (5.8 vs. 2.8 days) and shorter mean hospital LOS (10.7 vs. 5.7 days), although neither outcome was statistically significant. No difference in adverse event rates was observed.
Conclusion A fixed dose of 1,500 units of 4F-PCC was significantly more effective at lowering the INR to a threshold of less than either 2 or 1.6 when compared with a combination of factor IX complex and vitamin K with or without FFP. Further research is needed to investigate clinical outcomes and a possible reduction in ICU and hospital LOS.
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P347

Four-factor prothrombin complex concentrate (Beriplex® P/N) is superior to three-factor prothrombin complex concentrate for reversal of coumarin anticoagulation

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Introduction The study was conducted as a head-to-head comparison of a four-factor prothrombin complex concentrate (4F-PCC) and two different three-factor PCCs (3F-PCC) for effective reversal of vitamin K antagonist (VKA)-induced anticoagulation using an established rat model of acute bleeding [1]. The 4F-PCC (containing the human coagulation factors II, VII, IX and X) is indicated for the urgent reversal of acquired coagulation factor deficiency induced by VKA therapy in adult patients with acute major bleeding. In contrast, the 3F-PCCs (containing factors II, IX, X and only minimal VII) are indicated for the prevention and control of hemorrhagic episodes in hemophilia B patients. Nevertheless, the use of 3F-PCC for correcting hemostasis following warfarin overdose has been discussed but the lack of factor VII in these 3F-PCC products has raised questions about efficacy.
Methods Rats received an oral dose of 2.5 mg/kg phenprocoumon. At 15.75 hours post dosing, animals were treated with a single intravenous dose of saline, 4F-PCC (Beriplex® P/N, Kcentra®; CSL Behring) or 3F-PCC (Bebulin® VH; Baxter and Profilnine® SD; Grifols). Study endpoints included bleeding following tail clip, activated partial thromboplastin time (aPTT), and prothrombin time (PT). In addition, the plasma levels of vitamin K-dependent coagulation factors were determined.
Results Acute coumarin anticoagulation of rats induced a rise in median bleeding time by ≥2-fold from an average of 823 to 1,800 seconds (maximum observation period) compared with untreated animals. In parallel, PT and aPTT were prolonged from 8.9 to 29.9 seconds and from 14.5 to 25.5 seconds, respectively. Treatment with 4F-PCC was able to fully and statistically significantly reverse bleeding, achieving average bleeding times of 676 seconds. In parallel, the elevation in PT was reduced to 15.1 seconds. In contrast, the two 3F-PCC products were not or only partially able to reduce coumarin-induced bleeding with average bleeding times of 1,398 and 1,708 seconds post treatment, respectively. This also correlated with inferior reductions in PT which achieved minimum levels of 23.8 and 29.5 seconds, respectively. There was no reduction in aPTT seen for any treatment option.
Conclusion In conclusion, this first direct comparison of 4F-PCC and 3F-PCCs for the reversal of VKA anticoagulation in a rat model of acute bleeding suggests that replenishment of all four vitamin K-dependent coagulation factors including factor VII as achieved using a 4F-PCC may result in superior efficacy compared with the use of 3F-PCCs.
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P348

Four-factor prothrombin complex concentrate (Beriplex® P/N) mediated reversal of apixaban-induced bleeding in a rabbit model

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Critical Care 2015, **19(Suppl 1):**P348 (doi: 10.1186/cc14428)

Introduction This study assessed whether a four-factor prothrombin complex concentrate (4F-PCC; Beriplex®/Kcentra®; CSL Behring) can effectively reverse bleeding associated with the direct oral factor Xa inhibitor apixaban in an established *in vivo* rabbit model [1,2].
Methods For dose-finding purposes, anesthetized rabbits were treated with a single intravenous dose of apixaban (800 to 1,600 µg/kg). In a subsequent study phase, anesthetized rabbits were treated with apixaban (1,200 µg/kg) followed by 4F-PCC (6.25 to 100 IU/kg). Bleeding signals were quantified following a standardized kidney incision by measurement of the volume of blood loss and time to hemostasis over an observation period of 30 minutes. Blood samples were collected for monitoring of coagulation parameters.
Results Dose-dependent increases in time to hemostasis and total blood loss were observed post apixaban administration with maximum bleeding signals seen at 1,200 µg/kg. Treatment with 4F-PCC resulted in a statistically significant reversal in apixaban-induced bleeding time (all doses) and volume (doses ≥12.5 IU/kg). Of the coagulation parameters measured, thrombin generation initiated using phospholipids only was the *in vitro* coagulation parameter most sensitive to 4F-PCC-mediated bleeding reversal, although statistically significant 4F-PCC-mediated reductions in the prothrombin time and whole blood clotting time were also observed.
Conclusion In conclusion, 4F-PCC treatment effectively decreased apixaban-induced hemorrhage at a clinically relevant dose range.
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P349

Beneficial effects of prehospital versus immediate in-hospital blood products during resuscitation in two models of severe military injury

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Introduction Acute trauma coagulopathy (ATC) is seen in 30 to 40% of severely injured trauma casualties. Early use of blood products is thought to attenuate ATC. This study determined the potential impact

of prehospital versus immediate in-hospital packed red blood cells and fresh frozen plasma (PRBC:FFP) in two models of severe battlefield injury.
Methods This is a prospective randomised controlled trial using *in vivo* models of injury conducted in accordance with the Animals (Scientific Procedures) Act, 1986. Two injury strands were investigated in 43 terminally anaesthetised Large White pigs: whole body blast exposure (Bl) or no blast (ShBl) plus soft tissue injury and haemorrhage. Thirty minutes later animals were randomly allocated to a 60-minute simulated prehospital hypotensive resuscitation with either PRBC:FFP (1:1 ratio) or 0.9% saline (Early and Late groups respectively). This was followed by 150 minutes of simulated in-hospital resuscitation with a revised normotensive target whereby PRBC:FFP was initiated in the Late group and continued in the Early group.
Results In the ShBl injury strand there was a significant reduction in ATC in Early compared with Late PRBC:FFP treatment (TEG R and K times) in both the prehospital ($P = 0.004$ and $P = 0.003$ respectively, ANOVA) and early in-hospital ($P = 0.002$ and $P = 0.005$) phases, although clotting was normalised in the Late group within 60 minutes of initiating PRBC:FFP. Prehospital base deficit (BD) was significantly attenuated in ShBl Early versus Late (9.0 ± 2.1 vs. 14.4 ± 2.2 mM). BD improved in both Early and Late treatment groups during the in-hospital phase but remained greater in the Late group throughout ($P < 0.001$). In the Bl injury strand the trend in coagulation was similar to that seen in the ShBl injury strand (but the differences between Early and Late did not attain statistical significance). By contrast, Early versus Late PRBC:FFP treatment did not result in a difference in BD in the Bl strand. Finally, there was no difference in the total amount of PRBC:FFP used between the two treatments in either injury strand, but in both injury strands the Early treatment groups required significantly less saline ($P < 0.001$).
Conclusion Prehospital use of PRBC:FFP may attenuate ATC and improve physiological status. Furthermore the amount of crystalloid may be reduced with potential benefit of reducing the third-space effect and later tissue oedema.
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P350

Comparing prothrombin complex concentrate and fresh frozen plasma with blood viscosity characteristics in patients with trauma-induced coagulopathy

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Critical Care 2015, **19(Suppl 1):**P350 (doi: 10.1186/cc14430)

Introduction To compare the effectiveness of prothrombin complex concentrate and fresh frozen plasma (FFP) in patients with multiple injuries, complicated with coagulopathy bleeding.
Methods The study involved 51 patients who entered Odessa Regional Hospital with traumatic injuries (concomitant skeletal trauma) complicated with hypocoagulation. Patients were divided into two groups: in the first group (26 patients), as a treatment for coagulopathy, was administered PCC in a dose of 1 ml/kg (25 IU/kg); in the second group (25 patients) was administered FFP in a dose of 15 ml/kg. Evaluation of the functional state of the hemostasis system was carried out using low-frequency thromboelastography (LFTEG) on admission to hospital and 24 hours after the patient's admission to the ICU.
Results According to LFTEG, polytrauma patients had statistically significant abnormalities in platelet aggregation (intensity of contact coagulation (ICC)), in coagulation (intensity of coagulation drive (ICD), clot maximum density (MA)) and in fibrinolytic activity (index of retraction and clot lysis (IRCL)). ICC in patients with multiple injuries was decreased by 27.51%, ICD was decreased by 34.68%, MA was decreased by 75.16%, IRCL was 91.06% above the norm. Patients of group 1 according to LFTEG had significant changes in all parts of coagulation 24 hours after intensive care. Indicators of platelet hemostasis characterized by persistence of hypoaggregation: ICC was decreased by 24.51%, compared with the norm; parameters of coagulation and fibrinolysis had a reliable trend toward normal and decreasing the activity, the fibrinolysis index reached normal reference values. Patients in group 2 had hypoaggregation and hypocoagulation state with increased activity of fibrinolysis: ICC was reduced by 25.62%, ICD decreased by 19.76%, MA was decreased by 22.34%, IRCL was increased by 24.52%. Clinically, patients of group 1 had reduced indicators for infectious complications, reducing the term of mechanical ventilation and reducing the volume of blood transfusions.
Conclusion Patients with multiple injuries have violation in all parts of blood coagulation. The use of prothrombin complex concentrate can reduce the severity of pathological changes in the hemostatic system in patients with polytrauma.

P351

Efficacy of idarucizumab, prothrombin complex concentrate (PCC) and activated PCC to reverse the anticoagulatory potential of dabigatran in a porcine polytrauma model

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Introduction The anticoagulant effect of dabigatran can be reversed with idarucizumab or PCCs in porcine blood *in vitro* [1]. However, the impact on clinical parameters such as blood loss is not known. Thus, this study assessed the efficacy of idarucizumab in comparison with PCC and aPCC in dabigatran-anticoagulated swine following polytrauma on clinically relevant endpoints.
Methods After ethical approval, 28 male pigs were administered dabigatran etexilate (30 mg/kg twice daily p.o.) for 3 days. Dabigatran was administered intravenously in anaesthetised animals on day 4 to achieve consistent high concentrations. Animals were randomised to receive idarucizumab (60 mg/kg, $n = 7$), PCC (50 U/kg; $n = 7$), aPCC (50 U/kg; $n = 7$) or placebo ($n = 7$). Intervention started 12 minutes after bilateral femur fractures and a standardised blunt liver injury. The primary endpoint was blood loss (observation period 300 minutes). Further, histopathology, haemodynamics and several coagulation variables were also assessed. Data were analysed by repeated-measures ANOVA (mean ± SD).
Results Dabigatran levels were comparable between groups (571 ± 174 ng/ml) and resulted in altered coagulation variables. Blood loss was comparable 12 minutes post trauma between groups (801 ± 49 ml) and increased to 3,816 ± 236 ml in anticoagulated control animals post injury. Idarucizumab treatment reduced total blood loss to 1,086 ± 55 ml ($P < 0.005$ vs. all), aPCC to 1,639 ± 104 ml ($P < 0.05$ vs. control) and PCC to 1,797 ± 80 ml ($P < 0.05$ vs. control) after 5 hours. All animals in the intervention groups survived, whereas control animals died within the observation period (mean survival: 89 minutes, range: 62 to 145 minutes). In histopathology no signs of thromboembolic events were present. Altered coagulation variables returned to baseline levels after idarucizumab application and were also significantly, although inconsistently and to a lesser extent, ameliorated following PCCs.
Conclusion All medical interventions were associated with reduced blood loss and increased survival. However, idarucizumab, a specific antidote to dabigatran, reduced total blood loss more prominently and normalised coagulation parameters to a greater degree as compared with either PCC or aPCC.
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P352

Coagulation support algorithm with rapid TEG and functional fibrinogen TEG in critical bleeding: more results and less time

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Introduction Early coagulation support is essential in massively bleeding patients. A Coagulation Support Algorithm (CSA), integrating rapid TEG (r-TEG) and functional fibrinogen TEG (ff-TEG) could shorten the time to a tailored treatment (Figure 1).

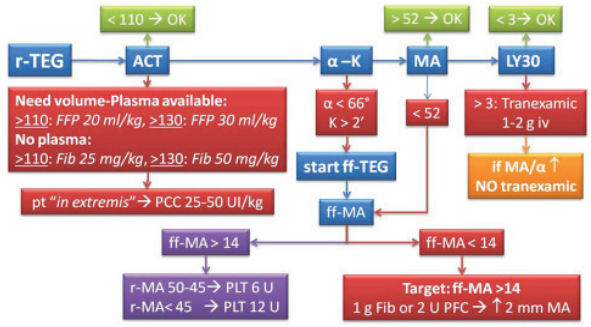


Figure 1 (abstract P352). Coagulation Support Algorithm.

Table 1 (abstract P352). Comparison of time to results

Test	k-TEG	r-TEG	r-TEG + ff-TEF	SCT
r (minutes)	13.8 ± 7.1	2.6 ± 2	–	
ACT (seconds)		265.7 ± 171.9	–	105.2 ± 46.3
TMA (minutes)	42.6 ± 12.4	25.4 ± 14.1	–	
CSAT (minutes)			21 ± 7.4	

Data presented as mean ± SD. ACT, activated clotting time; CSAT, Coagulation Support Algorithm total time; SCT, standard coagulation tests; TMA, time to maximum amplitude. r: r-TEG versus k-TEG, $P = 0.0000003$; r-TEG versus SCT, $P = 0.000000001$; k-TEG versus SCT, $P = 0.000000009$; TMA: r-TEG versus k-TEG, $P = 0.0001$; r-TEG versus SCT, $P = 0.00000004$; k-TEG versus SCT, $P = 0.000002$; ACT versus r of k-TEG (seconds), $P = 0.000004$; CSAT versus k-TMA, $P = 0.00000005$.

Methods A retrospective comparison of the time to available TEG and Standard Coagulation Tests (SCT: INR, aPTTr, fibrinogen level) results in two groups of bleeding and coagulopathic patients using citrate kaolin-TEG (k-TEG) or the CSA protocol (r-TEG/ff-TEG). Statistical analysis was performed with Student's *t* test for unpaired samples.
Results Twenty-three patients for each k-TEG and CSA group were compared. The time to available results was shorter using the CSA protocol in comparison with k-TEG (Table 1). The differences were both statistically (P <0.00001) and clinically (mean reduction time 21 minutes) significant. SCT needed the longest time to obtain the final results.
Conclusion The implementation of a CSA, including r-TEG and ff-TEG, could shorten the time to a targeted treatment in critically bleeding patients.
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P353

Use of albumin in spontaneous bacterial peritonitis is cost-effective

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Introduction Assessing the cost-effectiveness of therapeutic interventions is increasingly crucial for health decision-making. Spontaneous bacterial peritonitis (SBP) is one of the major complications of liver cirrhosis. The use of albumin in conjunction with antibiotics has been shown to be effective through clinical trials [1].
Methods A decision tree (TreeAge®) (Figure 1) was populated from published sources for clinical, cost and epidemiologic variables. The perspective taken was that of the US payer. The robustness of the model was checked using one-way and probabilistic sensitivity analyses. The clinical course was followed for 3 months or until death. Total medical costs and quality-adjusted life years (QALYs) [2] were calculated.

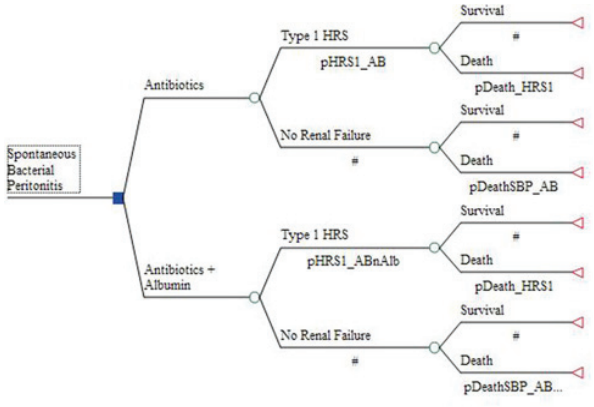


Figure 1 (abstract P353). Structure of decision tree for patients with SBP.

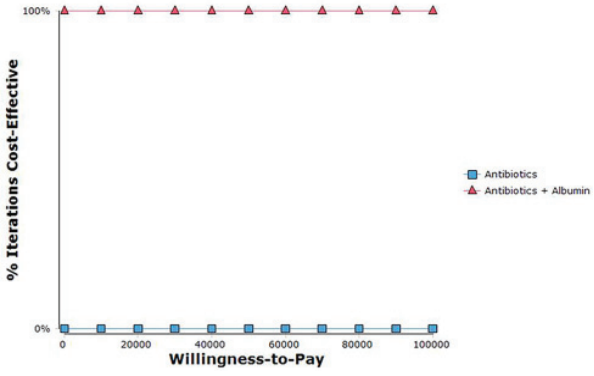


Figure 2 (abstract P353). Cost-effectiveness acceptability across range of WTP.

Table 1 (abstract P353). Results of the cost-effectiveness model

Treatment	QALYs	Total medical costs ($)	Total costs/ QALY ($)
Antibiotics + albumin	2.45	7,628	3,111
Antibiotics	1.48	7,682	5,182

Results Total costs were decreased when using albumin, and the improved survival resulted in an additional QALY for patients on albumin, decreasing the cost per QALY. See Table 1 and Figure 2.
Conclusion The use of albumin in the treatment of SPB is cost-effective.
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P354

Estimation of the latent therapeutic demand for albumin in the USA: a focus on three indications

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Introduction The use of albumin in therapeutics is controversial in several areas and requires assessment based on evidence for effective resource allocation. Supported indications include sepsis, areas of hepatic diseases and coronary artery bypass grafts (CABG). Latent therapeutic demand (LTD) [1] is the underlying evidence-based demand ensuring ample supplies of drugs are available and affordable. Estimating the LTD would assist decision-making and resource

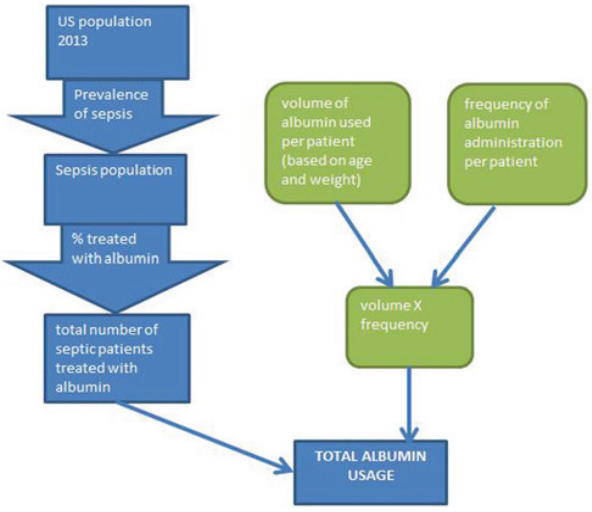


Figure 1 (abstract P354). Variables used to construct the LTD model in sepsis.

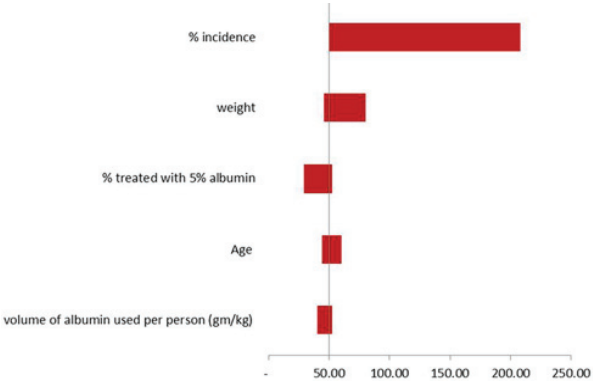


Figure 2 (abstract P354). Relative importance of inputs into the LTD model for sepsis.

allocation, but many of the clinical and epidemiologic variables are subject to uncertainty. Decision analysis [2] may assist in generating an assessment of the demand for albumin.

Methods A decision analysis model was constructed using Excel. The model is based on the relationships of the epidemiological and clinical factors shown in the influence diagram (exemplified in Figure 1 for sepsis). Data for the individual factors were obtained from the literature. One-way sensitivity analysis was used to generate Tornado diagrams (exemplified in Figure 2 for albumin use in sepsis) to determine the relative contribution of different factors to the LTD. Probabilistic sensitivity analysis was used to generate a probability distribution and calculate a mean level for the LTD of each indication.

Results On average, albumin use was calculated as 104 g per 1,000 inhabitants in severe sepsis, 157 g per 1,000 inhabitants in liver diseases and 61 g per 1,000 inhabitants in CABG. This shows a total LTD of 322 g per 1,000 use of albumin in the US annually.

Conclusion Albumin consumption in the USA currently averages 479 g per 1,000 population [3]. Hence, the LTD of these three evidence-based indications represents 67% of current usage. Further work is needed to assess the LTD for albumin in other, less well-defined areas.

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P355

Lactated Ringer Versus Albumin in Early Sepsis Therapy (RASP) study: preliminary data of a randomized controlled trial

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Critical Care 2015, **19(Suppl 1):**P355 (doi: 10.1186/cc14435)

Introduction Adequate fluid therapy is essential to the care of septic patients, aiming to optimize oxygen delivery without compromising microcirculation. In recent years, a few studies have suggested that albumin may be superior when compared with crystalloids in severe cases of septic shock. However, there are no data in the first hours of resuscitation. The aim of this study is to evaluate whether albumin 4% solution compared with lactated Ringer decreases 30-day mortality in cancer patients with septic shock.

Methods The Lactated Ringer Versus Albumin in Early Sepsis Therapy (RASP) study is a prospective, randomized, double-blind and controlled trial, with 360 patients. Until November 2014, at the Cancer Institute of University of São Paulo, we enrolled 110 patients with cancer and septic shock to receive as resuscitation fluid in the first 12 hours of ICU an admission bolus of albumin 4% solution or lactated Ringer. The primary outcome was 30-day mortality. Secondary outcomes include ICU mortality, ICU and hospital length of stay, 90-day mortality, daily SOFA score, rates and length of mechanical ventilation, renal replacement, needing of vasopressor drugs, status performance and fluid balance.

Results From 650 eligible patients, 110 patients were included in the study – 50 patients in the albumin group and 60 in the Ringer group. The mean age was 63 (57 to 70) years in the albumin group and 61 (51 to 71) in the Ringer group, $P = 0.508$. Most patients were male (58% in the albumin group vs. 56.1% in the Ringer group, $P = 0.846$). The ECOG was similar between the albumin and Ringer groups ((0) 26% vs. 8%, (1) 38% vs. 36.8%, (2) 20% vs. 38.6%, (3) 16% vs. 15.8%, $P = 0.05$). The SAPS 3 admission score was 51 ± 13 in the albumin group and 49 ± 10 in the Ringer group, $P = 0.492$. The total amount of administered fluid in the first 12 hours of resuscitation was 1,000 ml (1,000 to 1,500) in the albumin group and 1,000 ml (1,000 to 1,000) in the Ringer group, $P = 0.59$. The 12-hour fluid balance was 1,053 ml (385 to 1,700) in the albumin group and 990 ml (200 to 1,525) in the Ringer group. The 30-day mortality was similar in both groups (60% in the albumin group and 50.9% in the Ringer group, $P = 0.34$). No significant differences in the other secondary outcomes were observed between the two groups.

Conclusion In cancer patients with septic shock, resuscitation with albumin 4% as compared with lactated Ringer did not improve the rate of survival at 30 days.

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P356

Acid–base effects of different crystalloid solutions for ECMO priming: preliminary report

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Critical Care 2015, **19(Suppl 1):**P356 (doi: 10.1186/cc14436)

Introduction The induction of ECMO may result in metabolic acidosis [1] due to circuit priming with chloride-rich fluids, and the sudden decrease in plasma strong ion difference (SID). This effect can be attenuated using balanced solutions with a SID equal to the patient's plasma bicarbonate concentration (HCO_3^-) [2]. We aimed to compare the effects of a novel balanced solution (SID equal to patients' HCO_3^-) with those of commonly employed crystalloids for circuit priming in patients undergoing venovenous ECMO.

Methods We randomly assigned patients with acute respiratory failure in need of ECMO to receive either NaCl 0.9% (NS, SID = 0), Ringer lactate (RL, SID = 28), or a novel balanced solution (Solution X, SID equal to the patient's HCO_3^-) for circuit priming solution. Arterial blood gases and laboratory parameters were collected at 0, 5, 30, 60, 90, and

120 minutes after pump start. SID, base excess (BE) and total weak acids (Atot) were calculated.
Results We enrolled 20 patients (23 priming procedures – RL, n = 8; NS, n = 8; Solution X, n = 7). ECMO was initiated for ARDS (45%), bridge to lung transplant (25%), acute graft failure after transplant (15%), and acute on chronic respiratory failure (15%). Average priming volume was 10 ± 5 ml/kg; patients' baseline HCO_3^- was 28 ± 6 mEq/l. During the first 2 hours after ECMO initiation, arterial pH raised similarly in all groups (P = 0.39) due to CO_2 removal. In contrast, BE decreased starting after 5 minutes in both the NS and RL groups (BE variation, –2.2 ± 1.7 and –1.9 ± 1.3 mEq/l, P <0.001 vs. baseline; P = 0.04 for interaction, two-way ANOVA, 2-hour period). No BE changes were observed in the Solution X group (0.3 ± 0.8 mEq/l). In the NS group, BE reduction was associated with a reduction in SID (from 39 ± 8 to 34 ± 6 mEq/l at 5 minutes, P = 0.008), entirely due to an increase in Cl (103 ± 7 vs. 108 ± 6 mEq/l, P = 0.001). In the RL group, BE and SID reductions (40 ± 8 vs. 36 ± 8 mEq/l, P = 0.008) were associated with an increase in both Cl (105 ± 7 vs. 107 ± 7 mEq/l, P = 0.01) and lactate (1.4 ± 0.6 vs. 2.2 ± 1.0 mEq/l, P = 0.008). No changes were observed in other electrolyte concentrations. Dilution did not differ between groups (P = 0.25 for Atot variation). The acidifying effect of NS and RL was amplified in patients with higher baseline HCO_3^-.
Conclusion As compared with NS and RL, the use of a novel balanced solution with a SID equal to the patient HCO_3^- level for ECMO priming uniquely avoids the addition of metabolic acidosis to patients with uncompensated hypercapnia.
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P357

Intraoperative use of gelatin in living donor liver transplantation and postoperative acute kidney injury

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Introduction The aim of our study is to investigate the effect of intraoperative use of gelatin in living donor liver transplantation on postoperative acute kidney injury (AKI). It has been demonstrated that ischemia and chloride-liberal fluid management cause AKI in liver transplantation [1]. Gelatin has minimal side effects on renal functions [2]; however, it might be a reason for postoperative AKI.
Methods A total of 154 liver transplantation patients were retrospectively evaluated between September 2011 and September 2013, and among these, 128 patients were included in the study. The patients who were under 18 years old, transplanted from cadaveric donors and needed preoperative renal replacement therapy were excluded. The patients were divided into two groups as GI (without gelatin administration) and GII (with gelatin administration). The patient's age, gender, actual body weight, diagnoses, MELD score, APACHE II score, duration of operation, total clamping time, noradrenalin infusion rate, amount of erythrocyte suspension, fresh frozen plasma (FFP) and thrombocyte suspension used, intraoperative fluid balance, intraoperative and total clamping diuresis, serum creatinine levels on the postoperative 1st, 2nd, 4th and 7th days, duration of mechanical ventilation, length of ICU and hospital stay, hospital and 1-year mortality rate were recorded. The changes in creatinine levels on the 1st, 2nd, 4th and 7th days were evaluated according to the KDIGO guideline for AKI [3].
Results In total, 128 patients were categorized as GI (58, 45%) or GII (70, 55%). Total clamping time, intraoperative diuresis, intraoperative crystalloid use, intraoperative fluid balance, operation bleeding, erythrocyte suspension, FFP and thrombocyte suspension use and postoperative lactate levels of GII were statistically significantly higher than GI (P <0.001 for each). According to the KDIGO guideline, AKI in GII on the 1st, 2nd, 4th and 7th days (11.4%; 20%; 24.3%; 17.1%) was statistically significantly higher than GI (P <0.001 for each).
Conclusion In patients who received gelatin, kidney dysfunction in the postoperative period was observed more frequently. Also in this group, total clamping time was longer and amount of blood products used during surgery was more than the other group. Which of these factors is associated with AKI has to be revealed with further studies.
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P358

Incidence of acute kidney injury in critically burned patients resuscitated with crystalloid and colloid according to parameters of transpulmonary thermodilution, diuresis and lactic acid

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Introduction The purpose was to study the incidence of acute kidney injury (AKI) according to RIFLE and AKIN criteria in critically ill burn patients resuscitated with Ringer's solution and supplements of lower molecular weight hydroxyethyl starch (HES)130/0.4/6%, and to determine the relationship between RRT indication and mortality.
Methods We studied 165 consecutive patients admitted to the critical care burn unit. Resuscitation was performed using lactated Ringer's solution and HES at a low dose to achieve urine output, lactate levels, and transpulmonary thermodilution parameters. The contributions of colloids and crystalloids were measured, and renal function was evaluated. Statistical analysis was performed using the Spearman test.
Results The average total body surface area (TBSA) burned was 30 ± 15%, and the median of the total volume needed in the first 24 hours was 4.01 ml/kg/% TBSA burned. According to the RIFLE criteria, 10 (6.1%) patients presented with risk, 11 (6.7%) presented with injury, and 11 (6.7%) presented with failure. According to the AKIN criteria: 9.7% presented stage I, 3% stage II and 10.3% stage III. Replacement therapy (RRT) was performed in 15 patients (9.1%). In six of these patients RRT was employed in the final stages of multiorgan failure. In the remaining nine patients, for various reasons only one survived.
Conclusion During the resuscitation phase of the burn patients, the use of HES (130/0.4/6%) at low doses does not seem to cause more risk or injury according to RIFLE or AKIN criteria than those reported by studies in burn patients resuscitated without HES. However, the need for RRT is associated with a high mortality, although in many cases the display is terminal.

P359

Influence of anaesthetic factors on skin graft viability in a burns ICU

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Introduction Graft failure is a major cause of morbidity in patients with burns, resulting in increased length of hospital stay and increased number of operations. At our regional burns unit we collated the data from anaesthetic charts of patients admitted to our burns ICU who required skin grafting. The aim was to analyse whether any anaesthetic variables contribute to graft failure.
Methods Thirty-five patients were included in the analysis with a total of 191 operations. These were a combination of debridement, split skin grafts (SSG) and change of dressings. All patients were admitted to our burns ICU between January 2009 and October 2013. Exclusion criteria were death prior to discharge and initial surgery at a different hospital. Sixteen patients had good graft viability (Group A) and 19 patients had poor graft viability (Group B). Logistical regression was performed using SPSS (Version 22.0). Hosmer and Lemeshow testing was used to confirm goodness of fit. Independent variables were age, sex, preoperative haemoglobin, intraoperative fluid resuscitation, blood products, inotropes, volatile agents and temperature. Poor graft viability was defined as requiring at least one additional skin graft. Analysis was performed on all operations and then by subtype of operation (that is, SSG and debridement, SSG only).

Results There was no significant difference in age, %total burn surface area or Belgian Outcome Burns Injury score between the groups. For all operation data, use of colloids was found to significantly contribute towards poor graft viability (P = 0.035, 95% CI). When analysis was performed on only SSG and debridement operations, colloids remained significant (P = 0.034, 95% CI) and metarminol use was found to significantly contribute (P = 0.028, 95% CI) to poor graft viability. Overall use of inotropes was not significant between the two groups. Other variables including minimum and maximum temperature, preoperative haemoglobin and blood transfusion were not found to be significant.
Conclusion Our results suggest that the use of colloids is a contributor to poor graft viability in burns. This was found to be independent of temperature and overall inotrope use; however, the use of metarminol may be a contributing factor.

P360

Association of elevated levels of plasma chloride, in severity and mortality, in adult patients in the ICU

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Introduction For a long time, many investigators have tried to demonstrate increased mortality associated with acid–base disturbances. In this study, we sought to determine the association of hyperchloremia measured at ICU admission and whether this electrolyte disturbance is associated with an increase in morbidity and mortality.
Methods Data were retrospectively collected for consecutive adult patients admitted to Agustin O'Horan Hospital ICU, between January 2011 and July 2014, who underwent inpatient medical treatment using electronic files.
Results The dataset consisted of 936 medical files and serum chloride concentration values on admission, 853 being eligible. Hyperchloremia (serum chloride >110 mmol/l) is quite common, with an incidence of 47.71%. Patients were propensity matched based on their association with death and hyperchloremia. Of the 853 patients collected, patients with hyperchloremia after admission (n = 446, 52.3%), patients were matched to patients who had normal serum chloride levels after admission. These two groups were well balanced with respect to all variables collected. The hyperchloremic group was at increased risk of mortality at ICU discharge, relative risk ratio = 1.81; 95% confidence interval, 1.41 to 2.51 risk increase of 25.31%. Admission hyperchloremia was associated with increased morbidity, mortality and higher scores in severity scales; this association was statistically important. See Figure 1.
Conclusion This retrospective cohort trial demonstrates an association between hyperchloremia and poor ICU admission outcome (death). Additional studies are required to demonstrate a causal relationship between these variables.

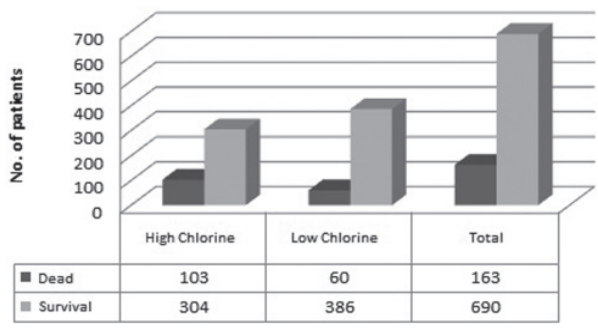


Figure 1 (abstract P360). Group mortality, high and low chlorine.

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P361

Urinary strong ion difference and acute kidney injury: an early marker of renal dysfunction?

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Introduction Kidneys play a crucial role in the regulation of electrolytes and acid–base homeostasis. Impaired renal function is associated with greater urinary strong ion difference (SIDu) in patients with metabolic acidosis [1]. In critically ill patients, several factors, such as infused fluids and acid endogenous production, would lead to changes in plasma SID and acid–base homeostasis without renal regulation of urinary electrolytes and SIDu [2]. Hence, AKI can be highlighted as an inability to address acid–base metabolic disturbances, which may be detected before major increases in creatinine or decreases in urine output. We evaluated the effects of renal function on urinary strong ion excretion using the Stewart approach to acid–base in critically ill patients with AKI.
Methods A retrospective study was conducted. Patients with a diagnosis of AKI according to KDIGO creatinine criteria and available urinary chemistry at one point during their ICU stay were evaluated. Day 0 was defined as the day when SIDu was calculated from urinary spot analysis (SIDu = Na+U + K+U – Cl–U). Patients were followed and staged for AKI in the next 3 days. AKI reversibility was defined according to the lack of criteria for AKI.
Results In total, 143 critically ill patients with a diagnosis of AKI were included. SIDu at day 0 did not differ between different AKI stages at day 0. SIDu at day 0 was statistically different between different AKI stages at days 1, 2, 3 (Table 1). SIDu at day 0 was statistically different between reversible and not reversible AKI at days 1, 2, 3 (Table 2). A conventional receiver-operating curve was generated to assess the accuracy of SIDu to predict AKI reversibility at day 1. AUC for SIDu was 0.82 (P <0.0001; 95% CI: 0.75 to 0.88).

Table 1 (abstract P361). SIDu (mEq/l) between different AKI stages at days 1, 2, 3 post admission

	AKI stage				
	3	2	1	0	*P* value
Day 1	48.1 (21)	46 (22)	37.9 (20)	17.3 (22)	<0.001
Day 2	40.2 (23)	45.9 (20)	45 (23)	29 (22)	0.004
Day 3	40.3 (26)	47.2 (18)	53.2 (23)	31 (23)	0.006

Table 2 (abstract P361). SIDu (mEq/l) between reversible versus not reversible AKI at days 1, 2, 3

	Reversible	Not reversible	*P* value
Day1	16.8 (23)	43.9 (21)	0.0001
Day2	28.5 (24)	45.3 (22)	0.0001
Day3	30 (24)	47.3 (21)	0.0001

Conclusion SIDu identified patients with reversible AKI with good accuracy. SIDu can be a promising, simple and cost-effective tool in AKI patient evaluation. Further research is needed to assess SIDu capability to early detect patients with renal dysfunction before increases in creatinine or decreases in urine output.

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P362

Evaluation of the effect of guidelines to reduce intravenous potassium infusions in ICU patients

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Introduction The aim was to evaluate whether guidelines for intravenous (i.v.) potassium replacement improved plasma potassium homeostasis in ICU patients. Prompt and effective treatment of hypokalaemia is an important intervention in the ICU, but concentrated i.v. potassium solutions may cause serious harm if used inappropriately [1]. There were previously no formalised guidelines on i.v. potassium supplementation in the ICU at Sheffield Teaching Hospitals. Practice was reviewed and guidelines were introduced to improve patient safety, plasma potassium homeostasis and reduce i.v. potassium supplementation requirements.
Methods A before and after evaluation of plasma potassium homeostasis in ICU patients requiring i.v. potassium supplementation was conducted over a period of 8 months (August 2013 to May 2014). Patient data on plasma potassium levels, i.v. and oral potassium supplements administered were obtained from the clinical information system. Clinical appropriateness of i.v. potassium acetate prescriptions, fluid and chloride intake related to potassium infusions and cost linked to the guidelines were also compared pre/post implementation. Impact of the guidelines on nurses' practice was assessed using questionnaires.
Results Median i.v. potassium replacement dose per patient was significantly reduced in the post-guidelines group from 215 (IQR: 94; 485) to 80 (IQR: 40; 160) mmol; $P < 0.001$. Although the percentage time per group for patients who were hypokalaemic was less in the post group (18.2% vs. 14.8%), there was no difference in mean patient values (24.2 (20.3)% vs. 22.1 (17.5)%; $P = 0.228$). The duration of hyperkalaemia was increased. Prescribing of i.v. potassium acetate was not always appropriate. Median patient fluid-related dose was increased (107.5 (IQR: 47.1; 242.4) vs. 250 (IQR: 100; 600) ml; $P < 0.001$), whilst chloride doses were reduced (170.7 (IQR: 91.3; 438.3) vs. 110 (IQR: 55; 250) mmol; $P < 0.009$). Nurses were satisfied with the new practice, reporting it was safe, effective and clinically useful. However, compared with baseline practice, they perceived the guidelines as less effective and felt the workload was higher.
Conclusion Implementation of i.v. potassium replacement guidelines improved the use of i.v. potassium in the ICU by reducing the requirement for i.v. potassium supplementation and increasing the overall time patients spent without hypokalaemia. Whilst nursing staff found the guideline useful and felt it increased safe use of i.v. potassium, more work is needed to ensure nurse workload is not increased significantly.
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P364

Marked exposure to the endocrine-disrupting chemicals phthalates and bisphenol A in the ICU

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Introduction Care for ICU patients has benefited from medical devices. Bisphenol A (BPA) and phthalates can leach from the plastic matrix. We hypothesized that ICU patients are exposed to BPA and phthalates through medical devices.
Methods Serum ($n = 118$) and urinary ($n = 102$) samples of adult ($n = 35$) ICU patients were analyzed for total BPA and di(2-ethylhexyl)phthalate (DEHP) and other phthalate metabolites (PMs). We also enrolled patients preoperatively before scheduled thoracic surgery and repeat samples were taken on days 1 to 4 during the ICU stay. Control data came from 44 healthy controls or from referenced literature.
Results Our results show that adult ICU patients are continuously exposed to phthalates (that is, DEHP) as well as to BPA, albeit to a lesser extent, resulting in detectable serum and urinary levels in almost every patient and at every studied time point. Moreover, these levels were significantly higher than in controls or compared with referenced literature. The chronology of exposure was demonstrated: the preoperative urine and serum levels of the DEHP metabolites were often below the detection limit. Medical devices are the source of these chemicals: patients on hemofiltration, extracorporeal membrane oxygenation or both showed serum levels 100-fold or 1,000-fold higher than the general population or workers in plastic industry. The serum and some of the urinary levels of the DEHP metabolites are the highest ever reported in humans; some at biologically highly relevant concentrations of even ≥10 to 50 μM.
Conclusion Adult ICU patients are exposed to plastic softeners, in particular PMs. Despite the continuously tightening regulations, BPA and DEHP are still present in medical devices. Because patient safety is a concern in the ICU, further research into the (possibly toxic and clinical) effects of chemicals released from medical devices should be undertaken.

P365

Low serum 25-hydroxyvitamin D at critical care initiation is associated with sepsis and morbidity in Dutch critically ill patients

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Introduction Vitamin D deficiency may frequently occur in critically ill patients and may be associated with sepsis and increased mortality. We therefore evaluated the prevalence of 25-hydroxyvitamin D deficiency in a Dutch ICU, and its relationship with sepsis, morbidity and mortality.
Methods We conducted a prospective observational study in a 10-bed mixed ICU. A total of 1,372 patients were admitted between July 2011 and June 2013 including 198 readmissions, of which 940 patients were studied. 25-Hydroxyvitamin D levels were determined within 24 hours after admission. 25-Hydroxyvitamin D levels were judged as sufficiency (>50 nmol/l), insufficiency (30 to 50 nmol/l) and deficiency (<30 nmol/l).
Results The prevalence of deficiency and insufficiency was 36% and 38%, respectively. Only 26% of the patients had sufficient vitamin D levels. Vitamin D deficiency is associated with sepsis ($P < 0.001$) at ICU admission. Patients with deficient levels had higher mean APACHE IV scores, 64 versus 52 ($P < 0.001$), and longer length of hospital stay, 12 versus 9 days ($P < 0.001$), respectively, as compared with patients with sufficient levels. Patients with deficient vitamin D levels had an odds ratio for in-hospital mortality of 1.4 (95% confidence interval of 0.84 to 2.29, $P = 0.2$) relative to patients with sufficient vitamin D levels.
Conclusion 25-Hydroxyvitamin D deficiency frequently occurs in Dutch critically ill patients. Although relating to sepsis, disease severity and morbidity, vitamin D deficiency is not an independent predictor of mortality in these patients, which was otherwise relatively low.

P366

Incidence and predisposing factors for the development of disturbed glucose metabolism and diabetes mellitus after intensive care admission: the DIAFIC study

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Introduction Stress hyperglycaemia (SH) is commonly observed during hospitalisation in the ICU and adversely influences outcome [1]. When SH occurs in previously nondiabetic patients, this might reflect a latent disturbance of glucose metabolism and predict future risk of diabetes. We wanted to assess the incidence of disturbed glucose metabolism (DGM) and identify predictors for future diabetes risk. This could support timely diagnosis, prevention, and early treatment of impending diabetes mellitus (DM).
Methods In this prospective observational study, we enrolled 338 patients without known DM, who were admitted for at least 36 hours to the ICU of the Antwerp University Hospital between September 2011 and March 2013. A 75 g oral glucose tolerance test was performed

6 to 9 months post ICU admission to screen for disturbed glucose metabolism. Furthermore, we examined whether post-discharge glucose disturbances could be predicted by the FINDRISC questionnaire [2], patient demographics, comorbidities, HbA1c at ICU admission, and by parameters related to ICU stay (glucose parameters, insulin need, caloric intake, disease severity).

Results In total, 246 patients (73%) experienced SH during their ICU stay. Eight months post ICU admission, glucose metabolism was disturbed in 119 (35%) subjects. Of these, 27 (8%) had impaired fasting glucose, 43 (13%) had impaired glucose tolerance, 25 (7%) had impaired fasting glucose and impaired glucose tolerance, and 24 (7%) were diagnosed with DM. A disturbed glucose metabolism tended to be more prevalent in subjects who experienced SH during ICU stay as compared with those without SH (38% vs. 28%, $P = 0.065$). HbA1c on admission correlated with the degree of SH ($r = 0.308$, $P < 0.001$). The FINDRISC score (9.5 vs. 11, $P = 0.001$), SAPS 3 score (median of 42 in both groups, $P = 0.003$) and daily caloric intake during ICU stay (222 vs. 197, $P = 0.011$) were associated with a DGM.

Conclusion Stress hyperglycaemia is frequent in nondiabetic patients and has a tendency towards future disturbances in glucose metabolism and DM. Glucose metabolism was disturbed in 35% of subjects 8 months post ICU admission, of whom 7% was diagnosed with diabetes mellitus. Predictors of elevated risk included a high FINDRISC score, high SAPS 3 score, and a lower daily caloric intake during ICU stay.

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P367

Associations between the degree of correction of hypoglycemia and ICU mortality

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Introduction It is conjectured that transition of hypoglycemia to hyperglycemia may be more harmful than hypoglycemia itself. We investigated the association between the degree of correction of hypoglycemia and ICU mortality in patients under moderately strict to strict glycemic control.

Methods This is a retrospective analysis from a pooled cohort from seven ICUs in the Netherlands over 6 years. ICU patients who developed hypoglycemia (<70 mg/dl) were included. We excluded patients who were readmitted, and patients with hypoglycemia in whom no follow-up blood glucose measurement was performed within 8 hours. We determined the association between three measures of correction of hypoglycemia within 8 hours after hypoglycemia and ICU mortality: predefined ranges of the 'highest blood glucose level' (<80 mg/dl; 80 to 110 mg/dl; 110 to 150 mg/dl (reference category); 150 to 180 mg/dl; and >180 mg/dl); quartiles of the 'delta glucose', defined as the difference between minimum and maximum blood glucose level with the third quartile as reference category; and quartiles of the 'standard deviation' of the blood glucose level with the third quartile as reference category.

Results In total, 4,516 ICU patients developed at least one episode of hypoglycemia. In three separate multivariate analyses for each of the three measures we adjusted for the respective confounders. The category 80 to 110 mg/dl of the 'highest blood glucose level' was associated with increased mortality compared with the reference category (odds ratio (OR) = 1.31, 95% confidence interval (CI) = 1.06 to 1.61). The lowest quartile of the 'delta glucose' (OR = 1.32, 95% CI = 1.03 to 1.69) and the lowest quartile of the 'standard deviation' (OR = 1.55, 95% CI = 1.23 to 1.96) were associated with higher ICU mortality than their reference categories.

Conclusion Not the transition to hyperglycemia, but insufficient recovery from hypoglycemia is associated with an increased ICU mortality in patients under moderately strict or strict glucose control with insulin.

P368

Computer versus paper insulin protocol for managing hyperglycemia in three ICUs

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Introduction The purpose of this study was to compare a computer protocol against a paper protocol in managing three domains of glucose control. Hyperglycemia is common in critically ill patients, and their risk of death is associated with hyperglycemia, hypoglycemia, and glucose variability. A safe and effective insulin protocol must minimize hyperglycemia and glucose variability while also avoiding hypoglycemia. Computer-based insulin protocols promise better performance by adjusting to each individual's sensitivity to insulin.

Methods This is a historical cohort study with 759 patients admitted to three ICUs (medical/cardiac, trauma, and neuroscience) at an academic tertiary care hospital. All adult patients from January 2012 to October 2013 on one of two continuous insulin protocols for at least 8 hours were included. At the start of the study period the paper protocol in use (Adult ICU) had a target glucose of 140 to 180 mg/dl and was used for any patient with a glucose higher than 180 mg/dl. In June 2013 this was replaced by a computer-based insulin protocol (EndoTool) that had the same criteria for initiation and had a target glucose of 150 mg/dl. The primary exposure was the insulin protocol, and the primary outcome was performance in maintaining glucose control.

Results The median glucose in the EndoTool group (141.5 mg/dl) was lower than in the Adult ICU group (159.9 mg/dl) ($P < 0.0001$). The standard deviation of glucose in the EndoTool group (32.3 mg/dl) was lower than the Adult ICU group (39.5 mg/dl) ($P = 0.0001$). The proportion of patients in each group with 10% or higher of measurements at a severe hyperglycemia level (≥200 mg/dl) in the EndoTool group (35.2%) was lower than the Adult ICU group (64.1%) ($P < 0.0001$). The proportion of patients who had at least one moderate hypoglycemic measurement (<70 mg/dl) was not significantly different between the EndoTool group versus the Adult ICU group (11.73% vs. 9.3%, respectively; $P = 0.34$). However, there was a higher overall incidence of hypoglycemia in the EndoTool group (5.65 hypoglycemic measurements/100 person-protocol days) compared with the Adult ICU group (3.43/100 person-protocol days) (RR = 1.65, 95% CI = 1.09 to 2.45, $P = 0.014$). Severe hypoglycemia (<40 mg/dl) was rare, only occurring in 1/179 (0.56%) in the EndoTool group and 4/580 (0.69%) in the Adult ICU group.

Conclusion Patients on the computer protocol had a lower median glucose, less variability, and less hyperglycemia than patients on the paper protocol. There was a higher risk of moderate but not severe hypoglycemia in the computer group.

P369

Continuous blood glucose monitoring reduces the risk to ICU patients

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Introduction GlySure Limited (Abingdon, UK) has developed a continuous intravascular glucose monitoring system (CIGMS) to simplify the application of hospital protocols for optimal glucose control at the point of care. We have previously reported on the early results achieved in cardiac patients [1] and MICU patients [2]. This initial success has been sustained and demonstrated in further patient groups. We have now reached the point where we can conjecture upon the regular application of the GlySure CIGMS in day-to-day ICU practice. This in turn prompts the question, 'How effective will continuous blood

glucose data prove in such routine use?' Using actual case data, we have shown how comparing the mean absolute relative difference (MARD) and integration of the area under the curve (AUC) from the continuous glucose monitoring and intermittent measurement can be used to measure patient risk.

Methods The analysis used aggregated case data generated from our recent clinical trials, where a GlySure sterile, single-use sensor and dedicated monitoring system was used to measure the blood glucose concentration in patients continuously and in real time. The measurement of risk was compared using the MARD, an accepted error calculation tool, and the AUC was calculated using an AUC analysis software program.

Results When MARD from the GlySure sensor and intermittent measurement using the hospital's existing protocol was compared, the measure of risk to the patient (that is, the uncertainty regarding the patient's absolute blood glucose status) for the GlySure sensor was 50.5% lower than the intermittent measurement. The results also showed that as the variability of the BG data increases, the benefit of continuous monitoring increases by significantly reducing patient risk. The continuous monitoring reduces the patient's risk by 88%, 73%, and 69% respectively in high, medium and low variability situations.

Conclusion It is more and more evident that continuous glucose technology will be instrumental in driving safe and effective glucose management protocols that will support more consistent glycemic management standards within ICUs and across institutions.

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P370

Point accuracy and reliability of an interstitial continuous glucose monitoring device in critically ill patients

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Introduction There is a need for continuous glucose monitoring in critically ill patients. The objective of this trial was to determine the point accuracy and reliability of a device designed for continuous monitoring of interstitial glucose levels in ICU patients (Sentrino; Medtronic MiniMed, Northridge, CA, USA).

Methods Critically ill patients with an anticipated life expectancy >96 hours were eligible for participation, if the platelet count was $>30 \times 10^{12}$ ml. Device readings were compared with glucose measurements in arterial blood using blood gas analyzers (RapidLab Siemens Healthcare Diagnostics, The Hague, the Netherlands). We used a linear mixed model to determine which factors affect point accuracy. In addition, we determined the reliability, including duration of device start-up and calibration, skips in data acquisition, and premature disconnections of sensors.

Results We included 50 patients, aged 65 (56 to 72) years with an APACHE II score of 23 (17 to 26). Admission types were medical (62%), elective surgery (22%) and emergency surgery (16%), and 22% had diabetes. For the accuracy analyses we had 929 comparative samples from 100 sensors in 45 patients (11 (7 to 28) samples per patient) during 4,639 hours (46 (27 to 134) hours per patient and 46 (21 to 69) hours per sensor). The Bland–Altman plot showed a bias of −0.6 mg/dl with limit of agreement between −57.2 and 56 mg/dl. Glucose prediction error analysis showed 60% of the glucose values <75 mg/dl within ±15 mg/dl and 75.8% of the glucose values ≥75 mg/dl within 20% of the comparative RapidLab results. Clarke error grid analysis showed 75.3% in zones A and 23.5% of the paired measurements in zones B, 0.3% of the paired measurements in zones C and 0.9% of the paired measurements in zones D. Point accuracy did not meet the ISO14971 standard for dosing accuracy, but improved with increasing numbers of calibrations, and was better in patients who did not have diabetes mellitus. Sixty out of 105 sensors were removed prematurely for a variety of reasons. The device start-up time was 49 (43 to 58) minutes. The number of skips in data acquisition was low, resulting in availability of real-time data during 95 (89 to 98)% of the connection time per sensor.

Conclusion The point accuracy of the device was relatively low in critically ill patients. The device reliability was relatively good, although sensors were removed prematurely for a variety of reasons.

P371

Effect of admission hyperglycemia in sepsis patients with or without a history of diabetes

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Introduction Hyperglycemia is common and often multifactorial in critically ill patients. The association of hyperglycemia with adverse outcome has repeatedly been established in a variety of settings. The objective of this study was to investigate whether hyperglycemia on admission to the ICU impacts presentation and outcome of sepsis patients and whether this effect is different for patients with a history of diabetes mellitus.

Methods A two-center, prospective observational cohort study was conducted including all consecutive critically ill patients admitted to the ICU between January 2011 and July 2013. Sepsis patients were identified using strict clinical and diagnostic criteria. The first glucose measurement within a time window of 4 hours before up to 4 hours after ICU admission was categorized into euglycemia (71 to 140 mg/dl), mild hyperglycemia (141 to 200 mg/dl) or severe hyperglycemia (>200 mg/dl), patients with hypoglycemia were excluded. A multivariable Cox proportional hazard model was used to determine the effect of admission hyperglycemia on mortality corrected for covariates.

Results Of the 1,059 patients admitted with sepsis, 526 (55.8%) had admission glucose levels within the normal range, 270 (25.5%) had mild hyperglycemia and 202 (19.1%) severe hyperglycemia. Patients with severe hyperglycemia were older, had higher APACHE IV scores and were more often diabetics compared with euglycemic patients. Shock on admission was more common in patients admitted with euglycemia. Crude mortality increased with increased admission glucose and a Cox regression analysis showed increased risk for 30-day (HR = 1.67, CI = 1.24 to 2.23), 60-day (HR = 1.42, CI = 1.08 to 1.87) and 90-day (1.31, CI = 1.02 to 1.70) mortality in patients admitted with severe hyperglycemia compared with euglycemia. The association between mortality and severe hyperglycemia on admission was only present in patients without known diabetes but not in patients with a history of diabetes (30-day mortality HR = 1.67, CI = 1.15 to 2.43 vs. 1.84, CI = 0.97 to 3.49). Severe hyperglycemia was associated with a blunted proinflammatory cytokine response (IL-6 and IL-8) on admission in patients without, but not in patients with diabetes.

Conclusion Severe hyperglycemia on admission is associated with increased 30-day, 60-day and 90-day mortality in sepsis patients without a history of diabetes mellitus.

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P372

Point and trend accuracy of continuous glucose monitoring using intravenous microdialysis in critically ill patients

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Introduction Insulin infusion in critically ill patients mandates frequent measurements of the blood glucose level [1]. Microdialysis is a well-established technology that offers the opportunity to sample blood analytes with high accuracy, without the need for drawing blood samples [2,3]. We aimed to determine point and trend accuracy of

microdialysis-based continuous glucose monitoring (CGM) (EIRUS®; Maquet Critical Care AB, Solna, Sweden).
Methods Patients with an expected stay in the ICU of >48 hours needing an arterial catheter and a central venous catheter (CVC) were eligible. For a maximum of 3 days, during 8 hours per day, 125 µl blood was drawn from the arterial line every 15 minutes. Point accuracy was expressed using Clarke error grids, Bland–Altman plots and glucose prediction error analysis [4,5]. Trend accuracy was expressed using continuous glucose error grid analysis [6].
Results Three-hundred and fifty-four paired samples were obtained from seven patients (66 (59 to 79) years old, APACHE II score 23 (20 to 28), 51 (19 to 77) samples per patient). Point accuracy: 91% of paired values were in zone A, with the remaining 9% of the values in zone B in the Clarke error grid. In the Bland–Altman, bias was 5.4 mg/dl with an upper limit of agreement of 32.5 mg/dl and a lower level of agreement of −21.8 mg/dl. Glucose prediction error analysis showed that 91% of the values ≥75 mg/dl within 20% of the values measured by the blood gas analyzer were within range. Trend accuracy: in the rate error grid of the continuous glucose error grid analysis, 96% of the paired values were in zone A, 3.7% were in zone B and 0.3% were in zone C.
Conclusion Point and trend accuracy of the tested microdialysis-based CGM are good in critically ill patients.
Acknowledgement Maquet Critical Care AB provided two CGM systems and disposables for the duration of the study, but had no influence on study design or study reporting.
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P373

Real-time continuous glucose monitoring in the ICU

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Introduction Hyperglycemia occurs in 50 to 85% of patients admitted to a medical ICU (MICU) and has been associated with poor prognosis [1,2]. Whether applying intensive insulin therapy to achieve tight glycemic control in critically ill patients is beneficial remains controversial [2]. Another important observation is a link between glycemic variability and mortality [3]. We performed a pilot study hypothesizing that when implementing intensive insulin therapy, real-time continuous glucose monitoring (RT-CGM) may help to safely achieve tight glucose control, while avoiding hypoglycemia and reducing glycemic variability in MICU patients.
Methods This two-center randomized controlled pilot study was performed during a 3-year period. To be included, patients had to be severely ill (APACHE II score ≥20) and CGM monitoring had to be started within 48 hours after admission in the MICU. Thirty-five patients (age 66 ± 10 years; nondiabetic/diabetic patients 27/8; APACHE II score 28 ± 6) were randomly assigned to RT-CGM (n = 16) or to blinded CGM. In both groups a microdialysis-based glucose sensor (GlucoDay®S) was used during a 96-hour period of glucose monitoring. Insulin infusion was performed using a modified Yale protocol. Outcome measures were percentage of time in normoglycemia and in hypoglycemia, glycemic variability, and CGM accuracy.
Results In the RT-CGM group the percentage of time at the target glycemia (80 to 110 mg/dl) was 37 ± 12% versus 34 ± 10% in the control group (NS) and glycemia averaged 119 ± 17 mg/dl versus 122 ± 11 mg/dl respectively (NS). Time spent in hypoglycemia (<60 mg/dl) was not statistically different between the group assigned to RT-CGM (0.6 ± 1.6% of the time) versus those with blinded CGM registration (2.4 ± 4.3% of the time). Parameters of glucose variability (standard deviation of mean glucose value, coefficient of variation, mean amplitude of glucose excursions) did not differ between the groups. The GlucoDay®S values and arterial glycemia correlated well with 98.6% of data falling in regions A and B of error grid analysis.
Conclusion In our study, the use of RT-CGM neither improved glucose control and variability, nor did it reduce hypoglycemic events. On the other hand we can state that our insulin infusion protocol already led to overall tight glucose control without a significant hypoglycemia risk, leaving little space for improvement.
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P374

Critically ill patients with faecal peritonitis: a 5-year review in a tertiary centre

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Introduction Faecal peritonitis (FP) is a common cause of sepsis and admission to the ICU [1]. We report a review of all patients admitted to our ICU over 5 years with FP. The aim was to define the clinical characteristics, outcomes and risk factors for mortality in ICU patients with FP.
Methods Data were extracted retrospectively from electronic case files. The primary outcome was ICU mortality. Secondary outcomes were hospital, 28-day, 90-day and 1-year mortality. Logistic regression analysis was used to identify independent risk factors for mortality.
Results Ninety-nine FP patients were admitted between April 2008 and January 2014. Median age was 73 (IQR 61 to 79), with a female preponderance (53.5%). The median ICU length of stay (LOS) was 5 days (IQR 2 to 16). On admission to critical care, clinical data included (all medians): temperature 36.6°C (IQR 36 to 37.2), systolic blood pressure (BP) 113 mmHg (IQR 104 to 136), diastolic BP 56 mmHg (IQR 49 to 67), lactate 2.3 mmol/l (IQR 1.5 to 3.7), bilirubin 12 µmol/l (IQR 9 to 20), haemoglobin 104 g/l (IQR 93 to 116), haematocrit 31 (IQR 28 to 36), creatinine 88 µmol/l (IQR 66 to 152), prothrombin time 13.1 seconds (IQR 11.9 to 14.4). In 86 patients the initial operation was an emergency laparotomy, with primary perforation in 53 cases. Subsequent anastomotic dehiscence and need for relaparotomy happened in 24 and 33 cases respectively. Forty per cent of patients underwent more than one surgical abdominal intervention. The most common antibiotic used was tazobactam and fluconazole was the commonest antifungal. The percentages of patients receiving mechanical ventilation, renal replacement therapy and inotropic/vasopressor support during ICU stay were 72.7%, 25.3% and 84.8% respectively. The ICU and hospital mortality rates were 23.5% and 26.1%, respectively, increasing to 26.7% at 28 days, 28.4% at 90 days and 32.2% at 1 year. None of the surgical factors or diabetes influenced survival. The strongest independent risk factors associated for ICU mortality were systolic BP on ICU admission (OR = 1.05, 95% CI = 1.01 to 1.09, P = 0.015), acute kidney injury (AKI) within the first 24 hours of ICU admission (OR = 0.15, 95% CI = 0.03 to 0.9, P = 0.026) and lactate on ICU admission (OR = 0.62, 95% CI = 0.39 to 1, P = 0.05).
Conclusion In this cohort of critically ill FP patients the ICU and 12-month mortality rates were 23.5% and 32.2%, respectively. The most consistent predictors of mortality across all time points were AKI within 24 hours of ICU admission and admission lactate.
Acknowledgement VP and AT are joint first authors.
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P375

Bowel and related complications after cardiac surgery

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Introduction Postoperative ileus appears to be underestimated after cardiac surgery. We conducted this study to analyse the incidence, risk factors and outcomes of postoperative ileus.

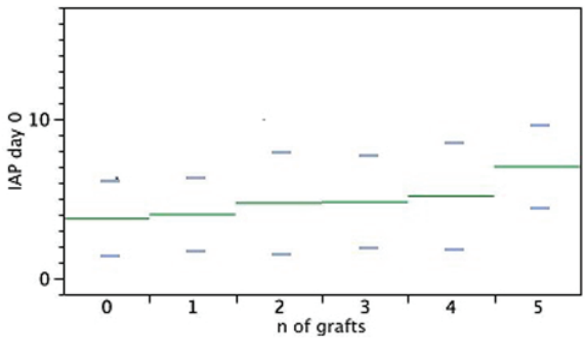


Figure 1 (abstract P375).

Methods In this single-centre observational study we prospectively enrolled all patients undergoing elective cardiac surgery. The primary output was the time to faeces (TTFE) as representing the postoperative ileus. Secondary outputs were the occurrence of ischaemic colitis and pneumonia. Quantitative variables were compared by ANOVA or Wilcoxon tests, qualitative variables by chi-square tests. Multivariate analyses were performed by logistic regression, P <0.1 for inputs P <0.05 for outputs.
Results We included 349 patients: age 67.5 ± 10.8 years, M/F sex ratio 252/97, preoperative left ventricle ejection fraction 58.8 ± 10.6%, bypass/valve ratio 234/154, number of grafts 2.7 ± 0.9, mammal arteries 1.8 ± 0.5. In univariate analyses, bypasses received more anaesthetic drugs (P <0.01), had shorter extracorporeal circulation duration, 67 ± 27 versus 75 ± 24 minutes (P <0.01), and received less blood products (P <0.0001). Bypasses had lower postoperative levels of troponin (3.9 ± 7.6 vs. 8.1 ± 21 pg/ml, P <0.01) and LDH (330 ± 162 vs. 420 ± 175 pg/ml). In contrast, the intra-abdominal pressure (IAP) was higher and related to the number of grafts at day 0 (Figure 1) and day 1 (P = 0.01 and 0.02 respectively), and to the number of mammal grafts at day 0 and day 1 (P = 0.01 and 0.04 respectively). The TTFE was longer but did not reach significance (P = 0.13) as well as the occurrence of abdominal ischaemia (P = 0.22). The occurrence of pneumonia was higher (P = 0.01). In multivariate analysis, the IAP at day 0 and day 1 was related to propofol quantities only. The predictors of pneumonia were: duration of mechanical ventilation, peak lactate in the postoperative 24 hours, and coronary bypass: OR = 163, 2.6, and 4.2 respectively.
Conclusion The number of coronary grafts and of mammal artery used in cardiac surgery is associated with higher IAP and higher risk of pneumonia. However, whether this is due to direct bowel ischaemia or longer anaesthesia remains to be studied in larger trials.

P376

ICU outcome of patients undergoing cytoreductive surgery followed by hyperthermic intraperitoneal chemotherapy: a single-center study

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Introduction Peritoneal carcinomatosis (PC) is associated with poor prognosis. The advent of complete cytoreductive surgery (CRRS) followed by hyperthermic intraperitoneal chemotherapy (HIPEC) has shown promise in improved survival for locally advanced intra-abdominal carcinomatosis. Such patients are routinely admitted to the ICU postoperatively. Little is known about the natural course of such patients while in the ICU.
Methods The procedure was introduced in our hospital in 2008 as the first regional center performing such therapy. A retrospective chart review of 129 cases of CRS-HIPEC admitted to a 22-bed surgical ICU in a tertiary care academic center between November 2008 and March 2014. Primary outcomes were ICU length of stay (LOS) and duration of mechanical ventilation (MV). Secondary outcomes were hospital LOS and hospital mortality.
Results Eighty-seven patients (69.9%) were females. Mean age was 48.9 years. Primary cancer was colorectal in 42 patients (32.5%), ovarian in 39 (30%), appendiceal in 29 (22%), others in 15.5%. Average operative time was 11 ± 2.1 hours. Average intraoperative crystalloids given were 12,217 ± 4,359 ml, packed RBCs were 2 ± 2.3 units, colloids 1,083 ± 898 ml, average blood loss was 1,108 ± 785 ml. All patients were admitted to the ICU post procedure. The average fluid balance during the OR was 9,481 ± 4,694 ml. Patients stayed in the ICU for an average of 6 ± 5.3 days. All patients survived the ICU stay. The duration of mechanical ventilation was 57 ± 83 hours, total fluid balance while in the ICU was 1,467 ± 3,399 ml. Hypomagnesemia was the most frequent electrolyte abnormalities in 79 (61%). Pleural effusions in 48 (37%), of which three patients only required drainage, Seven patients (5.6%) developed pneumonia, no patient required renal replacement therapy. Average hospital LOS was 33.7 ± 29 days. Only two patients died in the hospital. When the first 65 patients were compared with the last 64 patients, the duration of MV, ICU LOS and hospital LOS were all significantly shorter in the latter group (72 vs. 43 hours, 6.8 vs. 5.0 and 40 vs. 27 days respectively; P <0.01 for all).
Conclusion With proper selection of patients, CRS with HIPEC can be done safely with no major complications. There is a significant reduction in ICU utilization and shorter hospital LOS with more experience in such procedure, suggesting a learning curve as well as better utilization of resources by referring such patients to a high-volume center.

P377

Disseminated intravascular coagulation score predicts mortality in critically ill patients with liver cirrhosis

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Introduction The disseminated intravascular coagulation (DIC) score is a predictor of outcome in critically ill patients [1,2]. Yet disturbances of coagulation and hemostasis, as reflected by the DIC score, are a common finding in patients with liver cirrhosis. Thus, it is unclear whether the DIC score has prognostic value in critically ill patients with liver cirrhosis. The aim of this study was to assess the applicability and prognostic impact of the DIC score in critically ill patients with liver cirrhosis.
Methods Patients with liver cirrhosis admitted to the medical ICU were analyzed for this study. Detailed laboratory analyses including platelet count, D-dimer, fibrinogen and prothrombin index were performed on admission and the DIC score was calculated. Survival was assessed on site or by contacting the patients or the attending physician.
Results In total, 150 admissions to the ICU with liver cirrhosis were analyzed. Thirty-nine percent were female. Median age was 56 (IQR 49 to 63) years. The median SOFA score on admission was 9 (6 to 13), median MELD score 26 (IQR 18 to 36). Twenty-eight-day mortality was 59%. Median DIC score on admission was 5 (IQR 4 to 6). Overt DIC (DIC score ≥5) was found in 65%. DIC score was significantly higher in nonsurvivors compared with survivors (5 (IQR 4 to 7) vs. 4 (IQR 3 to 6); P <0.01). AUROC for the DIC score in prediction of 28-day mortality was 0.68 (95% CI = 0.59 to 0.77). Overt DIC on admission was significantly associated with 28-day mortality (OR = 3.4 (95% CI = 1.69 to 6.84), P <0.01). The 28-day mortality rate in admissions with cirrhosis and overt DIC was 70% compared with 40% in those with a DIC score <5.
Conclusion Disturbances in coagulation and hemostasis are found in the majority of cirrhotic patients admitted to the ICU. The DIC score is a suitable predictor of 28-day mortality in critically ill patients with liver cirrhosis.
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P378

Warm ischemia time, postreperfusion syndrome and initial poor function after liver transplantation: are they connected?

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Introduction Factors associated with initial poor graft function (IPGF) after liver transplantation are still under debate. Although the initial insult to the graft begins during the cold ischemia time (CIT), recent studies showed that most injuries occur during rewarming. Ischemic–reperfusion (I/R) injuries are present in all grafts and may be responsible for postoperative graft dysfunction. Along with other factors, I/R injury may also play a role in the development of postreperfusion syndrome (PRS) after revascularization of the liver graft. The aim of this study was to assess whether longer warm ischemia time (WIT) is associated with PRS or with IPGF after liver transplant. The secondary aim was to investigate whether patients with intraoperative PRS have a higher risk for postoperative IPGF.
Methods This retrospective observational study included 60 liver transplant patients. We excluded from the study group patients with retransplant procedures, and the recipients of divided grafts and of grafts from extended criteria donors. We recorded: demographic data, intraoperative PRS, CIT, WIT, ALT, AST levels and standard coagulation tests on postoperative days (POD) 1 to 5. Statistical analysis was performed using SPSS Statistics v.19.1 with significant *P* value under 0.05.
Results We used the criteria of Nanashima and colleagues for the diagnosis of IPGF (ALT and/or AST level above 1,500 IU/l within 72 hours after OLT). The study group included 33 men (55%) and 27 women. Mean (±SD) age was 50.56 (±13.26) years. WIT longer than 60 minutes correlated significantly with ALT and AST levels in POD 1 to 3 ($P < 0.0001$ for ALT in POD 1 to 3, $P = 0.001$ for AST in POD 1, $P = 0.007$ and 0.013 for AST in POD 2 and 3) and with prothrombin time ($P = 0.008$ in POD 1, $P = 0.03$ in POD 2 and $P = 0.015$ in POD 3). We could not find a correlation between PRS and WIT ($P = 0.566$), CIT ($P = 0.439$) or transaminase levels on POD 1 to 3. The correlation between WIT >60 minutes and IPGF was confirmed using the Pearson chi-square test ($P < 0.0001$). The same test was used to correlate IPGF with PRS with nonsignificant results ($P = 0.876$).
Conclusion Our study showed that PRS is not a risk factor for IPGF after liver transplantation. WIT over 60 minutes does not influence the development of PRS, but is associated with IPGF after liver transplantation. Close monitoring of liver tests in the early postoperative period is very important especially in recipients of grafts with WIT over 60 minutes. Further efforts to decrease WIT may prove useful for the reduction of IPGF in liver transplant patients.

P379

Seroprevalence of hepatitis B, hepatitis C and HIV in ICU patients

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Introduction Healthcare workers are at risk for infections caused by hepatitis B (HBV), hepatitis C (HCV) and human immunodeficiency (HIV) viruses that transmit via blood and body fluids. In the present study, it was aimed to investigate the seroprevalences of HBsAg, anti-HCV and anti-HIV in patients admitted to the ICU.
Methods HBsAg, anti-HCV and anti-HIV test results and demographical data of the patients admitted to the Reanimation ICU between January 2012 and December 2014 were evaluated retrospectively. HBsAg, anti-HCV and anti-HIV tests were assayed with a macro-ELISA method (Axsym-Abbott, Architect i2000; Abbott, USA). Statistical analysis was performed with the chi-square test.
Results The records of 462 patients admitted to our ICU were reviewed. The results of 36 patients could not be reached, so 426 patients were evaluated in the study. Among 426 patients, 169 (39.7%) were female and 257 (60.3%) were male. The mean age was 63.7 ± 18.7. HBsAg was positive in nine (2.1%) patients; all of these nine were male. Anti-HCV was positive in four (0.9%) patients; among these, three were male and one was female. Only one patient was positive for anti-HIV.
Conclusion In the present study, it was observed that the seroprevalences of HBsAg, anti-HCV and anti-HIV were not higher than in our city population. However, taking the safety precautions of the healthcare workers during surgical or invasive procedures such as catheterization, intubation or tracheostomy without any information about the serological test results of the patients will reduce the contamination of these agents.
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P380

Outcomes of decompensated chronic liver disease in a UK district general hospital critical care setting

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Introduction Patients with decompensated cirrhosis admitted to the ICU have historically had a very high mortality rate [1]. It has been suggested that improving patient selection can improve ICU outcomes in patients with cirrhosis [2]. The aim of this study was to determine the mortality and evaluate the risk factors that may influence the outcome of this group of patients in a large UK district general hospital with a view to introducing selection criteria for future ICU admission of patients with decompensated liver disease.
Methods A retrospective analysis was performed of all adult patients with decompensated chronic liver disease admitted to a general (nontransplant) critical care unit between January 2012 and December 2013. Data were collected regarding demographics, ICU mortality, hospital mortality, aetiology of chronic liver disease, severity scores, acute diagnoses, and organ support requirements.
Results Thirty-seven patients were identified, with a median age of 57 years, predominantly male (62%). Seventy-six per cent had alcohol-related cirrhosis. Overall ICU mortality was 29.7% and hospital mortality was 48.6% – these values were higher in the alcoholic group (39.3% and 57.1% respectively). All ICU deaths were in those with alcoholic liver disease. Median scores were: APACHE III 93, SOFA (day 1) 9, Child–Pugh 11, MELD 21. Seventy per cent were treated for sepsis, 22% had a GI bleed, 57% had encephalopathy, 24% had suspected/confirmed spontaneous bacterial peritonitis, and 70% had an acute kidney injury. Organ support requirements were: 35% respiratory (non-invasive or invasive ventilation), 38% vasoactive agent support, 24% renal replacement therapy (RRT). Alcoholic liver disease patients requiring respiratory or cardiovascular support had an ICU mortality of 64%, and those requiring RRT had a mortality of 75%. Alcoholic liver disease patients requiring combined respiratory, cardiovascular, and RRT support had 100% mortality.
Conclusion Those with decompensated chronic liver disease admitted to the ICU have a significant ICU/hospital mortality, which is increased in alcoholic liver disease. Sepsis and AKI were the most common acute diagnoses in this cohort. Alcoholic liver disease patients requiring organ support have a very high mortality, and the outlook for multiorgan failure requiring RRT in this group is dismal.
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P381

Prometheus® liver therapy in children with acute liver failure

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Introduction The Fractionated Plasma Separation and Adsorption System Prometheus® (Fresenius Medical Care, Germany) aims at being

a supportive therapy as a bridge to transplantation or recovery in adults with liver failure. The system offers specific challenges when applied in children due to the large extracorporeal volume (700 to 750 ml). We therefore developed an adapted protocol for the application in children.
Methods Priming of the blood circuit is performed using 2 l isotonic saline, whereas the plasma circuit, containing both adsorption devices, is filled with 2 U fresh frozen plasma or 400 ml stabilized solution of human plasma proteins. Next, for children with body weight (BW) <25 kg, a solution of 60 to 65% packed cells (PC) is infused in the inlet blood line at 40 ml/minute. The volume of PC needed is calculated based on the circuit priming volume and the maximum allowed extracorporeal blood volume of the child (= 8 ml/kg × BW). After the priming phase, blood and plasma flow are increased to at least 100 ml/minute and 200 ml/minute, respectively, and dialysate flow is set at 300 ml/minute. Regional citrate anticoagulation is done with a calcium-free dialysate, while, eventually, heparin is added to the priming solution. Post treatment, the circuit volume is either not reinfused (BW <25 kg) or reinfused using isotonic saline (BW >25 kg), with a volume depending on the hydration status and the originally infused volume of PC. Reduction ratios (RRs, %) of urea, creatinine (Crea), bilirubin (bili), and ammonia (NH_3) were calculated from pretreatment and posttreatment serum concentrations. Primary and secondary patient outcome was evaluated.
Results Eight children (five male/three female), 8.6 ± 5.9 years old (range 2 to 15.6 years), BW 32 ± 21 kg, GFR 71 ± 20 ml/minute/1.73 m^2, with an uncuffed double lumen dialysis catheter (8 to 14 Fr Femoralis ($n = 6$) and 9 Fr Jugularis ($n = 2$)) were treated according to this protocol. In total, 19 sessions were executed using FX40 ($n = 13$), FX50 ($n = 3$), and FX60 ($n = 3$) dialysers during 6.5 ± 0.9 hours. Blood flow was 149 ± 45 ml/minute, albumin flow 226 ± 49 ml/minute, and ultrafiltration flow 432 ± 517 ml. RRs were 70 ± 15% (urea), 34 ± 14% (Crea), 44 ± 16% (bili), and 36 ± 10% (NH_3). Primary survival rate was 100%. Four patients were transplanted (bridge to transplant) of which, however, one died within 30 days after discharge from the ICU. The fifth patient died due to primary disease 9 months after treatment, and the remaining three patients fully recovered (bridge to recovery).
Conclusion This adapted Prometheus® protocol is promising for the treatment of children with liver failure.

P382

Molecular adsorbent recirculating system treatment in 69 patients listed for liver transplantation

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Introduction The molecular adsorbent recirculating system (MARS) is used to remove circulating albumin-bound toxins in patients with liver failure. However, the application of MARS has not demonstrated improved survival in randomized clinical trials and the clinical utility has not been finally established. In our department, the use of MARS is now restricted to the most critically ill patients with acute or acute on chronic liver failure. We aimed to explore MARS efficacy in removing toxicity parameters and the safety of the system.
Methods Since 2005, we have treated 69 patients (30 males/39 females with median age of 39 years ranging from 1 month to 70 years) listed for liver transplantation with MARS. The median Model of End Stage Liver Disease (MELD) score in patients older than 12 years of age ($n = 56$) was 33 (interquartile range 26 to 39). The flow rate was 35 to 40 ml/kg/hour and treatment kits were changed every 8 to 12 hours. The patients were treated for a median of 31 hours (range 1 to 240 hours).
Results Fifty-five patients (79%) were successfully bridged to transplantation. Nine died before they could be transplanted, and five patients recovered without liver transplantation. Forty-four (81%) of the transplanted patients were alive 30 days after transplantation. Ammonium decreased modestly from a median of 148 to 124 μM ($P = 0.03$) during MARS treatment. We detected worsening of coagulopathy with significant decreases in platelet count and fibrinogen concentrations, and increase in International Normalized Ratio. Phosphate and magnesium decreased significantly during MARS treatment.
Conclusion Close observation and treatment of coagulopathy and electrolyte disturbances is essential when treating patients with MARS. MARS can reduce and stabilize ammonium and other biomedical markers in patients listed for urgent liver transplantation with high MELD score and liver encephalopathy. It seems that, in some cases and with our settings, the detoxification properties of MARS may be insufficient.

P383

First clinical experience with a new type of albumin dialysis: the HepaWash® system

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Introduction Liver failure (LF) is associated with prolonged hospital stay, increased cost and substantial mortality. With regard to a limited number of donor organs, extracorporeal liver support is an appealing concept to bridge to transplant or to avoid transplant in case of recovery. A new type of albumin dialysis, the HepaWash® system, was recently introduced. The HepaWash® system provides rapid re-generation of toxin-binding albumin by secondary circuits altering binding capacities of albumin by biochemical (changing pH) and physical (changing temperature) modulation of the dialysate.
Methods We evaluated the first 14 patients treated with the HepaWash® system with regard to safety and efficacy. Seven patients were treated in the context of the run-in phase of the studies (HEPATICUS 1 and HEPATICUS 2) and seven patients were treated since the HepaWash® system received the CE certificate in July 2013. Patients treated suffered under acute on chronic LF ($n = 9$) or secondary LF which resulted from nonhepatic diseases such as sepsis ($n = 5$). Primary endpoint: comparison of serum bilirubin, creatinine and serum BUN before and after the first treatment with the HepaWash® system. Statistics: IBM SPSS Statistics version 22. The Wilcoxon test for paired samples was used to detect significant treatment effects.
Results A total of 254 treatments (1 to 101 per patient) were performed in 14 patients (six female, eight male). Mean age 54 ± 13. MELD score 33.7 ± 7.0, CLIF-SOFA 14.6 ± 2.7. Main underlying disease: nine acute-on-chronic LF; five secondary LF. While bilirubin did not change significantly on the day before HepaWash® treatment (26.2 ± 15.4 vs. 26.0 ± 15.4 mg/dl; $P = 0.116$), serum bilirubin levels were significantly decreased by the HepaWash® procedure (26.0 ± 15.4 vs. 17.7 ± 10.5 mg/dl; $P = 0.001$). Similarly, serum creatinine (2.2 ± 0.8 vs. 1.6 ± 0.7 mg/dl; $P = 0.005$) and serum BUN (49.4 ± 23.3 vs. 31.1 ± 19.7 mg/dl; $P = 0.003$) were significantly lowered by the HepaWash® procedure. There were no serious adverse events observed in conjunction with the HepaWash® treatment.
Conclusion So far the HepaWash® system has proven to be a safe and feasible procedure to effectively eliminate water and protein-bound toxins in humans with LF.

P384

Intensive care referral and admission: do the criteria for liver disease match?

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Introduction Hospital admission and mortality rates for patients with cirrhosis in the UK are rising [1]. Cirrhotic patients are physiologically challenged and at increased risk of sepsis and death [2]. Mortality rates for cirrhosis in nontransplant ICUs are up to 37% [3]. Increased availability of medical therapies and public expectation places pressure on limited intensive care resources. There is a lack of research into factors used to decide which patients to admit or refer to the ICU.
Methods A prospective survey was sent to all consultant gastroenterologists and consultant intensivists in Scotland. Each recipient rated the significance of 18 physiological and social criteria on their decision to refer or admit a patient to intensive care from 1 to 5, with 1 being no influence and 5 denoting significant impact on the

decision. Recipients listed additional criteria used in their own practice and asked whether they would admit or refer individual grades of Child–Pugh cirrhosis with either a gastrointestinal bleed or sepsis.
Results Thirty-five consultant gastroenterologists and 65 intensive care consultants responded, representing a response rate of 34% and 45% respectively. The only criterion given an average rating of 5 by both gastroenterologists and intensivists was Child–Pugh score when stable. Presence on the transplant list, referral secondary to bleeding varices, recent discharge from the ICU, abstinence from alcohol, nutritional status, age under 30 and more than one additional organ failure all scored 4 or 5 from both groups. Sex, employment, smoking or drug use, deprivation and positive virology status did not influence the decision to refer or admit patients. Clinicians reported compliance with medication and outpatient appointments plus an obvious precipitant factor as important features in their decision. The majority of respondents would refer or admit all grades of Child–Pugh cirrhosis with gastrointestinal bleeding. Most would refer or admit Child–Pugh A or B with sepsis. A total 76.5% of gastroenterologists would refer Child–Pugh C cirrhosis with sepsis but only 33.3% of intensivists would accept.
Conclusion Referral and admission decisions for patients with cirrhosis are multifactorial. Child–Pugh status when stable appears to be of greatest significance. The difference in opinion of admission of patients with Child–Pugh C with sepsis requires further evaluation.
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P385

Mortality in patients with cirrhosis admitted to the ICU: time to rethink strategies?

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Introduction Cirrhotic patients admitted to the ICU are usually regarded as having a particularly poor prognosis when compared with other groups of critically ill patients. The aim of our study was to evaluate the prevalence, case mix and outcomes of patients with cirrhosis admitted to the general ICU of a nontransplant center.
Methods Data were collected from a running ICU database. We studied cirrhotic patients admitted to the ICU between January 2013 and November 2014.
Results A total of 30 patients with cirrhosis were admitted, accounting for 3% of total ICU admissions. Mean age was 54.5 years, with a male preponderance (76.7%). The main cause for cirrhosis was alcohol (53.3%), followed by alcohol plus chronic hepatitis C virus (HCV) infection (20%) and HCV virus infection alone (13.3%). The most common causes for admission were sepsis/septic shock (26.7%), surgical (23.4%), gastrointestinal bleeding and hepatic encephalopathy (16.7% each). At admission, these patients presented an average Model for End-Stage Liver Disease score of 23.5 ± 10.4 with 70% classified as grade C in the Child–Pugh score; mean Acute Physiology and Chronic Health Evaluation (APACHE II) 29.2 ± 8.7 and new Simplified Acute Physiology Score (SAPS II) 62.7 ± 29. Regarding organ failure at admission, the mean Sequential Organ Failure Assessment score was 12.8 ± 4.5. The ICU mortality of these patients was 43.3% and hospital mortality was 53.3%. The variables at admission that related significantly with ICU mortality were: all scores described except for Child–Pugh score, bilirubin, the International Normalized Ratio, creatinine, bicarbonate, lactate, pH and the use of renal replacement therapy during the ICU stay (P <0.05). The mortality rate of cirrhotic patients was superior to the general ICU mortality (43% vs. 26%). However, patients with cirrhosis presented significantly higher severity scoring systems (APACHE II; SAPS II) at admission compared with noncirrhotics, with high prevalence of organ dysfunction as assessed by SOFA score.
Conclusion The high severity of disease in conjunction with the high mortality rate observed in this group of patients should make us consider the possible benefits of earlier referring/admission to the ICU, ideally before multiorgan failure arises. On the other hand, in nontransplant centers where cirrhotic patients constitute a small percentage of total ICU admissions, the complexity and peculiarities of the management of these patients should prompt their early transfer to a specialized center.

P386

Intraabdominal pressure in critical burn patients

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Critical Care 2015, **19(Suppl 1):**P386 (doi: 10.1186/cc14466)

Introduction The aim was to study the evolution and incidence of intraabdominal hypertension in critical burn patients using a slightly restrictive fluid therapy protocol based on monitoring transpulmonary thermodilution and lactic acid.
Methods A prospective study of 132 consecutive patients admitted to the Critical Burn Unit between October 2008 and October 2011. In all of them resuscitation was performed by objectives: blood pressure (>65 mmHg), hourly diuresis (0.5 to 1 cm^3/kg), lactic acid clearance and thermodilution transpulmonary parameters (CI >2.5 l/minute/m^2, ITBI: 600 ml/m^2). We performed measurements of IAP with a bladder catheter every 8 hours in the first 72 hours.
Results Ninety-eight men and 34 women were studied. Mean age 48 ± 18 years and a TBSA of 35 ± 22%. The fluid provided by %TBSA in the first 8 hours was less than predicted by Parkland (4.05 ml/kg), although the total contribution in the first 24 hours was similar. The evolution of the intra-abdominal pressure was: admission 9.7 mmHg, 8 hours 11, 16 hours 10.5, 24 hours 12.1, 32 hours 12.0, 40 hours 12.0, 48 hours 11.1, 56 hours 10.3, 64 hours 10.0 and 72 hours 10.0. A total of 44 patients (33.3%) had a determination higher than 12 mmHg, distributed: 15 patients between 12 and 15 mmHg (IAHT I grade), 14 between 16 and 20 mmHg (II), nine between 21 and 25 mmHg (III) and six >25 mmHg (IV). See Figures 1 and 2.
Conclusion IAH incidence when a slightly restrictive fluid protocol used is less than expected.

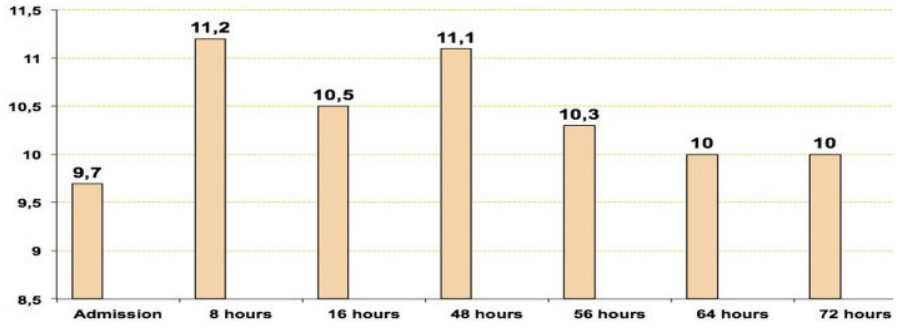


Figure 1 (abstract P386). Intraabdominal pressure.

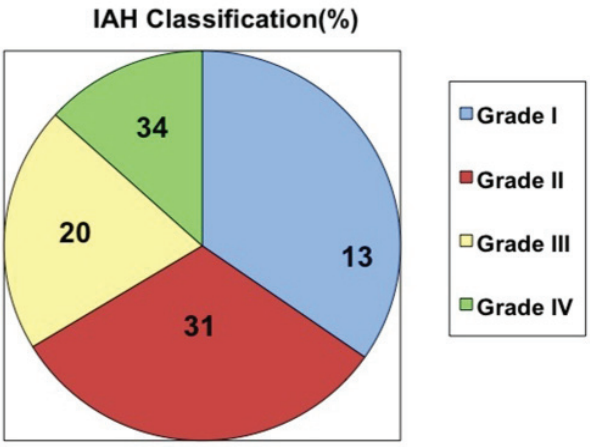


Figure 2 (abstract P386). IAH classification.

P387

Intraabdominal hypertension in burn patients

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Introduction Intra-abdominal hypertension (IAH) is frequent in the ICU and has been associated with adverse outcomes and worse prognosis. The purpose of our study was to assess risk factors for IAH and prognosis of major injured patients during burn resuscitation.
Methods Adult burned patients with a burn injury exceeding 20% of total body surface area, from 1 April to 30 November 2013, were included. IAP was measured when IAH was suspected, according to the Kron method via the Foley catheter. Monitoring of IAP was performed every 6 hours during 5 days until normalization.
Results Twenty patients were enrolled in the study. The mean age was 36 ± 13 years. There were 14 males and six females. The average TBSA was 44 ± 17%. Screening and monitoring of IAP were applied by: oliguria (42%), abdominal distension (31.5%) and gastrointestinal trouble (21%). IAH occurred between day 2 and day 3 after early burn resuscitation, respectively in 52% and 63%. IAH was observed in 69% of cases in patients admitted to the ICU with a delay of 1.6 days post burn injury. IAH was noted in 13 patients; of these, five patients developed an abdominal compartment syndrome. The mean IAP was 16 ± 7 mmHg. Patients were assigned into two groups: G1 (IAH+; n = 13) and G2 (IAH–; n = 7). Comparative study of the two groups shows that HIA increases significantly body weight gain within the first 5 days after injury: 8 kg for G1 versus 2 kg for G2 (P = 0.04), occurrence of ARDS (70% for G1 vs. 16.7% for G2, P = 0.02), respiratory failure (77% for G1 vs. 28.5% for G2, P = 0.06), shock (70% for G1 vs. 16.7% for G2, P 0.02) and mortality (61.5% vs. 50%).
Conclusion IAH was frequent in early burn resuscitation of major injured patients. It seems to be associated with fluid overload in burns and contributes to organ damage.

P388

Effects of sepsis on respiratory mechanics in a porcine model of intra-abdominal hypertension

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Introduction The aim of our study was to investigate the effects of sepsis on respiratory mechanics in a porcine model of intra-abdominal hypertension (IAH).
Methods Sixteen pigs were divided into two groups of eight (G-A/G-B). All animals received general anesthesia and were mechanically ventilated. Parameters recorded included respiratory system, chest wall and lung compliance (CRS, CCW, CL) and respiratory system and chest wall inspiratory and expiratory resistances (RRSisp, RRSexp, RCWisp, RCWexp). After baseline measurements (0 minutes), intra-abdominal pressure IAP was raised by helium insufflation to 25 mmHg in both groups and remained at that level for the whole study. In G-B, sepsis was induced 60 minutes after IAP increase, by i.v. administration of *Escherichia coli* endotoxin. Parameters were recorded every 20 minutes. The last measurement was made at 180 minutes, right after deinsufflation, and IAP return to baseline levels.
Results CRS decreased statistically significantly in both groups after IAP increase and increased after deinsufflation only in G-A. Similarly, CCW decreased in both groups but returned to baseline values in both groups after deinsufflation. CL decreased more significantly in G-B and returned to baseline values only in G-A. RRSisp increased only in G-B and did not decrease after deinsufflation, whereas RRSexp increased in both groups, in a more significant manner in G-B, and decreased only in G-A after deinsufflation. RCWisp and RCSesp did not show any alterations during the study period. Results are depicted as mean values ± SD in Tables 1 and 2.
Conclusion Both sepsis and IAH have negative effects on respiratory mechanics. However, their combination has even more detrimental effects, which do not ameliorate after deinsufflation.

Table 1 (abstract P388). Compliance alterations during the study

	C_{RS} (ml/cmH_2O)			C_{CW} (ml/cmH_2O)			C_L (ml/cmH_2O)		
Minutes	**A**	**B**	***P* value**	**A**	**B**	***P* value**	**A**	**B**	***P* value**
0	35 ± 8	31 ± 4	NS	58 ± 20	46.1 ± 11	NS	99 ± 22	98 ± 14	NS
20	14 ± 4**	12 ± 3**	NS	20 ± 6**	17.7 ± 3**	NS	52 ± 21**	35 ± 11**	NS
40	13 ± 4**	12 ± 1**	NS	19 ± 6**	16.8 ± 3**	NS	47 ± 23**	36 ± 13**	NS
60[a]	12 ± 3**	11 ± 2**	NS	20 ± 5**	18.4 ± 4**	NS	41 ± 20	28 ± 7**	NS
80	13 ± 3**	10 ± 1**	NS	20 ± 6	18.2 ± 44	NS	41 ± 21**	24 ± 6**	<0.05
100	12 ± 3**	10 ± 2**	NS	21 ± 8**	19.9 ± 5**	NS	37 ± 20**	19 ± 4**	<0.05
120	12 ± 3**	10 ± 1**	NS	20 ± 6**	21.9 ± 7**	NS	37 ± 20**	17 ± 3**	<0.05
140	12 ± 3**	9 ± 1**	NS	21 ± 7**	21.8 ± 6**	NS	37 ± 20**	17 ± 5**	<0.05
160	12 ± 3**	9 ± 1**	NS	21 ± 7**	22.3 ± 7**	NS	37 ± 19**	16 ± 4**	<0.05
180	33 ± 7**	16 ± 5**	<0.001	50 ± 18	77.0 ± 18**	<0.05	81 ± 20*	21 ± 7**	<0.001

[a]Sepsis induction. Comparison with baseline: *P <0.05, ** P<0.01.

Table 2 (abstract P388). Respiratory system resistance alterations during the study

	R_{RSisp} (cmH_2O/l/minute)			R_{RSexp} (cmH_2O/l/minute)		
Minutes	**A**	**B**	***P* value**	**A**	**B**	***P* value**
0	8.1 ± 0.8	8.3 ± 0.7	NS	13.6 ± 4.1	15.5 ± 3.7	NS
20	7.8 ± 0.6	8.1 ± 0.7	NS	17.1 ± 5.2**	19.3 ± 2.2**	NS
40	7.8 ± 0.8	7.6 ± 0.9	NS	18.1 ± 5.4**	20.6 ± 3.1**	NS
60[a]	7.6 ± 0.9	7.5 ± 1.1	NS	18.9 ± 4.4**	19.9 ± 4.7**	NS
80	7.8 ± 1.2	8.2 ± 1.2	NS	18.6 ± 4.2**	21.1 ± 4.12**	NS
100	7.8 ± 0.9	7.9 ± 0.9	NS	18.2 ± 4.5**	22.7 ± 4.5**	NS
120	8 ± 0.6	9.1 ± 1.1	<0.05	18.6 ± 4.3**	20.9 ± 2.2**	NS
140	7.7 ± 0.6	9.5 ± 1.2	<0.01	18.8 ± 3.5**	22.9 ± 3.2**	<0.05
160	7.3 ± 0.7	9.6 ± 1.5*	<0.01	17.7 ± 3.5**	22.2 ± 2.3**	<0.01
180	8.1 ± 0.8	9.7 ± 1.2*	<0.01	14.9 ± 3.3	18.9 ± 2.3*	<0.05

[a]Sepsis induction. Comparison with baseline: **P* <0.05, ***P* <0.01.

P389

Severity markers in acute pancreatitis

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Introduction CD73/ecto-5'-nucleotidase is an enzyme that generates adenosine, which dampens inflammation and improves vascular barrier function in several disease models. CD73 also circulates in a soluble form in the blood [1]. We studied whether levels of soluble form of CD73 and cytokines/chemokines predict the development of organ failure in acute pancreatitis [2,3].
Methods Altogether, 161 patients with acute pancreatitis (107 were subclassified according to the revised Atlanta criteria into mild, 29 into moderately severe and 25 into severe forms) were studied. Serum and blood cell samples were collected at admission. Protein levels of soluble form of CD73 in serum were determined using a novel enzyme-linked immunosorbent assay, activity of soluble form of CD73 using radioactive enzyme assays, and CD73 messenger RNA levels from leukocytes using quantitative PCR. Serum levels of 48 cytokines and growth factors were determined using Bio-Plex Pro Human Cytokine Assay 21-plex and 27-plex magnetic bead suspension panels.
Results Activity and protein concentration of soluble form of CD73 and messenger RNA level of CD73 all decreased along with the disease severity ($P \leq 0.01$ for all). The activity of soluble form of CD73 at admission predicted the development of severe pancreatitis in different groups of the patients. Especially, activity of soluble form of CD73 was better than C-reactive protein or creatinine in predicting the severity of pancreatitis in the group of patients without any signs of organ failure at admission. In subgroup analyses of patients with severe pancreatitis and without organ dysfunction upon admission, IL-8, hepatocyte growth factor and granulocyte colony-stimulating factor (G-CSF) levels predicted the development of severe pancreatitis, with G-CSF being the most accurate cytokine.
Conclusion Activity of soluble form of CD73 and levels of certain cytokines at admission to the hospital have prognostic value in predicting the development of the severe form of acute pancreatitis. The possibility that combining them with other prognostic markers might improve prognostic accuracy requires further studies.
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P390

Randomized, double-blind, placebo-controlled study of the efficacy of four probiotics to modify the risk for postoperative complications in colorectal surgery

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Introduction Heterogeneous published results led us to conduct a clinical trial to assess the efficacy of a new formulation of four probiotics (P) as prophylaxis for complications after colorectal surgery.
Methods A double-blind, placebo-controlled randomized study was conducted enrolling patients undergoing colorectal cancer surgery. Placebo or a formulation of *L. acidophilus*, *L. plantarum*, *B. lactis* and *S. boulardii* was administered starting 1 day before operation and continuing for 15 days post operation. Patients were followed-up for 30 days with the development of postoperative complications as the primary outcome. PAXGene tubes and serum were collected on postoperative day 4 for measurement of gene expression and serum cytokines (ClinicalTrials.gov NCT02313519).
Results Administration of P significantly decreased the rate of all postoperative major complications (28.6% vs. 48.8% of placebo, $P = 0.010$, odds ratio: 0.42). Major benefit was found in the reduction of the postoperative pneumonia rate (2.4% vs. 11.3%, $P = 0.029$), of wound infections (7.1% vs. 20.0%, $P = 0.020$), of anastomotic leakage (1.2% vs. 8.8%, $P = 0.031$) and of the need for mechanical ventilation (20.2% vs. 35.0%, $P = 0.037$). The time until hospital discharge was shortened as

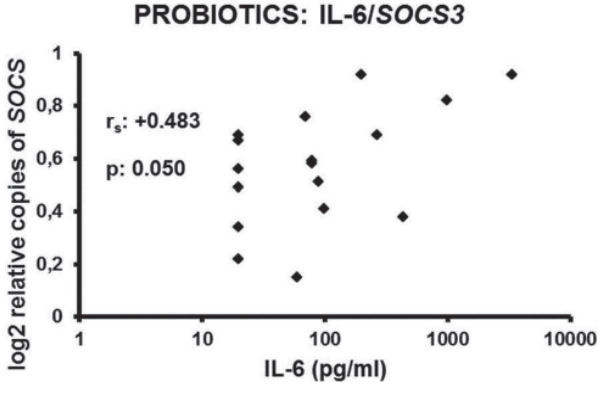


Figure 1 (abstract P390).

well. Gene expression of SOCS3 was positively related with circulating IL-6 in the P group but not in the placebo group (Figure 1).
Conclusion The studied P formulation significantly decreased the risk of postoperative complications, namely mechanical ventilation, infections and anastomotic leakage. Modulation of the gene expression of SOCS3 is one suggested mechanism.

P391

Role of ultrasonography in detection of the localization of the nasoenteric tube

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Introduction In this study, we aimed to determine the success rate of nasoenteric tube (NET) insertion into the postpyloric area by ultrasonography (USG) and compare it with the commonly used method, direct abdominal radiography.
Methods Patients admitted to an adult ICU between April and July 2014 with an indication for NET insertion for enteral feeding were included in the study after informed consent was given from patients' relatives. Nasoenteric feeding tubes were placed using the blind bedside method by a single anesthesiologist. Any motility stimulant agent was not used. The outside of the polyurethrane 8 F with unweighted NET (Bexen, Spain) and its guiding wire were lubricated with gel. The NET was inserted into the nostril after determination of the mouth–posterior ear–xiphoid distance and pushed on at least such a distance. Followed by auscultation of the gastric area and air infusion of 30 to 50 ml into the tube, the patient was positioned on their right side and the tube was advanced 20 to 30 cm more. Then the guiding wire inside the NET was removed. The patient was then brought to the supine position and NET was visualized by two radiologists simultaneously by M5 portable USG (Mindray, PRC), with a 3.5 MHz convex probe whether it passes through the postpyloric area or not. Localization of the tube was confirmed with abdominal radiography in all patients. During the first insertion of the NET, the ratios for inaccurate localization and correct placements through the postpyloric area were recorded and results were compared with abdominal radiography.
Results In this study, the bedside blind method was used for NET insertion into 34 patients. Eleven of the tubes were detected passing through the postpyloric area by USG. In one case the NET could not be seen in the postpyloric area by USG, but it was detected in the postpyloric area by control abdominal radiography. In 22 patients, NETs were detected in the stomach with control abdominal radiography. Success for NET placement with the bedside blind method and USG imaging was 35% versus 91.6%, respectively.
Conclusion The success rate of the bedside blind method in the NET placement was low. It is clear that if any other placement techniques with high success rate will be applied, USG will be useful in a higher number of patients reducing the need for abdominal radiography.

P392

Thiamine as a metabolic resuscitator in septic shock: a randomized, double-blind, placebo-controlled, pilot trial

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Introduction The objective was to determine whether the administration of thiamine mitigates elevated lactate levels in patients with septic shock. Thiamine is essential for aerobic metabolism and we have found that thiamine levels are low and inversely correlated with lactate levels in patients with sepsis.
Methods We performed a randomized, double-blind, placebo-controlled, two-center trial from January 2010 to October 2014. We enrolled patients with septic shock, elevated lactate (≥3 mmol/l) and no obvious competing cause of lactate elevation. Patients received thiamine 200 mg or placebo i.v. twice/day for 7 days. The primary outcome was lactate levels at 24 hours. Secondary outcomes included the SOFA score at 24 hours and mortality. Lactate levels at 24 hours were compared between groups using the Wilcoxon rank-sum test and categorical variables were compared using the Fisher's exact test. Lactate values at 24 hours, for those who died before 24 hours, were imputed according to a predefined plan. We performed a preplanned analysis in those with baseline thiamine deficiency (≤7 nmol/l).
Results We enrolled 88 patients; 43 received thiamine and 45 placebo. Baseline characteristics were similar between groups. We found no overall statistical significant difference in 24-hour lactate levels between thiamine and placebo groups (2.5 (IQR: 1.5 to 3.4) vs. 2.6 (IQR: 1.6 to 5.1), $P = 0.40$). Fewer patients in the thiamine group had lactate levels >4 mmol/l at 24 hours (21% vs. 38%, $P = 0.10$) and this was statistically significant if only evaluating survivors at 24 hours (7% vs. 33%, $P = 0.03$), although our preplanned analysis was to impute data. We found no difference in 24-hour SOFA score or mortality. A total of 28 (35%) patients were thiamine deficient. Of the deficient patients, those receiving thiamine had statistically significant lower lactate levels at 24 hours (2.1 (IQR: 1.4 to 2.5) vs. 3.1 (IQR: 1.9 to 8.3), $P = 0.03$) and more patients in the placebo group had a lactate >4 mmol/l (38% vs. 7%, $P = 0.07$). Mortality in the thiamine and placebo groups was 13% and 46%, respectively ($P = 0.10$).
Conclusion Thiamine deficiency is prevalent in septic shock. Thiamine did not decrease overall median lactate levels at 24 hours. In the patients with thiamine deficiency, there were statistically significant lower lactate levels at 24 hours in the thiamine group and a large, although nonsignificant, difference in mortality.

P393

Unraveling the link between malnutrition and adverse clinical outcomes: association of acute and chronic malnutrition measures with blood biomarkers from different pathophysiological systems

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Introduction Malnutrition is common in hospitalized medical patients and is associated with poor clinical outcomes. Whether malnutrition has a direct link to adverse outcomes or is rather a mirror of the severe patient condition remains debated. Our aim was to study the association of acute and chronic malnutrition status with blood biomarkers from different pathophysiological concepts to better understand the underlying mechanisms of malnutrition.
Methods We prospectively followed consecutive adult medical inpatients hospitalized between February 2013 and October 2013 in a tertiary care Swiss hospital. Nutritional risk was assessed using the Nutritional Risk Screening (NRS 2002) score, which incorporates acute and chronic measures of malnutrition. Multiadjusted regression models were used to investigate the associations between acute and chronic nutritional risk and biomarkers mirroring inflammation (CRP, PCT, proADM, leucocytes), stress (copeptin), renal dysfunction (creatinine, urea), nutritional status (vitamin D25, albumin, calcium, glucose), and hematological function (platelets, INR, Hb, RDW). Biomarker levels were transformed into deciles due to skewed distributions.
Results A total of 529 patients (mean age 72 years, 57.1% male) were included. Overall, there was a significant association of NRS and most biomarkers of inflammation, stress, renal function, nutrition and the hematological system (coefficient and 95% CI): CRP 0.021, $P = 0.0021$, PCT 0.28, $P = 0.003$, proADM 0.4, $P < 0.001$, copeptin 0.44, $P < 0.001$, urea 0.28, $P = 0.002$, vitamin D25 −0.23, $P = 0.012$, albumin −0.6, $P < 0.001$, hemoglobin −0.5, $P < 0.001$, RDW 0.46, $P < 0.001$. These associations remained robust after adjustment for sociodemographics (model 1), comorbidities (model 2) and main medical diagnosis (model 3). Subgroup analysis suggested that mainly the acute part of malnutrition and not chronic malnutrition was associated with an increase in biomarker levels.
Conclusion Acute malnutrition was associated with a pronounced inflammatory response and an increase in biomarkers from different pathophysiological systems which may partly explain the link between malnutrition and adverse medical outcomes. However, interventional trials are needed to prove causal relationships.

P394

Evaluation of the provision of nutrition in a South African provincial hospital

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Introduction The provision of nutrition in the critical care unit (CCU) has shifted from nutrition support to nutrition therapy, and the potential benefits derived from this in the recovery of the critically ill is being explored [1]. We audited the management of nutrition in the CCU in a South African Hospital against the American Society of Parenteral and Enteral Nutrition Guidelines. Furthermore, we reviewed the knowledge and confidence of healthcare providers in the management of nutrition in the CCU.
Methods Retrospective data collection of patients admitted to a four-bed CCU over a 4-month period in 2013. A survey was distributed to different disciplines involved in patient nutrition in the CCU.
Results Seventy-two patients were admitted to the CCU during this time period, and notes were able for 44. Three paediatric patients were excluded. Twenty-nine patients stayed for 2 or more days (the audit population). The median age of the audit population was 38, 19 were female. Sixteen were postoperative admissions. The median APACHE II score of the patients with sufficient available data ($n = 16$) was 14 (range 6 to 34). The audit found that 21 of the patients had nutrition started in the CCU, with 15 having nutrition started within 48 hours. Only eight patients had a nutritional assessment done. A total of 45 responded to the survey: eight anaesthetists, 25 from surgical disciplines, seven CCU nurses, and five dieticians. All agreed that nutrition should be started in the first 48 hours, except from the surgeons only 14 (56%) agreed. The average self-rating of knowledge of nutrition management in the CCU (1 = lowest, 5 = highest) was 2.1 with the dieticians and CCU nurses showing the highest confidence with 3.4 and 2.6, respectively. The anaesthetists rated their knowledge at 1.9 and the surgeons rated themselves at 1.8.
Conclusion We found that there is poor management of nutrition in the CCU. This is paired with limited knowledge and low confidence in management amongst the attending staff. Evidence would suggest that the development and dissemination of clear hospital guidelines could improve rates of correct management [2]. However, the lack of uniform guidance based on strong evidence from the leading global authorities on nutrition suggests that, in order to improve implementation of adequate nutrition, more research is urgently required.
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P395

Quality improvement project to optimize enteral nutrition in a tertiary hospital's surgical ICU

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Critical Care 2015, **19(Suppl 1):**P395 (doi: 10.1186/cc14475)

Introduction Optimizing enteral nutrition early has been shown to be beneficial in critically ill patients. However, underfeeding is still a common problem. The critically ill surgical patient often presents with additional challenges to optimal enteral feeding. The objective of this study was to improve enteral feeding practices in a surgical ICU.
Methods The Clinical Practice Improvement Programme is a local quality improvement initiative involving a multidisciplinary team aimed at identifying and improving deficiencies in the process of delivery of care. A team led by an intensivist, consisting of doctors, surgeons, nurses and a pharmacist, was formed to improve enteral feeding practices in a surgical ICU. The quality improvement methodology was employed. An audit was carried out to determine the problem of underfeeding in the unit. Root cause analyses were conducted and team members identified key barriers to optimal feeding and areas for improvement. Protocols were developed to standardize and encourage early enteral feeding as well as to reduce the time feeds are interrupted for patients who were going for surgeries or for various other reasons. Educational interventions were conducted with lectures to physicians and nurses. Visual aids in the form of screensavers at each bedside computer served as reminders to the team to optimize feeding. A subsequent audit was then conducted to determine the improvement in achieving the desired outcomes, namely the amount of calories and proteins received as well as the proportion of patients who achieved >70% of their target calories and proteins. We considered target calories to be 25 kcal/kg/day and target proteins to be 1.5 g/kg/day.
Results Patients received more calories (78.3% vs. 59.1%) and more proteins (70.2% vs. 54.6%) post implementation. The mean percentage of patients in the post group who achieved >70% of required calories was 80.1% versus 30.9% in the pre group. The mean percentage of patients who achieved >70% of required proteins was 58.3% versus 32.1% in the pre group.
Conclusion The multipronged approach of the quality improvement methodology helped to increase the provision of calories and proteins in our population of critically ill surgical patients. However, there is still room for improvement in terms of achieving optimal enteral nutrition targets early in our population. There is also a need to look into sustaining such results.

P396

Could preoperative and postoperative optimal nutrition support modulate the inflammatory response and clinical outcome of severe malnourished surgical patients with gastrointestinal neoplasia?

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Critical Care 2015, **19(Suppl 1):**P396 (doi: 10.1186/cc14476)

Introduction Our aim was to assess whether perioperative and postoperative optimal 7-day nutrition support could modulate the inflammatory status and clinical outcome of severe malnourished patients with surgery for gastrointestinal neoplasia.
Methods A prospective randomized study of 64 patients with gastrointestinal neoplasia, severe malnourished BMI <18.5, albumin level <3 g/dl, BW loss >10%, NRS >3, scheduled for surgery, allocated into two groups. Group A: 32 patients, minimal enteral nutrition in the postoperative period according to tolerance, medium 500 kcal/day. Group B: 32 patients received optimal parenteral nutrition support (25 kcal/kg/day) 3 days before surgery and continued for at least 4 days postoperatively. We measured CRP, fibrinogen, IL-6, TNF, albumin level preoperative and at 96 hours, the incidence of complications, and the length of ICU stay.
Results There was a significant decrease in the values of CRP, IL-6, TNF, albumin at 96 hours in group B. No difference in fibrinogen. A significantly lower rate of complications and a shorter time of ICU stay were observed in group B. See Figures 1 and 2 (overleaf).
Conclusion Perioperative optimal nutrition support for at least 7 days could modulate the inflammatory status and clinical outcome of severe malnourished surgical neoplasic patients.

P397

Does discontinuation of the use of hydroxyethyl starches in the critically ill cardiac surgery patient have an impact on caloric intake?

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Introduction After research revealed unwanted effects of the use of starches in critically ill patients, its use in the immediate postoperative period of cardiac surgery patients came to an abrupt ending. However, they constitute an important source of non-intended calories, providing 4 calories per gram. We investigated whether this phenomenon (involuntary) attributed to an increase in caloric debt for this critically ill patient population.
Methods We retrospectively searched a database of 417 elective cardiac surgery patients, representing 5,004 observation-days. Caloric

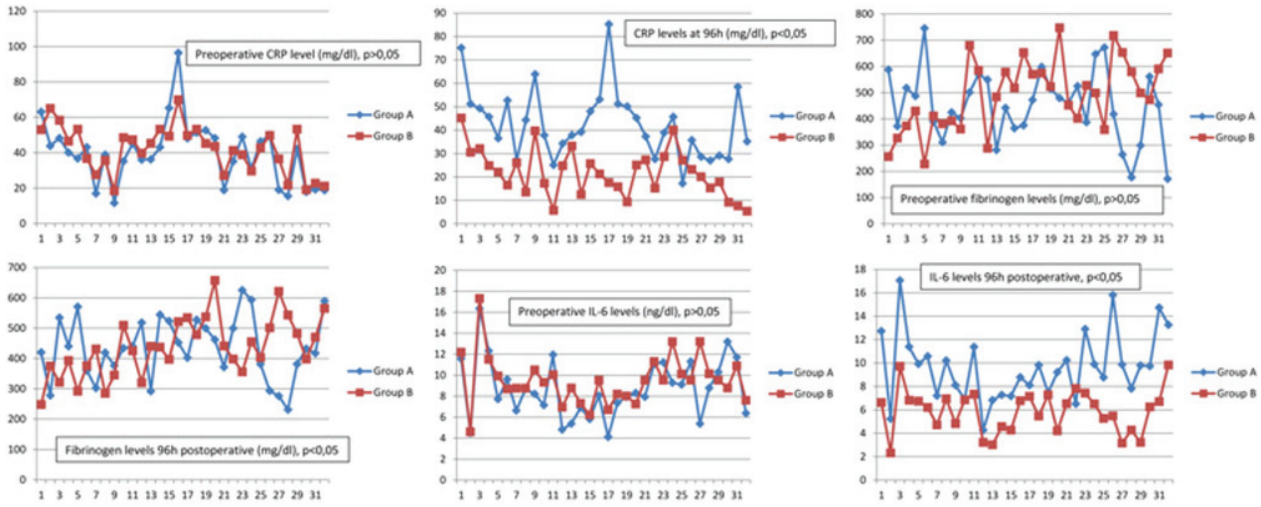


Figure 1 (abstract P396). Results 1.

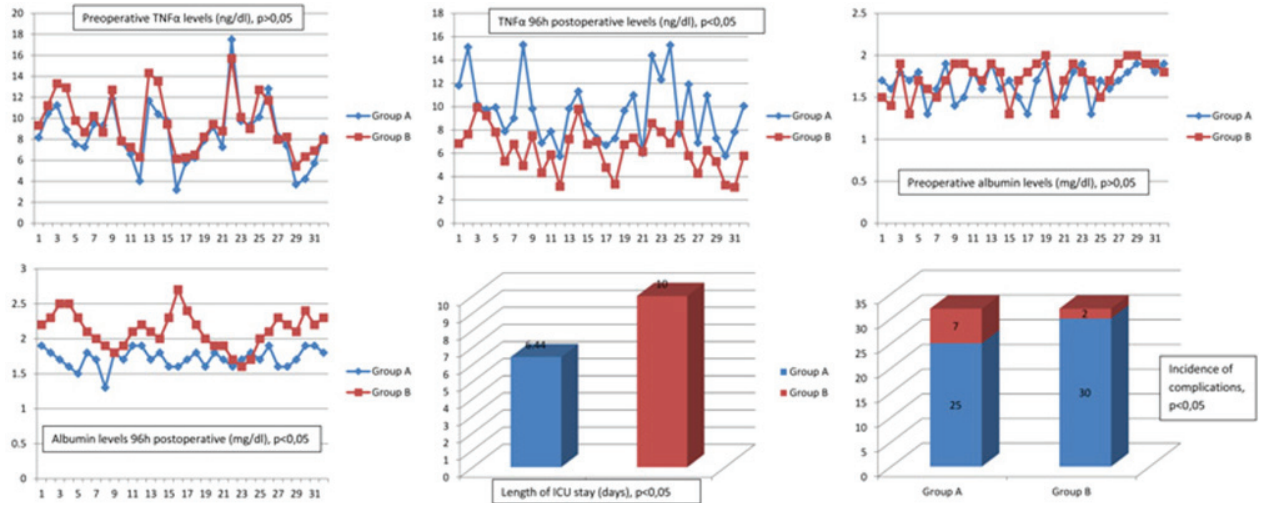


Figure 2 (abstract P396). Results 2.

intake was evaluated in the group of patients before and after the cessation of starch use.
Results Patient characteristics and caloric needs were comparable: 2,054 ± 395 kcal/day and 2,056 ± 347 kcal/day. The 140 patients who in the immediate postoperative period had volume resuscitation without the use of starches had a mean non-intended fluid caloric intake of 69 (± 36.3) kcal/day. The group of 277 patients who received starches in the postoperative period had a mean non-intended fluid caloric intake of 105 (± 100.2) kcal/day.
Conclusion Withdrawal of the use of starches resulted in a 34% decrease of non-intended caloric intake by fluids, contributing to caloric debt. Whether outcome is influenced and/or whether these findings are clinically relevant needs further research.

P398

NUTRIC score in oncologic patients

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Critical Care 2015, **19(Suppl 1):**P398 (doi: 10.1186/cc14478)

Introduction The NUTRIC score is a tool designed to quantify the risk of critically ill patients developing adverse events that may be modified by aggressive nutrition therapy, in the general population of an ICU. Cancer patients are more prone to be at nutritional risk due to the disease and treatment complications. Our aim was to characterize NUTRIC score behavior in the population of patients admitted to an oncologic ICU.
Methods Between January and June 2014 we applied the NUTRIC score to all patients, age >18 years, without cerebral death criteria and with a length of stay (LOS) >72 hours. Data were collected and analyzed using SPSS v20.0. To evaluate the impact on mortality we used logistic regression.
Results Sixty-nine patients were included, 23 women (33.3%) and 46 men (66.7%). Most patients were aged between 50 and 75 years (72.5%) and had normal range weight 58% (n = 40). The mean LOS was 11.56 (minimum: 3 to maximum: 69). The most common motive for admission was sepsis (7.7%, n = 26). APACHE II score was above 15 in 77% of the patients (n = 53) and SOFA score was superior to 6 in 56.5% (n = 30). The NUTRIC score was low risk in 42% (n = 29) of the patients and high in 58% (n = 40). Twenty-eight-day mortality was 26.1% (n = 18). A high NUTRIC score corresponded to a 22-fold increased odds of dying in the first 28 days (P <0.001). Both APACHE II and SOFA were mortality predictors alone, with an increase of 1 point in APACHE score corresponding to an increase of 14% (P = 0.002) and an increase of

1 point in SOFA corresponding to an increase in the odds of being dead at 28 days ($P = 0.002$). Body mass index, age, number of comorbidities, and days in the ICU did not correlate with mortality.
Conclusion The NUTRIC score is a good tool in cancer patients to predict 28-day mortality. Nevertheless, the only compounds of the NUTRIC score that correlated independently with mortality were APACHE II and SOFA scores. Further investigation towards the inclusion of other categories such as tumor staging and the type of tumor could be useful to develop a specific prognostic tool for this population.

P399

Early calorie-dense immune nutrition in haemodynamically compromised cardiac patients

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Critical Care 2015, **19(Suppl 1):**P399 (doi: 10.1186/cc14479)

Introduction The aims of present study were to test the hypothesis that early enteral nutrition (EN) with calorie-dense food supplemented with glutamine improves recovery of nutritional status in critically ill cardiac patients and to evaluate their resting energy expenditure (REE).
Methods A prospective randomised study of 40 adult cardiac patients undergoing elective cardiopulmonary bypass surgery no more than 24 hours before eligibility assessment, complicated with acute heart failure syndrome. Patients were randomised to receive either standard isocaloric isonitrogenic early EN (standard group, $n = 20$) or immunomodulating early EN (immune group, $n = 20$). The daily energy target was set using REE measured by indirect calorimetry (CCM Express; Medgraphics, St. Paul, MN, USA). Serum prealbumin, transferrin, C-reactive protein, blood lactate and clinical characteristics were analysed.
Results The actual REE was an average of 6.8 and 7.5 kcal/kg/day higher than the REE calculated using the Harris–Benedict equation and empiric approach (25 kcal/kg/day), respectively (Figure 1). Early EN with immune formula was associated with higher levels of prealbumin concentration on the 14th day (0.13 ± 0.01 g/l and 0.21 ± 0.1 g/l; $P = 0.04$) and transferrin on the 3rd, 5th, 7th, and 14th day ($P < 0.05$) after surgery.
Conclusion Haemodynamically compromised cardiac patients have increased REE, which in the absence of indirect calorimetry should be set at 30 kcal/kg/day. Early EN using a calorie-dense immune formula leads to better recovery of nutritional status as assessed by serum protein levels.

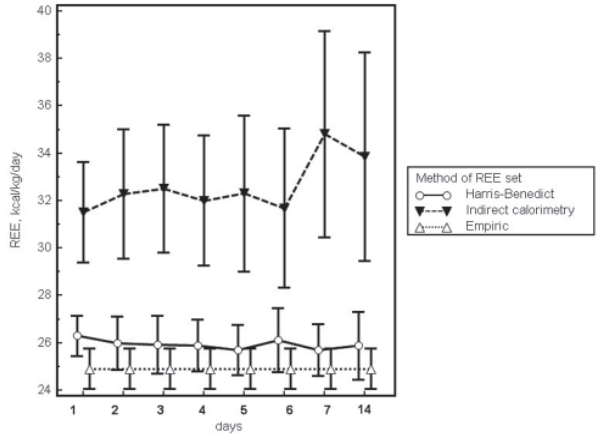


Figure 1 (abstract P399). Indirect calorimetry measured significantly higher resting energy expenditures.

P400

Measurement of skeletal muscle glycogen status in critically ill patients: a new approach in critical care monitoring

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Introduction Critically ill patients experience hypermetabolism increasing substrate utilization, especially glucose oxidation. Glycogen is the main source of glucose in the body, being 85% and 15% stored in skeletal muscle and liver respectively. Since glycogen stores are limited we evaluated the hypothesis that critical illness could be associated with glycogen depletion leading to skeletal muscle catabolism for gluconeogenesis and eventually resulting in cachexia, an important determinant of future ICU survival and ICU-acquired weakness.
Methods Nine critically ill patients (58.75 ± 25 to 75 years old) with an ICU stay from 1 day to 5 weeks were evaluated for skeletal muscle glycogen content using a rapid, non-invasive high-frequency ultrasound methodology (MuscleSound®, Denver, CO, USA). Scans were obtained from the rectus femoris and vastus lateralis muscles. Glycogen content was measured with a score from 0 to 100 according to the MuscleSound® scale. Patients had a variety of primary diagnoses including septic shock ($n = 3$), hemorrhagic shock/abdominal hypertension ($n = 1$), hypovolemic shock/post major oncologic surgery ($n = 1$), trauma ($n = 3$), and burn injury ($n = 1$).
Results Six out of nine patients had no glycogen present in the muscle (score = 0). The other three patients had glycogen scores between 5 and 15 which are well below scores of healthy individuals (reference 50 to 70). As a comparison we collected post-competition levels in competitive athletes, which decrease their glycogen stores (score 15 to 25) but are well above those of most critically ill patients we have studied.
Conclusion This is the first time that muscle glycogen stores have been evaluated in critical illness. Our data show severe glycogen depletion in ICU patients which probably leads to muscle catabolism necessary for gluconeogenesis, eventually resulting in cachexia. This finding poses severe metabolic challenges for ICU patients in which interfering with recovery can contribute to poor survival. In light of our findings, re-evaluation of nutritional protocols and potential anabolic/anti-catabolic therapy to decrease muscle catabolism may improve survival. Different therapeutics that may prevent hypermetabolism (such as beta-blockers) should be re-evaluated along with anabolic agents (that is, oxandrolone) which could counteract the severe catabolic response in critical illness. Monitoring of muscle glycogen repletion could signal the transition from the catabolic to anabolic phase.

P402

Plasma glutamine after acute or elective admission on the ICU

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Critical Care 2015, **19(Suppl 1):**P402 (doi: 10.1186/cc14482)

Introduction Low plasma glutamine concentrations are associated with unfavourable outcome at acute ICU admission. We questioned whether there is a difference in plasma glutamine level after acute or elective ICU admission.
Methods We performed a single-centre prospective observational study in a 22-bed mixed ICU. Exclusion criteria were age <18 years and total parental nutrition at admission. Patients were divided into two groups: elective surgery and acute admissions. Blood samples were taken at ICU admission and daily at 6.00 a.m. Glutamine levels were measured using the Bioprofile 100 plus analyser (Nova Biomedical UK, Cheshire, UK). A Mann–Whitney U test was used to detect differences between groups and a Bonferroni method to correct for multiple comparisons.
Results We included 88 patients after elective surgery (76 cardiac and 12 general surgery) and 90 patients after acute admission (27 sepsis, 17 acute surgery, two trauma and 44 medical). Baseline characteristics are presented in Table 1. Plasma glutamine levels at admission were significantly lower in acute patients compared with elective surgery, 0.25 mmol/l (IQR 0.09 to 0.37) versus 0.43 mol/l (IQR 0.33 to 0.55)

Table 1 (abstract P402)

	Elective	Acute
Age (years)	68 ± 10	59 ± 17*
APACHE IV	46 ± 14	67 ± 29*
LOS ICU	2 (2 to 2)	4 (2 to 7)*
Survival (*n*)	88	85*

Mean ± SD or median (IQR). *P <0.01.

(P <0.001). There appeared to be a significant correlation between the APACHE IV score and glutamine levels (R = 0.52, P <0.001). Moreover, in a backward linear regression analysis this correlation was independently associated with APACHE IV scores and the presence of infection, but not with the type of admission.

Conclusion Plasma glutamine levels were significantly lower after acute admission compared with elective surgery. In both groups a considerable amount of patients had decreased glutamine levels, but this was not independently associated with the type of admission. In contrast to previous studies we found that glutamine levels were determined by severity of illness and the presence of an infection.

P403

Intravenous fish oil lipid emulsions in ICU patients: an updated systematic review and meta-analysis

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Critical Care 2015, **19(Suppl 1):**P403 (doi: 10.1186/cc14483)

Introduction Intravenous fish oil (FO) lipid emulsions (LEs) are rich in ω-3 polyunsaturated fatty acids, which exhibit anti-inflammatory and immunomodulatory effects. We previously demonstrated that FO-containing emulsions may be able to decrease mortality and ventilation days in the critically ill. Over the last year, several additional randomized controlled trials (RCTs) of FO-based LEs have been published. Therefore, the purpose of this meta-analysis was to update our systematic review aimed to elucidate the efficacy of FO-based LEs on clinical outcomes in the critically ill.

Methods We searched computerized databases from 1980 to 2014. Overall mortality was the primary outcome and secondary outcomes were infections, ICU and hospital length of stay (LOS), and mechanical ventilation (MV) days. We included RCTs conducted in critically ill adult patients that evaluated FO-based LEs in parenteral nutrition (PN) or enterally fed patients. We analyzed data using RevMan 5.1 (Cochrane IMS, Oxford, UK) with a random effects model.

Results A total of 10 RCTs (n = 733), including four trials published over the last year, met inclusion criteria. There was considerable heterogeneity in interventions tested in these trials. No effect on overall mortality was found. When the results of five RCTs that reported infections were aggregated, FO-containing emulsions significantly reduced infections (RR 0.64; 95% CI, 0.44 to 0.92; P = 0.02, heterogeneity I^2 = 0%). Furthermore, FO-based LEs were associated with a trend toward a reduction in MV days (WMD, –1.41; 95% CI, –3.43 to 0.61; P = 0.17, heterogeneity I^2 = 0%), and hospital LOS (WMD –4.06; 95% CI, –10.14 to 2.03; P = 0.19, I^2 = 89%, P <0.00001), without effect on ICU LOS. See Figure 1.

Conclusion FO-based LEs may be associated with a reduction in infections, as well as clinically important reductions in duration of ventilation, and hospital LOS. Nevertheless, according to current literature there is inadequate evidence to give a final recommendation on the routine use of FO-containing emulsions in PN and/or as a pharmaconutrient strategy in enterally fed critically ill patients. Further large-scale RCTs which should aim to consolidate potential positive treatment effects are warranted.

P404

Glutamine administration in sepsis: enteral, parenteral or both? Experimental study in swine

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Critical Care 2015, **19(Suppl 1):**P404 (doi: 10.1186/cc14484)

Introduction Glutamine (GLN) is recommended in the critically ill for i.v. administration but enteral use is not quite clarified. We decided to measure GLN plasma levels in healthy and septic swine after GLN given by i.v., enteral or both routes, over a 3-hour period.

Methods Sepsis was induced by *E. coli* LPS. GLN was infused: i.v. through the femoral vein (0.5 g/kg); enterally (E) through jejunostomy (0.5 g/kg); and i.v. + E. Blood was drawn continuously from the femoral artery and the portal vein for GLN plasma levels in systemic-S and portal-P circulation.

Results In healthy swine, GLN levels remained stable, both in S and P; i.v. infusion, and even more i.v. + E significantly increased GLN in the S circulation (P <0.001), whereas E infusion failed to do so (P = 0.4). On the contrary, GLN P levels were significantly increased after i.v. + E infusion, as well as after E infusion (P <0.001) and to a lesser extent, after i.v. (P <0.001). In sepsis, both S and P GLN levels decreased significantly.



Figure 1 (abstract P404).

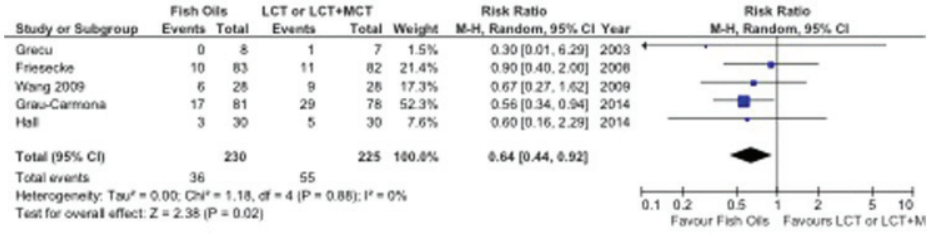


Figure 1 (abstract P403). Effects of parenteral fish oil lipid emulsions on infections.

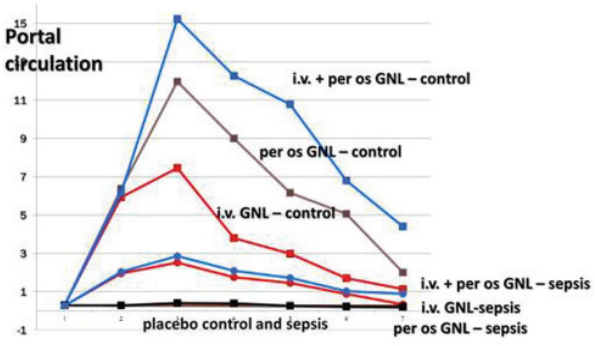


Figure 2 (abstract P404).

As previously, i.v. ($P = 0.001$) and even more i.v. + E ($P < 0.001$) infusion significantly increased S GLN levels, while E infusion failed to have any effect. In the P vein, both i.v. ($P = 0.02$) and i.v. + E ($P < 0.001$) GLN increased significantly, whereas the E had no effect ($P = 0.08$). See Figures 1 and 2.

Conclusion In our experimental early sepsis model, a combination of E and i.v. GLN seems to be the most appropriate; this results in high GLN levels for the functional needs, including those of the gut mucosa.

Reference

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P405

Prehospital factors associated with an ICU admission from the emergency department

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Critical Care 2015, **19(Suppl 1):**P405 (doi: 10.1186/cc14485)

Introduction This study aimed to describe the patient characteristics and prehospital factors associated with an ICU admission from the ED. There is a paucity of information about the early recognition of critical illness by paramedics; especially in the Australian prehospital setting.

Methods A retrospective cohort study, July 2012 to June 2014, conducted in the Perth metropolitan area, which is served by a single ambulance service. Adult patients were included if transported to a public hospital ED that used the ED information system (EDIS) (seven of eight EDs) and were admitted to the ICU from the ED (ED-ICU group). Patients aged <16 years, those from rural areas or transfers were excluded. We used existing ambulance clinical data linked to EDIS data. Prehospital cohort characteristics are described using univariate statistical techniques. Logistic regression was conducted with admission to the ICU from the ED (critical illness surrogate) as the outcome variable. Variables included in regression models were age, sex, paramedic-identified urgency, that is the time patients should be seen by a doctor based on the Australasian Triage Scale, paramedic-identified patient problem and the time taken from the ambulance service receiving the call to hospital arrival. Physiological variables: systolic blood pressure (SBP), heart rate (HR), respiratory rate (RR), temperature, oxygen saturation, and GCS were included in the logistic models.

Results Of the 142,448 eligible patients transported by ambulance, 1,076 (0.75%) were admitted to the ICU from the ED: the ED-ICU group was younger (mean 53 vs. 61 years, $P < 0.001$). Seventeen percent of ICU patients were transported as Urgency 1 (resuscitation/immediate) and 58% as Urgency 2 (within 10 minutes) while 70% of non-ICU patients were transported as Urgency 3 to 5 ($P < 0.001$). Thirteen percent of ICU patients had a SBP <90 mmHg, 15% had a HR ≥130 and 19% had a RR >30. Drug overdose (21%) and respiratory conditions (18%) were the most common ICU conditions identified by paramedics for the ED-ICU group. All variables entered into the logistic models were significant (all $P < 0.001$) except the time taken from receiving the call to hospital arrival ($P = 0.48$).

Conclusion Three-quarters of the ED-ICU patients were transported to the ED with high urgency. Currently no prehospital severity of illness or early warning system (EWS) is used in our ambulance service. Given the small proportion of ED-ICU patients who presented with abnormal observations, it is unlikely that introducing an EWS would alter practice or patient outcome.

P406

Reliability of a new French-language triage algorithm for out-of-hours primary care calls: the SALOMON rule

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Critical Care 2015, **19(Suppl 1):**P406 (doi: 10.1186/cc14486)

Introduction Because of increased workloads associated with primary care physician (PCP) shortage, many western countries have been facing the difficult challenge of optimizing their out-of-hours primary care services. PCPs initially gathered in small rotation groups, and then further collaborations led to larger-scale cooperatives. In such models, implementation of patient call triage is mandatory to increase the efficiency, quality and safety of care [1]. Organization models differ, from the PCP performing all patient calls to nurses and nurse assistants answering calls and performing triage, but no validated triage algorithm has been reported to date. We developed a specific French-language triage algorithm called SALOMON (Système Algorithmique Liégeois d'Orientation pour la Médecine Omnipraticienne Nocturne) in order to guide nurse triage PCP out-of-hours calls. The present study tested this algorithm reliability.

Methods The SALOMON algorithm is based on 53 common presentation flowcharts using specific discriminators to triage calls into four categories according to the level of care required: emergency medical services, nonemergent visit to local emergency department, PCP home visit or PCP delayed consultation. Using an appropriate statistical test, we assessed the accuracy of presentation flowchart and triage category selections attributed to 130 clinical scenarios, by 10 different nurses, in comparison with references established by a local team of experts, at two different time periods: immediately after training (T0) and 3 to 6 months after algorithm practice (T1).

Results Overall selection of flowcharts was accurate for 94.1% of scenarios at T0 and 98.7% at T1. Triage category selection was correct for 93.3% of scenarios at T0 and 98.4% at T1. Both flowchart selection and triage category were correct in of 89.5% case in T0 and at 97.5% T1. When an incorrect flowchart was used, triage category remained accurate in 64.9% and 70.5% respectively. Both flowchart and triage selection accuracy improved significantly from T0 to T1 ($P < 0.0001$).

Conclusion The results of the present study revealed that using the SALOMON algorithm is reliable for out-of-hours PCP call triage by nurses. Validity of this rule may be further evaluated through its actual implementation in real-life conditions.

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P407

Adequacy of trained assistance, emergency equipment and drugs at emergency calls in the ICU and in remote areas of the hospital

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Critical Care 2015, **19(Suppl 1):**P407 (doi: 10.1186/cc14487)

Introduction We aimed to identify the adequacy of assistance provided and to assess correct anaesthetic equipment and drug availability at emergency calls made in the ICU and in remote areas of the hospital. Emergency calls often involve managing critically ill patients with the highest mortality results. The importance of a clinical team with the necessary competencies and the right level of resources are paramount.

Methods We undertook a prospective survey of all adult patients with emergency calls put out to the anaesthetic team in a London district

general hospital over a 6-week period. We performed a snapshot audit of equipment in resuscitation trolleys across each ward and in the radiology department. We compared the data collected on available equipment with the standard set by the Resuscitation Council (UK) Recommended Minimum Equipment Checklist [1]. The survey addressed the availability, clinical competency and appropriate duration of stay of the anaesthetic assistant at the emergency calls. Further qualitative data were collected on the availability of required emergency drugs.

Results During the study period 44 emergency calls were attended. Twenty-three (52%) of these calls were in the accident and emergency department, and four (9%) in the ICU. Survey results demonstrated two cases where no anaesthetic assistant arrived at the emergency call put out to them. In cases where timely assistance was available, the assistant did not have the adequate clinical and anaesthetic skills required by the attending physician. In 6% of cases where skilled assistance was required ($n = 2$), it was felt that the assistant did not stay for the clinically required length of time. Emergency drugs required were found to not be available in 11% of cases ($n = 5$) and in 17% of cases ($n = 6$) the necessary emergency equipment was not available. Data were collected on equipment from 17 resuscitation trolleys. The inadequacies identified were the oxygen cylinders were filled less than 75% full in 41% cases ($n = 7$) and end-tidal capnography was identified to be absent.

Conclusion Emergency calls require standards to be met involving the competency of responding team members and adequate resources. This leads us to question whether guidelines should exist regarding the clinical competency and timeliness of the assistant available to the physician at emergency calls.

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P408

Use of an electronic early warning score and mortality for patients admitted out of hours to a large teaching hospital

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Introduction There is widespread concern regarding excess mortality for patients admitted to hospital out of hours. We introduced an electronic track and trigger system (Patientrack) with automated alerts in a large university teaching hospital between 2010 and 2012. The system computes the patient's early warning score and alerts medical staff via a pager. It is operational 24 hours a day, 7 days a week and could be an effective tool to reduce variations in mortality throughout the working week.

Methods We extracted hospital outcome data for all admissions during the financial years between 2007 and 2014. We identified variables that predicted mortality and incorporated them into a multivariate logistic regression model to assess risk of death for admissions in hours (9:00 am to 5:00 pm, Monday to Friday) versus out of hours (all other times).

Results Data were available for 1,180,268 hospital admissions, of which 7,264 (0.6%) died. Predictors for hospital mortality included: age, male sex, unplanned admission and admission from supportive care. Risk of death for out-of-hours admissions was not significantly different to in-hours for any year (1.01 (0.92 to 1.11), $P = 0.784$). There was a significant fall in risk of death over the 7-year period compared with baseline values in 2007/08 (Table 1).

Table 1 (abstract P408). Overall risk of death ratios compared to 2007/08

Year	ROD	95% CI
2008/09	1.01	0.73 to 1.5
2009/10	1.03	0.74 to 1.5
2010/11	0.46*	0.33 to 0.7
2011/12	0.31*	0.22 to 0.4
2012/13	0.27*	0.2 to 0.39
2013/14	0.26*	0.2 to 0.37

*P <0.001.

Conclusion In our cohort there was no evidence of increased mortality for patients admitted out of hours compared with in hours. This remained true after adjustment for age, sex, emergency admissions and admission source. Our data demonstrated an overall fall in risk of death over the study period. The introduction of Patientrack could have contributed to this reduction in mortality.

P409

Revitalising the medical emergency team call

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Introduction Medical emergency team (MET) calls are quickly becoming an integral part of the response to a deteriorating patient in Australia. Conceptually the MET call response incorporates a structured approach, but in practice this can quickly disintegrate. This collapse of method can leave patients without clear treatment plans and staff disenfranchised. We sought to improve the process of the MET call response at our regional hospital by introducing targeted interventions focused on teamwork, communication, leadership and role allocation.

Methods We invited junior doctors and nurses to complete a survey designed by a multidisciplinary MET Call Working Group; 138 staff (40% of population) completed the survey. Based on analysis of responses, a focused three-pronged intervention was formulated and implemented hospital wide. The arms of the intervention were: identification of the name and role of each staff member using highly visible labels; role allocation according to policy written through a multidisciplinary working group; and a time out during the response allowing a structured synopsis of the patient's current status to be communicated to the team. The intervention was preceded by extensive staff education, and 175 staff (50%) completed the survey 6 months later to assess its success.

Results The intervention significantly increased satisfaction amongst staff regarding: identification of the team leader and other key staff members at the response; and time out effectiveness in reducing repetition and improving staff understanding of the patient's status and medical issues. We found no significant change in staff perceptions regarding the clarity of the ongoing treatment plan at the end of the MET call response.

Conclusion Utilising a low-cost intervention in a regional setting, we were successful in improving staff perceptions of role allocation and communication within our MET call responses. The intervention also led to significantly increased overall satisfaction with the MET call system. Through our surveys we have identified other facets of the MET call response that also require attention. Given our encouraging results we are designing a follow-up intervention incorporating structured multidisciplinary training in MET call scenarios.

P410

Successful implementation of a medical emergency team: 2-year experience in a teaching hospital

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Introduction A medical emergency team (MET) was introduced in our institution in January 2012 to provide timely response to the needs of acutely ill inpatients and cardiac arrest calls. The MET assesses the patient and prescribes a management plan for the responsible team to follow; promptly stabilising and transferring patients to a place of safety where required. We aimed at evaluating the effects of introducing the MET on clinically relevant processes and outcomes.

Methods Prospective data were analysed using STATA 10.1. The primary outcome measure was immediate mortality (defined as mortality at

conclusion of the MET intervention); the secondary outcome measures were admission to critical care after a MET call and cardiac arrest.
Results A total of 5,763 MET calls were made between 9 January 2012 and 4 March 2014, of which 5,310 (92.1%) were MET calls, 349 (6.1%) cardiac arrest calls, 36 (0.6%) false alarms and 68 (1.2%) unclassified. The number of calls increased by 32.7% from 2,255 in 2012 to 2,993 in 2013, with all month-specific comparisons showing significant increases in MET activity (ranging from 0.5% to 103.6% increases). MET activity displayed cyclical yearly changes, with the winter months and the month of August (junior doctors' changeover period) being particularly busy. Median response time (interquartile range) was 1 (1 to 2) minutes, with 99.1% calls attended to within 3 minutes. There were 210 (3.64%) immediate deaths (with no significant differences between years), 112 (1.9%) patient transfers to critical care, 233 (4%) patients were transferred to other locations (other than critical care) while 4,697 (81.5%) patients remained on the ward of origin. In 408 cases (7.1%) a do-not-resuscitate order was instituted. On multiple logistic regression analyses, when the type of call was taken into consideration, the response time had no influence on primary (mortality OR = 0.83, 95% CI = 0.63 to 1.09, $P = 0.18$) and secondary outcomes (admission to critical care OR = 0.85, 95% CI = 0.62 to 1.17, $P = 0.33$; subsequent cardiac arrest OR = 0.57, 95% CI = 0.27 to 1.2, $P = 0.14$).
Conclusion The MET has been successfully implemented, with demand for its services having increased by 32.7% in 1 year. The unadjusted immediate mortality rate of patients for whom a MET/cardiac arrest call is activated is 3.64%. Response time had no influence on mortality, most probably due to the rapid response time. Immediate mortality was low, probably as a result of early adequate intervention. Further evaluation of overall hospital mortality is warranted for future studies.

P411

Evaluation of emergency call Code Blue over a 5-year period

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Introduction Code systems are the emergency call and management systems for rapid response in healthcare institutions. The main aim of these systems is to provide common institutional understanding of what is necessary to be done immediately at the time of an event. Code Blue (CB), which is used throughout the world and was described in the 2008 service quality standards of Turkey, defines the necessary emergency intervention in cases of respiratory or cardiac arrest. This study aimed to evaluate the clinical and application data of patients for whom a CB call was made between 2009 and 2013.
Methods After approval of local ethics committee, retrospective examination was made of CB forms. The age and gender of the patient, diagnosis, department to which admitted, time of CB call, reason for CB, whether or not CB was appropriate, whether or not CPR was applied, duration of CPR if applied, APACHE II and PRISM scores and predicted mortality were recorded from the hospital automated record system and the CB form. Patients who refused treatment or who could not reach the necessary parameters for the calculation of APACHE II and PRISM scores were excluded.
Results From CB calls for a total of 1,195 patients over the 5-year period, 1,035 (86.6%) were evaluated. The rate of erroneous CB was 36.9%. Patients comprised 413 (39.9%) females and 622 (60.1%) males with a mean age of 59.73 ± 23.13 years (range, 0.1 to 102 years). The distribution of total cases over the 5 years (2009 to 2013) was 15.5%, 25.2%, 26.5%, 19% and 13.8% respectively. Distribution according to clinic was emergency internal (37.5%), internal (16.5%) and emergency surgical (9.5%). Clinical diagnosis was cardiac 28.8%, neurological 15.6% and end-stage cancer 13.5%. A total 19.9% of the patients were those discharged from intensive care. The total survival rate was 59.6%. The duration of CPR in survivors was statistically longer than in nonsurvivors ($P < 0.01$). There was no statistically significant relationship between the duration of CPR and age ($P > 0.05$). The overall mean time taken to reach the patient was 102.71 ± 22.47 seconds, which reduced to 93.64 ± 19.91 seconds in 2013. The APACHE II–PRISM scores and mortality rates were low in the cases of erroneous CB ($P < 0.05$).
Conclusion The time taken to reach patients conformed with the global standard mean 2 to 3 minutes [1]. The rates of erroneous CB and time to reach patients reduced each year due to more staff experienced and knowledgeable in CB and the structuring of the emergency clinic.
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P412

Attention Code Blue: a comprehension of in-hospital cardiac arrest from a multispeciality hospital in South India

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Introduction Numerous American and European studies have associated survival rates of in-hospital cardiac arrest (IHCA) with different quality markers. There has been a paucity of studies that explain IHCA in Asian populations. This study was conducted to assess the characteristics and survival among patients suffering from IHCA.
Methods All Code Blue activations from 1 January 2012 to 31 December 2012 were analyzed retrospectively. Data were gathered from the Code Blue form and finer details of individual patients were linked through their medical records. Code Blue was activated only for events that happened outside the medical and surgical ICUs.
Results A total of 260 Code Blue activations were made, out of which there were 203 true cardiac arrest events among 40,168 in-patients; the cumulative incidence of the same was 0.51%. Mean (SD) duration of arrival of the Code Blue Team (CBT) to the scene was 64.5 (27.7) seconds. Cardiovascular illness was the predominant baseline morbidity but none of the baseline illness showed increased risk of mortality in this group. Among true cardiac arrest events, 92.6% was due to pulseless electrical activity/asystole and 7.7% was due to ventricular fibrillation (VF)/pulseless ventricular tachycardia (VT); both of these did not have any difference on the initial outcome. But having an initial rhythm of VF/pulseless VT had 90% more chance for discharge from the hospital, with $P = 0.04$. Although arrival time of the CBT did not have any influence on the final outcome, duration of resuscitation ≤20 minutes had an odds ratio of 10.6 with $P < 0.001$ favoring return of spontaneous circulation over death after controlling for age. Of the 203 patients who had true cardiac arrest events, 43 (21.2%) were discharged from the hospital. Good neurological outcome at discharge was seen among 22 (10.8%) of the patients based on Cerebral Performance Category Score.
Conclusion Our experience shows that out of every 1,000 patients admitted to our hospital, about five sustained cardiac arrest, of whom only 11.3% survived to hospital discharge with good neurological recovery. Variation in the effectiveness of the cardiopulmonary resuscitation quality in comparison with world data could be due to the inherent difference in the severity of the primary illness in the patients and diversity in the reported data.
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P413

Are we failing to teach cardiopulmonary resuscitation (CPR) in schools? A pilot study to assess CPR and automated external defibrillator training in London schools

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Introduction Mortality from cardiac arrest remains high [1]. Bystander cardiopulmonary resuscitation (CPR) and the use of automated external defibrillators (AED) are two of the most important factors favouring survival [2]. CPR/AED training in schools is a recommended intervention for significantly improving training rates across a large population [3]. The current practice for CPR/AED training in London schools is unknown. The primary aim of this study was to assess current

practices relating to CPR and AED training in London secondary schools.
Methods We conducted a registered audit of CPR and AED training in London schools. Secondary schools were identified via web links for each of the London Borough Councils. Telephone interviews with school staff familiar with CPR and AED training practices were conducted prospectively using a standardized web-based survey. All survey response data were captured electronically. We defined universal training as any programme which delivers CPR and AED training to all students in the school. We used simple descriptive statistics to summarise the results.
Results A total of 51 schools completed the survey covering an estimated student population of 54,037. There were four (8%) schools that provide universal training programmes and an additional 23 (45%) offer optional training programmes for students. There were 16 (31%) schools which have an AED available on the school premises. The most common reasons for not having a universal CPR training programme is the requirement for additional class time (15/51; 29%) and that funding is unavailable for such a programme (12/51; 24%). There were three students who died from sudden cardiac arrest over the period of the past 10 years.
Conclusion CPR and AED training rates in London secondary schools are low. The majority of schools do not have an AED available on premises. The most common reason for not providing CPR training is the requirement for additional class time. These data highlight an opportunity to vastly improve CPR training rates in a large population. Future studies should assess programmes which are cost-effective and which do not require significant amounts of additional class time.
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P415

Magical manoeuvre: a 5-second instructor's intervention helps lightweight female rescuers achieve the required chest compression depth

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Introduction Adequate chest compression (CC) depth is crucial for resuscitation outcomes. Lightweight rescuers, particularly women, are often unable to achieve the required 5 to 6 cm CC depth. This nonrandomised cohort study investigated new strategies to improve CC performance.
Methods Data were prospectively collected from January 2011 to January 2012 from 336 female medical and pharmacy students undergoing CPR training at the Lithuanian University of Health Sciences. During the training process, the instructors performed a simple 5-second intervention (Andrew's manoeuvre) with all of the rescuers in the study group. The instructor pushed 10 times on the shoulders of each trainee while she performed CCs to achieve the maximal required compression depth. Immediately after training, the participants were asked to perform a 6-minute BLS test on a manikin that was connected to a PC with SkillReporter™ System software (Laerdal, Norway); the quality of the participants' CPR skills was then evaluated.
Results The CC depth in the study group increased by 6.4 mm ($P < 0.001$) compared with the control group (52.9 vs. 46.6 mm). A regression analysis showed that Andrew's manoeuvre increased the depth of the CCs among women by $14.87 \times (1 - 0.01 \times \text{weight})$ mm.
Conclusion Andrew's manoeuvre during CPR training significantly improved the performance of the female rescuers and helped them achieve the CC depth required by 2010 resuscitation guidelines. It is most effective among the women with the lowest body weight.
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P416

TRACE: a new protocol for ultrasound examination during out-of-hospital cardiac arrest

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Introduction Implementation of point-of-care ultrasound examination into cardiopulmonary resuscitation (CPR) may increase diagnostic accuracy for determining the cause of cardiac arrest. However, current protocols either do not reflect all causes detectable by ultrasound or are too complicated for prehospital use. Thus, we decided to construct and validate a new protocol TRACE (ThoRacic and Abdominal sonography in Cardiac arrEst) for ultrasound examination during out-of-hospital cardiac arrest (OHCA).
Methods We designed a new protocol for ultrasound examination during OHCA to increase the success rate for the establishment of OHCA cause. The subcostal view was performed during planned rhythm check to assess the presence of cardiac tamponade and size of the right and left ventricle and inferior caval vein. Thereafter, during ongoing cardiac compressions, Morrison's pouch and right pleural space were investigated to exclude intraperitoneal and inrapleural free fluid. The same procedure was applied on the left side of the body. Finally, the anterior thoracic view was done to exclude pneumothorax. Working diagnosis was compared with the final in-hospital diagnosis or autopsy.
Results We examined 40 consecutive OHCA patients. Correct cause of OHCA during CPR was recognised in 38 patients (95%). Leading causes were acute coronary syndrome (55.0%), pulmonary embolism (15.0%) and complication of chronic heart failure (10.0%). Incorrect recognition was performed in one patient with respiratory cause, originally considered as pulmonary embolism, and in another with pulmonary embolism, considered as respiratory cause. One rhythm check was sufficient to perform TRACE in 31 patients, in the other two interruptions of cardiac compressions were required. Return of spontaneous circulation was achieved in 15 (37.5%) patients, favourable neurological outcome at hospital discharge in eight (20%) patients. Specific therapy to affect the cause of OHCA was applied during OHCA in 12 (30%) patients.
Conclusion Implementation of the TRACE protocol to the CPR process was feasible, required minimal interruption of cardiac compressions and resulted in a high recognition rate for the cause of OHCA.

P417

Body position during transport in a refractory cardiac arrest porcine model

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Introduction Cardiac arrest patients are not transported only supine. The effect of body position on resuscitability and cerebral perfusion in a 30° and 60° incline is not known.
Methods Twenty-five female pigs were subjected to a simulated cardiac arrest (3 minutes no flow, 5 minutes mechanical CPR). Next, animals were randomly assigned to one of the three groups: GROUP 60 (n = 8), 60° incline for 3 minutes to simulate transport in space restricted elevator; GROUP 30 (n = 8), 30° incline for 8 minutes to simulate staircase transport; and GROUP 0, with no incline. During subsequent standard CPR including rescue ECMO, resuscitability and cerebral perfusion were assessed.
Results Attainment of ROSC (3, 5, 5 in respective groups, $P = 0.021$), time to ROSC (15:24 (13:26; 16:02) vs. 19:19 (18:28; 19:37) vs. 9:10 minutes (8:28; 9:41), respectively, P = 0.005) significantly differed. Changes in carotid blood flow according to the respective periods of the protocol

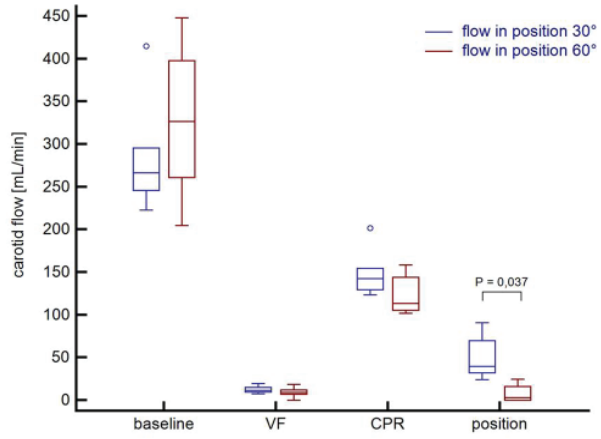


Figure 1 (abstract P417).

(baseline, cardiac arrest, initial supine CPR and 30° vs. 60° CPR) are depicted in Figure 1.

Conclusion Positional changes during simulated refractory cardiac arrest in this experimental model significantly affect resuscitability and brain perfusion. Animals subjected to shorter time in a more inclined (GROUP 60) position were more easily resuscitated; however, cerebral blood flow was better preserved in GROUP 30.

P418

Predictors of return of spontaneous circulation and survival in in-hospital cardiac arrest: a retrospective study in a single institution

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Introduction Despite several large studies concerning out-of-hospital cardiac arrests in recent years, it is not clear whether their in-hospital counterparts have benefited from advances in resuscitation as well as post-resuscitation care.

Methods We identified all cases of in-hospital cardiac arrest (IHCA) occurring in the National University Hospital in Singapore from 1 June 2008 to 31 May 2009. Patients for which IHCA occurred but where no resuscitation was attempted were excluded. Key outcomes were classified as primary (survival to discharge) and secondary (return of spontaneous circulation). Additionally, various arrest characteristics were analysed to identify predictive factors for survival to discharge with level of significant set at $P < 0.05$.

Results Among 353 unique cases of IHCA analysed, 63 patients (17.8%) had a shockable rhythm (ventricular fibrillation and pulseless ventricular tachycardia) of which 17 (27.0%) survived to discharge. While 290 (82.2%) patients presented with nonshockable rhythm (asystole or pulseless electrical activity), only 32 patients (11%) survived to discharge. For patients who survived to discharge, univariate analysis showed that event location ($P = 0.016$), nationality ($P = 0.035$), paying class ($P = 0.038$), use of ECG monitoring ($P = 0.048$), initial cardiac rhythm ($P = 0.000$) and presence of a house officer ($P = 0.005$) were statistically significant. Multivariate analysis showed that patients with shockable rhythms were 2.52 times more likely to survive but other factors were not significant. For patients who attained ROSC, univariate analysis showed that time of day ($P = 0.006$), event location ($P = 0.000$), and number of adrenaline doses administered ($P = 0.000$) were statistically significant. Multivariate analysis showed that an arrest occurring in the ICU setting was 2.9 times more likely to attain ROSC (95% CI: 1.02 to 5.59, $P = 0.044$).

Conclusion The results of this study have described some key predictive factors regarding positive outcomes in IHCA in Singapore. These are vital in understanding important features regarding IHCAs and will aid in developing policies to help improve care and survival in this group of patients.

P419

Comparison of complications secondary to cardiopulmonary resuscitation between out-of-hospital cardiac arrest and in-hospital cardiac arrest

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Introduction Chest compression during cardiopulmonary resuscitation (CPR) could bring out unintended complications which are mainly composed of chest injuries. The aim of this study was to assess whether there was a significant difference in the complications of CPR between out-of-hospital cardiac arrest (OHCA) and in-hospital cardiac arrest (IHCA) survivors using multidetector computed tomography (MDCT).

Methods We performed a retrospective cohort study in the emergency departments of two academic tertiary care centres from January 2009 to May 2014. We enrolled both OHCA and IHCA patients who underwent successful CPR. The enrolled patients had undergone a chest CT within 48 hours after ROSC. We evaluated the MDCT findings of the CPR-related chest injuries and compared complications between OHCA and IHCA patients.

Results A total of 148 patients were finally enrolled in this study, OHCA were 89 (60.1%) and IHCA were 59 (39.8%). The mean CPR time, both in-hospital and total, was longer in OHCA survivors. Rib fractures were

Patient demographics and clinical findings			
Variables	OHCA (N=89)	IHCA (N=59)	p-value
Age (yr), mean±SD	62.9±17.3	65.1±15.7	0.43
Gender, N(%)			0.71
Male	51(57.3)	32(54.2)	
Female	38(42.7)	27(45.8)	
Cause of arrest, N(%)			0.50
Cardiogenic	14(15.7)	7(11.9)	
Noncardiogenic	75(84.3)	52(88.1)	
Bystander CPR, N(%)	47(52.8)		
Initial rhythm, N(%)			0.20
Shockable	10(11.2)	3(5.1)	
Nonshockable	79(88.8)	56(94.9)	
Duration of CPR (Out), min, mean±SD	17.6±9.1	0±0	<.0001
Duration of CPR (In), min, mean±SD	11.0±7.3	7.9±5.6	0.005
Duration of CPR (Total), min, mean±SD	28.6±12.4	7.9±5.6	<.0001

Figure 1 (abstract P419). Patient demographics and clinical findings.

Comparison complications of CPR between OHCA group and IHCA group			
Variables	**OHCA(N=89)**	**IHCA(N=59)**	***p*-value**
Rib Fracture, N(%)	74(83.2)	37(62.7)	**0.01**
Side of rib fracture, N(%)			0.07
Unilateral	16(18.0)	9(15.3)	
Bilateral	58(65.2)	28(47.5)	
None	15(16.9)	22(37.3)	
Multiple rib fracture, N(%)	69(77.5)	34(57.6)	**0.01**
Number of rib fracture, n, mean±SD	5.2±3.9	3.8±4.0	**0.05**
Location of rib, N(%)			
Anterior	70(78.7)	34(57.6)	0.01
Lateral	50(56.2)	26(44.1)	0.15
Posterior	6(6.7)	3(5.1)	>.9999
Distance from midline, cm, mean±SD	9.7±1.9	9.5±1.6	0.68
Sternum fracture, N(%)	34(38.2)	18(30.5)	0.34
Upper	10(11.2)	5(8.5)	0.59
Middle	20(22.5)	10(17.0)	0.41
Lower	22(24.7)	8(13.6)	0.10
Lung contusion	31(34.8)	15(25.4)	0.23
Pneumothorax	19(21.4)	3(5.1)	0.08
Major complication	8(9.0)	3(5.1)	0.53
Survival	45(50.6)	27(45.8)	0.57

Figure 2 (abstract P419). Comparison complications of CPR between the OHCA group and the IHCA group.

detected more in OHCA survivors. Frequency of multiple rib fractures was higher in OHCA survivors. Frequency of sternum fractures was higher in OHCA survivors, showing no significant difference. In lung injuries, lung contusion and pneumothorax account for the large part, and OHCA survivors had higher incidence in both complications but statistically insignificant. Major complications occurred in eight cases in OHCA survivors and three cases in IHCA survivors during the study period. After adjusting for the time factor in multiple logistic regression analysis, rib fractures and multiple rib fractures became statistically significant in OHCA survivors. See Figures 1 and 2.

Conclusion Frequency of rib fractures and multiple rib fractures were higher in OHCA survivors. Further investigation is needed into the relation between the location of CPR and the CPR-related injuries, efforts to reduce the complications after CPR.

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P420

Impact of intra-arrest fluid loading with different doses of crystalloid infusion on hemodynamics in experimental cardiac arrest

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Introduction Fluid loading during cardiopulmonary resuscitation for nonhypovolemic cardiac arrest remains controversial. Thus, we conducted an experimental study comparing the impact of two different doses of balanced crystalloid infusion on hemodynamics in a porcine model of ventricular fibrillation.

Methods Ventricular fibrillation was induced for 15 minutes in 19 anesthetized domestic pigs. Before induction, the animals were randomized to receive either 1,000 ml (34 ± 3 ml/kg, group A, n = 7) or 500 ml (16 ± 2 ml/kg, group B, n = 7) of balanced crystalloid solution or to undergo no fluid loading during CPR (group C, n = 5). After spontaneous circulation (ROSC) was restored, the animals were observed for 90 minutes.

Results In all groups, significant increase of intracranial pressure followed by its decrease after ROSC was observed. While in groups B (from 12 ± 2 to 18 ± 2 mmHg, P <0.05) and C (from 13 ± 1 to 18 ± 3 mmHg, P <0.05) it was comparable (P >0.05), the rise of intracranial pressure in group A was significantly higher (from 12 ± 3 to 23 ± 3 mmHg, P <0.05). Whereas coronary perfusion pressure was lower in group A than in control group C during volume loading, fluid infusion induced its mild increase in group B (group A: 12.1 ± 2.4, group B: 16.0 ± 2.6, group C: 13.6 ± 2.8 mmHg, P = 0.043). Decrease of cerebral perfusion pressure was equal in all groups. Cardiac index 10 minutes after ROSC significantly differed among all groups (group A: 8.9 ± 2.2, group B: 7.1 ± 1.3, group C: 4.9 ± 1.9 l/minute/m^2, P = 0.007) and the dose of crystalloid infusion during cardiac arrest positively correlated with cardiac index increase (r = 0.815, P <0.001).

Conclusion Fluid loading during CPR had significant impact on hemodynamics in our experimental model. While a high dose led to unintentional increase of intracranial pressure and decrease of coronary perfusion pressure, a low dose did not affect intracranial pressure and was associated with mild increase of coronary perfusion pressure during cardiac arrest.

P421

Near-death experiences in survivors of cardiac arrest: a study about demographic, medical, pharmacological and psychological context

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Introduction Near-death experiences (NDEs) are increasingly being reported as a clear reality of clinical significance. Previous studies, essentially, have been trying to estimate their incidence in various populations, notably after cardiac arrest resuscitation, and to understand the implication of resuscitation characteristics [1,2]. Using the Greyson NDE scale [3], the present retrospective study aimed at exploring cardiac arrest survivors and the correlations between NDE and physiological, medical, psychological and pharmacological context.

Methods In a retrospective study from 2005 to 2012, 295 consecutive cardiac patients who were successfully resuscitated after cardiac arrest were enrolled. In total, 204 (69%) were alive during the research period (mean delay: 55 months). A total of 118 (40%), over 18 years, able to answer a short standardized interview were included in the study when they accepted to participate. Demographic, medical, pharmacological and psychological data were recorded and we used the Greyson NDEs scale to identify and characterize NDEs. Descriptive and unifactorial analysis was performed using the Jacknife method and Wald test according to low event frequency.

Results From our 118 reports, 20 described a core experience and 18 (15.3%) met the criteria for NDEs (Greyson NDEs total score >6/32 (7 to 19)). Only one patient recounted a negative experience. Regarding the risk factors for NDEs, using univariate analysis, we found for demographic data: woman (CI: 1.11 (1.10 to 1.12), P <0.0001), age under 60 (CI: 1.23 (1.21 to 1.24), P <0.0001), prior knowledge of NDEs (CI: 1.97 (1.95 to 1.99)) and previous NDE (CI: 5.82 (4.19 to 8.08)). According to the history of previous disease, we found an increased risk for pulmonary disease (CI: 1.75 (1.73 to 1.77)), rheumatic disease (CI: 3.79 (3.75 to 3.84)), endocrine disease (CI: 1.45 (1.43 to 1.46)), and a decrease for cardiac disease (CI: 0.65 (0.64 to 0.66)), psychiatric disease (CI: 0.71 (0.69 to 0.72)) and digestive tract disease (CI: 0.71 (0.69 to 0.72)). For previous pharmacological treatment we found a decrease of risk for all classes and particularly when two drugs were simultaneously given (CI: 0.37 (0.36 to 0.38)).

Conclusion Although our study has a number of methodological limitations, these results about incidence in cardiac arrest survivors corroborate previous retrospective reports. It is possible that every cardiac arrest survivor has had to live a NDE, regardless of brain mechanisms associated with experience, but only some patients remember it. If some chronic medications, such as benzodiazepine, may decrease memorization, the role of the elements of the clinical context about NDE during resuscitation is speculative

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P422

Utilisation and prognostic impact of cathlab investigation prior to intensive care admission for patients following out-of-hospital cardiac arrest

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Introduction Our 700-bed hospital has a 24–7 cathlab service that routinely investigates patients with indications prior to ICU admission following out-of-hospital cardiac arrest (OOHCA). Our aim was to compare survivors and nonsurvivors and evaluate utilisation and

prognostic impact of angiography and primary percutaneous coronary intervention (PPCI) in this patient group.
Methods A retrospective analysis using Trust electronic databases (Symphony, WardWatcher, PICIS, PRISM) of all OOHCA patients admitted to our ICU over 3 consecutive years between 1 November 2011 and 31 October 2014.
Results A total of 351 patients presented to our emergency department (ED) following OOHCA in this period, and of these 50% died in the ED, 37% were admitted to the ICU and 13% were admitted elsewhere. Of the 129 patients admitted to the ICU, median age was 66 (range 18 to 93), 71% were male, 68% had a shockable presenting rhythm, median ICU LOS was 3.75 (range 1 to 34 days) and ICU and hospital mortalities were 50% and 60% respectively. Eighty-nine percent ($n = 48$) of OOHCA survivors admitted to the ICU had a shockable rhythm compared with 55% ($n = 41$) of nonsurvivors. Eighty-three percent ($n = 45$) of survivors admitted to the ICU went to the cardiac cathlab before ICU admission compared with 53% ($n = 39$) of nonsurvivors. Forty-three percent of survivors had PPCI compared with 26% of nonsurvivors. Eighty-one percent ($n = 44$) of survivors received therapeutic hypothermia compared with 62% ($n = 48$) of nonsurvivors.
Conclusion Over 3 consecutive years our annual case mix, ICU and hospital mortalities for OOHCA patients admitted to the ICU have remained stable, while our annual pre-ICU cathlab and PPCI utilisation have risen consistently in both survivors and nonsurvivors. ICU survivors were more likely to have had a shockable rhythm, been to the cathlab, and received PPCI and TH, but all may simply reflect selection bias. Any benefit these conferred to cardiac patients may have been offset by our liberal ICU admission policy to OOHCAs with nonshockable rhythms. Access to 24–7 PPCI in this group may determine survival and we suggest that OOHCA patients should be taken directly to regional heart attack centres.

P423

Utilisation and prognostic impact of angiography and primary percutaneous coronary intervention prior to intensive care admission for patients following out-of-hospital cardiac arrest

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Introduction Our 700-bed hospital has a 24–7 cathlab service that routinely investigates patients with indications prior to ICU admission following out-of-hospital cardiac arrest (OHCA). Our aim was to compare ICU survivors and nonsurvivors and evaluate the utilisation and prognostic impact of angiography and primary percutaneous coronary intervention (PPCI) in this patient group.
Methods A retrospective analysis using Trust electronic databases (Symphony, WardWatcher, PICIS, PRISM) of all OHCA patients admitted to our ICU over 3 consecutive years between 1 November 2011 and 31 October 2014.
Results A total of 351 patients presented to our hospital following OHCA in this period, and of these 50% died in the ED, 37% were admitted to the ICU and 13% elsewhere. Of the 129 patients admitted to the ICU, median age was 66 (range 18 to 93), 71% were male, 68% had a shockable presenting rhythm, median ICNARC score was 31 (range 10 to 66), median ICU LOS was 3.75 (range 1 to 34 days) and ICU and hospital mortality were 50% and 60% respectively. ICU survivors were more likely to have had a shockable rhythm (89 vs. 55%), been to the cathlab (83 vs. 53%), received PPCI (43 vs. 26%) and TH (82 vs. 62%) and had lower median ICNARC scores (26 vs. 35) than nonsurvivors. Over the 3 consecutive years, pre-ICU cathlab and PPCI utilisation increased annually in ICU survivors (73 vs. 86 vs. 89% and 45 vs. 54 vs. 59% respectively) and nonsurvivors (40 vs. 38 vs. 50% and 20 vs. 27 vs. 31% respectively). However, our annual ICU and hospital mortality remained unchanged (46 vs. 51 vs. 51% and 60 vs. 57 vs. 62% respectively).
Conclusion ICU survivors were more likely to have had a shockable rhythm, been to the cathlab, received PPCI and TH and been less sick than nonsurvivors, but these may simply reflect selection and other biases. Any benefit these factors did confer to cardiac patients may have been offset by our liberal ICU admission policy to OHCAs with nonshockable rhythms. However, access to 24–7 PPCI may determine survival and we suggest that all OHCA patients should be taken directly to regional heart attack centres.

P424

Targeted temperature management after cardiac arrest and fever control with an esophageal cooling device

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Introduction Mild hypothermia and fever control have been shown to improve neurological outcomes post cardiac arrest. Common methods to induce hypothermia include body surface cooling and intravascular cooling; however, a new approach using a catheter placed into the esophagus has recently become available.
Methods We report the first three cases of temperature control using an esophageal cooling device (ECD). The ECD was placed orally in a similar fashion to orogastric tubes. Temperature reduction was achieved by connecting the ECD to a commercially available heat exchange unit (Blanketrol II or III).
Results The first patient, a 59-year-old male (73 kg), was admitted after successful resuscitation from a protracted out-of hospital cardiac arrest. His initial temperature was 35°C, which is within our current institutional protocol of 34 to 36°C. Several hours after arrival, his temperature slowly increased to 35.8°C despite application of a cooling blanket and ice packs to the groin and axilla. The ECD was inserted and a reduction of temperature to 34.8°C was achieved within 3 hours. The patient expired on day 3. The second patient, a 54-year-old female (95 kg), was admitted after resuscitation from an out-of-hospital PEA arrest. Despite initiating our cooling protocol with surface-cooling blankets and cold intravenous saline, she mounted a fever peaking at 38.3°C shortly after admission. After ECD insertion and confirming the external heat exchanger connection, her temperature gradually dropped to 35.7°C over a period of 4 hours. She subsequently made a favorable neurological recovery and was discharged home at day 23. The third patient, a 47-year-old male patient (86 kg) presented with an ongoing fever secondary to necrotizing pneumonia in the postoperative period after coronary artery bypass grafting. His fever was unresponsive to empiric antibiotic therapy, antipyretics, cooling blankets, and ice packs. ECD insertion resulted in a decrease in temperature from 39.5°C to 36.5°C in less than 5 hours. The patient eventually made a full recovery and was discharged home after 59 days. In all three patients, placement of the device occurred in less than 3 minutes and ease of use was reported as excellent by nursing staff and physicians.
Conclusion The ECD is a novel technology that can be used for temperature management post cardiac arrest and for fever control in critically ill patients. Despite patients mounting a febrile response, temperature control was achieved and maintained successfully. The device was reported as being easy to use, by both physicians and nurses.

P425

Is selective nasopharyngeal brain cooling detrimental to neuroprotection?

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Introduction Clinical outcomes vary depending on the method used to induce therapeutic hypothermia following stroke or cardiac arrest. In swine, we tested the hypothesis that selective nasopharyngeal brain cooling (SNBC), in contrast to systemic hypothermia, adversely impacts cerebral perfusion.
Methods In two groups of animals (34 to 35 kg), blood flow in the right middle cerebral artery (MCA) was measured using transcranial Doppler (TCD). In group 1, SNBC was initiated using perfluorohexane aerosol (1 ml/kg/minute) and oxygen (1 l/kg/minute) through a nasopharyngeal catheter atomizer. In group 2, the animals were body surface cooled using water-circulating blankets (4°C). In both groups,

Table 1 (abstract P425). Cerebral vasospasm during SNBC

Intervention	MCA flow velocity (cm/second)	ICA flow velocity (cm/second)	Lindegaard ratio	Pulsatility ratio	ICP (mmHg)
Baseline	62	41	1.51	0.77	13
SNBC cooling	128	52	2.46	0.48	−15
SNBC rewarming	96	44	1.74	1.12	21

brain temperature, intracranial pressure (ICP), core temperatures and vital signs were continuously recorded. Cooling was terminated once the brain reached 32°C and the animals were allowed to passively rewarm.
Results In the SNBC group, the brain target temperature was reached in 54 ± 11 minutes. The mean ICP dropped precipitously to a nadir of −15 mmHg. TCD showed significant vasospasm in the MCA, compared with the internal carotid artery (ICA), during the entire cooling phase (Table 1). Upon termination of cooling, the brain temperature spontaneously rewarmed to core temperature in 13 ± 4 minutes. Rewarming was associated with hyperemia and elevation of ICP. In group 2, there was no cerebral vasospasm or hyperemia during cooling and rewarming respectively.
Conclusion SNBC is associated with significant vasospasm of the MCA. In addition, spontaneous and rapid rewarming of the brain, vasodilation, rapid reperfusion, and rebound elevation of ICP, all occurring minutes after termination of SNBC, are likely to be detrimental to an already ischemic brain.

P426

Hemodynamic targets during therapeutic hypothermia after cardiac arrest: a prospective observational study

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Introduction In analogy with sepsis, current postcardiac arrest (post-CA) guidelines recommend to target mean arterial pressure (MAP) above 65 mmHg and SVO_2 above 70%. This is unsupported by mortality or cerebral perfusion data. The aim of this study was to explore the associations between MAP, SVO_2, cerebral oxygenation and survival.
Methods A prospective, observational study during therapeutic hypothermia (24 hours −33°C) in 82 post-CA patients monitored with near-infrared spectroscopy.
Results Forty-three patients (52%) survived in CPC 1 to 2 until 180 days post CA. The mean MAP range associated with maximal survival was 76 to 86 mmHg (OR = 2.63, 95% CI (1.01; 6.88), $P = 0.04$). The mean SVO_2 range associated with maximal survival was 67 to 72% (OR = 8.23, 95% CI (2.07; 32.68), $P = 0.001$). In two separate multivariate models, a mean MAP (OR = 3.88, 95% CI (1.22; 12.33), $P = 0.02$) and a mean SVO_2 (OR = 8.79, 95% CI (1.69; 18.36), $P = 0.01$) in the optimal range persisted as independently associated with increased survival after correction for presence of early bystander CPR and presenting shockable rhythm. Based on more than 1,625,000 data points, we found a strong linear relation between SVO_2 (range 40 to 90%) and average cerebral saturation ($R^2 = 0.86$) and between MAP and average cerebral saturation for MAPs between 40 and 87 mmHg ($R^2 = 0.70$). Based on our hemodynamic model, the optimal MAP and SVO_2 were determined to be 87 mmHg and 72%.
Conclusion The optimal SVO_2 (72%) and MAP (87 mmHg) derived from our hemodynamic model matched with the observed SVO_2 (67 to 72%) and MAP (76 to 86 mmHg) associated with maximal survival. Prospective interventional studies to reach or maintain these targets are needed to confirm these findings.

P427

Pharmacologic evaluation of shivering management in neurologically injured patients utilizing therapeutic normothermia

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Introduction Uncontrolled shivering may have negative consequences by increasing metabolic demand and subsequently neutralize the benefits of therapeutic normothermia [1]. Previous anti-shivering protocols that utilize the least sedation have been described in therapeutic temperature modulation (TTM) [2]. Our aim is to describe and evaluate an anti-shivering protocol that emphasizes the least sedating regimen with the least number of pharmacologic agents for patients undergoing therapeutic normothermia.
Methods This retrospective chart review includes patients with neurologic injury who underwent TTM from March 2013 to November 2014 and were evaluated for the following outcomes: percentage of total patient hours in each score of the Bedside Shivering Assessment Scale (BSAS) at 72 hours, 168 hours, and total duration of TTM; percentage of total patient days in each tier of the anti-shivering protocol at 72 hours, 168 hours, and total duration of TTM; de-escalation of anti-shivering agents with or without the necessary need for re-escalation; ICU and hospital length of stay (LOS); rescue agents utilized; and hospital mortality.
Results Evaluation of 47 patients who underwent TTM resulted in a total of 505 patient-days of TTM with 6,967 BSAS hours. Overall, patients spent 85.5% of total hours at BSAS 0, 11.4% of total hours at BSAS 1, 2.5% of total hours at BSAS 2, and 0.6% of total hours at BSAS 3. Patients were in tier 0 of the anti-shivering protocol 33.1% of the time, in tier 1 of the anti-shivering protocol 20.6% of the time, in tier 2 of the anti-shivering protocol 43.6% of the time, and in tier 3 of the anti-shivering protocol 2.8% of the total duration of TTM. There were 487 rescue doses of fentanyl and 243 rescue doses of meperidine that were required for shivering. Patients had a mean ICU LOS of 19 days, mean hospital LOS of 21 days, and a mortality rate of 23.4%.
Conclusion This study demonstrates a high level of efficacy of our protocol and the feasibility of de-escalation to limit the number of pharmacologic interventions. With our patient population spending a large percentage of time without shivering, it would suggest that this protocol could be revised further by utilizing rescue agents more frequently in order to prevent escalation of therapy to the next tier.
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P428

Predictors of survival of therapeutic hypothermia based on analysis of a consecutive American inner-city population over 4 years

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Introduction Therapeutic hypothermia (TH) is the international standard of care for all comatose patients after cardiac arrest, but criticism focuses on poor outcomes. We sought to develop criteria to identify American urban patients more likely to benefit from TH.
Methods A retrospective chart review of 107 consecutive adults undergoing TH in downtown New Orleans from 2010 to 2014 yielded records for 99 patients with all 44 survivors or families contacted up to 4 years.
Results Sixty-nine males and 38 females with a mean age of 60.2 years showed 63 dead (58%) and 44 survivors (42%). Presenting cardiac rhythm was divided into shockable (pulseless ventricular tachycardia, ventricular fibrillation) and nonshockable (pulseless electrical activity, asystole). Presenting in shockable rhythms with ROSC <20 minutes were 21 patients with 15 (71%) survivors ($P = 0.001$). Time >20 minutes until ROSC in shockable rhythms had five patients with three survivors (78%, $P = 0.001$). Presenting in nonshockable rhythms with ROSC <20 minutes were 54 patients with 18 survivors (33%, $P = 0.001$). ROSC >20 minutes in nonshockable rhythms had 19 patients with two survivors (8%, $P = 0.001$). Survivors of shockable rhythms showed 19 (100%) living post TH. Fifteen survivors (79%, $n = 19$, $P = 0.001$) had CPC

score 1 or 2 with four survivors (21%, *n* = 19) having a CPC score of 3. A total of 25 survived nonshockable rhythm. Acute survival of patients with nonshockable rhythm showed 18 expired <72 hours (72%, *n* = 25) with long-term survival of four patients (5%, *n* = 74) and CPC scores of 1 or 2 (*P* = 0.001). Interestingly, patients with time to ROSC <20 minutes exhibiting more than one loss of sustained ROSC showed 100% mortality (*P* = 0.001). Patients presenting with shockable >20 minutes ROSC had overall survival of 70% (*P* = 0.001), but those undergoing >3 cardiac rhythm changes had 100% mortality (*P* = 0.001).
Conclusion Patients presenting with shockable rhythms undergoing TH had overall acute survival of 70% followed by long-term survival of 100% after 4 years. In contrast, patients presenting with nonshockable rhythm had long-term survival of 5%. TH is not recommended.

P429

Difference in cerebral saturation during cardiopulmonary resuscitation between survivors with favorable neurological outcome and compromised neurological outcome at hospital discharge

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Introduction During out-of-hospital cardiac arrest (OHCA) monitoring possibilities are limited. Recently, the role of cerebral oximetry, using near-infrared spectroscopy, during ALS was investigated. In this study we determined whether the magnitude of increase in cerebral saturation (rSO_2) or mean rSO_2 during prehospital ALS was associated with good neurological outcome at hospital discharge (Cerebral Performance Category (CPC) 1 or 2).
Methods With IRB approval, we prospectively measured rSO_2 during ALS in consecutive OHCA patients. One sensor of the Equanox™ 7600 (NONIN) was applied on the patient's forehead's right side when the medical emergency team arrived in an OHCA. ROSC was defined as ROSC >20 minutes.
Results We included 88 prehospital cardiac arrest patients between December 2011 and October 2014 with eight (9%) patients with CPC 1 or 2. Twenty-seven patients of the nonsurvivors had ROSC >20 minutes and one patient had CPC 3 at hospital discharge. We observed no significant difference between both groups in age (*P* = 0.161), time between emergency call and start of ALS (*P* = 0.788) and duration of basic life support performed by bystanders, general practitioners or paramedics (*P* = 0.649). The initial rhythm was asystole in one (12.5%) survivor and in 50 (62.5%) nonsurvivors (*P* = 0.009), ventricular fibrillation in six (75%) survivors and 13 (16%) nonsurvivors (*P* = 0.001), and pulseless electrical activity in one (12.5%) survivor and 17 (21%) nonsurvivors (*P* = 1.00). The cardiac arrest was witnessed in all survivors (100%) and in 49 (61%) nonsurvivors (*P* = 0.046). First measured rSO_2 was 38% (27 to 67) in the survivor group compared with 22% (8 to 32) in the nonsurvivor group (*P* = 0.004). Also a significant difference was found in mean rSO_2 until 1 minute before ROSC between survivors and nonsurvivors, respectively 46% (40 to 74) and 34% (22 to 42). We observed no significant difference in increase of rSO_2 until 1 minute before ROSC between survivors 12.5% (5 to 21) and nonsurvivors 11% (5 to 18) (*P* = 0.719).
Conclusion We observed a significant difference in first measured rSO_2 and mean rSO_2 until 1 minute before ROSC between patients with good neurological outcome (CPC 1 or 2) at hospital discharge and patients with worse neurological outcome or nonsurvivors (CPC 3 or 4 or 5). However, no significant difference was observed in the increase between both groups. Larger studies are necessary to confirm these results.

P430

Association between hemoglobin, cerebral oxygenation and neurologic outcome in postcardiac arrest patients

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Critical Care 2015, **19(Suppl 1):**P430 (doi: 10.1186/cc14510)

Introduction The safety of a restrictive transfusion threshold of 7 g/dl applied in all critically ill patients can be questioned in postcardiac arrest (post-CA) patients since these are phenotypically clearly distinct. The aims of this study were to investigate the association between hemoglobin, cerebral oxygenation ($SctO_2$) and outcome in post-CA patients.
Methods A prospective observational study in 82 post-CA patients during hypothermia in the first 24 hours of ICU stay. Hemoglobin was determined hourly together with a corresponding $SctO_2$ by NIRS and SVO_2 in patients with a pulmonary artery catheter (*n* = 62).
Results Based on 2,099 paired data, we found a strong linear relationship between hemoglobin and average $SctO_2$ ($SctO_2 = 0.70 \times \text{hemoglobin} + 56$ ($R^2 = 20.84$, $P = 10^{-6}$)). Given the previously suggested $SctO_2$ target between 66 and 68%, hemoglobin levels below 10 g/dl generally resulted in suboptimal brain oxygenation. Forty-three patients (52%) had a good neurological outcome (CPC 1 to 3) at 180 days post CA. There was a significant association between average hemoglobin above 12.3 g/dl and good neurological outcome (OR = 2.88, 95% CI = 1.02; 8.16, *P* = 0.04). In a multivariate model, this association persisted after correction for comorbidities and age by the modified Charlson score (OR = 2.99, 95% CI = 1.05; 8.53, *P* = 0.03). This association was entirely driven by results obtained in patients with an average SVO_2 below 70% (OR = 17.55, 95% CI = 1.67; 184.41, *P* = 0.01).
Conclusion There is a steep linear relationship between hemoglobin and $SctO_2$ in post-CA patients with hemoglobin levels below 10 g/dl generally resulting in cerebral desaturation. Average hemoglobin below 12.3 g/dl was independently associated with worse neurological outcome 180 days post CA. An interventional trial is necessary to investigate whether maintaining higher hemoglobin would improve outcome.

P431

Somatosensory evoked high-frequency oscillations and prognostication after cardiac arrest

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Introduction Electrical median nerve stimulation elicits a burst of high-frequency oscillations (HFOs) superimposing onto the cortical short-latency potential. Digital filtering of somatosensory evoked potentials (SSEPs) enables non-invasive analysis of these HFOs. The late HFO component following the cortical N_2O peak is ascribed to spiking activity of cortical neurons.
Methods We retrospectively studied late HFO components of median nerve SSEPs obtained 24 hours to 4 days after cardiac arrest in patients treated with mild hypothermia (33°C for 24 hours). Cortical average recordings were digitally filtered at 450 to 750 Hz and noise-corrected maximum peak-to-peak amplitudes of the cortical late HFO bursts determined. Outcome upon ICU discharge was dichotomized according to the Cerebral Performance Category (CPC) scale. CPC 1 to 3 was classified as good outcome, CPC 4 to 5 (unresponsive wakefulness syndrome and death) as poor outcome.
Results Of 307 consecutive patients, 153 (50%) achieved good outcome (CPC 1 to 3) and 154 (50%) had poor outcome. Late HFO bursts were present in 102 (33%) recordings. Among patients with late HFO amplitudes above 0.1 μV, 26 had CPC 1 to 3, none had CPC 4 and eight died. Case review indicated causes of death other than hypoxic encephalopathy in all patients who died despite HFO amplitudes above 0.1 μV.
Conclusion We found cortical late HFO bursts, obtained by digital filtering of standard SSEP recordings, in a significant proportion of patients after cardiac arrest treated with mild hypothermia. Our data indicate that the presence of late HFO bursts with amplitudes above 0.1 μV may confirm absence of severe hypoxic encephalopathy early after cardiac arrest with high specificity.

P432

One-size-fits-all or patient-tailored hemodynamic targets in post-cardiac arrest patients: an observational near-infrared spectroscopy study on cerebral autoregulation

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Introduction A subgroup of post-CA patients with disturbed cerebral autoregulation might benefit from higher mean arterial pressures

(MAPs). We aimed to (1) investigate whether patients with disturbed autoregulation have a worse prognosis, (2) phenotype these patients, (3) define an individual optimal MAP and (4) investigate whether time under this individual optimal MAP is associated with outcome.
Methods A prospective observational study in 51 post-CA patients monitored with near-infrared spectroscopy.
Results (1) In multivariate analysis, patients with preserved autoregulation (33.65%) had a significant higher 180-day survival rate (OR = 4.62, 95% CI (1.06; 20.06), $P = 0.04$). (2) Phenotypically, a higher proportion of patients with disturbed autoregulation had pre-CA hypertension (31 ± 47 vs. 65 ± 49%, $P = 0.02$) suggesting that right shifting of autoregulation is caused by chronic adaptation of cerebral blood flow to higher blood pressures. Based on an index of autoregulation (COX), the average COX-predicted optimal MAP was 85 mmHg in patients with preserved and 100 mmHg in patients with disturbed autoregulation. (3) An individual optimal MAP could be determined in 33/51 patients. (4) The time under the individual optimal MAP was negatively associated with survival (OR = 0.97, 95% CI (0.96; 0.99), $P = 0.02$). The time under previously proposed fixed targets (65, 70, 75, 80 mmHg) was not associated with a differential survival rate.
Conclusion Cerebral autoregulation was shown to be disturbed in 35% of post-CA patients of which a majority had pre-CA hypertension. Disturbed cerebral autoregulation within the first 24 hours after CA is associated with a worse outcome. In contrast to uniform MAP goals, the time spent under a patient-tailored optimal MAP, based on an index of autoregulation, was negatively associated with survival.

P433

Response of regional oxygen saturation technologies during hypoxia

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Introduction The purpose of this study was to determine the rate and magnitude of response to hypoxia for three different regional oxygen saturation (rSO_2) devices. rSO_2 technologies are focused on absolute accuracy without consideration of response characteristics. Current rSO_2 technologies assume that the oxygen saturation is a fixed ratio of arterial and venous blood. Cerebral arteries have an oxygenation-related vasoactivity that may change the arterial/venous ratio during hypoxia. Thus, absolute rSO_2 accuracy may be less important compared with sensitivity to changes in cerebral rSO_2.
Methods Ten subjects completed the study and are included in the analysis. One INVOS sensor (SAFB-SM) was placed on the left side and one Equanox (8000CA) or Foresight (1 July 2007 or 1 July 2005) sensor (alternated between subjects) was placed on the right side of the forehead for bilateral monitoring. Desaturation was induced by adjusting the inspiratory gas mixture of O_2/N_2. Desaturation was titrated from room air to achieve a plateau of 70% arterial oxygen saturation (SpO_2). Resaturation was induced by rapid change in FiO_2 to 1.0. After 5 minutes of SpO_2 100%, the process was repeated by desaturation to SpO_2 70% and rapid return to SpO_2 100%. Cerebral and pulse oximetry data were recorded during the study and the time of each FiO_2 change and plateau was recorded. rSO_2 levels at 10, 20, 40, 60 and 80% of the total SpO_2 response were calculated for each device to assess the rate of rSO_2 change. The rate of rSO_2 change in seconds and total rSO_2 change were compared.
Results The rate of rSO_2 change during desaturation was similar for all devices with an average slope factor of 0.17 for Foresight, 0.16 for Equanox and 0.21 for INVOS. The rate of rSO_2 change in seconds during resaturation from SaO_2 70% to SaO_2 100% was significantly faster for INVOS (42 ± 16) compared with Foresight (57 ± 20) ($P < 0.05$). There was significant difference in total rSO_2 change between INVOS (23 ± 4%) and Equanox (15 ± 4%) during desaturation and resaturation ($P < 0.005$) and between INVOS compared with Foresight (20 ± 5%) ($P < 0.05$).
Conclusion All rSO_2 devices followed the SpO_2 slope during desaturation as expected. The differences between the devices in terms of total rSO_2 change reached statistical significance. There were also significant differences in the rate of rSO_2 change in seconds between INVOS and Foresight during resaturation. The rate of absolute change in seconds and the magnitude of absolute change may result in better resolution to detect physiological changes. Clinical studies are required to elucidate the clinical relevance of the differences.

P434

Use of bispectral index EEG monitoring for a fast and reliable detection of epileptic activity in postcardiac arrest patients

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Introduction Assessment of prognosis in postcardiac arrest (post-CA) patients became very challenging since the introduction of therapeutic hypothermia (TH). Continuous EEG monitoring has been proposed to improve prognostication; however, its use is limited due to difficulties in ready interpretation. Thus emerges the need for a simple EEG montage. The bispectral index (BIS) monitor is a simplified EEG system, mainly calculating an index ranging from 0 (isoelectric EEG) to 100 (full consciousness) to provide information on hypnotic depth of anaesthesia. The aim of the study was to validate the accuracy of simplified EEG monitoring in a CA setting.
Methods BIS monitoring (BIS VISTATM) was applied to collect frontotemporal data in TH-treated CA patients. A standard 19-channel EEG was performed after return to normothermia. Afterwards, small EEG frames coincident with the time of full EEG registration were extracted from the BIS monitor. We asked two neurophysiologists to indicate the presence of status epilepticus (SE), cerebral inactivity (CI), burst suppression (BS), periodic epileptiformic discharges (PEDs) or a diffuse slowing pattern (DS). In addition, these samples were analysed by two inexperienced physicians, who were asked to indicate the presence of SE.
Results Thirty-four simplified EEG samples were analysed. According to standard EEG, 11 patients showed a DS pattern, three had CI, six showed BS, four showed PEDs and 10 had an SE. Neurophysiologists interpreted all samples with a high accuracy. Mean sensitivity was 82.12% and mean specificity was 91.88%. Only one SE was missed by one neurophysiologist. Unfortunately, only one PED was confirmed by both neurophysiologists. Interobserver reliability was high ($\kappa = 0.843$). High correlations were found for the comparison of full and simplified EEG for both neurophysiologists ($r = 0.809$). Further, the two inexperienced physicians identified SE with a sensitivity of 85% and specificity of 98%.
Conclusion Simplified EEG monitoring, using BIS, resulted in high accuracy of a simple classification system in post-CA patients. Not only neurophysiologists, but also treating physicians were capable to identify SE, which may play an important role in the early detection of SE. We suggest using BIS as a screening tool in post-CA patients to save valuable time in the detection of SE, without replacing the need for full EEG monitoring for confirmation.

P435

Differences in cerebral saturation measured during prehospital advanced life support, between patients with presumed cardiac origin and noncardiac origin of cardiac arrest

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Introduction During out-of hospital cardiac arrest (OHCA) cerebral saturation may provide relevant information on cerebral oxygenation. In this study we examined the time course in cerebral saturation (rSO_2) during prehospital ALS comparing patients with a presumed cardiac origin (survivor = Sc, nonsurvivor = NSc) of arrest and noncardiac origin (survivor = Snc, nonsurvivor = NSnc) of arrest.
Methods With IRB approval, we prospectively measured rSO_2 from the start of ALS in consecutive OHCA patients. One sensor (Equanox™ 7600; Nonin) was applied on the patient's forehead's right side when

the medical emergency team arrived at the OHCA setting. ROSC was defined as ROSC >20 minutes. Retrospectively, included patients were divided into two groups with respect to their presumed origin of arrest.
Results Between December 2011 and October 2014, 113 OHCA patients were included. We observed a significant difference in asystole and VF as initial rhythm between NSc and NSnc, respectively ($P = 0.035$ and $P = 0.001$). In both groups of NS, duration of ALS was significant longer compared with the two S groups ($P = 0.001$ in both comparisons). We observed no significant difference in first measured rSO_2, mean rSO_2 until 1 minute before ROSC and increase in rSO_2 until 1 minute before ROSC (respectively $P = 0.123$, $P = 0.501$, $P = 0.265$) between Sc and Snc. However, when we compare the nonsurvivors of cardiac with noncardiac origin, we observed a significant difference in mean rSO_2 until 1 minute before ROSC, 35% (27 to 44) in the NSc group and 27 (21 to 34) in the NSnc group ($P = 0.026$). First measured rSO_2 was 24.5% (13 to 34) in the NSc group and 14 (4 to 28) in the NSnc group ($P = 0.069$) trending to be significantly different. No significant difference was observed in increase until 1 minute before ROSC between both groups of NS ($P = 0.920$). Significant differences was observed in mean rSO_2 until 1 minute before ROSC and increase in rSO_2 between Snc and NSnc ($P = 0.033$; $P < 0.001$) and between Sc and NSc ($P = 0.001$; $P < 0.001$).
Conclusion We can conclude that NSc have a significant higher mean rSO_2 and trend to have a significant difference in first measured rSO_2 compared with NSnc. However, no significant difference was observed between Sc and Snc.

P436

Amplitudes of cortical somatosensory evoked potentials and outcome prediction after cardiac arrest

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Introduction Bilaterally absent cortical somatosensory evoked potentials (SSEPs) predict poor outcome after cardiac arrest. A threshold for the amplitude of early cortical SSEPs above which patients may survive with good outcome has not been determined. Thus, tolerable noise levels for the interpretation of cortical SSEPs are poorly defined. Furthermore, it has not been systematically investigated whether high amplitudes of cortical SSEPs may exclude severe hypoxic encephalopathy incompatible with re-awakening.
Methods We prospectively studied SSEPs after median nerve stimulation obtained 24 hours to 4 days after cardiac arrest in patients treated with targeted temperature management at 33°C for 24 hours. Amplitudes of cortical SSEPs were determined, if at least two peripheral, spinal and cortical recordings per side were available, spinal potentials were bilaterally reproducible and cortical noise level was below 0.25 μV. Cortical SSEP amplitude was defined as largest amplitude of a reproducible cortical SSEP of four cortical recordings (two per side) within 50 milliseconds after stimulation. Outcome was assessed upon ICU discharge using the Cerebral Performance Category (CPC) scale. CPC 1 to 3 was defined as good outcome, CPC 4 to 5 as poor outcome.
Results Of 318 consecutive patients examined, 293 had complete SSEP recordings with reproducible spinal potentials and cortical noise levels below 0.25 μV. Of those, 137 (47%) had good outcome and 156 (53%) had poor outcome. The lowest amplitude of the early cortical SSEPs in a survivor with good outcome was 0.62 μV. All 79 patients with amplitudes below this threshold had poor outcome. None of 27 patients who survived with CPC 4 (unresponsive wakefulness syndrome) had cortical SSEP amplitudes above 2.5 μV. Twenty-four patients with amplitudes above this limit died. Detailed case review indicated a cause of death other than hypoxic encephalopathy in these patients.
Conclusion Our data indicate that the prognostic value of SSEP after cardiac arrest extends beyond a mere absent–present dichotomy. Bilaterally absent as well as very low amplitude SSEPs predict poor outcome with high positive predictive value. SSEPs should not be used for prognostication, if noise in cortical recordings could mask critically low amplitudes. High amplitudes of early cortical SSEPs strongly argue against severe hypoxic encephalopathy incompatible with re-awakening.

P437

Prognostic value of neuron-specific enolase after cardiac arrest and targeted temperature management

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Introduction The serum concentration of neuron-specific enolase (NSE) has been established as a highly specific predictor of poor outcome after cardiac arrest. Recent studies have indicated that patients treated with targeted temperature management at 33°C for 24 hours may have good outcome despite NSE serum concentrations considerably higher than the cutoff established for normothermic patients. The threshold above which survival with good outcome becomes very unlikely, its positive predictive value and sensitivity for prediction of poor outcome have not been established in this patient group. Furthermore, a threshold below which hypoxic encephalopathy may be largely excluded has not been determined.
Methods From 2006 through 2014 we prospectively included in-hospital and out-of-hospital cardiac arrest patients treated with targeted temperature management at 33°C for 24 hours. The NSE serum concentration was determined 3 days after cardiac arrest and the outcome was assessed according to the Cerebral Performance Category (CPC) upon ICU discharge. CPC 1 to 3 was defined as good outcome and CPC 4 to 5 as poor outcome. Individual case review was performed in patients with good outcome despite very high NSE serum concentration and in patients with poor outcome despite very low NSE serum concentration.
Results Of 601 included patients, 309 (51%) had good outcome. An NSE serum concentration threshold of 90 μg/l predicted poor outcome with a positive predictive value of 0.98 and a sensitivity of 0.51. Three patients survived with good outcome despite an NSE serum concentration >90 μg/l. In two of these patients NSE elevations had been documented prior to cardiac arrest. One patient had a neuroendocrine tumor of the pancreas, the other patient suffered from encephalitis of unknown etiology and an osteomyelofibrosis. Potential confounders in the third patient were an ovarian carcinoma, the use of an intra-aortic balloon pump and blood transfusions shortly after cardiac arrest. Only 16 of 205 patients with NSE <17 μg/l had poor outcome, the majority of these patients died from causes other than hypoxic encephalopathy.
Conclusion In patients with cardiac arrest and targeted temperature management at 33°C, an NSE serum concentration of >90 μg/l strongly indicates poor outcome. NSE producing tumors, acute brain diseases, severe hematologic diseases, use of an intra-aortic balloon pump and blood transfusions need to be considered as potential confounders. An NSE serum concentration of <17 μg/l largely excludes hypoxic encephalopathy incompatible with re-awakening.

P438

Resuscitated cardiac arrest in patients admitted with acute heart failure: analysis of a large prospective AHEAD network registry

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Introduction Heart failure is a frequent cause of cardiac arrest and *vice versa*, cardiac arrest frequently complicates acute heart failure episodes. We aimed to characterize the influence of cardiac arrest on outcome of acute heart failure patients admitted to hospital.
Methods The AHEAD registry includes patients hospitalized for acute heart failure from 10 PCI and five non-PCI centers in the Czech Republic. The data were collected from September 2006 to October 2012.
Results In the respective period, a total of 6,242 patients were enrolled into the registry. Resuscitated cardiac arrest occurred in 313 patients prehospitally and in 484 after admission; the remaining 5,445 patients were not resuscitated during their index hospitalization. Patients resuscitated after admission in comparison with prehospitally resuscitated were older, had lower left ventricle ejection fraction, more

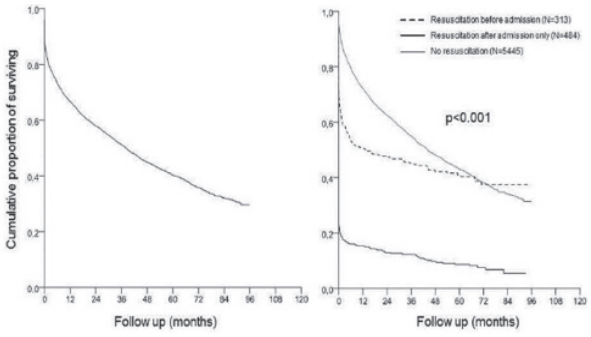


Figure 1 (abstract P438). Overall mortality (including hospitalization). Total *n* = 6,242.

frequently suffered cardiogenic shock, had more organ dysfunctions and died more frequently, respectively, with hospital mortality of 79.5% versus 29.1%, *P* <0.001; see also Figure 1.
Conclusion In patients hospitalized for acute heart failure, both prehospital and postadmission resuscitated cardiac arrest is a severe complication associated with significantly morbidity and mortality.

P439

Outcome of cardiopulmonary resuscitation in cancer patients in an Indian tertiary cancer center

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Introduction Cardiopulmonary resuscitation (CPR) after cardiac arrest in cancer patients is often discouraged as it is associated with poor outcome. In our 700-bed tertiary cancer hospital in Mumbai, India, the ICU runs an in-hospital cardiac arrest team (CAT). We reviewed our data to determine outcome from CPR, identify factors associated with improved outcomes and justify the presence of a CAT in our cancer hospital.
Methods All in-hospital patients from November 2012 to November 2014 (2-year period) with unanticipated cardiorespiratory arrests were included. Data were recorded prospectively using the Utstein template. Only patients with cardiac arrest rhythms were included. Patients with anticipated progression towards arrest, those with seizures, hypotension without dysarrythmias or other medical emergencies were excluded. The outcomes studied were return of spontaneous circulation (ROSC) and survival on hospital discharge (SOHD). Binary logistic regression analysis was performed to determine factors associated with ROSC and SOHD.
Results One hundred and ninety-three patients (110 males, 83 females, mean age 48.2 ± 18.3 years) were studied. The mean time interval between collapse and onset of resuscitation was 2.3 ± 2.1 minutes. A total of 65.3% arrests were witnessed. Sustained ROSC occurred in 36.8% patients and the SOHD was 24.9%. The initial rhythm recorded during CPR was asystole in 133 patients, pulseless electrical activity in 21 patients and ventricular fibrillation/tachycardia (VF/VT) in 39 patients. SOHD for these rhythms was 8.3%, 33.3% and 76.9%, respectively. On univariate analysis, type of rhythm, witnessed arrests and time to resuscitation were associated with sustained ROSC and SOHD. On multivariate analysis, only type of rhythm, VF/VT (*P* = 0.000) and PEA (*P* = 0.017), were significantly associated with SOHD, while witnessed arrest and time to resuscitation were not.
Conclusion Sustained ROSC occurred in 36.8% patients and the SOHD was 24.9%. A reduced response time, witnessed arrest and type of rhythm are associated with ROSC and improved SOHD. The type of rhythm was independently associated with SOHD, with VF/VT and PEA having improved survival while asystolic patients had a poor outcome. These considerations justify the presence of a CAT in our cancer hospital.

P440

Outcome after CPR: when we cannot save lives, we can save organs

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Introduction Patients resuscitated after cardiac arrest (CA) who suffer bad neurologic outcome or become brain dead might become organ donors (OD) when well managed and identified. We report on the cohort of patients resuscitated after in-hospital or out-of-hospital CA becoming OD in a tertiary community hospital with an intensive donor identification program.
Methods Data from our 28-bed mixed medical/surgical adult ICU in a 900-bed tertiary hospital were analyzed from 2010 to 2014.
Results Our ICU admitted 2,320 patients/year. Overall ICU mortality in this period was 7.4%. A summary of the results is presented in Table 1. Of the 219 patients admitted after CA, 21 (10%) became OD. This resulted in 55 successfully transplanted organs (28 kidneys, 17 livers, seven lung pairs, three hearts). Of note, good outcome (CPC 1 and 2) was achieved in 55 patients (25%).

Table 1 (abstract P440)

Year	Organ donors	Donors after CA	DCD/DBD	ICU admission after CA
2010	11	3	0/3	40
2011	9	5	3/2	41
2012	18	4	3/1	47
2013	17	5	4/1	53
2014	13	4	1/3	38
Total	68	21 (31%)	11/10	219

Conclusion Ten percent of patients resuscitated after CA and admitted to the ICU become OD, consisting of up to 31% of the total number of OD in our center. Patients resuscitated after CA who suffer severe irreversible brain damage or are brain dead can thus substantially expand the donor pool. This justifies extensive resuscitation efforts, if not to save lives, then to save organs. This might be reassuring for families, staff and the community.

P442

Effect of alcohol in blood on neurological outcome and survival of patients with combination of polytrauma and head injury

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Introduction The association between blood alcohol level (BAL) on mortality and neurologic outcome in patients with polytrauma and head injury is not clear and the data in the literature are sometimes conflicting. Some studies suggest a possible neuroprotective effect of alcohol and increased survival while others show the opposite. The rationale for this study was to investigate whether BAL has any impact on presentation, neurologic outcome and survival in patients with combination of polytrauma and head injury.
Methods This is a retrospective study of 43 polytraumatized patients with head injury who were intubated and treated by the prehospital unit and transported to the trauma center. Patients were grouped according to their BAL into BAL+ (>0.5 mg/l) and BAL– (≤0.5 mg/l). Inclusion criteria were age ≥18, Injury Severity Score ≥16 and head Abbreviated Injury Scale (AIS) ≥3. Physiological parameters and outcome with respect to survival to hospital discharge (STHD) and functional outcomes were analyzed. Severity of injuries was measured using the Trauma–Injury Severity Score (TRISS) and head injury using AIS. Functional outcome was measured using the Glasgow Outcome Scale (GOS), Cerebral Performance Category (CPC) and Glasgow Coma

Scale (GCS) at discharge. Differences among groups were analyzed using Student's t test, the Mann–Whitney U test and the chi-square test.
Results BAL did not have a significant effect on presenting physiological parameters. There was a significant difference in the age of the groups, showing that patients in the BAL+ group were younger (32.6 vs. 56.8 years; 95% confidence level; $P = 0.000$). BAL had a lasting effect on functional measures of neurological outcome which showed better results in the BAL+ group; it had significantly better GOS (4.7 vs. 3.9; 95% confidence level; $P = 0.027$), and GCS at discharge was on the border of statistical significance (15 vs. 14; 95% confidence level; $P = 0.05$). Other variables (TRISS, AIS, STHD, CPC) did not show statistically significant differences among groups.
Conclusion Presence of alcohol in the blood had a positive effect on neurological outcome but there was no significant difference in survival. However, the positive results in neurologic outcome in the BAL+ group may also be due to the fact that this group was younger. The small number of patients in the study is another limiting factor of the interpretation. Therefore, the neuroprotective role of alcohol needs further clarification.

P443

Endothelial dysfunction in acute brain injury and the development of cerebral ischemia

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Introduction Cerebral ischemia (CeI) is a major complicating event after acute brain injury (ABI) in which endothelial dysfunction is a key player.
Methods We studied cellular markers of endothelial dysfunction and peripheral reactive hyperemia index (RHI) in 26 patients with ABI at admission and after 6 and 12 days, and compared these with healthy volunteers ($n = 15$). CeI was determined clinically or using computer tomography.
Results In patients with ABI, RHI at admission was significantly reduced compared with healthy subjects ($P = 0.003$), coinciding with a decrease in circulating endothelial progenitor cells (EPC) ($P = 0.002$) (Table 1). The RHI recovered in eight patients without development of CeI (Figure 1, black), but failed to fully recover by day 12 in three out of four patients that developed CeI (Figure 1, red). Despite recovery of the RHI within 12 days in these patients ($P = 0.003$), the EPC count remained significantly lower after 12 days in patients with ABI ($P = 0.022$) (Table 1). $CD31^+$ T cells and endothelial microparticles were not different between controls and patients. No differences were noted in cellular markers of endothelial dysfunction in patients developing CeI and those not.
Conclusion Patients with ABI exhibit impaired microvascular endothelial function measured as RHI and a decreased circulating level of EPC.

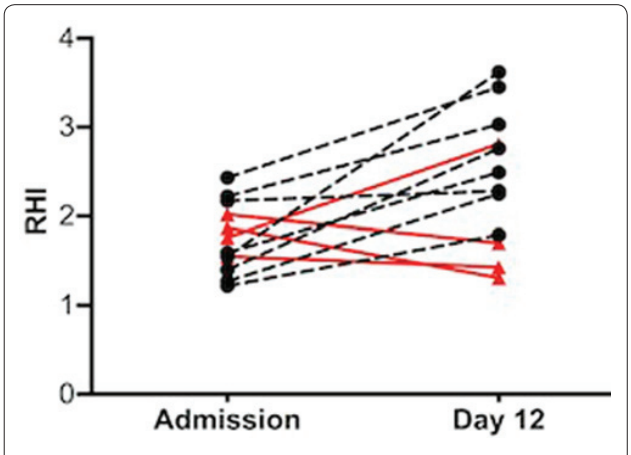


Figure 1 (abstract P443).

Table 1 (abstract P443). Evolution in time of markers of endothelial dysfunction after acute brain injury

	Healthy volunteers ($n = 15$)	D0	D6	D12
EPC/10^5 PBMC	24.1 ± 6.3	11.9 ± 2.2	11.0 ± 1.8	12.6 ± 2.3
%$CD31^+$ of T cells	43.1 ± 2.6	42.4 ± 2.4	40.1 ± 3.0	43.4 ± 2.8
RHI ($n = 12$)	2.41 ± 0.14	1.68 ± 0.12	2.14 ± 0.15	2.46 ± 0.21

P444

Survey on ICP, target CPP and MAP measurement level in patients with severe acute brain injury in different ICUs

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Introduction Since most patients with acute brain injury are treated head-up at 30 to 45°, there can be a height difference of up to 15 cm between the heart and the ear canal. This causes a difference between mathematical CPP and true CPP of up to 11 mmHg depending on the zero reference level used and the body length of the patient (Figure 1). We conducted a survey to analyze the current practice on CPP targets and zero reference levels in different ICUs.
Methods Neuro-ICU physicians were invited to participate in a survey on ICP and CPP targets and the level of measurement.
Results The results of 30 centers are summarized in Table 1. Most centers (83.3%) use head-up elevation of 30 to 45° and consider an ICP of 20 mmHg as the threshold to start treating ICP (80%). More variation is noted in minimal and maximal CPP threshold. All centers measure ICP at the ear canal. Twenty-seven centers (90%) measure MAP at the heart, three centers measure MAP at the ear canal. These three centers use >50, 60 and 65 mmHg as minimal CPP and raise the bed to 30 to 45°. The two centers using minimal CPP >60 mmHg do not apply an upper limit.
Conclusion Considering the influence of position on CPP, the variations among centers and the narrow range of CPP thresholds, future studies and guidelines should describe where MAP is measured. Alternatively, we propose a new formula for CPP: true CPP = MAP(heart) – ICP(ear) – height difference (heart to ear canal (cm)) × 0.73.

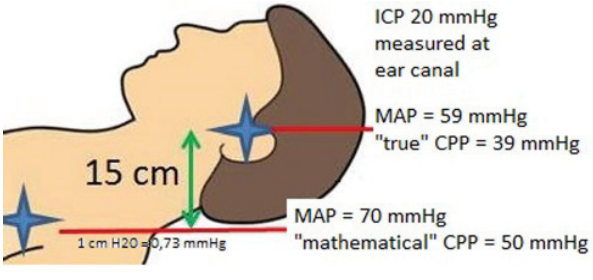


Figure 1 (abstract P444).

Table 1 (abstract P444)

ICP threshold (mmHg); *n* (%)	**>15; 2 (6.7%)**	**>18; 1 (3.3%)**	**>20; 24 (80%)**	**>25; 3 (10%)**
Minimal CPP (mmHg); *n* (%)	>50; 6 (20%)	>55; 4 (13.3%)	>60; 16 (53.3%)	>65 to 70; 4 (13.3%)
Maximal CPP (mmHg); *n* (%)	<70 to 75; 8 (26.7%)	<80; 8 (26.7%)	<85; 2 (6.7%)	No limit; 12 (40%)

P445

Comparison of ^{15}oxygen positron emission tomography and near-infrared spectroscopy for measurement of cerebral physiology

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Introduction The gold standard technique for imaging cerebral blood flow (CBF) and metabolism is ^{15}oxygen positron emission tomography (^{15}O PET). Continuous near-infrared spectroscopy (NIRS) has been used to assess adequacy of cerebral oxygenation following stroke, traumatic brain injury and subarachnoid haemorrhage [1], and measurements have been compared with jugular oxygen saturation. In this study we compared NIRS with ^{15}O PET within healthy volunteers.
Methods Fifteen healthy subjects were recruited (12 male, average age 38 years); PET precluded females of reproductive age. Steady-state ^{15}O PET with arterial sampling was performed to measure CBF, cerebral metabolic rate of oxygen ($CMRO_2$), oxygen extraction ratio (OEF) and cerebral blood volume (CBV) [2]. Simultaneously, NIRS data were collected using a Hamamatsu NIRO 200 with sensors on either side of the forehead. NIRS OEF was calculated from tissue oxygen saturation, SaO_2 and an assumed arterial/venous blood volume ratio of 30/70 [3].
Results The frontal region ^{15}O PET CBF, $CMRO_2$, OEF and CBV were mean (SD) 44.9 (10) ml/100 ml/minute, 158.7 (24.7) µmol/100 ml/minute, 45.8 (7.3)%, and 2.8 (0.8) ml respectively, and there was no relationship between NIRS and ^{15}O PET (Figure 1).

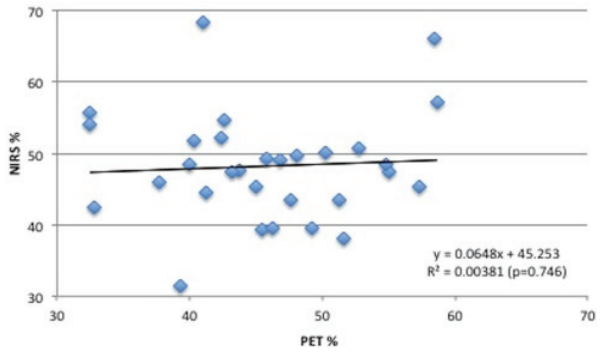


Figure 1 (abstract P445). Linear correlation between NIRS and PET OEF.

Conclusion We found no relationship between NIRS and baseline physiology as determined by ^{15}O PET. Further studies should assess the dynamic response of NIRS to a measured change in physiology in patients. Further confines of NIRS include its limited and focal brain coverage.
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P446

Evaluation of infection risk and antibiotic exposure in traumatic brain injury patients treated with therapeutic normothermia

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Introduction The purpose of this study is to assess the rate of confirmed infections, antibiotic exposure, and monitoring practices with normothermia protocol utilization for traumatic brain injury patients. Treatment and prevention of fever is a focus of therapy for patients with severe neurological injury as fever has been identified as an independent risk factor for morbidity and mortality [1].
Methods The retrospective chart review analyzed outcomes of maintaining normothermia at 36.5°C versus a similar population without temperature control as a standard of care in patients admitted with traumatic brain injuries defined as a Glasgow Coma Score <8 upon admission. Patients included were 18 to 59 years of age and were mechanically ventilated with intracranial pressure monitoring for greater than 72 hours. The primary outcome evaluated was the number of patients treated for confirmed infections. Secondary outcomes included the antibiotic length of therapy (LOT), antibiotic days of therapy (DOT), number of cultures, and ICU and hospital length of stay (LOS). DOT was defined as the sum of days on which each antibacterial drug was administered.
Results A total of 23 patients treated with normothermia and 119 patients in the control group were evaluated between January 2009 and September 2014. The number of patients treated for confirmed infections was similar between groups (normothermia: 73.9%, control: 80%, $P = 0.803$). Empiric antibiotic therapy was more commonly utilized in the normothermia group at 34% versus 20.5% ($P = 0.173$). Antibiotic LOT and DOT were 13.8 versus 10.8 days ($P = 0.157$) and 18.3 versus 16.2 days ($P = 0.575$) in the normothermia versus control groups, respectively. Total culture rate was lower in the normothermia group with 13.2 versus 8.78 ($P = 0.0002$) cultures per patient. No significant difference in hospital LOS (normothermia: 23 days, control: 18 days, $P = 0.158$) or ICU LOS (normothermia: 17 days, control: 15 days, $P = 0.185$) was demonstrated.
Conclusion Rates of confirmed infections and number of antibiotic days were similar between the normothermia and control groups, suggesting that normothermia does not increase infection risk. However, the number of cultures obtained in the control group was significantly greater than the normothermia group with a trend toward increased empiric antibiotic use.
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P447

Effect of osmotherapy with mannitol or hypertonic saline on cerebral oxygenation and metabolism in patients with intracranial hypertension after severe brain injury

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Introduction Osmotherapy with mannitol (Man) or hypertonic saline (HTS) is currently used to treat elevated intracranial pressure after severe acute brain injury (sABI); however, their effect on cerebral oxygenation and metabolism has not been extensively evaluated.
Methods A retrospective analysis of a cohort of patients with sABI after traumatic brain injury (TBI) and subarachnoid hemorrhage (SAH) monitored with cerebral microdialysis (CMD), brain oxygen ($PbtO_2$) and ICP, who were treated with Man (20%, 0.5 g/kg) or HTS (7.5%, 100 ml) for ICP >25 mmHg. Osmotherapy was administered over 20 minutes and each patient's individual response to intervention was analyzed up to 120 minutes following infusion. Only episodes where no other hypertonic solute was administered within 2 hours before or after treatment were selected. Variables analyzed included CMD lactate, pyruvate, glucose, glutamate, lactate/pyruvate ratio, and main brain physiologic variables ICP, $PbtO_2$, CPP. Analysis was conducted using mixed-effects multilevel regression.
Results Sixty-four treatments (32 HTS, 32 Man) were studied among 26 patients (19 TBI, seven SAH; age 42 ± 17 years, time from injury to treatment 2.6 ± 1.9 days). Man and HTS effectively decreased ICP (coefficient = –2.5 mmHg, 95% CI = –3.2 to –1.8 mmHg and –2.9 (–3.8 to –2.0) respectively; both $P < 0.0001$). No significant difference was found in CMD lactate, pyruvate, glucose and $PbtO_2$ after HTS or Man treatment. CMD glutamate decreased significantly after Man (–0.73 (–1.41 to –0.052); $P < 0.05$), but not after HTS.
Conclusion Osmotherapy with Man and HTS treatment had no effect on cerebral oxygenation and metabolism. Man, but not HTS, favorably reduced brain glutamate. These findings support further investigation to test the value of alternative osmotic agents (such as hypertonic lactate) that may reduce ICP and at the same time improve cerebral metabolism after sABI.
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P448

Neuroenergetic response to prolonged cerebral glucose depletion after severe brain injury and the role of lactate

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Introduction In patients with acute brain injury (ABI), increased cerebral energy demand is frequent, potentially leading to cerebral glucose depletion (GD) and poor outcome. In this setting, lactate may act as supplemental fuel. We examined dynamics of cerebral lactate supply during prolonged GD in ABI.
Methods We retrospectively analyzed severe ABI (18 TBI, eight SAH) monitored with brain oxygen and cerebral microdialysis (CMD) to measure hourly levels of cerebral extracellular glucose, lactate, pyruvate and lactate/pyruvate ratio (LPR). Variations of CMD variables were analyzed as a function of GD (defined as spontaneous decreases of CMD glucose from normal to low (<1.0 mM), at least 2 hours) and increased cerebral energy demand (LPR >25).
Results During GD (60 episodes; 26 patients), we found an increase of CMD lactate (4 ± 2.3 vs. 5.4 ± 2.9 mM) and LPR (27 ± 6 vs. 35 ± 9; all P <0.005) while brain oxygen and blood lactate remained normal. Dynamics of lactate and glucose supply were studied by analyzing the relationship between blood and CMD samples. No correlation between blood and brain lactate was found when brain glucose and LPR were normal (r = –0.12, P = 0.48; Figure 1), while this correlation became linear during GD, progressively rising to r = 0.53 (P <0.0001) when energy demand increased, suggesting increased cerebral lactate availability. The correlation between blood and brain glucose changed in the opposite direction, decreasing from r = 0.78 to 0.37 (P <0.0001) during GD and at LPR >25.

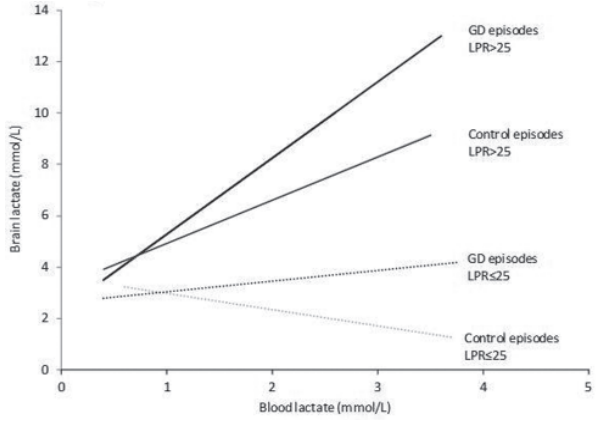


Figure 1 (abstract P448). Correlations between blood and brain lactate.

Conclusion Energy dysfunction is associated with increased supply of nonhypoxic cerebral lactate. Our data suggest lactate may act as alternative substrate after ABI when availability of cerebral glucose is reduced.

P449

Correlation between intracranial pressure and pulsatility index measured by transcranial Doppler in children with severe trauma brain injury

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Introduction This study was designed to see whether there is a correlation between the transcranial Doppler (TCD) parameters and the CCP and intracranial pressure (ICP) monitoring during the cerebral hemodynamic changes and to evaluate ICP indirectly by TCD.
Methods A prospective and descriptive study conducted in our PICU from June 2011 to December 2013. We investigated 51 children with severe trauma brain injury (TBI). The TCD measurements were routinely performed bilaterally on the middle cerebral artery parallel to the ICP registration. The ICP and CPP data were correlated to PI and the correlation coefficient calculated. To control the linear correlation, the residuals were tested for normal distribution around the regression line.
Results ICP registrations were made parallel with all TCD measurements in 51 patients. Intraparenchymal ICP monitoring was inserted within the first 3 hours after trauma and there was no complication (infections, intracranial hemorrhage, or technical failure) related to invasive ICP monitoring. Increased ICP was noted upon transducer insertion in 38 children with male prevalence (10 girls, 28 boys). Median GCS was 6, indicating the magnitude of injury in this group of patients. The overall results of the 38 patients showed a strong correlation between the ICP and PI and during outbursts of ICP with a correlation coefficient of r = 0.89 (ICP >20 mmHg) and r = 0.90 (ICP <20 mmHg). The relation between ICP and PI was estimated by the linear regression equation: ICP = 22,299 × PI – 10,705 (ICP >20 mmHg) and ICP = 38,592 × PI – 16,972 (ICP <20 mmHg). The CPP and PI were correlated significantly during the changes in intracranial pressure. However, a better correlation was found when ICP >20 mmHg and PPC <50 mmHg (PI was 2.4 ± 0.89 when CPP was 35.96 ± 4.48 with a correlation coefficient of Pearson r = 0.80) than when ICP <20 mmHg and CPP >50 mmHg (PI was 0.78 ± 0.14 when CPP was 57.11 ± 9.62 with a correlation coefficient of Pearson r =0.76).
Conclusion The absolute value of the PI is a reliable noninvasive indicator of ICP in pediatric severe TBI. A strong correlation between PI and ICP was demonstrated. Therefore, PI may be of guiding value in the invasive ICP placement decision in the neurointensive care patient when ICP monitoring is not systematically performed. In particular, ICP monitoring remains as grade C in the latest guidelines of management of STBI in children published in 2012.

P450

Bispectral index as a predictor of unsalvageable traumatic brain injury

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Introduction The aim was to evaluate the accuracy of bispectral index (BIS) monitoring for the diagnosis of brain death in severely comatose patients. We aimed to determine the utility of the BIS as a tool for clinical evaluation of the moment of brain death.
Methods A prospective observational study with waiver of consent was conducted in the trauma ICU for 2 years from October 2012 to September 2014. Monitoring of BIS occurred during patient stay in the ICU. Population: 62 severely comatose patients (Glasgow Coma Score less than 6) admitted to the ICU mainly because of intracerebral hemorrhage, head injury, or postanoxic coma. BIS was recorded continuously during the hospitalization in the ICU. Where necessary, clinical brain death was confirmed by EEG or brain stem test.
Results Twenty-nine patients were already clinically brain dead at the time of admission, and their individual BIS values were 0. Twenty-four patients were not clinically brain dead at the time of admission, and their individual BIS values were between 20 and 30. These patients became brain dead, and their individual BIS values dropped to 0 in a few hours to a few days. Seventeen patients who did not become brain dead during their hospitalization in the ICU had persistent electrocerebral activity on EEG, and their average BIS values remained above 31.
Conclusion The BIS is a noninvasive, simple, and easy to interpret method, showing a perfect correlation with the other diagnostic methods. BIS can be used in severely comatose patients as an assessment of brain death.

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P451

Neuromonitoring of patients with severe traumatic brain injury at the bedside

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Introduction Measurement of intracranial pressure (ICP) and arterial blood pressure is used to derive cerebral perfusion pressure (CPP) and to guide targeted therapy of severe traumatic brain injury (TBI) necessitating ICU admission. In this review we discuss the evidence for ICP monitoring, CPP calculation, and ICP/CPP-guided therapy after severe TBI. Despite its widespread use, there is currently no class I evidence that ICP/CPP-guided therapy improves outcomes. Similarly, no class I evidence can currently advise the ideal CPP.
Methods A review of current literature with special focus on autoregulation (PRx)-guided CPP treatment in TBI patients.
Results Optimal CPP is probably patient, time, and pathology specific and related to cerebral autoregulation status. The fact that optimal CPP and autoregulation status varies between individual patients and over time makes it an attractive bedside tool to serve as a (simplified) model to investigate the use of autoregulation (PRx) status to fine tune or feedback clinical treatments in individual sedated TBI patients (optimal CPP concept) [1]. Evidence is emerging for the role of other monitors (representing (local) metabolism, oxygen supply/use, perfusion, neuronal functioning) that enable the intensivist to employ an individualized multimodality monitoring approach in TBI [2].
Conclusion The management of TBI is likely to become increasingly based on a more comprehensive monitoring and management approach rather than relying on absolute numbers of ICP and CPP in isolation. This will allow individual optimization of perfusion and therefore of oxygen and energy substrate delivery. We await further robust, high-quality evidence to support the benefits of using more sophisticated monitoring tools like the autoregulation-guided CPP concept during the ICU management of TBI. For the near future, more important is a greater understanding of the underlying pathophysiology.
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P452

Technique for continuous bedside monitoring of the global cerebral energy state

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Introduction In the present experimental study we explore whether cerebral venous lactate/pyruvate ratio (LP ratio) measured by intravascular microdialysis during induced hemorrhagic shock may be used as a surrogate marker for compromised cerebral oxidative metabolism.
Methods Six female pigs were anesthetized and vital parameters was recorded. Microdialysis catheters were placed in cerebral hemisphere parenchyma, the superior sagittal sinus and femoral artery. Brain tissue oxygenation ($PbtO_2$) and intracranial pressure (ICP) was recorded. Hemorrhagic shock was achieved by bleeding the animals to a mean arterial pressure (MAP) of approximately 35 mmHg. Animals were kept at a MAP of about 30 to 40 mmHg for 90 minutes. The animals were resuscitated with reinfusion of shed blood followed by 3 hours of observation.
Results In the cerebral hemisphere, hemorrhagic shock caused a marked increase in the LP ratio, while a significant but minor increase was observed in the sagittal sinus. The LP ratio increased and continued doing so to a very high level. In the femoral artery, the shock period was associated with a slight increase of the LP ratio. The increase in the LP ratio in the sagittal sinus was markedly and significantly higher than in the arterial blood. Further, the dynamic changes in the LP ratio in the sagittal sinus followed that of the parenchyma, not the arterial blood. After infusion of blood ICP increased, cerebral perfusion pressure and $PbtO_2$ decreased and the microdialysis showed continuous signs of ischemia and cellular degradation.
Conclusion This experimental study documents that during protracted pronounced hemorrhagic shock, cerebral energy metabolism was severely compromised and exhibited a biochemical pattern typical of ischemia and cellular degradation. After retransfusion this pattern continued. From intravenous microdialysis in the sagittal sinus, it is possible to achieve semiquantitative information of the intracerebral redox state. Accordingly, it might be possible to monitor the global cerebral energy state continuously with a strictly extracerebral technique. This technique might be valuable in various severe conditions during critical care when cerebral energy metabolism may be compromised; for example, resuscitation after cardiac standstill, open heart surgery, multitrauma and so forth. Interestingly the study also showed that after reinfusion of blood other parts of the body recovered, evaluated by microdialysis, but the brain showed signs of damage, making the brain the limiting organ in hemorrhagic shock.

P453

Amantadine sulfate treatment in cases with brain injury in the ICU: a retrospective clinical trial

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Introduction Improvement of recovery is a challenging process in cases with varying degrees of severe brain injury (BI) requiring intensive care. Amantadine sulfate (AS) is recommended for use in cases with brain injury. The Coma Remission Scale (JFK-CRS) consists of auditory–visual–motor–mouth–tongue functions, communication and awareness scales; provides a score between 0 and 23; and shows numeric recovery from coma. The aim of this study was to evaluate outcomes and effects of AS used for neurorecovery on the Glasgow Coma Scale (GCS) and JFK-CRS in our ICUs during the last 5 months.
Methods After approval of the Ethics Committee, we recruited 12 patients with brain injury resulted from trauma or hemorrhage who had initial GCS of ≤9 and received AS (500 mg, twice daily over 10 days) during the recovery period. In all subjects, age, gender, diagnosis, initial APACHE II score, time of initiation of AS therapy, JFK-CRS and GCS scores, aspartate aminotransferase, alanine aminotransferase, BUN, creatinine, platelet count, electrocardiography findings, electrolyte values and arterial blood gas values on days 1, 6, 10 and 14 were recorded.
Results The patients' diagnoses included two post-CPR, five intracranial and one subdural hematoma, one CVA, one postoperative aneurysm, one subarachnoid hemorrhage and one brain contusion. Table 1 (overleaf) presents the findings. The AS therapy was initiated between days 3 and 33 of admission in all patients other than Patients 2 and 8. A dramatic improvement was observed in a patient with both GCS and JFK-CRS score of 5 when AS therapy was initiated in month 5 and the patient was discharged for home care. In Patient 9, AS therapy was withdrawn on day 5 due to persistent thrombocytopenia (TP) despite exclusion of other reasons; subsequently, improvement was observed in TP. The complications were relatively less severe with average acceptability.
Conclusion We suggest that an AS dose of 1,000 mg/day (over 10 days) seems to improve neurorecovery in BI patients with good tolerability. Prospective controlled studies with large, homogeneous BI populations will better define the role of AS for recovery and complications.

P454

Prognostic value of ubiquitin carboxy-terminal hydrolase L1 in patients with moderate or severe traumatic brain injury: a systematic review

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Introduction Traumatic brain injury (TBI) prognostication is a developing field striving to identify indicators, notably neurochemical

Table 1 (abstract P453). Findings of 12 patients receiving amantadine sulfate

Patient number	Sex/age (years)	APACHE II	GCS A/B/C	Initiation of AS therapy (day)	CRS score D/E/F/G	Complications	Outcome
1	M/14	24	3/5/7	6	0/4/5/6	H, J	Still in ICU
2	F/78	33	8/8/10	84	0/0/0/0	K	Ex
3	F/75	35	5/6/4	4	1/1/0/Ex	K, L	Ex
4	M/24	29	3/3/3	6	0/0/Ex	K, L	Ex
5	M/27	27	4/4/15	6	1/13/18/22	L, M, J	Discharged
6	F/70	45	3/3/3	20	0/0/0/0	–	Ex
7	F/72	22	5/5/12	3	4/7/11/17	K, L, I	Discharged
8	F/53	27	3/5/10	150	5/7/10/14	K	Discharged
9	F/38	34	4/4/4	33	0/0/1/1	H, J	Still in ICU
10	M/50	26	4/6/13	8	0/7/18/19	L, J	Discharged
11	M/63	24	8/10/12	14	6/8/8/12	–	Discharged
12	M/50	31	4/6/11	6	2/5/7/9	L, J	Still in ICU

F, female; M, male. GCS, Glasgow Coma Scale: A, at admission to ICU; B, at initiation of AS therapy; C, outcome value. CRS: D, value on day 1; E, value on day 6; F, value on day 10; G, value on day 14. Complications observed: H, low platelet; J, ALT increase by twofold; K, BUN increase by twofold; L, AST increase by twofold; M, convulsion.

biomarkers, of long-term outcomes. Among these, ubiquitin carboxy-terminal hydrolase L1 (UCH-L1) is currently being investigated to define its potential prognostic value. The objective of this systematic review is to determine the ability of UCH-L1 to predict prognosis following a moderate or severe TBI.

Methods The MEDLINE, Embase, The Cochrane Library and BIOSIS electronic databases, conference abstracts and existing narrative reviews were searched from their inception to July 2013. Cohort studies including patients with moderate or severe TBI having evaluated the prognostic value of UCHL-1 according to mortality or the Glasgow Outcome Scale (GOS) were considered. Data concerning patients, outcomes, study methods, and laboratory methods were abstracted. Pooled results were planned to be presented using mean differences and analyzed using random effect models, as well as sensitivity analyses to explain potential heterogeneity.

Results Our search strategy yielded 2,257 articles, of which five studies corresponded to our inclusion criteria (n = 730). All studies were performed by the same group of researchers. Five studies reported mortality (n = 515), two studies reported GOS (n = 58). Results from all included studies observed that UCHL-1 was a significant predictor of mortality. However, only two studies represented a unique study population, thus precluding a meta-analysis.

Conclusion In this systematic review, we observed that all published studies on UCHL-1 were conducted by the same group of investigators and presented results from an intersecting cohort of patients. Due to the paucity of data, we could not perform a pooled analysis and conclude on the association of this biomarker with long-term prognosis. Assays using UCHL-1 were only recently developed and further studies done by different research teams will be needed to determine the reproducibility and validity of UCH-L1 as a potential prognostic tool.

P455

Cannabinoid 2 receptor antagonism reverses central nervous system injury-induced immune deficiency syndrome

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Introduction Central nervous system (CNS) injury, such as stroke, is known to increase susceptibility to infections that adversely affect clinical outcome. This impaired immune response to infection is termed CNS injury-induced immune deficiency syndrome (CIDS). Activation of the cannabinoid 2 receptor (CB2R) suppresses immune function suggesting that antagonism of this receptor may overcome CIDS. The main purpose of this study was to determine the impact of CB2R inhibition on leukocyte activation within the microcirculation following endotoxin challenge in an experimental stroke model.

Methods This was a prospective, randomized animal study. Five experimental groups (male C57BL/6 mice, age: 6 to 8 weeks) were subjected to the following treatments: control; endotoxemia (LPS 5 mg/kg, i.v.); transient cerebral hypoxia–ischemia (HI) + endotoxemia; HI + endotoxemia + CB2R antagonist (AM630 2.5 mg/kg, i.v.). HI was induced by unilateral carotid artery occlusion, followed by 50-minute exposure to a low oxygen atmosphere (8% O_2). The CB2R antagonist was given 15 minutes prior to LPS administration. Intravital microscopy was carried out 2 hours after LPS administration. Brains were then extracted and stained with tetrazolium chloride to calculate the infarct volume. The primary outcome measurement in this study regarding the immune response after stroke was the quantification of leukocyte adhesion following endotoxin challenge in submucosal venules of the gut – an important organ in the development of multiorgan failure in endotoxemia and sepsis.

Results Compared with endotoxemic animals without CNS injury, mice subjected to HI displayed reduced leukocyte activation in intestinal submucosal venules indicative of CIDS. Administration of the CB2R antagonist in animals with CIDS challenged with endotoxin restored peripheral leukocyte recruitment without a detrimental impact on infarct size.

Conclusion CB2R-related modulation of leukocyte activation is involved in the impaired immune response following CNS injury. Future studies will explore the CB2R pathway in order to develop novel therapies to improve the immune response in CIDS.

P456

Implementation process of a large multicenter study in trauma

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Introduction Our purpose was to evaluate the time from shipping of the study start-up package to study screening, as well as conditions that may impact this process, in the context of a large-scale multifaceted and multicenter clinical study in trauma.

Methods We designed a survey questionnaire based on four domains: REB characteristics and process, centers' characteristics, experience of the study and clinical teams, and center-specific implementation approaches. The questionnaire was self-administered to all lead research coordinators of the 17 level 1 participating trauma centers in

the ongoing Pan-Canadian TBI-Prognosis Study. Descriptive statistics were used.
Results Overall, 33.4 weeks (95% CI = 24.8 to 42.1) were required on average from the start-up package mailing to centers and the start of the screening process. Data sharing and financial agreement were mainly responsible for this delay with an average of 28.6 weeks (95% CI = 20.4 to 36.7) needed to complete the agreement with the coordinating center. REB approval was obtained on average 17.5 weeks (95% CI = 13.8 to 21.2) from the shipping of the study package to the participating centers. Eighty percent of the REBs had members with prior experience in multicenter clinical research, and more than half with specific clinical expertise in critical care medicine or neurology/neurosurgery. A standardized electronic REB submission process was used in most REBs (60%). All centers had experience in implementing multicenter clinical studies. PIs had experience conducting from zero to 40 prior clinical studies and from 3 to 24 years of research experience with protected research time ranging from 5 to 75%. RCs had managed from zero to more than 50 clinical studies. Most centers (87%) organized specific presentation of the study to the critical care medical staff (93%), while some (60%) presented the study to other medical teams. Agreements from other departments such as radiology (87% of centers), electrophysiology (80%) and clinical imaging (73%) were requested in most centers.
Conclusion The implementation of a large Canadian multicenter and multifaceted clinical study in the trauma population involved a significant amount of time and energy from both the coordinating and the participating sites. The variable experience of participating sites and teams, as well as the involvement of different medical disciplines, may have had an impact on study implementation time. Delays for REB approval but also for data sharing and financial agreement must be taken into consideration in the timeline for implementing large multicenter clinical studies in trauma.

P457

Optic nerve sheath diameter by bedside ultrasound is a reliable screening test for cerebral edema in the comatose ICU patient

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Introduction ICU patients may remain comatose after resolution of critical illness. Frequently this is due to delayed sedative clearance but may also result from increases in intracranial pressure (ICP) and cerebral edema. We proposed that measurement of the optic nerve sheath diameter (ONSD) is a rapid, bedside screening test that can be used to quickly identify patients with cerebral edema and increased ICP.
Methods This was a prospective, observational study carried on consecutive patients admitted to a multidisciplinary medical and surgical ICU. Stable patients with unexplained coma and scheduled for brain imaging were included. Patients with obvious ocular trauma or on sedative, narcotic infusions were excluded. ONSD was measured using a 7.5 to 10 MHz linear array ultrasound transducer probe placed on the closed eye in the transverse axis. The ONSD was measured at a predefined point 3 mm posterior to the globe. Both eyes were measured and the mean value used. The study protocol was approved by the Hospital Research Ethics Committee (RAC Prop No. 2141 103). Statistical analysis was carried out using SPSS version 20.0.
Results ONSD was measured in 43 patients; mean age was 62 ± 19.2 years, 48% (n = 20) were female. Admitting diagnosis was sepsis in 24% (n = 10), intracranial vascular event in 21% (n = 9), cardiac arrest in 12% (n = 5), hepatic encephalopathy in 7% (n = 3), malignancy with metastases in 7% (n = 3) and other causes in 28% (n = 12). The ONSD measured correlated highly between eyes, Spearman's ρ = 0.799, $P \leq 0.001$. The area under the ROC curve for detecting cerebral edema was 0.812 (95% CI = 0.667 to 0.957). Using a 0.58 cm cutoff ONSD diameter, the sensitivity was 86%, specificity 74%, negative predictive value 96% and the positive likelihood ratio = 3.3.
Conclusion This study suggests that bedside measurement of ONSD by ultrasound performs well as an initial screening test for cerebral edema. The identified cutoff value of 0.58 cm can be used to detect cerebral edema with reasonable accuracy.

P458

Levels of N-terminal pro-brain natriuretic peptide in brain injury patients

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Introduction Currently, the most common way to predict the outcome of acute brain damage is to study the level of protein S-100 in the serum. This method lacks specificity as the concentration of protein S-100 significantly increases with age, more for men than women, and there are no data on prognostically significant changes in the level of S-100 after removal of the tumor and cerebral hemorrhages. Endothelins, vasopressin, some cytokines, excess sodium or calcium in serum, activation of the sympathoadrenal system, and tachycardia are the stimulants of brain natriuretic peptide production. The rise of the natriuretic peptide level in cases of acute brain damage has a functionally adaptive nature, based on vasodilation, diuretic action peptide and ability to reduce sympathoadrenal system activity. Thus, we can suppose that the more severe the damage, the higher the stimulation of natriuretic peptide. In this study we investigate the level of N-terminal pro-brain natriuretic peptide (NT-proBNP) in patients with severe brain damage and find correlation between the level of peptide and outcome.
Methods We studied 110 patients having brain injuries of various origins. All patients were divided into four groups. All patients were 20 to 72 years old, 58 men and 52 women. Group 1 (n = 17) – acute TBI, group 2 (n = 29) – patients operated on for the brain tumor, group 3 (n = 36) – hemorrhagic stroke, group 4 (n = 28) – vegetative state. We measured the level of brain natriuretic peptide on days 1 to 3, and then every 7 days for 21 days.
Results All patients with severe acute brain damage (groups 1, 2, 3) had a level of NT-proBNP higher than normal (normal 0 to 125 pg/ml). Significant difference in values between the groups was not observed. Level of NT-proBNP above 700 pg/ml and/or the absence of its reduction to normal dynamic indicators was marked by an unfavorable outcome of the disease – severe disability (n = 25) or death (n = 18). For patients from group 4 regardless of their age, sex, severity of condition and treatment results in a level of NT-proBNP below 250 pg/ml.
Conclusion In cases of acute severe brain damage the level of NT-proBNP significantly increased. Correlation between the level of NT-proBNP and etiology of acute brain damage was not observed. If the level of NT-proBNP is above 700 pg/ml and/or in the absence of its reduction to normal, then poor outcome of the disease – severe disability or death – can be predicted. Level of NT-proBNP cannot be used as an indicator for the severity of the status for patients in a vegetative state in contrast to patients with acute brain damage.

P459

Cerebral oximetry monitoring in pediatric seizure patients in the emergency department

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Introduction During ictal/post-ictal events, altered cerebral physiology occurs: increased neuronal activity causes significant increase in cerebral metabolism with changes in ipsilateral cerebral blood flow. Standard PED seizure monitoring is by O_2SAT and $ETCO_2$ which yield no direct data about regional cerebral oxygenation/physiology (rSO_2). Significant abnormal hemispheric cerebral physiology resulting in neurological injury can occur without knowing because the current monitoring system could not detect the abnormal hemispheric abnormality. Cerebral oximetry can provide a rapid, non-invasive detection of each hemisphere's cerebral physiologic changes during ictal/post-ictal phases. The aim was to study left and right rSO_2 values in patients in the pre and post seizure periods and in nonseizing controls.
Methods An observational study of seizing and nonseizing patient's left and right rSO_2 readings compared with nonseizure patients.

Comparison of Left and Right Cerebral between Seizure Cases and Control Cases

		Seizure Cases N = 185	Control Cases 133	P Value[3]
Age		2.96 ± 2.95	6.32 ± 5.52	<0.001
		N = 45	N = 133	
before seizure	Left Cerebral[1]	72.5 ± 8.9	70.2 ± 8.3	0.12
	Right Cerebral[1]	70.1 ± 10.0	70.5 ± 7.7	0.83
	Difference between side means[2]	5.9 (3.8,7.9)	3.8 (3.4,4.1)	0.002
		N = 185	N = 133	
First seizure	Left Cerebral[1]	56.7 ± 20.3	70.2 ± 8.3	<0.001
	Right Cerebral[1]	53.3 ± 22.1	70.5 ± 7.7	<0.001
	Difference between side means[2]	10.8 (9.4,12.2)	3.8 (3.4,4.1)	<0.001
		N = 151	N = 133	
Second seizure	Left Cerebral[1]	53.7 ± 17.3	70.2 ± 8.3	<0.001
	Right Cerebral[1]	50.1 ± 20.1	70.5 ± 7.7	<0.001
	Difference between side means[2]	14.1 (12.4,15.9)	3.8 (3.4,4.1)	<0.001
		N = 87	N = 133	
Third seizure	Left Cerebral[1]	58.5 ± 19.2	70.2 ± 8.3	<0.001
	Right Cerebral[1]	53.0 ± 23.9	70.5 ± 7.7	<0.001
	Difference between side means[2]	13.6 (11.4, 15.8)	3.8 (3.4,4.1)	<0.001
		N = 47	N = 133	
Fourth seizure	Left Cerebral[1]	53.2 ± 16.3	70.2 ± 8.3	<0.001
	Right Cerebral[1]	49.2 ± 20.0	70.5 ± 7.7	<0.001
	Difference between side means[2]	14.0 (11.1,16.9)	3.8 (3.4,4.1)	<0.001
		N = 27	N = 133	
Fifth seizure	Left Cerebral[1]	57.1 ± 18.3	70.2 ± 8.3	<0.001
	Right Cerebral[1]	49.8 ± 19.0	70.5 ± 7.7	<0.001
	Difference between side means[2]	16.6 (12.4,20.8)	3.8 (3.4,4.1)	<0.001
		N = 183	N = 133	
After the last seizure 10 min	Left Cerebral[1]	67.6 ± 8.3	70.2 ± 8.3	0.028
	Right Cerebral[1]	65.9 ± 9.5	70.5 ± 7.7	<0.001
	Difference between side means[2]	5.8 (4.9,6.6)	3.8 (3.4,4.1)	0.001

Comparison of left and right cerebral in focal seizures

	Focal Left				Focal Right			
	Left Cerebral	Right Cerebral	Difference between sides	P value[3]	Left Cerebral	Right Cerebral	Difference between sides	P value[3]
First Seizure		N = 15				N = 20		
	51.7 ± 19.5	68.8 ± 9.2	22.6 (10.9,28.2)	<0.001	73.9 ± 7.4	58.5 ± 23.6	22.7 (18.2,29.2)	<0.001
Second seizure		N = 21				N = 34		
	48.5 ± 15.8	66.7 ± 11.5	22.9 (18.5,27.3)	<0.001	62.1 ± 13.2	47.7 ± 20.8	24.5 (20.6,28.4)	<0.001
Third seizure		N = 5				N = 28		
	51.1 ± 21.4	63.9 ± 6.3	24.2(10.6,29.7)	0.15	63.8 ± 12.7	54.6 ± 23.7	21.3 (17.8,25.1)	0.05
All seizures		N = 39				N = 82		
	53.7 ± 20.3	65.6 ± 9.7	22.6 (20.9,26.2)	<0.001	62.7 ± 12.7	51.6 ± 20.8	20.6(18.8, 23.3)	<0.001

Comparison of duration between general case and focal case; focal left and focal right

	Focal Case	General	P value	Focal Left	Focal Right	P value
	N = 168, N' = 84	N = 295, N' = 162		N = 47, N' = 39	N = 103, N' = 62	
Duration(s)	14.2 (12.3,16.2)	18.9(16.7,20.3)	<0.001[3]	17.1 (13.3,20.9)	12.9 (10.7,15.1)	0.04[3]

Figure 1 (abstract P459).

Results No difference for ictal left and right rSO_2 readings across ages. See Figure 1.

Conclusion We have demonstrated abnormal hemispheric cerebral physiology during focal or generalized ictal activity. In patients with generalized seizures, the left and right rSO_2 values were significantly decreased. In patients with focal seizures, the ipsilateral rSO_2 values were significantly different from the contralateral rSO_2 readings and correlated to the hemisphere experiencing the focal seizure. In certain patients, during the ictal phase their rSO_2 readings rose and stayed or rose then dropped. Overall, cerebral oximetry has shown great monitoring potential for actively seizing patients in the emergency department.

P460

Neurophysiological tests in the neuro ICU

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Introduction Neurophysiological tests (NPTs) are important prognostic and diagnostic tools for patients admitted to the modern neuro ICU (NICU) [1]. Electroencephalography (EEG), somasensorial evoked potentials (SSEP), auditory brainstem response (ABR) and electromyography (EMG) complete clinical examination and radiological findings in patients suffering from post-traumatic brain injury, post-anoxic brain injury, refractory male epileticcus status, and neuromuscular illness. We evaluate the spread of NPTs in our NICU.

Methods We collected data from patients admitted to our NICU from January 2014 to November 2014. We recorded the admission diagnosis and the NPT applied.

Results From January 2014 to November 2014 we performed 521 EEG, 45 SSEP/ABR and 10 EMG. In post-anoxic and post-traumatic brain-injured comatose patients we performed EEG, SSEP and ABR 24 to 48 hours after the admission to predict later prognosis and expected neurological deficit [2]. In the presence of a benign pattern no further evaluation was performed; in the presence of a malignant pattern the NPTs were repeated every 48 to 72 hours according to the protocol of our institute. In post-anoxic comatose patients we recorded EEG during hypothermia to assure burst suppression. In post-traumatic brain-injured patients with a persistent comatose state we use EEG to detect nonconvulsive states which potentially can increase secondary brain injury if untreated. In malignant epilepticus status we use EEG to monitor the effect of therapy and to modify it. In patients who present profound weakness of legs and hands we performed EMG to distinguish primary peripheral myopolyneuropathy (Guillian Barrè, miastenia gravis) from secondary illness acquired in the ICU (critical polyneuropathy, critical myopathy) [3].

Conclusion NPT can improve management of patients admitted to the neuro ICU. The data provided can modify therapeutic strategies and improve outcome in these settings of patients.

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P461

Goal-directed cerebral hemodynamic strategy decreases the incidence of postoperative delirium in patients with intracranial hypertension in major abdominal surgery

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Introduction Increased intracranial pressure (ICP) adversely affects anesthesia due to a disturbed cerebral blood flow. In older patients this disturbance may increase the incidence of postoperative delirium (POD) and may lead to a poor outcome [1]. The standard hemodynamic protocol involves maintaining the mean arterial blood pressure (MAP), but in patients with intracranial hypertension it may not be enough to maintain adequate cerebral perfusion. The purpose of this study was to evaluate the protocol of maintaining cerebral perfusion pressure (CPP) in the prevention of postoperative delirium in older patients in abdominal surgery.

Methods A total of 132 ASA 3 patients, undergoing major abdominal surgery (duration 5.2 (4.3 to 6.5) hours) with ICP >12 mmHg evaluated by a venous ophthalmodynamometry [2], were included in our research. Patients were randomized into two groups: MAP group, in which MAP

was maintained above 70 mmHg or within 20% from baseline (n = 78); or CPP group, in which CPP was maintained above 60 mmHg or within 20% from baseline (n = 54). ICP, MAP and CPP were assessed every hour of anesthesia. Time of recovery of consciousness, incidence of POD and length of stay in the ICU and in the hospital were also evaluated.
Results Initial ICP was 14 ± 3 mmHg in the MAP group and 15 ± 2 mmHg in the CPP group. During the anesthesia it was stable without any significant change. Decreasing of MAP after induction of anesthesia was similar in two groups and it was stable during the anesthesia. The frequency of use of vasopressors and infusion rate was higher in the CPP group. Time of recovery of consciousness in the MAP group was higher (28 ± 7 minutes vs. 18 ± 5 minutes (P <0.05)). The incidence of postoperative delirium was higher in the MAP group (18% vs. 11% in the CPP group (P <0.05)). There were no significant differences between two groups in other complications. Total length of stay in the ICU and in the hospital was higher in the MAP group (6 ± 2 days vs. 4 ± 2 (P <0.05) and 15 ± 3 days vs. 12 ± 2 in the N group (P <0.05)).
Conclusion A goal-directed hemodynamic protocol of maintaining CPP can decrease the incidence of POD in older patients with intracranial hypertension after major abdominal surgery compared with a protocol of maintaining MAP.
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P462

Hydroquinone shows neuroprotective potential in an experimental ischemic stroke model via attenuation of blood–brain barrier disruption

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Introduction Hydroquinone (HQ), a major benzene metabolite, occurs naturally in various plants and food, and is also manufactured for commercial use. Although many studies have demonstrated the various biological effects of HQ, the neuroprotective effects of HQ following ischemic stroke have not been investigated. Therefore, in this study, we first examined the neuroprotective effects of HQ against ischemic damage in a focal cerebral ischemia rat model.
Methods It was proven that pre and post treatment with 100 mg/kg HQ protects from ischemia-induced cerebral damage, which was confirmed by evaluation of neurological deficit, positron-emission tomography and 2,3,5-triphenyltetrazoliumchloride staining.
Results In addition, pre and post treatment with 100 mg/kg HQ significantly attenuated ischemia-induced Evans blue dye extravasation, and significantly increased the immunoreactivities and protein levels of SMI-71 and glucose transporter-1 (GLUT-1), which were well known as useful makers of endothelial cells, in ischemic cortex compared with a vehicle-treated group.
Conclusion Briefly, these results indicate that pre and post treatment with HQ can protect from ischemic damage induced by transient focal cerebral ischemia, and the neuroprotective effects of HQ may be closely associated with the prevention of BBB disruption via increase of SMI-71 and GLUT-1 expressions.

P463

Impact of hyperthermia before and during ischemia reperfusion on neuronal damage and gliosis in the gerbil hippocampus induced by transient cerebral ischemia

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Introduction Hyperthermia can exacerbate the brain damage produced by ischemia. In the present study, we investigated effects of hyperthermia before and during ischemia–reperfusion on neuronal damage and glial changes in the gerbil hippocampus following transient cerebral ischemia using cresyl violet staining, NeuN immunohistochemistry and Fluoro-Jade B histofluorescence staining.
Methods The animals were randomly assigned to four groups: sham-operated animals with normothermia (normothermia + sham group); ischemia-operated animals with normothermia (normothermia + ischemia group); sham-operated animals with hyperthermia (hyperthermia + sham group); and ischemia-operated animals with hyperthermia (hyperthermia + ischemia group). Hyperthermia (39.5 ± 0.2°C) was induced by exposing the gerbils to a heating pad connected to a rectal thermistor for 30 minutes before and during ischemia–reperfusion.
Results In the normothermia + ischemia group, a significant delayed neuronal death was observed in the stratum pyramidale (SP) of the hippocampal CA1 region (CA1) 5 days after ischemia–reperfusion. In the hyperthermia + ischemia group, neuronal death in the SP of the CA1 occurred at 1 day post ischemia, and neuronal death was observed in the SP of the CA2/3 region at 2 days post ischemia. In addition, we examined activation of astrocytes and microglia using immunohistochemistry for anti-glial fibrillary acidic protein (GFAP) and anti-ionized calcium-binding adapter molecule 1 (Iba-1). GFAP-positive astrocytes and Iba-1-positive microglia in the ischemic hippocampus were activated much earlier and much more accelerated in the hyperthermia + ischemia group than those in the normothermia + ischemia group.
Conclusion Based on our findings, we suggest that experimentally hyperthermic precondition before cerebral ischemic insult produces more extensive neuronal damage and glial activation in the ischemic hippocampus.

P464

Effects of long-term exercise on memory recovery in the aged gerbil hippocampus after transient cerebral ischemia

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Introduction Therapeutic exercise is an integral component of rehabilitation for patients with stroke. Despite the high prevalence of cerebral ischemia in the older population, the mechanisms linking restorative exercise to memory recovery from ischemic stroke have not been completely understood in aged animals. In this study, we investigated effects of long-term exercise on neuronal death and memory recovery in the aged gerbil hippocampus after transient cerebral ischemia. We also investigated changes in gliosis, ischemia-induced myelin repair, microvessels, neurogenesis, and growth factor immunoreactivity in the hippocampus to study possible mechanisms of restorative exercise in memory recovery.
Methods The gerbils were divided into four groups (n = 12 in each group): the sham-operated group (Sham), 4-week sedentary group following ischemia (SD4), 1-week treadmill group following ischemia (TR1) and 4-week treadmill group following ischemia (TR4). Treadmill exercise was stared at 5 days after ischemia/reperfusion (I/R) and lasted for 1 or 4 weeks, and the animals were sacrificed 31 days after ischemia.
Results In this study, 4 weeks of treadmill exercise facilitated memory recovery despite neuronal damage in the CA1 region after I/R. On the other hand, the long-term treadmill exercise alleviated the increased gliosis in the CA1 region, and increased the myelin repairing and microvessels in the CA1 region and DG, and enhanced the ischemia-induced cell proliferation, neuroblast differentiation, neuronal maturation of the newly generated cells, and BDNF expression in the ischemic DG of the aged gerbil.
Conclusion These results suggest that, in the aged gerbil, long-term treadmill exercise after ischemic stroke could restore the impaired short-term memory function through the cumulative effects of multiple neurorestorative processes.

P465

Association between high arterial oxygen tension and long-term survival after intracerebral hemorrhage

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Introduction Liberal use of oxygen after brain insults remains controversial [1,2]. We studied whether high arterial oxygen tension

(PaO_2) is associated with decreased long-term survival in patients with spontaneous intracerebral hemorrhage (ICH) treated in the ICU.
Methods Data on primary admissions for adult patients (>18 years) treated for ICH in Finnish ICUs between 2003 and 2012 were collected from a nationwide ICU database. Patients were divided into three groups according to the PaO_2 value associated with the lowest measured PaO_2/FIO_2 ratio during the first 24 hours after ICU admission. High arterial oxygen tension was defined as PaO_2 >19.9 kPa; intermediate as PaO_2 13 to 19.9 kPa; and low as PaO_2 <13 kPa. The primary outcome was 6-month mortality.
Results Of the 3,033 patients, 63% (n = 1,923) had low PaO_2, 29% (n = 892) intermediate PaO_2, and 7% (n = 218) high PaO_2. Forty-nine percent of the patients died during the 6-month follow-up. Of these, 75% died before discharge from hospital. Univariate analysis showed that 6-month mortality was higher in the high PaO_2 group (61%) compared with the intermediate and low PaO_2 groups (52% and 46% respectively, P <0.001). Multivariate analysis, however, showed no statistically significant correlation between high PaO_2 and mortality (with the low PaO_2 group as the reference category, odds ratio for death (OR) for high PaO_2 = 1.10, 95% confidence interval (CI) = 0.76 to 1.58 and for intermediate PaO_2 = 0.96, 95% CI = 0.78 to 1.17).
Conclusion High PaO_2 is not predictive of 6-month mortality in patients treated for spontaneous ICH in the ICU. Therefore, targeting higher PaO_2 values appears to be a safe approach in order to avoid hypoxemia.
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P466

Prognostic value of blood lactate and glucose levels after aneurysmal subarachnoid hemorrhage

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Introduction In critically ill patients, blood lactate on admission is associated with outcome, but in patients with aneurysmal subarachnoid hemorrhage (SAH) this has not been investigated. We studied the association of early circulating lactate and glucose with unfavorable disease course. The prognostic role of both lactate and glucose was studied, hypothesizing that both may be increased due to sympathetic activation after SAH [1].
Methods In this retrospective cohort study we included consecutive patients with aneurysmal SAH admitted to the ICUs of two university hospitals in the Netherlands between November 2006 and December 2011. Exclusion criteria were: nonaneurysmal SAH, ICU admission >24 hours after ictus, death ≤48 hours after admission and no lactate measurement <24 hours after admission. Maximum blood lactate and glucose levels within the first 24 hours after SAH were used for analyses. The outcomes were DCI, defined as a new hypodensity on brain CT due to DCI, and poor outcome, defined as a modified Rankin Scale of 4, 5 or death 3 to 6 months after the ictus. We performed proportional hazard analyses to assess the associations of lactate and glucose with DCI, and logistic regression was used to assess the associations with poor outcome. Multivariable analyses were adjusted for established predictors for DCI and poor outcome.
Results Two hundred and eighty-five patients were included in the analyses. DCI occurred in 84 patients (29%) and 106 patients (39%) had poor outcome. Lactate was independently associated with DCI (adjusted HR = 1.16, 95% CI = 1.04 to 1.30) and poor outcome (adjusted OR = 1.53, 95% CI = 1.25 to 1.94). Maximum lactate and glucose were strongly related (Spearman's ρ = 0.55, P <0.001). In multivariable analyses including both lactate and glucose as independent variables, only lactate was independently related to poor outcome (OR = 1.42, 95% CI = 1.11 to 1.81), and only glucose was independently associated with DCI (HR = 1.10, 95% CI = 1.02 to 1.19).
Conclusion Maximum lactate in the acute phase after aneurysmal SAH is associated with both DCI-related infarction and poor outcome. Once glucose was considered, early lactate remained independently associated with poor outcome, while glucose, instead of lactate, was associated with DCI. These routinely available laboratory measurements may improve identification of patients at risk for complications or poor outcome after SAH. Confirmation of the pathophysiological significance of lactate and glucose in prospective research is warranted.
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P467

Prediction of 60-day case fatality after aneurysmal subarachnoid hemorrhage: external validation of a prediction model

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Introduction Aneurysmal subarachnoid hemorrhage (SAH) is a devastating disease with substantial morbidity and mortality. Prognostic modeling is an important instrument to identify high-risk patients in both clinical practice and research settings. Recently, a prognostic model to predict 60-day case fatality after aneurysmal SAH was developed with data from the International Subarachnoid Aneurysm Trial (ISAT) [1]. Our aim was to externally validate this model in a retrospective cohort of consecutive SAH patients.
Methods We included consecutive aneurysmal SAH patients admitted to one university hospital between October 2007 and October 2011. Exclusion criteria were: age <18 years, hospital admission >28 days after SAH, nonaneurysmal SAH, explicit objection by the patient to view the medical data and missing data on 60-day case fatality. The model's predictors were age, maximum lumen size of the aneurysm, Fisher grade and World Federation of Neurological Surgeons (WFNS) grade. Two versions of the model were validated: one with WFNS grade scored on admission and the other with WFNS grade assessed at the time of treatment decision, as a proxy to WFNS grade at randomization used in the ISAT. The outcome was 60-day case fatality. Model performance was assessed by studying discrimination, expressed by the area under the receiver operating characteristic curve (AUC), and calibration.
Results A total of 307 patients were included in the validation cohort. The observed 60-day case fatality rate was 30.6%. Discrimination was good, and was considerably better for the model with WFNS grade at treatment decision (AUC = 0.89) compared with the model with WFNS grade on admission (AUC = 0.82). Calibration was poor, with mean predicted probabilities of 17.0% for the model with WFNS grade on admission and 17.7% for the model with WFNS grade at the time of treatment decision.
Conclusion Our results indicate that the ISAT prediction model is generalizable, since the model showed adequate performance in an independent, unselected cohort of aneurysmal SAH patients. The model discriminated well between patients who died and those who survived the first 60 days after SAH. Additionally, use of WFNS grade at the time of treatment decision of the ruptured aneurysm improved model performance. However, since predicted probabilities were lower than observed probabilities, the ISAT prediction model needs to be adapted before use in clinical practice.
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P468

Cortical spreading depolarizations in patients with intracerebral hemorrhage: preliminary data

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Introduction Perihematomal edema (PHE) expansion contributes to increased morbidity and mortality after spontaneous intracerebral

hemorrhage (ICH). Pathophysiology of PHE is incompletely understood. Recently, the role of cortical spreading depolarizations (CSDs) in secondary brain injury was established in subarachnoid and traumatic brain injury patients. However, the value of CSDs after ICH is not known.
Methods Patients with ICH fulfilling the inclusion criteria were prospectively enrolled in the observational COSBID study (Co-operative Study on Brain Injury Depolarisations). g.BSamp (g.tec, Austria) connected to PowerLab and LabChart software (Adinstruments) was used for electrocorticography (EcoG). Electrocardiogram patches at the patient's shoulder and bed served as groundings, and a surface reference electrode was glued on the mastoid. The duration of EcoG depressions was defined as the time between depression onset and start of EcoG recovery in the integral of power calculations (0.5 to 45 Hz; 60 seconds time constant decay). Brain tissue oxygen tension ($PbtO_2$), cerebral blood flow (CBF), cerebral metabolism and intracranial pressure were monitored in the PHE region. Data are presented as median and interquartile range.
Results Eighteen patients with ICH (ICH volume: 54 (33 to 69) ml) were analyzed. Hematoma evacuation was performed in 17 patients, one subject underwent craniectomy only. Patients were 60 (55 to 67) years old and 38% female. Monitoring time per patient was 10 (6 to 14) days. A total of 129 CSDs with 16 (10 to 29) minutes of EcoG depression were observed. Eighty-four percent (n = 15) of patients showed expansion of PHE by 25 (10 to 50) ml within 3 to 6 days after bleeding. Neuromonitoring probes were 35 (23 to 58) mm distant from the EcoG strip. CSDs occurred in 73% (n = 11) of patients with PHE expansion. The interval between CSDs was 98 minutes (25 to 308). CSDs were associated with a significant decrease of $PbtO_2$ (–4 mmHg (–3; –7); duration 10 (5 to 23) minutes) in 68% (52/77), CBF changes in 95% (19/20) and metabolic derangement in 80% (80/100) of CSDs. PHE expansion was observed in all patients with spreading convulsions (n = 2) and patients with repetitive CSDs occurring as clusters (n = 3).
Conclusion CSDs are common in ICH patients and associated with perihematomal $PbtO_2$ decreases and metabolic derangement. Especially, clusters of CSDs might be associated with detrimental metabolic changes of the perihematomal brain tissue.

P469

Troponin level as a predictor of prognosis in patients with acute ischemic stroke

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Critical Care 2015, **19(Suppl 1):**P469 (doi: 10.1186/cc14549)

Introduction The aim of this study was to identify the association between troponin level and the outcome in patients with acute ischemic stroke.
Methods We retrospectively investigated 152 patients admitted to our reanimation ICU for cerebrovascular accident between 1 January 2013 and 31 December 2013. Inclusion criteria were as follows: patients with acute ischemic stroke, measurement of serum troponin level and electrocardiography performed within 24 hours of admission. Not included were patients with intracerebral hemorrhage, no brain imaging or electrocardiography, previous myocardial infarction, stable or unstable angina pectoris before admission, previous coronary angioplasty or coronary bypass surgery.
Results Of 152 patients, 51 patients were excluded from the study because of the exclusion criteria. The serum troponin level was elevated in 81 patients. The patients were divided into two groups; patients in group 1 (n = 81) with serum troponin level >0.01, and those in group 2 (n = 20) with serum troponin level ≤0.01. For 1-month follow-up results of patients, death had occurred in 50.6% (n = 41) of patients in group 1 and in 25% (n = 5) of patients in group 2. There was a significant positive correlation between the increase in troponin level and death within 1 month (r = 0.205; P = 0.040). The best cutoff point revealed by the ROC curve of troponin was 0.291 mg/l; at which the sensitivity was 73% and the specificity was 79% when used for prediction of death within 1 month (area = 0.319, CI = 0.214 to 0.423, P = 0.021; Figure 1).
Conclusion These results suggest that increased serum troponin level at admission is associated with higher mortality rate. Troponin positivity on admission is an independent prognostic predictor in acute ischemic stroke.

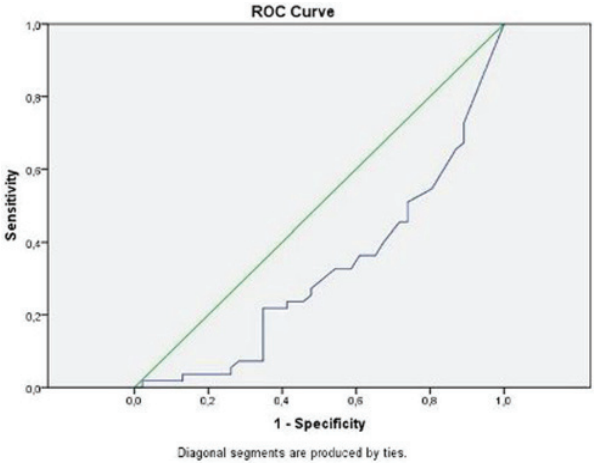


Figure 1 (abstract P469).

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P470

Increased risk of ischemic stroke in patients with burn injury: a nationwide cohort study in Taiwan

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Introduction The results of studies attempting to assess the risks of ischemic stroke in patients with burn injury have been conflicting. We investigated the risks of ischemic stroke in hospitalized burn injury patients in Taiwan to evaluate whether the risk is higher compared with the general population.
Methods The data from 1 million National Health Insurance beneficiaries were utilized. All adult beneficiaries were followed from 1 January 2005 until 31 December 2012 to identify those who developed ischemic stroke. Meanwhile, each identified patient with burn injury was matched with 100 unexposed patients based on the high-dimensional propensity score. Cox regression models were applied to compare the hazards of ischemic stroke in the matched cohorts.

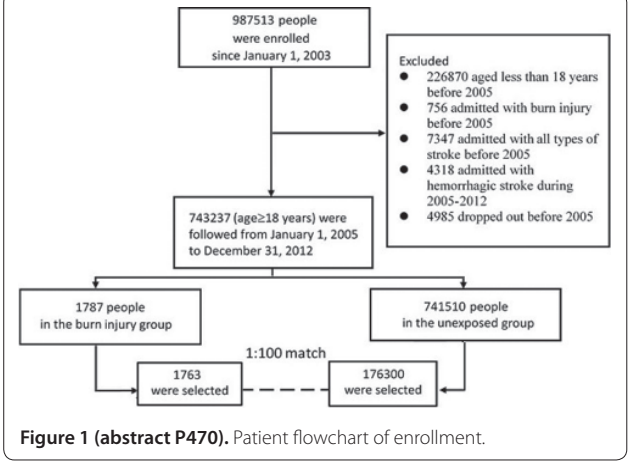


Figure 1 (abstract P470). Patient flowchart of enrollment.

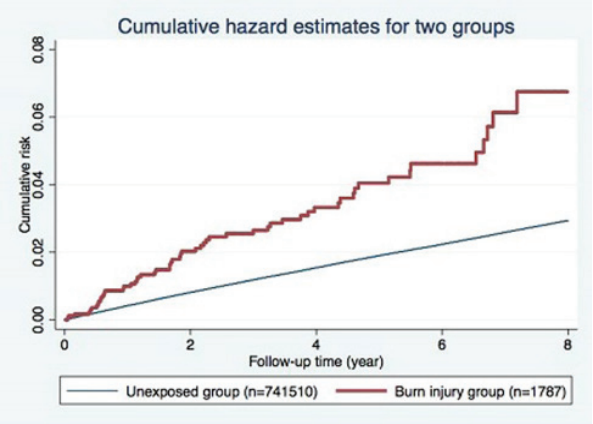


Figure 2 (abstract P470). Burn injury patients have higher adjusted hazard ratio of ischemic stroke.

Results A total of 743,237 patients were enrolled. After matching, 1,763 burn injury patients and 176,300 unexposed patients were selected. The adjusted hazard ratio of ischemic stroke was significantly increased in burn injury patients (1.84; 95% CI, 1.43 to 2.36). Such phenomenon remained significantly after 12 months (1.54; 95% CI, 1.11 to 2.13). See Figures 1 and 2.
Conclusion The risk of ischemic stroke is higher in patients hospitalized with burn injury than in the general population, and the effects may be extended longer than expected previously.
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P471

Effect of coronary artery bypass grafting surgery with a pump on cerebral blood flow in high-risk patients

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Introduction Coronary artery bypass grafting (CABG) surgery usually improves myocardial contractility, reducing cardiovascular events. However, it is a high-risk procedure associated with significant neurological complications, including stroke, delirium and cognitive impairment. The pathophysiology of these complications is not very well known, and may include low flow state after surgery, low cardiac output, embolism and reperfusion lesion. The aim of this study is to prospectively evaluate the cerebral hemodynamics through transcranial color and spectral Doppler sonography in high-risk patients undergoing cardiac surgery with a pump.
Methods This was a prospective, single-center study, performed at the Heart Institute from University of São Paulo. From May to November 2014 we included 35 patients in the study, aged older than 18 years old, submitted to CABG with a pump, with EuroSCORE higher than 6 or left ventricular ejection fraction lower than 40%. Transcranial color and spectral Doppler sonography was performed 48 hours before surgery (T0), 7 days (T1) and 6 months after surgery (T2). We used a probe of 2.5 to 2 MHz (Doppler Box DWL/Compumedics, Singen, Germany). All recordings were taken with the patient in a supine position. We measured the middle cerebral artery mean flow velocity and pulsatility index. The end-expiratory pressure of CO_2 ($PETCO_2$) was measured with infrared capnography attached to a face mask. Blood pressure, hematocrit and axillary temperature was also recorded.
Results The mean age of patients was 64 years; most patients were male (74%). Middle cerebral artery mean flow velocity increased significantly after cardiac surgery. It was 53.89 ± 17.23 m/second at T0, 61.48 ± 15.18 m/second at T1 and 59.27 ± 16.12 m/second at T2 (P = 0.029). The pulsatility index was similar at all time points (0.88 ± 0.25 at T0, 0.85 ± 0.24 at T1 and 0.91 ± 0.25 at T2, P = 0.146). There was a significant difference in the levels of hemoglobin (13.19 ± g/dl 1.97 at T0 and 9.64 ± 1.48 g/dl at T1, P = 0.002). However, this difference was not maintained at T2 (12.7 ± 2.02 g/dl at T2, P = 0.252). There were no differences regarding $PETCO_2$ at the time points.
Conclusion After cardiac surgery with a pump in high-risk patients, improvement of cerebral hemodynamic occurs, perhaps due to the optimization of cardiovascular function. These findings must be better investigated.

P472

Increased early systemic inflammation in patients with ICU-acquired weakness

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Introduction Inflammation may be important in the pathogenesis of ICU-acquired weakness (ICU-AW) since SIRS, sepsis and multiple organ failure are the main risk factors. Local inflammation has been found in muscle and nerve tissue of patients with ICU-AW, but little is known about the association with systemic inflammation. We hypothesized that systemic inflammation is increased in patients who develop ICU-AW compared with patients who do not develop ICU-AW.
Methods Newly admitted ICU patients ≥48 hours on mechanical ventilation were included. Daily plasma samples were collected from leftover plasma. Muscle strength was evaluated as soon as patients were awake and attentive. ICU-AW was defined by a mean Medical Research Council score <4. IL-1β, IL-6, IL-8, IL-10, IL-13, TNFα, IFNγ, fractalkine, GM-CSF, sICAM-1, sE-selectin and sP-selectin were measured in plasma samples of days 0, 2 and 4 using cytometric bead arrays and FACS. Differences of maximum levels between patients with and without ICU-AW were calculated using Mann–Whitney U tests. Principal component (PC) analysis was used to avoid multicollinearity and to reduce the set of mediators into a smaller set of PCs. To investigate whether different inflammatory profiles are associated with development of ICU-AW, we used multivariable logistic regression models of selected PCs, corrected for *a priori* selected variables, being age, gender, BMI, sepsis, SOFA score, APACHE IV score, immune insufficiency and corticosteroids.
Results Ninety-nine of 204 included patients developed ICU-AW. Patients with ICU-AW had higher APACHE IV and SOFA scores, a longer duration of mechanical ventilation, longer ICU stay, and died more often on the ICU compared with ICU patients without ICU-AW. Maximal levels of IL-1β, IL-6, IL-8, IL-10, TNFα, IFNγ, fractalkine and sICAM-1 were higher in patients who developed ICU-AW compared with patients who did not develop ICU-AW (univariable analysis). PC 1 to 4 derived from maximal levels explained >69% of the total variance in the data. Multivariable logistic regression models showed that PC 1 (mainly loaded by IL-6, IL-8 and IL-10) and PC 4 (mainly loaded by sP-selectin) were significantly higher in patients with ICU-AW compared with patients without ICU-AW (OR of 1.27 (95% CI = 1.02 to 1.60) and 1.55 (1.06 to 2.27) respectively).
Conclusion Development of ICU-AW is associated with increased systemic inflammation in the first days after ICU admission.
Acknowledgement This research was supported by the Center for Translational Molecular Medicine (MARS).

P473

Effect of prolonged critical care admissions on upper and lower limb muscle architecture

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Introduction Muscle wasting is a common consequence of long-term stay in the critical care environment, which may slow down the rehabilitation of survivors. Previous ultrasound studies have

demonstrated a loss of cross-sectional area of lower limb muscles during a 10-day intensive care stay. In this study, we have looked at how markers of muscle architecture (muscle thickness, pennation angle and fascicle length) change in the lower limb, as well as looking at changes in muscle thickness in the upper limb.

Methods Following ethical approval, patients who were intubated and ventilated in one of two critical care departments were assented to take part in the study by their next of kin. B-mode ultrasound scans of the right biceps, vastus lateralis and the medial head of gastrocnemius were performed on days 1, 5 and 10. Scans were not performed in patients once they were free of sedation. Muscle thickness (MT) was measured in all three muscles, with pennation angle (PA) being measured in the lower limb muscles. Fascicle length (FL) was derived from PA and MT.

Results Twenty patients were recruited, of which 15 were scanned on day 5, and eight were scanned on day 10. In the biceps, there were no alterations in MT over 5 or 10 days. MT of the vastus lateralis significantly decreased on day 5 (1.77 ± 0.06 mm muscle loss, $P = 0.03$) and day 10 (5.58 ± 0.09 mm muscle loss, $P = 0.01$). There was also a significant loss in PA over 5 days (1.48 ± 0.63°, $P = 0.01$) and 10 days (2.96 ± 0.72°, $P = 0.01$). However, FL was unchanged over time. There was a significant relationship between size of PA and percentage loss of PA and FL in over 5 days. Loss of MT and PA (MT: 3.21 ± 2.08 mm lost, PA: 2.19 ± 1.64°) was observed in the medial gastrocnemius over 10 days, but did not approach significance. Large fascicles on day 1 were associated with greater percentage loss of FL on day 5 ($P = 0.012$).

Conclusion In the lower limb, we have shown that MT and PA alterations occur in the first 10 days. Patients with larger PA and FL appear to lose a greater percentage of angle and fascicle length in the first 5 days. In contrast, we have demonstrated a sparing effect on the muscles of the upper limb compared with the lower limb. These findings may have implications for rehabilitation and interventions to preserve muscle mass.

P474

Predictive value for weakness and 1-year mortality of screening electrophysiology tests in the ICU

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Introduction Muscle weakness in long-stay ICU patients contributes to 1-year mortality [1]. Whether electrophysiological screening is an alternative diagnostic tool also in unconscious/uncooperative patients remains unknown. The aims of this study were to determine the diagnostic properties of abnormal compound muscle action potential (CMAP), sensory nerve action potential (SNAP) and spontaneous electrical activity (SEA) for Medical Research Council (MRC)-sum score defined weakness and their predictive value for 1-year mortality.

Methods Data were prospectively collected during the EPaNIC trial (ClinicalTrials.gov NCT00512122) [2] from October 2008 to November 2010. From day 8 onwards, nerve conduction studies and electromyography were performed weekly in 642 long-stay and 88 randomly selected short-stay patients and muscle strength was assessed in cooperative patients using the MRC-sum score. The electrophysiologist was blinded for the clinical assessments of the physiotherapists and *vice versa*. The two primary outcomes were: sensitivity, specificity, positive and negative predictive values of abnormal CMAP, SNAP and SEA for weakness (MRC-sum score <48); and the predictive value for 1-year mortality of abnormal findings on first electrophysiological screening. This association was assessed by univariate and multivariate analyses correcting for weakness and other risk factors, including baseline risk factors, comorbidities, illness severity and ICU exposures.

Results A total of 730 patients were electrophysiologically screened, of which 432 were tested for weakness. On day 8, only normal CMAP excluded weakness with a high negative predictive value (80.5%). By day 15, abnormal SNAP and the presence of SEA revealed a high positive predictive value (91.7% and 80.0%, respectively). On day 8, only a reduced CMAP was associated with higher 1-year mortality (35.6% vs. 15.2%, $P <0.001$). This association remained significant after correction for weakness and other risk factors (OR: 2.463 (95% CI: 1.113 to 5.452), $P = 0.026$). Also among conscious/cooperative patients without weakness, reduced CMAP was independently associated with a higher likelihood of death within 1 year (HR: 2.818 (95% CI: 1.074 to 7.391), $P = 0.035$).

Conclusion The diagnostic properties of electrophysiological screening vary over time. Abnormal CMAP documented early during critical illness carries information about longer-term outcome, which should be further investigated mechanistically.

Acknowledgement HVM and GH contributed equally.

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P475

Psychometric properties of the de Morton Mobility Index in ICU patients

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Introduction Many ICU patients develop ICU-acquired muscle weakness (ICU-AW) due to inactivity and critical illness. ICU-AW is associated with short-term and long-term physical impairments and impaired functional status [1]. The de Morton Mobility Index (DEMMI) was developed to measure changes in mobility across clinical settings and proved to be reliable, feasible and sensitive to small but clinically relevant changes in functioning [2]. Our aim was to evaluate the psychometric properties of the DEMMI in ICU patients.

Methods The inter-rater reliability and validity were determined in a prospective observational study. Patients were included and assessed by two independent raters until hospital discharge. Reliability was expressed using the intraclass correlations (ICC). To evaluate the validity, the DEMMI scores were compared with the Barthel Index (BI), Katz-ADL and manual muscle testing (MMT).

Results A total of 115 ICU patients were included. The average age was 61 years and 67% of the patients were male. ICU admission diagnoses were 53% acute surgery, 14% elective surgery and 33% were admitted for medical nonsurgical reasons. Inter-rater reliability of the DEMMI was high: intraclass correlation coefficient (ICC) ranging from >0.91 (range 0.85 to 0.94) at ICU admission, >0.98 (range 0.96 to 0.99) at the MICU and >0.97 (range 0.96 to 0.98) at the general ward. Internal consistency reliabilities (Cronbach α) of the DEMMI were 0.84, 0.87 and 0.98 at the ICU, MICU and hospital ward respectively. Validity coefficients (Spearman's rank correlations) with BI, Katz-ADL and MMT were 0.63, –0.45 and 0.62.

Conclusion The DEMMI is a reliable, responsive and feasible measurement instrument for the assessment of mobility in critically ill ICU patients.

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P476

B-type natriuretic peptide and estimated glomerular filtration rate at ICU admission as a predictor of delirium

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Introduction Delirium in the ICU is a predictor of mortality and cognitive impairment at hospital discharge. Although several pathways for delirium have been described, it is very difficult to predict the occurrence of delirium. In this study, we examined plasma biomarkers in delirious and nondelirious patients at admission and whether the biomarkers can predict onset of delirium.

Methods We targeted 103 ICU patients in Okayama University Hospital between April 2013 and February 2014. Delirium was diagnosed using the Confusion Assessment Method – ICU. On admission, blood was obtained for biomarker analysis. Patients with severe head injury and under 16 years old were excluded. P <0.05 was considered statistically significant.
Results Thirty-seven delirious and 66 nondelirious patients were included. We found that delirious patients tented to have higher B-type natriuretic peptide (BNP) levels and to have lower estimated glomerular filtration rate (eGFR) (BNP: delirious patients 188.6 pg/ml, nondelirious patients 78.2 pg/ml (P = 0.001); eGFR: delirious patients 58.6 ml/minute/1.73 m^2, nondelirious patients 81.3 ml/minute/1.73 m^2 (P = 0.020)). Procalcitonin (PCT) and D-dimer were almost the same between delirious and nondelirious patients (PCT: delirious patients 0.202 ng/ml, nondelirious patients 0.150 ng/ml (P = 0.613); D-dimer: delirious patients 5.25 ng/ml, nondelirious patients 5.35 ng/ml (P = 0.714)).
Conclusion BNP and eGFR in ICU admission was associated with delirium. PCT and D-dimer in ICU admission was not associated with delirium. BNP and eGFR might evaluate a predictor of delirium in ICU.
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P477

Prevalence of psychiatric disorders in trauma patients: results from a major trauma unit

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Introduction Mental illness has been recognised as a potential risk factor both for intentional and unintentional injury. About 50% of patients presenting with self-inflicting injuries in emergency departments had previous known psychiatric disorder (PD) [1,2], whereas individuals with mental illness were admitted for unintentional injury twice as often as those without [3]. We aimed to assess the prevalence of PD in trauma patients being admitted to a major trauma ICU and compare it with the nontrauma population.
Methods We retrospectively reviewed all admissions from January 2010 to December 2013 in a tertiary, mixed ICU that serves a London major trauma centre (MTC) hospital. Data obtained were age, APACHE II score, reason for admission, length of stay (LOS), mortality and a diagnosis of depression, bipolar, self-harm, psychosis, schizophrenia and suicide attempt.
Results Of 978 trauma patients admitted to the ICU, 68 (7%) had a known PD. Their diagnoses are shown in Figure 1. Median APACHE II score and unadjusted mortality were 13 and 18% respectively in the PD group (15 and 12% in the entire cohort, P >0.05). Patients suffering from more than one diagnosis or self-harm alone had increased median LOS (6 vs. 4 days in the entire cohort, P >0.05).

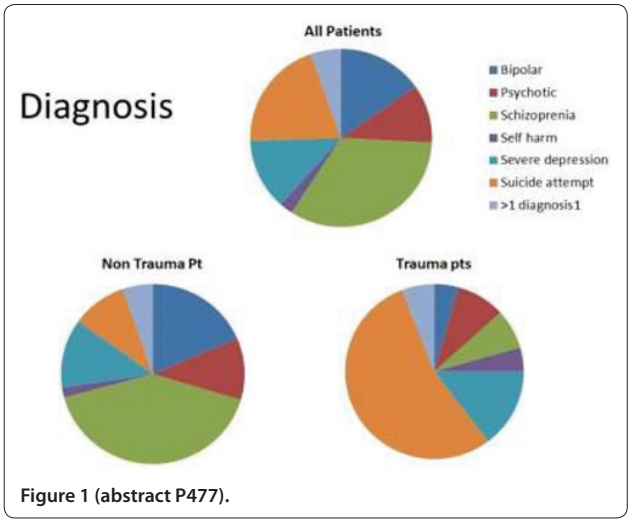


Figure 1 (abstract P477).

Conclusion Trauma patients with PD have increased mortality and LOS. MTCs provide a unique opportunity to identify mental illness during hospitalisation through screening and intervention programmes. Integration of mental health services into ICU care should be examined, as it might provide an efficient and cost-effective way of decreasing the risk of reinjury.
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P478

Modifiable risk factors for delirium in critically ill trauma patients: a multicenter prospective study

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Introduction Delirium is associated with significant morbidity and mortality in critically ill medical and surgical patients. However, patients suffering from trauma are generally excluded from these studies. Our objectives were to assess the incidence of delirium and identify modifiable risk factors associated with delirium among critically ill trauma patients.
Methods This was a prospective observational study of trauma patients from two critical care trauma centers. We excluded patients who had ICU stay <48 hours and those with severe traumatic brain injury (TBI) (GCS ≤8). Patients were followed until ICU discharge, resolution of delirium, death or ICU length of stay >28 days. Delirium was assessed daily using the Confusion Assessment Method for the ICU until the end of the follow-up period. Demographic and admission data, daily consumption of medications, and environmental factors (that is, presence of clock, TV/radio, and so forth) were collected daily. Univariate analysis was performed using Cox regression analysis to identify risk factors for delirium. The independent effect of modifiable risk factors was assessed using multivariate Cox regression analysis adjusting for severity of illness and nonmodifiable risk factors.
Results We enrolled 150 trauma patients resulting mostly from falls (40%) and motor vehicle accidents (28.7%) over 14 months. Patients with TBI accounted for 56.7% while polytrauma patients without TBI accounted for 43.3%. Mean ICU length of stay was 8.1 ± 7.1 days, 69.3% required mechanical ventilation, 14.7% required a tracheostomy. Delirium developed in 58 patients (38.7%) (mean age 62.9 ± 15.7, mean APACHE score 15.4 ± 6.1, mean ISS score 23.4 ± 9.1). Univariate analysis revealed that delirium was significantly associated with the following nonmodifiable risk factors: age (per 10-year range), APACHE II score (per 10-point increase), need of mechanical ventilation, presence of TBI and pre-existing diabetes. In a multivariate analysis when adjusting for the nonmodifiable risk factors, opioids (adjusted HR = 0.37, 95% CI (0.14 to 1.0)), presence of a TV/radio in the room (adjusted HR = 0.28, 95% CI (0.12 to 0.67)), and number of hours mobilized (adjusted HR = 0.77, 95% CI (0.68 to 0.88)) had a protective effect on delirium; whereas use of physical restraints (adjusted HR = 2.20, 95% CI (1.11 to 4.35)) and active infection (adjusted HR = 2.08, 95% CI (1.16 to 3.71)) remained strongly associated with delirium.
Conclusion Considering the long-term consequences of delirium, steps should be implemented to prevent its development in trauma and include optimizing opioids and mobilizing patients while limiting use of physical restraints.

P479

Evaluation of the PRE-DELIRIC delirium prediction tool on a general ICU

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Introduction Delirium is a frequently occurring complication of critical care, occurring in approximately 45% of unplanned UK ICU admissions

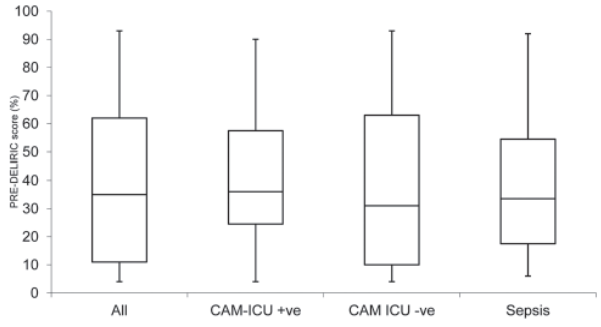


Figure 1 (abstract P479). Range of PRE-DELIRIC scores.

[1]. The presence of delirium in critical care is an independent risk factor for mortality; for every day of delirium, there is an additional 10% relative risk of death at 1 year [2]. A delirium prediction tool PRE-DELIRIC has been recently developed and calibrated in a multinational project [3]. This study aimed to determine the utility of PRE-DELIRIC on our ICU.

Methods This study prospectively investigated 41 patients. Medical and surgical general ICU patients were included after 24 hours of sedation and mechanical ventilation. The researchers calculated PRE-DELIRIC scores for each patient. PRE-DELIRIC involves recording 10 variables, submitted into an online algorithm that estimates the percentage risk of delirium. We diagnosed delirium with the CAM-ICU which was performed 12 hourly [4].

Results The PRE-DELIRIC scores predicted a mean rate of delirium of 39%. PRE-DELIRIC risk scores ranged from 4 to 93% (Figure 1). Six (15%) patients developed delirium in the first 24 hours following extubation. Fifteen (37%) of patients were predicted 20% or less probability of delirium. Twelve (29%) patients developed delirium at any point during their ICU stay. This resulted in 36 total delirium bed-days.

Conclusion Our observation that <30% of patients experienced delirium is less than the reported prevalence in similar settings and our own audits. This study demonstrates that there is some agreement between recorded rates of delirium and predicted rates using PRE-DELIRIC. We suggest that PRE-DELIRIC can be used in quality/audit work on UK ICUs in order to assess attempts to improve the management of delirium. Further work is required to assess the utility of PRE-DELIRIC as a risk assessment tool in individual patients.

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P480

Short-term propofol infusion syndrome (PRIS): fact or fiction? A systematic review on early PRIS in intensive care and anesthesia

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Introduction Propofol infusion syndrome (PRIS) is a rare propofol complication, leading to cardiac failure. It was first described in critically ill children and in adults with traumatic brain injury. Pathophysiology is unknown although common factors are the prolonged (>48 hours) use of high-dose (>5 mg/kg/hour) propofol combined with elevated levels of catecholamines and corticosteroids. Recently, case reports of early-onset PRIS during anesthesia and in the early postoperative setting were published. In many of these, lactic acidosis is interpreted as onset of PRIS. Criticism offers that it might concern a poor differential diagnostic approach or an observational bias. Also, lactic acidosis is not an obligate PRIS symptom and incidence of lactic acidosis during propofol sedation is unknown. To gain insight into the incidence and characteristics of early PRIS, we performed a systematic review on early PRIS cases.

Methods A literature study via MEDLINE and Embase search with keywords 'PRIS', 'lactic acid', 'propofol' and 'sedation'. All cases in English, French and Spanish were indentified. Exclusion criteria were onset >48 hours, unclear description of time pattern and dose.

Results Twenty-two cases of early PRIS were found. These concerned 10 pediatric versus 12 adult patients. Eleven were identified in the ICU versus 11 in the operating room. The survival rate of early PRIS was 95.5%, and morbidity was restricted to four patients. In the adult subgroup, the mean propofol dose was 4.9 mg/kg/hour. Triggering factors such as use of catecholamines and corticosteroids were found in 36.4% and 45% of patients. In total, 3/22 cases matched Bray's definition of PRIS. In 14/22 cases, lactic acidosis was interpreted as onset of PRIS.

Conclusion Compared with a review by Fudickar [1], we found significant differences in critical dose, risk factors, symptomatology and morbidity/mortality between PRIS and early PRIS cases. As criticisms are offered, a question is whether these cases really are the onset of the fatal syndrome PRIS. Therefore, we completed differential diagnosis of lactic acidosis and found that not all possible causes (for example, hyperglycemia, ketonemia, pharmacologic confounders as biguanides, epinephrine) were ruled out in most cases. This is important since PRIS is an exclusion diagnosis. The existence of early PRIS should indeed be questioned and investigated by large, multicenter observational trials.

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P481

Propofol sedation reduces contraction and motion of diaphragm in humans: preliminary results

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Introduction Among drugs used for sedation, propofol has a primary role [1]. Despite propofol being described to exert a relaxant effect on skeletal muscle, no data showing its action on diaphragm are reported. The aim of this observational study on humans is to apply ultrasound to assess propofol's effect on diaphragmatic contraction and motion during endoscopic procedures.

Methods We investigated seven consecutive patients undergoing gastroscopy or colonoscopy in the endoscopy unit of our hospital. Patients received propofol at a dose able to induce and maintain sedation to level 6 of the Ramsay Sedation Scale during the procedure. Measurements were obtained on right side of the thorax in millimeters; diaphragmatic motion (DM) and diaphragmatic motion at maximal inspiration (DM forced) were measured in M-Mode with a 3.5 MHz array convex probe placed on the midclavicular line using the liver acoustic window. Thickness at end inspiration (TEI) and thickness at end expiration (TEE) were measured in M-Mode with a 10 MHz vascular probe. The thickening fraction (TF) was calculated: (TEI – TEE) / TEE [2]. Time points of measurements were taken when the patient arrived in the surgery room (Baseline), 1 minute after level 6 of the Ramsey Sedation Scale was obtained (Sedation) and 5 minutes after the patient had a recovery to level 1 on the Ramsey Sedation Scale (Awakening).

Table 1 (abstract P481)

Variable	Baseline	Sedation	Awakening	*P* value
Thickness end inspiration (mm)	3.25 (0.21)	[a]2.66 (0.20)	[b,c]3.22 (0.30)	<0.001*
Thickness end expiration (mm)	2.11 (0.20)	[d]2.00 (0.15)	2.07 (0.15)	0.112*
Thickening fraction	0.54 (0.07)	[e]0.36 (0.10)	[f,g]0.49 (0.11)	<0.001*
Diaphragmatic motion (mm)	18.66 (2.23)	[h]13.27 (4.93)	15.31 (0.40)	0.055
Diaphragmatic motion forced (mm)	54.61 (19.34)	–	56.34 (13.75)	0.298

[a]*P* <0.001 versus baseline. [b]*P* = 0.043 versus baseline. [c]*P* <0.001 versus sedation. [d]*P* = 0.030 versus baseline. [e]*P* =0.012 versus baseline. [f]*P* =0.353 versus baseline. [g]*P* = 0.041 versus sedation. [h]*P* = 0.022 versus baseline.

Data analyzed are reported in Table 1 and expressed as mean (SD). *ANOVA was used to compare data for repeated measurements. *Post hoc* statistical comparison with Bonferroni's test was used to identify significant variations.

Results During propofol administration TEI reduced 19% whereas after awakening it increased 14.5% but did not reach baseline. Conversely TEE did not change during the study. During propofol sedation, TF decreased 34% and returned to baseline after recovery. DM showed 29% reduction during propofol administration whereas the forced diaphragmatic motion tested when patients were conscious (forced DM) did not evidence any change.

Conclusion In this observational study, ultrasound assessed that propofol causes a reduction of diaphragmatic contraction and motion during endoscopic procedures.

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P482

Delirium knowledge and assessment by ICU practitioners in South Africa: results of a national survey

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Introduction Delirium recognition in critically ill patients is considered to be important taking into account the poor outcomes associated with its occurrence. The purpose of this study was to evaluate knowledge pertaining to delirium as well as the implementation of screening practices. This study constituted a component of a survey that explored current sedation-related practices in South African ICUs.

Methods Following approval from the University Human Research ethics committee, a validated questionnaire was distributed electronically to physician members of various medical databases in South Africa as South Africa does not have a formal registry of critical care practitioners.

Results One hundred and twenty-six of 174 respondents indicated that they practice in the ICU setting. Sixty-six per cent were specialists and mainly anaesthesiologists (42%), whilst 32% were critical care subspecialists. The respondents indicated that on average 30 ± 20% of their patients experience delirium. Eighty per cent of the respondents indicated that delirium impacts significantly negatively on patient outcomes whilst 1% indicated that there was no such association. Delirium screening is achieved mainly by clinical assessment (77%). Twenty-four per cent utilise an objective tool to screen for delirium and amongst them the CAM-ICU is utilised by 80%. Amongst delirious patients the sedative of choice is dexmedetomidine in the majority. However, 20% prescribe midazolam as a first choice in this setting.

Conclusion The findings are comparable with reports of similar surveys conducted in other regions. The delirium screening method is inadequate as the vast majority do not utilise an objective method.

P483

Loxapine to control agitation during weaning from mechanical ventilation: a randomized controlled trial

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Introduction Weaning from prolonged mechanical ventilation (MV) in the ICU may be impeded by the occurrence of agitation. Loxapine had the ability to control agitation without affecting the efficacy of spontaneous ventilation in an observational study, justifying the implementation of a randomized controlled trial.

Methods We conducted a multicenter, placebo-controlled, parallel group, randomized trial at five French ICUs between November 2011 and November 2013. Patients (aged >18 years) under MV for more than 48 hours who were potential candidates for weaning from the ventilator and who exhibited agitation defined by a Richmond Agitation Sedation Scale (RASS) >2 after sedation withdrawal were randomly assigned to receive either loxapine or placebo. All participants were masked to group of allocation. After randomization, patients received 150 mg loxapine or placebo by nasogastric tube. RASS was monitored every 4 hours. A second dose of loxapine or placebo was administered if agitation persisted or worsened. In case of severe agitation, usual sedation (benzodiazepines and morphinic agents) was immediately resumed. Extubation was contemplated when patients were conscious and calm. The primary endpoint was the time between the first administration of loxapine or placebo and successful extubation (no reintubation in the following 48 hours). Three hundred patients were necessary to have 90% power to detect a 2-day reduction of weaning time in the loxapine group with a one-sided type I error rate of 5%.

Results The trial was discontinued after 101 patients had been randomized because of insufficient enrollment. Fifteen patients withdrew consent, leaving 86 patients for analysis. Forty-seven patients were assigned to the loxapine group and 39 to the placebo group. Median time to successful extubation was 3.2 days in the loxapine group and 5 days in the placebo group (RR = 1.2, 95% CI = 0.75 to 1.88; $P = 0.45$). During the first 24 hours, sedation was more frequently resumed in the placebo group (44% vs. 17%, $P = 0.01$). One patient had a transient seizure in the loxapine group.

Conclusion These results are consistent with the hypothesis of 2 days reduction of the median weaning time in the loxapine group, but the difference was not statistically significant. Loxapine reduces the need for resuming sedation during weaning from MV. Given the quality of the data and methodology, these results may be useful in future meta-analyses.

P484

Prolonged dexmedetomidine infusion and drug withdrawal in critically ill children

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Introduction We investigated the incidence, symptoms and risk factors for withdrawal associated with prolonged dexmedetomidine use. Dexmedetomidine is an α_2-adrenergic receptor agonist, with anxiolytic, analgesic and sedative properties. Intended for short-term use, there is increasing literature describing prolonged use for sedation. However, this raises the potential of withdrawal syndrome and there is no recommendation for the discontinuation of dexmedetomidine. Other goals included determining the hemodynamic effects of discontinuation of dexmedetomidine and role of clonidine in patients with prolonged dexmedetomidine use.

Methods A retrospective review of patients admitted to the critical care unit who had exposure to dexmedetomidine for longer than 48 hours, between 1 January 2014 and 15 July 2014. Data included patient demographics, dexmedetomidine exposure (bolus dose, total cumulative dose, duration), other sedative exposure, withdrawal symptoms measured by WAT-1 score, nursing subjective assessment and treatment given for withdrawal. Each potential withdrawal episode was reviewed by two reviewers. Hemodynamic parameters were analyzed to assess hemodynamic changes associated with discontinuation of dexmedetomidine. Descriptive statistics were used with *t* test and chi-square test. Median and interquartile range (IQR) are reported.

Results A total of 53 patients accounted for 69 unique dexmedetomidine treatment courses. Median age at the time of dexmedetomidine infusion was 5 months (range 1 day to 3 years). Dexmedetomidine dose ranged from 0.1 to 2 μg/kg/hour with a median cumulative dose of 87 μg/kg (IQR 53, 156). Median duration of exposure to dexmedetomidine was 124 hours (IQR 76, 178) with a maximum duration of 466 hours. We identified 24 separate episodes of withdrawal (incidence 35%). Most common symptoms were agitation (100%), fever (67%), vomiting/retching (46%), loose stools (29%) and decreased sleep (20%). Statistical analysis showed that factors significantly associated

with withdrawal were cumulative dose ($P = 0.01$) and duration of use of dexmedetomidine ($P = 0.02$). Duration of opioids exposure prior to dexmedetomidine wean was also a risk factor for withdrawal ($P = 0.01$). Use of clonidine as a transition from dexmedetomidine did not protect against withdrawal ($P = 0.59$).
Conclusion This study showed that withdrawal syndrome is associated with prolonged infusion of dexmedetomidine. Patients with higher cumulative doses and longer duration of exposure were more at risk. Our results suggested that clonidine use is not protective for withdrawal from dexmedetomidine.

P485

Weaning from extracorporeal membrane oxygenation: experience with dexmedetomidine in seven adult ARDS patients

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Introduction Sedation in the ICU is a basic therapeutic procedure to increase tolerance of invasive treatments and reduce discomfort. Extracorporeal membrane oxygenation (ECMO) is a highly invasive treatment and prolonged sedation may be required. Patients undergoing ECMO represent a challenge with respect to sedation. Initially, deep sedation may be required to optimize ventilation and circuit–patient flows and to minimize oxygen consumption. The other critical phase is represented by weaning from ECMO support. Optimal sedation is not clearly defined, moreover there are no data on sedation practices with dexmedetomidine (DEX) in adult patients undergoing ECMO. In contrast to other sedatives, DEX has analgosedative effects without respiratory depression, and could be useful to facilitate spontaneous respiratory activity during recovery from sedation.
Methods We investigate the role of DEX as a sedative agent used during recovery from deep sedation and weaning from extracorporeal support in patients on vv-ECMO. From May 2014 to October 2014 we prospectively enrolled seven patients affected by ARDS of different etiologies treated with vv-ECMO. The mean age was 53.7 ± 7.9 years and the mean ICU stay was 21.4 ± 11.5 days. Initially, all patients were sedated with association of opioids and GABA receptor agonists, following the internal protocol. At the time of weaning from ECMO, ruled out cardiovascular instability, we started the administration of DEX (0.7 µg/kg/hour, without initial bolus) with progressive decrease of the dose of other sedative drugs.
Results The mean duration of DEX infusion was 6.1 ± 4.8 days. Except for one patient, who received DEX as a single drug after suspension of other sedatives, a low-dose infusion of another sedative (<50% compared with initial dose) was maintained. Three patients presented adverse events: two bradycardia and one hypotension. In four patients DEX was discontinued after recovery of respiratory function; in two patients deeper sedation for ventilatory dyssynchrony was needed so other sedative drugs were started. Only in one patient was the drug suspended for extreme bradycardia, resolved after suspension.
Conclusion In our study, DEX allowed the reduction of doses of other sedative drugs during weaning from vv-ECMO; this may lead to a cooperative sedation, promoting spontaneous breathing. Side effects described and the cost–benefit ratio must still be verified extensively in patients during weaning from ECMO.

P486

Short-term sedation of mechanically ventilated ICU patients with propofol, benzodiazepines, or dexmedetomidine: systematic review and meta-analysis on awakening and recovery times

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Introduction Sedation in the ICU is crucial in reduction of patients' discomfort, in particular in patients undergoing mechanical ventilation to help tolerate intubation and reduce pain and anxiety. Propofol (Pr) is a widely used option, but other viable alternatives for short-term sedation (STS; that is, <24 hours) include benzodiazepines (BDZ) and dexmedetomidine (Dx). We aimed at pooling all available evidence on the comparative effects of Pr in terms of awakening and recovery times after STS in mechanically ventilated ICU patients.
Methods We planned a systematic literature review searching Medline and Scopus and performed a meta-analysis on direct comparisons reporting on weaning time (Tw), duration of mechanical ventilation (Tmv), time to extubation (Tex) and length of stay in the ICU (Ticu). The primary analysis considered only data from RCTs, while in a secondary analysis observational studies were also included.
Results The literature search identified 15 relevant RCTs, of which 11 versus BDZ, and a further five observational studies, of which one versus BDZ. When compared with BDZ, Pr associated with significantly reduced Tw (–1.6 hours, 95% CI: –2.5 to –0.8), Tmv (–2.0 hours, 95% CI: –3.7 to –0.2), and Ticu (–5.0 hours, 95% CI: –8.5 to –1.4); no statistically significant difference resulted when comparing Pr and Dx. When nonrandomized evidence was included, results did not change significantly.
Conclusion In conclusion, Pr is associated with shorter awakening and recovery times after STS than BDZ, while no difference could be shown when Pr was compared with Dx.

P487

Effects of administration of dexmedetomidine on inflammatory responses and severity in severe septic patients

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Introduction Recently, several animal studies observed that dexmedetomidine (DEX), a new sedative and α_2-adrenoceptor agonist, inhibited the inflammatory responses [1-3]. Moreover, DEX was reported to have anti-inflammatory effects in patients [4,5]. However, these studies were the small-sized studies and there are few studies about the effects of long-term administration of DEX in severe septic patients. The present study evaluated the effects of long-term administration of DEX on inflammatory responses and severity in severe septic patients. We hypothesize that the administration of DEX has beneficial effects for severe septic patients.
Methods In 66 patients (M/F 44/22, mean age 66 years) with severe sepsis, who were administered propofol (0.5 to 4.0 mg/kg/hour) only for sedation, 42 patients (M/F 28/14, mean age 67 years) were administered DEX (0.2 to 0.7 µg/kg/hour) for more than 24 hours in addition to propofol (DEX group). Twenty-four patients were not administered DEX (Control group). Primary outcome were changes in inflammatory responses at 48 hours after the administration of DEX or none, and secondary outcomes were changes in APACHE II and SOFA scores at 48 hours after the administration of DEX or none.
Results The administration of DEX occurred for a mean 130 hours (24 to 433 hours) in the DEX group. White blood cell counts, C-reactive protein (CRP) and procalcitonin (PCT) in both groups significantly decreased after the administration of DEX or none. However, CRP and PCT in the DEX group were significantly lower than those in the control group: CRP 7.7 (5.0) versus 13.6 (7.9) mg/dl; $P < 0.05$, PCT 7.6 (11.7) versus 18.6 (11.6) ng/ml; $P < 0.05$, mean (SD). APACHE II and SOFA scores in both groups decreased after the administration of DEX or none, but APACHE II and SOFA scores in the DEX group were lower than those in the control group: APACHE II 10.8 (4.8) versus 15.2 (5.1); $P < 0.05$, SOFA 3.6 (2.0) versus 5.8 (2.9); $P < 0.05$, mean (SD).
Conclusion In the present study, the long-term administration of DEX has beneficial effects of inflammatory responses and severity for severe septic patients.
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P488

Characteristics of the use of dexmedetomidine in critically ill children: a Brazilian study

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Introduction To describe the main indications, doses, infusion length and side effects of dexmedetomidine (DEX) administered to children and adolescents admitted to the pediatric ICU (PICU).
Methods A retrospective observational study including children (<18 years) admitted to a Brazilian PICU who received DEX between November 2011 and June 2014. Demographic data, indications, initial dose, maximum dose and time of infusion of DEX, side effects and impact on heart rate (HR) and mean arterial pressure (MAP) 6 and 24 hours after the start of infusion.
Results A total of 77 children with a median age of 15 (4 to 84) months, weight of 10 (5.7 to 20) kg and length of ICU stay of 8 (5 to 14) days received DEX, with a mortality rate of 9%. Indications were: weaning from mechanical ventilation (32.5%), neurosurgical postoperative (NCI) and upper airway surgery (VAS) (24.7%), non-invasive ventilation (13%), refractory tachycardia (6.5%) and other indications (23.3%). There was no difference between the initial and maximum doses and infusion length. There was a significant decrease in MAP and HR after 6 hours infusion of DEX in the total group; however, no significant difference occurred between groups when analyzing MAP and HR 24 hours after the start of infusion ($P = 0.798$ and 0.379, one-way ANOVA, respectively). In six patients (8%) DEX was suspended for possible side effects.
Conclusion Increased DEX indications have been observed in the pediatric population. In this study DEX was demonstrated to be a safe and tolerable drug with few side effects, especially related to the cardiovascular system.
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P489

Psychometric comparison of three behavioral scales for the assessment of pain in critically ill patients unable to self-report

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Introduction Pain assessment is associated with important outomes in ICU patients but remains challenging, particularly in noncommunicative patients. Use of a reliable tool is paramount to allow any implementation of sedation/analgesia protocols in a multidisciplinary team. This study compared psychometric properties (inter-rater agreement primarily; validity, responsiveness and feasibility secondarily) of three pain scales: Behavioural Pain Scale (BPS/BPS-NI, that is BPS for non-intubated patients), Critical Care Pain Observation Tool (CPOT) and Non-Verbal Pain Scale (NVPS), the pain tool routinely used in this 16-bed medical ICU.
Methods In a prospective observational study of ED polytraumatized patients ($n = 23$, mean Acute Physiology and Chronic Health Evaluation II (APACHE II) score of 11 ± 6) we measured (in the first 24 hours) plasma TAC by the ferric reducing activity/antioxidant power (FRAP). For control subjects, we used age-matched and gender-matched volunteers ($n = 32$). We also evaluated the contribution of antioxidant molecules (uric acid, bilirubin, and albumin) to these values.
Results Polytraumatized patients show differences in TAC with reference to control subjects. ED polytraumatized patients show high FRAP values. We found that FRAP values were inversely correlated with APACHE II score ($r = -0.266$, $P < 0.01$) suggesting that, in trauma patients, increased antioxidant response, as measured by the FRAP assay, could be a pathophysiological response to stress. Albumin and uric acid concentrations reproduced the FRAP trend with severity.
Conclusion FRAP values in trauma ED patients are independently influenced by age ($\beta = 0.271$, $P < 0.021$), APACHE II score ($\beta = -0.356$, $P < 0.002$) and head trauma ($\beta = -0.219$, $P < 0.045$). These results accentuate the influence of trauma location and severity in TAC changes. The TAC response in ED patients reinforces the need for adequate tailoring of treatments aimed at their recovery, such as antioxidant therapies.

P490

Best pain management for critical older patients in the surgical ICU

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Introduction To determine which of three methods of pain management provided the best pain control in severe ASA III older patients in the surgical ICU (SICU). As technology improves, more older patients benefit from surgery and need SICU care. Older surgery patients frequently present two medical problems. First is unspecific symptoms and decreased pain sensation resulting in delayed diagnosis. Second, they usually are not given enough perioperative pain relief. Optimal pain management results in perioperative stable hemodynamic status and decreased morbidity, mortality, length of stay and medical costs.
Methods A retrospective cohort study chart review of 1,872 all-cause patients in a 16-bed SICU during April 2011 to September 2012. Unconsciousness, uncooperative, ASA <III and <65-year-old patients were excluded. The primary point was to compare effectiveness of three different methods of pain management: P.R.N. i.v. Demerol/NSAID (D/N), i.v. patient-controlled analgesia (PCA) and patient-controlled epidural analgesia (PCEA), in three different conditions: rest, movement and coughing, with visual analogue scales (VAS 0 to 100). Secondary point was patient satisfaction.
Results A total of 1,292 patients were excluded. VAS results are presented in Table 1 as mean ± SD. At rest, the PCEA group is significantly better than the other two groups. When at movement, there is no difference between the PCEA group and the D/N group but both are better than the PCA group. While coughing, the PCEA group is worse than the D/N group, although there is no difference between the PCEA group and the PCA group. The PCEA group gets the best grades in patient satisfaction.

Table 1 (abstract P490)

	Demerol/NSAID ($n = 449$)	PCA ($n = 62$)	PCEA ($n = 69$)	*P* value
VAS (rest)	21 ± 14 *	19 ± 9*	12 ± 10	<0.001
VAS (movement)	35 ± 20	41 ± 12*	33 ± 11	0.02
VAS (coughing)	40 ± 24*	58 ± 14	51 ± 14	<0.001

*Significant difference.

Conclusion PCEA provided better pain control at rest than the other two methods, whereas P.R.N. Demerol/NSAID and PCEA were somewhat better than PCA when patients were moving. While coughing, P.R.N. Demerol/NSAID provided the best pain control. However, patient satisfaction was significantly better with PCEA.

P491

Subanesthetic xenon increases erythropoietin levels in humans and remains traceable in the first 24 hours after exposure: a randomized controlled trial

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Introduction The noble gas xenon was recently amended to the list of prohibited substances by the World Anti-Doping Agency as

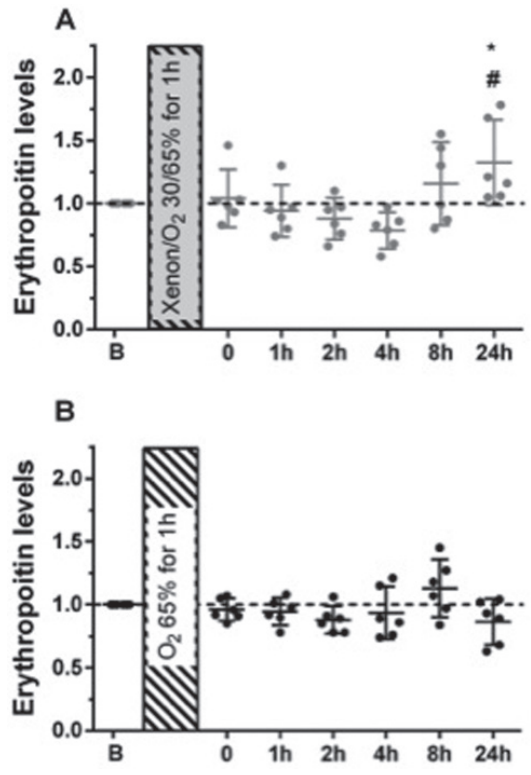


Figure 1 (abstract P491). Erythropoietin levels after 30% xenon exposure.

it is supposed to trigger the production of HIF-1α and subsequently erythropoietin. Subsequently, researchers and clinicians started a scientific discussion about the potential clinical benefit in support of humans exposed to high demand, such as critically ill patients. The objective of this study was therefore to evaluate the effect of xenon on serum levels of erythropoietin in healthy volunteers.

Methods This is a monocenter, randomized, blinded, crossover trial, which was registered at ClinicalTrials.gov (NCT01285271). Healthy study test persons were spontaneously breathing randomly 1 hour of xenon 30% (Xe/O_2 30%/65%) or control gas (N_2/O_2 30%/65%). The primary outcome parameter was the erythropoietin level 24 hours after exposure. Secondary outcome parameters are xenon's elimination kinetics measured in blood and exhalation samples.

Results The application of xenon increases erythropoietin levels with a maximum 24 hours after exposure (1.32 (0.99 to 1.66) P = 0.033) compared with the baseline values and compared with control values (0.87 (0.68 to 1.05) P = 0.012, Figure 1). Xenon was gas chromatographically traceable in blood and exhalation probes up to 24 hours after exposure.

Conclusion One hour of a subanesthetic level of xenon increases erythropoietin levels in healthy study test persons and remains gas chromatographically traceable in blood and exhalation probes 24 hours after exposure. These findings may stimulate larger studies to confirm these results and to open new avenues for the therapeutic use of xenon in critically ill patients.

P492

MIRUS™, a new system for sedation with halogenates in the ICU: a preliminary study of feasibility in postsurgical patients

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Introduction Sedation is standard practice in the ICU [1]. The aim of this study was to investigate the efficiency and safety of the MIRUS™ system (Pall Medical), a new device for sedation in ICU patients [2]. The system delivers volatile anesthetics in mechanically ventilated patients. An open reservoir scavenger and a dedicated gas filter avoid residual volatile anesthetic halogenate escaping into the room air.

Methods Ten mechanically ventilated patients electively admitted for ICU postoperative monitoring were sedated with sevoflurane delivered with the MIRUS™ system. Two patients were excluded from the analysis because inclusion criteria had been lost during the study period. Analgesia was obtained with morphine sulfate: bolus 0.1 mg/kg i.v. at the end of surgery and 0.2 to 0.4 mg/kg/24 hours. The primary endpoint was to achieve predefinite levels of sedation (Riker scale 4). Secondary endpoints were the assessment of hemodynamic stability (MAP and HR), blood lactates, any type of side effects, and sevoflurane consumption. Data were collected at the following times: admission to the ICU (T1), 1 hour after initiation of sedation (T2), and 1 hour after sedation withdrawal (T3). Results were expressed as median (IQR) or mean (SD), where appropriate.

Results The local ethical board approved the protocol. Median duration of sedation was 4 (5.5 to 2) hours. Predefinite levels of sedation were achieved in all patients with a median MAC of sevoflurane of 0.5 (0.5 to 0.3)% and with a median gas consumption of 9.9 (14.3 to 5.3) ml/hour. MAP and HR values at T1 were 86.5 (97 to 80.8) mmHg and 81.5 (103.8 to 65) bpm, respectively; at T2, 74.5 (89 to 69.5) mmHg and 74 (82 to 58.3) bpm, respectively; and at T3 92.5 (101 to 76.8) mmHg and 74 (88.5 to 66.3) bpm, respectively. Lactates were always normal. Mechanical ventilation was interrupted 5.4 (3.1) minutes after withdrawal of sevoflurane and respiratory parameters always were within normal values. Finally, no side effects were registered at any phase of the study.

Conclusion This pilot study shows that MIRUS™ is effective and safe in delivering sevoflurane for sedation at a predefinite target level in postsurgical patients, without side effects. Further data with a larger number of patients and for a longer duration of sedation are required to confirm these positive, preliminary observations.

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P493

Bispectral index-guided anesthesia on time to tracheal extubation after onpump cardiac surgery

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Introduction Electroencephalographic-based cerebral monitors such as the bispectral index (BIS) have been used for titration of both inhalational and intravenous anesthetics during general anesthesia. Titration of anesthetics using these monitors may facilitate an earlier recovery from general anesthesia and less consumption of anesthetics. The primary aim of this study was to investigate whether BIS-guided anesthesia would reduce time to tracheal extubation when compared with minimum alveolar concentration (MAC)-guided anesthesia in patients undergoing onpump cardiac surgery.

Methods Fifty patients undergoing elective coronary artery bypass grafting surgery from a single tertiary referral university hospital were randomized to BIS-guided anesthesia (Group BIS, n = 25) and MAC-guided anesthesia (Group MAC, n = 25). The inspired desflurane concentration was titrated to maintain a BIS value of 40 to 60 in Group BIS and an age adjusted minimum alveolar concentration of 0.7 to 1 was used in Group MAC. Time to tracheal extubation across the two groups was the primary outcome measure. Secondary outcomes included intraoperative desflurane consumption, postoperative complications, and lengths of stay in the ICU and hospital.

Results Demographic features, logistic EuroSCOREs, duration of cardiopulmonary bypass and surgery were similar in both groups. Mean desflurane consumption was significantly lower in Group BIS (11.9 ± 1.7 ml/hour) compared with Group MAC (13.4 ± 3.0 ml/hour) (P = 0.031). Time to tracheal extubation was not significantly different between the groups (13.3 ± 9.6 hours vs. 17.0 ± 22.4 hours) (P = 0.68). Incidences of postoperative complications were similar and lengths of stay in the ICU and hospital were 2.4 ± 0.7 days versus 3.2 ± 2.7 days

and 5.3 ± 1.2 days versus 6.5 ± 3.1 days in Group BIS and Group MAC respectively (P >0.05 for all).
Conclusion Intraoperative use of BIS monitoring in patients undergoing onpump cardiac surgery reduced desflurane requirement but BIS-guided anesthesia did not facilitate time to extubation and lengths of stay in the ICU and hospital.

P494

Use of sevoflurane in the medical ICU: 2-year experience, patient and safety profile

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Introduction The aim of this study is to present our experience with sevoflurane in the ICU, outline which patients were sedated with sevoflurane and present the safety profile. Sevoflurane has some potential advantages over intravenous sedation: rapid elimination and few interactions. The optimal role of sevoflurane in ICU is not known.
Methods We performed a retrospective study on adult patients who were sedated with sevoflurane in the medical ICU. The decision to use sevoflurane was left to the attending physician. Institutional ethics committee approval was obtained. The target mean alveolar concentration in all patients was 0.5 to 1%. The AnaConDa® device (Sedana Medical, Uppsala, Sweden) was used along with the Anastasia® (Sedana Medical) gas monitor. Data were obtained from patients' medical records.
Results We included 61 adult patients who were admitted from April 2012 to November 2014. Mean age was 62.6 ± 14.9 years, 39 (63.9%) were male. ICU mortality was 41%, hospital mortality was 43%. Mean duration of sevoflurane use was 3.56 ± 2.31 days. Admission diagnoses were: successful resuscitation after cardiac arrest (44.2%), sepsis (37.7%), cardiogenic shock (4.9%), pancreatitis (3.3%) and liver failure, acute exacerbation of COPD, asthma, tetanus and intracerebral hemorrhage (1.6% each). During treatment with sevoflurane, no patients developed malignant hyperthermia, new hyperkalemia or QT prolongation. In three (4.9%) patients, worsening liver function tests prompted sevoflurane discontinuation. Ischemic hepatitis was considered an alternative in all three patients. Seven (11.4%) patients developed renal failure while receiving sevoflurane. Sevoflurane was continued in all patients and renal failure was attributed to alternative diagnoses. No self-extubations were recorded. In seven (11.4%) patients, sevoflurane was discontinued because of worsening ventilation. In six (9.8%) patients, unexpected awakening occurred. Eight patients (13.1%) had symptoms of delirium after sevoflurane inhalations were concluded.
Conclusion We identified sevoflurane as an appropriate sedation agent in a diverse group of patients. Sevoflurane advantages over intravenous sedation could be more pronounced in some patient groups (for example, successful resuscitation after cardiac arrest). The safety profile of sevoflurane sedation was comparable with intravenous sedation [1].
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P495

Automated control of end-tidal volatile anaesthetic concentration using the MIRUS™ system: a comparison of isoflurane, sevoflurane and desflurane in anaesthesia

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Introduction The new MIRUS™ system as well as the established AnaConDa® system uses a reflector to conserve volatile anaesthetics (VA) [1]. Both systems act with commercially available ICU ventilators. In contrast to AnaConDa®, MIRUS™ includes an automated control of end-tidal VA concentrations. In this study we compared feasibility, costs and recovery times after anaesthesia with isoflurane (ISO), sevoflurane (SEVO) or desflurane (DES) in ventilated and spontaneously breathing patients.
Methods The study was approved by the appropriate institutional review board. After written informed consent, 63 ASA I to III patients undergoing elective hip or knee replacement surgery under general anaesthesia were included. Patients were randomly organised into three groups (20 to 22 each). Anaesthesia was induced with intravenous anaesthetics. After tracheal intubation MIRUS™ automatically adjusted the end-tidal VA concentration to 1.0 MAC. Patients were ventilated with the Puritan Bennett 840 ICU ventilator. After 1 hour of anaesthesia with 1.0 MAC the ventilator mode was switched from SIMV VC+ (totally controlled ventilation, passive patient, with a tidal volume of 8 ml/IBW) to proportional assist ventilation with 50% support (active patient). At the end of surgery the MIRUS™ system was stopped (MAC set to 0.0) and recovery times were measured.
Results Patients were comparable in age, height, weight and operation time. In 60/63 patients a MAC of 1.0 was reached by MIRUS™. Therefore, ISO 11.2 ± 3.3 ml/hour, SEVO 24.3 ± 4.8 ml/hour or DES 41.7 ± 7.9 ml/hour (mean ± SD; t test: P <0.001) were used during passive ventilation. During patients' active ventilation, mean VA consumptions of ISO 9.6 ± 5.1 ml/hour, SEVO 19.4 ± 9.6 ml/hour or DES 35.5 ± 23.0 ml/hour were detected (NS between passive and active patients). ISO was the cheapest VA (€2.70 ± 3.10/hour passive patient, €1.90 ± 2.30 active patient), followed by SEVO (€8.40 ± 3.70 passive patient and €6.8 ± 3.8 active patient) and DES (€9.6 ± 4.1 passive patient and €8.6 ± 6.5 active patient). Recovery times were significantly shorter after SEVO and DES compared with ISO (minutes:seconds; ISO 9:31 ± 6:04, SEVO 6:19 ± 2:56, DES 5:27 ± 1:59).
Conclusion This study showed that MIRUS™ could automatically control end-tidal VA concentrations in ventilated and spontaneously breathing patients. Using ISO reduces costs. Further studies must be taken to analyse feasibility, costs and recovery times of ISO, SEVO and DES used for sedation in an ICU setting.
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P496

Interaction between etomidate and beta tumoral necrosis factor on hemodynamic response after cardiac surgery

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Introduction The use of etomidate is a risk factor for relative adrenal insufficiency in patients undergoing cardiopulmonary bypass (CPB) [1]. The objective was to determine the possible interaction between

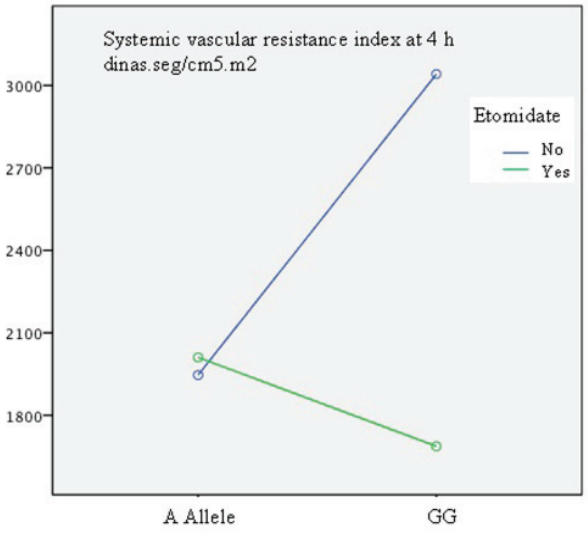


Figure 1 (abstract P496).

etomidate and beta tumoral necrosis factor (TNFβ) polymorphism on hemodynamics after CPB.
Methods A prospective cohort study on CPB patients who received etomidate or not during anesthetic induction during 2008 to 2011. Demographic and postoperative variables were collected. We tested the Hardy–Weinberg equilibrium in order to avoid selection bias. V18 SPSS was used.
Results We studied 433 patients undergoing CPB, 285 (65.8%) men and 148 (34.2%) women, 66 ± 6 years, EuroSCORE I 5.3 ± 4%. TNFβ was in Hardy–Weinberg equilibrium (χ^2: 0.6; P = 0.42). A total of 254 (58.7%) patients received etomidate, 152 out of them required vasoactive drugs. Homozygous G was defined as unfavorable TNFβ versus the A allele [2]. Using the general linear model after adjusting for sex and amines dose at 4 hours, an independent association was observed between the systemic vascular resistance index (SVRI) at 4 hours and the use of etomidate (F: 18; P <0.001): 1,849 (95% CI: 1,673 to 2,024) versus 2,493 (95% CI: 2,258 to 2,729) dinas.seg/cm^5.m^2, the presence of homozygous G (F: 6.5; P = 0.01), and also showed a significant etomidate–homozygous G interaction (F: 22.8: P <0.001): 1,687 (95% CI: 1,350 to 2,023) versus 3,041 (95% CI: 2,589 to 3,492) dinas seg/cm^5. m^2 (Figure 1).
Conclusion Etomidate use is associated with lower postoperative SVRI which is increased in the presence of G homozygosity for TNFβ polymorphism.
References
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P497

Sedation practices in South African ICUs: results of a national survey

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Introduction There has been a paradigm shift in the approach to sedation of critically ill patients. The purpose of this study was to evaluate current sedation-related practices in South African ICUs.
Methods A validated questionnaire was distributed electronically to physician members of various medical databases in South Africa as South Africa does not have a formal registry of critical care practitioners.
Results One hundred and twenty-six of 174 respondents indicated that they practice in the ICU setting. Sixty-six per cent were specialists and mainly anaesthesiologists (42%), whilst 32% were critical care subspecialists. The public and private-sector representation was 64% and 46% respectively. A written sedation guideline is implemented by 42%. Forty-three per cent utilise a sedation scale, with the Ramsey Sedation Scale being the commonest in use. However, 38% of sedation scale users do so infrequently. Daily interruption of sedation is practiced by 75%. Light sedation is targeted by 42% and 14% do not follow any sedation targets. Upon admission and on subsequent days, sedation targets are achieved most of the time by 48% and 69% of the respondents respectively. Whilst a wide variety of sedatives are prescribed, midazolam constitutes the most commonly prescribed agent. Dexmedetomidine is the agent of choice for postcardiac surgery patients with cardiovascular comorbidities, delirious patients, during weaning and for non-invasive ventilation. Propofol is the agent of choice amongst neurological patients. The respondents indicated that there is a need for local sedation guidelines.
Conclusion The findings are comparable with reports of sedation surveys conducted in other countries. There is an evidence–practice gap that needs to be addressed.

P498

Epidemiology of operation-related medical errors in inpatients in Japan: the JET study

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Introduction Operation therapy is more invasive than medication therapy and then operation-related medical errors (MEs) might be of more significant impact than medication errors. We assessed the incidence and characteristics of operation-related MEs to improve patient safety in such patients.
Methods The Japan Adverse Event (JET) study was a prospective cohort study which had evaluated AEs and MEs at two tertiary care hospitals. We included all adult patients aged ≥15 years old who had operations over a 2-month period. The primary outcome of this study was the operation-related MEs, defined as any deviation from appropriate process of an operation or perioperative care. Trained nurses placed at each participating hospital reviewed all charts daily on weekdays, along with laboratories, incident reports, and prescription queries to collect any potential event. They also collected the characteristics of the patients in the cohort. Some operation-related MEs are associated with operation-related AEs, which are operation-related preventable AEs. After those suspected events were collected, physician reviewers independently evaluated them and classified them as operation-related MEs, AEs, or rule violations. Physician reviewers assessed and rated operation-related AEs according to the symptom and the severity of injury.
Results This study included 389 patients with 6,624 patient-days. The median age of patients was 69 years and 224 (58%) were male. Among these 389 patients, 31 patients had 46 operation-related MEs during their hospital stay and the incidence of operation-related MEs was 12 per 100 patients. Operation-related AEs occurred in 29 patients with 43 events. The most frequent symptoms for operation-related MEs were skin (26%), bleeding (21%), and central nervous system (14%). Among 46 operation-related MEs, 43 (93%) were not intercepted, and they resulted in operation-related AEs that were considered as preventable operation-related AEs. Nine of preventable operation-related AEs (21%) were fatal or life-threatening: five were nerve injury during operation and stroke after neurosurgical operation, and one biliary peritonitis after gastrectomy and cholecystectomy, and tension pneumothorax after lung lobectomy, and two unexpected massive bleeding due to vessels injury.
Conclusion Ninety-three percent of operation-related MEs resulted in operation-related AEs and 21% of them resulted in life-threatening events. Prevention of operation-related MEs should improve the mortality of surgical patients.

P499

Visualising patients' dynamics in the ICU and predicting mortality in real-time using big data

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Introduction As informatisation of hospitals continues to spread, increasing amounts of healthcare related data are being collected, and the ICU is no exception. Large datasets are being made available to the scientific community, and offer the potential to answer clinical questions and to develop the next generation of clinical tools. A demonstration of such a tool is presented here, built using data from the Multiparameter Intelligent Monitoring in Intensive Care II (MIMIC-II) open database.
Methods All of the adult patients who died during their stay in the ICU were included, as well as a matched cohort of patients who survived for more than 28 days after discharge. Data regarding their vital signs, laboratory tests and demographics were collected. Using Matlab, a graphical method involving principal component analysis was developed. The expected mortality was computed using the k-nearest neighbours' method and compared with several classification algorithms (logistic regression, random forest, support vector machine, Gaussian mixture models).
Results A total of 6,084 patients were included in the analyses, adding up to more than 12 million data points. Using this multidimensional dataset, a 3D representation of the clusters of survivors and nonsurvivors was built, showing how their trajectories diverge through time. Patterns in the evolution of individuals or subgroups of patients can be identified using this approach. For example, the evolution of a new patient can be visualised, progressing through the clusters as his severity changes. His expected mortality can be predicted at any point in time, with an AUC ROC constantly above 0.85.

Conclusion Machine learning tools offer an appealing mathematical framework for modelling complex medical situations. This proof of concept demonstrates that the application of computational sciences to high-quality data such as the MIMIC-II database has the potential to lead to the development of meaningful tools which will ultimately be capable of assisting physicians in making the right decision at the right time for an individual patient. Only tight cooperation between clinicians and data scientists can help close the gap that currently separates these two worlds, for the ultimate benefit of patients.

P500

Organizational factors and patient outcomes in Brazilian ICUs: the ORCHESTRA study

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Critical Care 2015, **19(Suppl 1):**P500 (doi: 10.1186/cc14580)

Introduction The aim was to investigate the impact of organizational factors on patient outcomes in a large sample of Brazilian ICUs.
Methods A retrospective cohort study of 59,483 patients admitted to 78 ICUs in 51 hospitals during 2013. We retrieved demographic, clinical and outcome data from an electronic ICU quality registry (Epimed Monitor System). We surveyed ICUs using a standardized questionnaire regarding hospital and ICU structure, organization, staffing patterns, process of care, and family care policies. We used multilevel logistic regression analysis to identify characteristics associated with hospital mortality.
Results ICUs were mostly medical or medical–surgical (62.79%) and located in private hospitals (67.86%). Approximately half (40.51%) had critical care training programs. Median physician and nurse staff–bed ratios were 0.15 (IQR, 0.12 to 0.19) and 0.71 (0.61 to 0.84); board-certified intensivists were present 24/7 in 16 (21%) of ICUs. Routine clinical rounds occurred in 67 (86%) and daily clinical checklists were used in 36 (46%) ICUs. Most frequently implemented protocols focused on sepsis management and VAP and CLABSI prevention. Median number of patients per center was 898 (IQR 585 to 1,715) and there were 67% medical admissions; 18% patients received mechanical ventilation (MV). Median SAPS 3 score was 41 (33 to 52) points. ICU and hospital mortality rates were 9.6% and 14.3%, respectively. Adjusting for relevant patients' characteristics (SAPS 3 score, diagnostic admission category, chronic health status, comorbidities, MV use), case-volume and type of ICU, the ICU size (OR = 1.50 (95% CI, 1.45 to 1.95), for 11 to 20 beds; OR = 2.02 (1.40 to 2.92), for >20 beds) and ≥2 clinical protocols (OR = 0.65 (0.42 to 0.99)) were the organizational characteristics associated with mortality.
Conclusion In a large sample of Brazilian ICUs, the implementation of clinical protocols was associated with better outcomes. Conversely, mortality was higher in larger ICUs.
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P501

Hamilton Early Warning Score: predict, prevent and protect

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Introduction This study determined the pattern of decline prior to an inpatient arrest. We implemented the Hamilton Early Warning Score (HEWS) within our electronic vital signs documentation to track and trigger care for deteriorating patients. Other EWS have been described in the literature with varying success [1]. In contrast to previous observational studies, we chose to implement a score modified from published EWS using the consensus opinion of a steering committee and evaluate the score in real time.

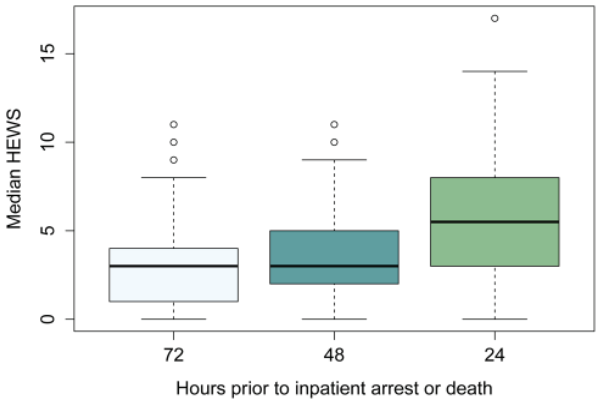


Figure 1 (abstract P501). HEWS prior to critical event.

Methods We conducted a prospectively identified, retrospectively gathered cohort study at two hospitals of consecutively admitted medical and surgical patients over a 6-month period. One hospital had a rapid response team (RRT) and used HEWS with a trigger of 5 while the other was undergoing implementation of the HEWS without a RRT. HEWS was calculated for each patient on the first day of admission and for the 3 days prior to inpatient arrest or death. A study investigator reviewed all events for accuracy. Our outcome of interest was a composite of inpatient cardiac arrest and hospital mortality.
Results There were 7,138 patients admitted over 6 months. We found 0.5% of patients suffered an inpatient arrest and 3.6% of patients died. Moreover, 66% of patients who died or arrested were admitted to the hospital without a RRT. Patients who arrested or died had more comorbidities defined by the Charlson Comorbidity Index (CCI) of 6.0 and 8.2 respectively compared with the general population, which had a CCI of 5.2. The median and mean HEWS at time of admission was 1 and 1.7 for the general population, 2 and 2.4 for patients who suffered an inpatient arrest and finally 3 and 3.8 for those who died. There was a rise in median HEWS from 2 to 5 in the 24 hours prior to in patient arrest or death. See Figure 1.
Conclusion We found that a 2.5-fold increase in HEWS occurred 24 hours prior to critical events. Similar to previous studies, a RRT in conjunction with HEWS is the best system to reduce unanticipated adverse events. An absolute HEWS of 5 and/or a rapidly increasing HEWS should trigger rapid assessment and treatment to reduce preventable inpatient deaths and arrests.
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P502

Ethnicity and trial recruitment

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Critical Care 2015, **19(Suppl 1):**P502 (doi: 10.1186/cc14582)

Introduction Surrogate consent and time-sensitive recruitment in critical care research is challenging, yet low enrolment numbers or omitting ethnic groups skew results and conclusions. Patients from different ethnic groups may respond differently to therapeutics [1]. There are few data about the effect of ethnicity on recruitment into ICU trials. Our ICU recruits to national trials and serves an increasingly non-White British population (24% of population). We undertook this study to determine whether ethnicity affects ICU consent rates.
Methods We performed a retrospective review of screening logs from three national UK trials (PROMISE, BALTI-P, GAiNS) and one local trial (Nociceptin in Sepsis). We analysed consent rates of eligible patients by ethnicity, age, sex, interventional or observational trial, and ethnicity of the researcher seeking consent. We performed chi-squared analysis, and entered significant values into a logistic regression model using SPSS v22.

Results We identified 332 eligible patients across all trials, of whom 37 (11%) were not White British (nWB). Analysis demonstrated consent/assent refusal being significantly associated with: nWB (14, 38%, P <0.001), interventional trial (21, 25%, P = 0.003) and different researcher–patient ethnicities (P <0.001). Logistic regression analysis confirmed these as independent factors (nWB OR = 4.5, 95% CI = 2.1 to 9.8, P <0.001; interventional trial OR = 2.7, 95% CI = 1.4 to 5.2, P = 0.003; data points missing for researcher–patient ethnicity so variable excluded).
Conclusion This initial study suggests that ethnicity may affect assent/consent to ICU research, with patients from different ethnicities being four times less likely to be recruited. Whilst data are incomplete for researcher–patient ethnicity, our data suggest that this may be an important factor and may influence future consent processes. We believe that the role of ethnicity warrants further investigation, not only in clinical trials but also in areas such as organ donation.
Reference

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P503

Validation of an electronic early warning score using decision tree analysis: proposal

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Critical Care 2015, **19(Suppl 1):**P503 (doi: 10.1186/cc14583)

Introduction Decision tree analysis uses an algorithm to classify data items by recursively posing a series of questions about items within a dataset. Each question leads to another node and potentially more questions until a predefined end condition is reached or no more questions can be asked (Figure 1). We hypothesize that scores generated using the decision tree method will improve upon our existing Hamilton Early Warning Score (HEWS) for a composite endpoint of cardiac arrest, unplanned ICU admission or death.
Methods A database of 156,642 electronically captured vital signs from 6,757 consecutively admitted patients to eight medical and surgical wards will be used to train and test the decision tree early warning score. One-third of the data will be withheld from the algorithm for use as a testing set. The algorithm will look for significant changes in vitals 72 hours prior to an outcome and develop the score based upon the resulting relative risk of the composite endpoint happening given a certain vital sign. The scores and predictions generated by the decision tree analysis will then be compared with that of the inception HEWS cohort.

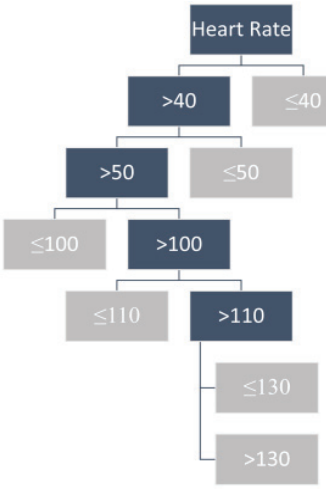


Figure 1 (abstract P503). Sample heart rate decision tree.

Results The planned analysis for determining the discriminatory and predictive ability of the decision tree HEWS will be conducted with area under the receiver operating characteristic curves. We will test whether the current HEWS has the appropriate sensitivity and specificity when compared with that of the decision tree score. The AUROC will be calculated for both the training set of data as well as the separate population of additional medical and surgical patients. The two scores will also be plotted along an efficiency curve, comparing the percentage of vitals that precede a critical event with the percentage of vitals that produce a EWS value greater than or equal to a given EWS value.
Conclusion Decision tree analysis methodology with real-life vital signs can produce an EWS superior to previous observational studies. Using a decision tree, especially one that composites all vitals, may show that certain vitals are more predictive of critical events than others. Data will be used to further improve our current HEWS score.

P504

Can an electronic ICU support timely renal replacement therapy in resource-limited areas of the developing world

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Critical Care 2015, **19(Suppl 1):**P504 (doi: 10.1186/cc14584)

Introduction Timely availability of a kidney specialist poses a formidable challenge in ICUs located in tier II and tier III cities of the developing world. Renal replacement therapy (RRT) is often required in the ICU for acute renal failure patients but availability of a nephrologist/specialist is scarce, leading to unnecessary and risky transfer to higher centers in metropolitans or even worse to death. We explored whether a remotely monitored ICU – an electronic ICU (eICU) – would help mitigate this demand–supply gap.
Methods This retrospective study was conducted at four Critinext affiliates where the eICU was being used to provide 24 × 7 support on 89 ICU beds from a remote command center with intensivist and other requisite staff. The eICU had complete access to the patient's real-time vitals, hemodynamic parameters, imaging, laboratory values, audiovisuals and appropriately engineered smart alerts. The eICU model was further extended in initiating and getting RRT done in patients whenever deemed necessary in times of unavailability of a specialist at the same site. Patient baseline demographics, including risk factors, severity score, all-cause mortality at 30 days, transfers to higher center for RRT and its prevention were recorded. Descriptive analysis was performed. Between-group comparison was performed by applying the chi-squared statistic, significance was assumed at a value of P <0.05. Out of a total of 5,146 admissions, 752 inpatient files with acute kidney injury/acute renal failure were reviewed, January to July 2013 (n = 373) and July 2013 to January 2014 (n = 379) pre and post eICU implementation respectively.
Results While baseline demographics and the patient profile in the two groups did not show statistically significant difference, mean APACHE II score was 14.25 ± 1.94 and 14.65 ± 1.76 pre and post eICU respectively; there was a statistically significant difference in all-cause mortality at 30 days which decreased from 31 (8.3%) to 16 (4.2%) pre and post eICU respectively, a reduction of >49% (P = 0.030) and transfer out for RRT came down by >77%, from 15 (4%) to two (0.5%) post eICU implementation (P <0.002).
Conclusion Over the years there is now broad consensus over the benefits of eICU intervention in deprived areas [1]. There is now a need for a paradigm shift to elevate specialized care to improve outcomes. Our small study has clearly indicated the benefits in outcome and economics even while providing intervention in such remote areas. An eICU as a bridge to the demand–supply gap needs to be explored and utilized further to its full potential in the emerging world.
Reference

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P505

Outcomes and resource use in Brazilian ICUs: results from the ORCHESTRA study

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Introduction The aim was to evaluate outcomes and resource use and to investigate the association between organizational factors and efficient resource use in a large sample of Brazilian ICUs.
Methods A retrospective cohort study in 59,483 patients (medical admissions: 39,734 (67%)) admitted to 78 ICUs (private hospitals, n = 67 (86%); medical or medical–surgical, n = 62 (79%)) during 2013. We retrieved demographic, clinical and outcome data from an electronic ICU quality registry (Epimed Monitor System). We surveyed ICUs using a standardized questionnaire regarding hospital and ICU structure, organization, staffing patterns, process of care and family care policies. Efficient resource use was assessed by estimating standardized mortality rates (SMR) and standardized resource use (SRU) adjusted for the severity of illness according to the SAPS 3 score, as proposed by Rothen and colleagues [1].
Results The median admissions per center was 898 (IQR 585 to 1,715) and SAPS 3 score was 41 (33 to 52) points. Median ICU length of stay was 2 (1 to 5) days, and ICU and hospital mortality rates were 9.6% and 14.3%, respectively. Estimated SMR and SRU were 0.97 (0.72 to 1.15) and 1.06 (0.89 to 1.37), respectively. There were 28 (36%) most efficient (ICUs with both SMR and SRU <median), 28 (36%) least efficient (ICUs with both SMR and SRU >median), 11 (14%) overachieving (ICUs with low SMR and high SRU) and 11 (14%) underachieving (ICUs with high SMR and low SRU) ICUs. Most efficient ICUs were usually located in private and accredited hospitals, with step-down units and training programs in critical care. In univariate analyses comparing most and least efficient ICUs, ≥2 clinical protocols (OR = 7.22 (95% CI, 1.41 to 36.97)) and graduated nurse/bed ratio >0.25 (OR = 4.40 (1.04 to 18.60)) were associated with efficient resource use. Daily checklists also tended to be associated with efficient resource use (OR = 2.89 (0.95 to 8.72), P = 0.057).
Conclusion We observed a great variability in outcome and resources in a large sample of Brazilian ICUs. Implementation of clinical protocols and nursing staffing patterns can be targets to improve the efficiency in resource use in emerging countries such as Brazil.
Acknowledgements Funded by IDOR, CNPq and FAPERJ. Endorsed by BRICNet.
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P506

Blood pressure and heart rate changes during shifts in ICU nurses in relation to their work experience

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Critical Care 2015, **19(Suppl 1):**P506 (doi: 10.1186/cc14586)

Introduction The aim of the study was to assess the blood pressure (BP) and heart rate (HR) changes during shifts in ICU nurses in relation to their work experience. Our hypothesis was that less experienced nurses, in comparison with more experienced ones, would be subjected to more work stress and this could be demonstrated by higher changes in BP and HR during shifts.
Methods We enrolled 23 nurses working in an 8-hour shift schedule at a general adult ICU. Demographic and clinical data were obtained by completing a short questionnaire. The nurses were invited to measure their BP and HR at the beginning, in the middle and at the end of their shift. An ESH/BSH-certified automatic device was used for the BP and HR measurements.

Table 1 (abstract P506). Mean change in systolic and diastolic BP and HR in relation to ICU work experience

	Group 1	Group 2	*P* value
SBP (mmHg)	3.22	–0.40	0.053
DBP (mmHg)	2.08	–0.27	0.061
HR (bpm)	4.46	1.16	0.048

Results The mean duration of working in an ICU was 7.3 ± 5.32 years (from 2 to 18 years). The nurses were grouped according to experience – Group A: 17 nurses with <10 years of experience (mean: 4.4 years), Group B: six nurses with >10 years (mean: 15.6 years). There were 640 BP–HR measurements. The mean systolic BP, diastolic BP and HR did not differ between the two groups (systolic BP: 111.2 ± 10.9 vs. 113.7 ± 14.1 mmHg, P = 0.654; diastolic BP: 72.8 ± 8.2 vs. 71.9 ± 8.1 mmHg, P = 0.835; HR: 81.4 ± 7.2 vs. 78.1 ± 8.4 bpm, P = 0.365). Nevertheless, the mean change in BP and HR during the shift did differ between the two groups, with the more experienced nurses showing a trivial reduction in systolic and diastolic BP and minor increase in HR whereas the less experienced ones showed slight increase in both BP and HR measurements (Table 1), reaching almost statistical significance. For the less experienced nurses in Group 1, it was noted that the mean changes were bigger in night shifts although the limited number of measurements did not allow robust statistical analysis.
Conclusion The less experienced ICU nurses, with <10 years of ICU work experience, tended to increase their BP and HR levels during the shift, a finding probably heightened during night shifts. Further research, including not only cardiovascular parameters, is warranted to uncover the effects of shift-work pattern in ICU nurses, taking into account this specifically stressful work environment.

P507

Prehospital transported patients: a resource for accessing prognostic risk factors

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Critical Care 2015, **19(Suppl 1):**P507 (doi: 10.1186/cc14587)

Introduction The survival of patients transported by ambulance to the emergency department (ED) depends on clinical conditions, patient-related factors and organisational prehospital set up. Data and information concerning patients in the prehospital system could form a valuable resource for assessing potential risk factors associated with adverse outcomes and mortality. Our aim was to describe ambulance transports to the ED and identify prognostic factors accessible in the prehospital phase and associated with 7-day mortality.
Methods We included all adult patients (≥18 years) with a first-time ambulance transport to the ED at Odense University Hospital in the period 1 April 2012 to 30 September 2013. Ambulance personnel recorded vital signs and other clinical findings on a structured form on paper during the ambulance transport. Each contact was linked to information from population-based healthcare registers in order to identify comorbid conditions and information on mortality. Demographic factors and first registered vital sign were analysed by univariate logistic regression analysis, with 7-day mortality as outcome.
Results In total, 18,572 first-time ambulance contacts were identified in the period of inclusion. Overall 7-day mortality was 4.3% (95% CI = 4.0 to 4.6). Univariate analysis showed increasing age, Charlson Comorbidity Index ≥2, vital parameters outside the normal reference range and summoned physician-assisted mobile emergency care units to be associated with 7-day mortality. Further analyses are currently being carried out.
Conclusion We found that several prehospital-registered vital signs recorded by ambulance personnel at first contact with the patient were prognostic factors of 7-day mortality.

P508

Contribution of medical senior house officers to a medical referral in the emergency department

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Introduction In Irish hospitals, the medical senior house officer (SHO) is the most junior fully qualified doctor on the medical on-call team. After a patient has been seen by an emergency department doctor of any level, they are almost always referred directly to the medical SHO. This process has been shown to delay a patient's ward admission by 3 hours 30 minutes [1]. We attempted to quantify the additional benefit for the patient of being seen by the on-call medical SHO, in terms of patients discharged, new diagnoses reached, and new treatments initiated.
Methods The emergency department notes and clinical charts of 182 patients were assessed. This constituted a random sample of patients referred by emergency department doctors to the medical team on call over a 2-month period (November to December 2011).
Results Discharged: 3/182 (1.6%) of patients referred to the medical team were discharged directly by the medical SHO. Diagnosed: medical SHOs suggested a diagnosis which was different from, or additional to, the ED doctor, in 52/182 cases (28.6%). However, the medical consultant only agreed with this diagnosis in 25 cases (13.7%). This means an incorrect new diagnosis was reached more often than not (14.9%). Treatment: the majority of cases (116/182 (63.7%)) saw no new treatment initiated by the medical SHO. Of the rest, only 31 (17%) had a new treatment initiated by the medical SHO which was continued on by the medical consultant through the admission.
Conclusion Few direct discharges, new diagnoses, or key new treatments were initiated by the medical SHO in the emergency department. A paper from our hospital shows that more patients referred in by GPs to ED are admitted compared with those referred in to the acute medical assessment unit, with comparable disease severity (43% vs. 12.5) [2]. That paper highlighted the fact that the junior level of the medical NCHDs who see patients in the ED may contribute to their lack of discharging/decision-making zeal. Our survey further illustrated this feature. Our study provided no evidence that a formal medical assessment should delay a patient progressing to the medical ward. Additional genuine urgent OPD appointment slots could be another beneficial measure.
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P509

Achieving a time to first consultant review of under 12 hours for acutely ill medical patients

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Introduction In 2007, the Acute Medicine Task Force made recommendations about the operation and staffing of acute medical units (AMU). Consultant-led care was seen as critical to ensuring high standards of care for patients and maintaining efficient patient flow [1]. It also recommended that during the hours when the AMU is staffed by a consultant, all new patients should be seen within 6 to 8 hours. Patients admitted overnight should have a consultant review within 12 to 14 hours. Following the introduction of a 4:00 pm consultant ward round of newly admitted acute medical patients to the existing 8:00 am and 2:00 pm rounds, it was our intention to establish whether our trust was meeting those recommendations.
Methods We conducted a prospective survey of all new acute medical admissions over a 2-week period. Data collected included date and time of admission to the hospital, location on arrival, time of first medical clerking, and time of first consultant review.
Results Data were collected for 420 admissions. Sixty-seven percent of patients were admitted to the hospital between 12:00 am and 12:00 pm with a peak occurring between 4:00 pm and 6:00 pm. Sixty-two percent of patients were first seen by a consultant within 12 hours of admission, with a range from 23 minutes to 26 hours. When looking at patients admitted during the weekdays, 63% of them were seen within 12 hours; for those admitted at the weekend the figure was 57%.
Conclusion In 2011 the Royal College of Physicians emphasized the impact that the quality of the care provided within the first 48 to 72 hours had on clinical outcomes. An evaluation of consultant input into acute admissions management revealed that hospitals in which two or more ward rounds of all acute medical unit patients were performed daily had a lower adjusted case fatality rate for patients with hospital stays over 7 days. Despite twice-daily consultant ward rounds of all new acute admissions and the addition of a third 4:00 pm round from Monday to Friday, only 62% of patients were seen by a consultant within 12 hours. With 67% of patients being admitted between the hours of 12:00 am and 12:00 pm, it is possible that the substitution of an evening round for one of the afternoon rounds would help increase the number of patients seen within the target time frame. This would require a change in the working pattern of the acute medicine consultants.
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P510

Interhospital critical care transfer delays result from organisational not geographical factors: secondary analysis of deteriorating ward patients in 49 UK hospitals

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Introduction Critically ill patients may require interhospital transfer for specialist care or because of a lack of local ICU capacity. Harm is assumed from delays that result, but it is not clear whether these delays are due to transfer distances or deficiencies in the organisation of care.
Methods In total, 151 of 15,602 deteriorating ward patients in the (SPOT)light study [1] were transferred rather than admitted locally. We defined delay as the time from critical care assessment in the first hospital to arrival in critical care in the second hospital. We used hospital postcodes to derive latitude and longitude, and calculated both geodesic (straight-line) distances (Figure 1) and road distances between the sites using R version 3.1.1 [2]. We compared daytime versus overnight (7:00 pm to 7:00 am) transfer durations assuming traffic would contribute less to delay overnight. Mapping and visualisation was performed on Quantum GIS version 2.4 [3].
Results The median delay to admission was 22 hours (range 41 to 167 hours). The median geodesic distance was 18 km (range 1 to 141 km), and road distance was 24 km (range 2 to 180 km). Correlations between time delay and geodesic/road distances were weak (Figure 2,

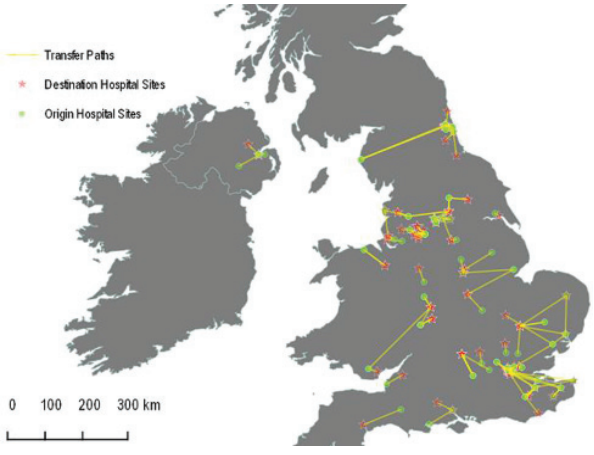


Figure 1 (abstract P510). Map of transfers.

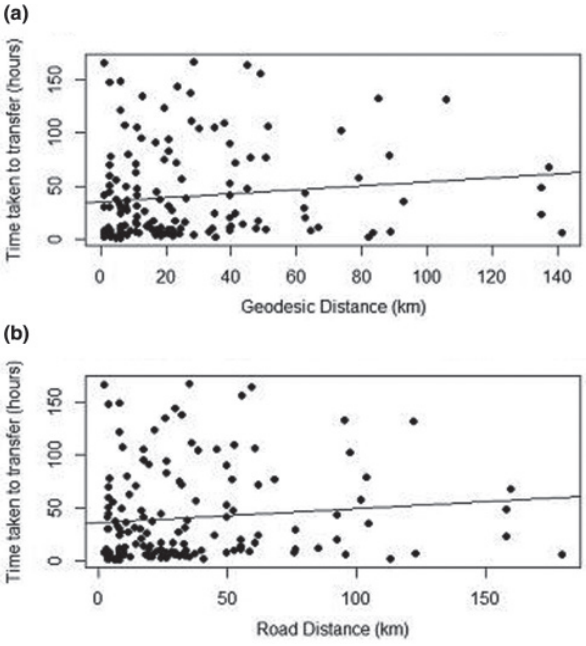


Figure 2 (abstract P510). (a) Time duration versus geodesic distance (R^2 = 0.015). **(b)** Time duration versus road distance (R^2 = 0.011).

R^2 = 0.015 and 0.011, respectively). Transfer delays in the daytime and overnight were similar (Wilcoxon rank sum, P = 0.6).

Conclusion Interhospital transfers are subject to clinically significant delays, and substantial travel distances. Delays are only weakly correlated to distances travelled and may reflect delays resulting from organisational inefficiencies. We infer that efforts to improve the efficiency of transfer should focus on local organisational issues. There was no difference in the duration taken for overnight versus daytime transfers.

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P511

Delayed ICU discharges and medical follow-up: a cause of increased mortality?

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Introduction Discharge from intensive care is a potentially vulnerable time for patients who are recovering from critical illness. Recent data from the ANZICS group have highlighted that the mortality difference in those patients who are discharged out of hours is nearly twice that of those discharged during the day [1]. These results have been replicated in our institution with a mortality of 8.7% (discharged 22:00 to 06:59) versus 4.8% (discharged 07:00 to 21:59). In the UK, NICE CG50 advised that transfer from critical care to the ward out of hours should be avoided and documented as an adverse event. We postulated that one important factor in our hospital is the decreased medical and nursing cover overnight and so looked at the delay from discharge to first medical review and to outreach review.

Methods The case notes of 100 consecutive patients discharged to the ward between September 2013 and October 2013 were examined to identify the time of discharge from the ICU and the subsequent first review by the receiving medical team and the Critical Care Outreach team. The grade of the doctor reviewing the patient was recorded.

Results Of these 100 patients, 22 were discharged between 22:00 and 07:59. From the 100 case notes requested, only 50 were available for examination. Forty patients were discharged to the wards, with only 37 having further documented medical reviews in the notes. Only 62% of patients were reviewed by a consultant following intensive care, with over 20% of patients waiting more than 24 hours for any medical review. During this time 18% of patients received a review by the nurse-led outreach team. See Figure 1.

Conclusion It is clear that a highly vulnerable group of patients who are recovering from critical illness [2] receive inadequate early follow-up within the hospital. We postulate that the delay in medical review and the lack of senior review may be caused by over 40% being discharged overnight and contribute to the increased mortality seen in our institution and the ANZICS study [1] with nighttime discharges.

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P512

Evaluation of patients with wild mushroom poisoning in the emergency department

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Introduction Wild mushroom poisoning (MP) is an important medical emergency that may have bad clinical outcome. We aimed to evaluate the clinical and laboratory features of patients with wild MP admitted to our emergency department in the Central Black Sea Region and to inform the emergency department physicians about early diagnosis and management of wild MP in the light of obtained data.

Methods This study was designed retrospectively by examining files of the patients with wild MP who were admitted to Ondokuz Mayis University Emergency Department, between January 2008 and December 2012. Patients older than 18 years were included in the study. Patients were evaluated according to gender, age, location, duration between mushroom intake and the start of clinical symptoms, time of application to hospital, clinical features and findings and treatment method. The number of patients has been compared with the regional distribution of population, monthly temperature and average annual rainfall.

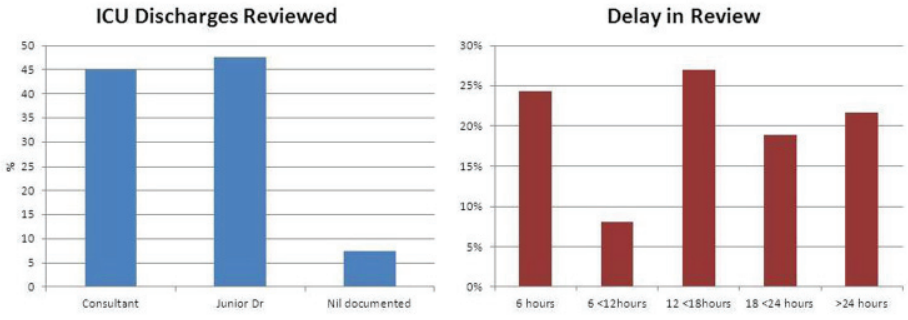


Figure 1 (abstract P511).

Results A total of 420 patients poisoned by wild mushrooms were studied. The male/female ratio was 1/1.5. The age of patients changed from 18 to 92 and mean age was 46 years. MP constituted 13.3% of all intoxication cases. The time when the first symptom occurred after mushroom intake was a mean 2 (0.17 to 2.15) hours. Of the patients, 47.6% lived in villages, 38.6% in towns and 13.8% in city centers. Admissions were mostly made in autumn, with 57.6%. Eighty-six percent of intoxications happened because of wild mushrooms collected in nature. The most frequent symptoms were nausea (93.8%), and vomiting (87.1%). Increase in liver function tests in 47 patients was observed. Two of these patients died while 10 patients were transferred to further centers for liver transplantation. The remaining patients were discharged from the hospital.
Conclusion Wild MP can cause bad clinical outcome. The public should be informed about the probable hazards of wild mushroom ingestion because collection and consumption of wild mushrooms from nature is common. Public health units should take protective precautions against wild MP. Education of health personals regarding MP will lead to successful results in patient management.

P513

Triage after drug overdose: effect of the introduction of a medical psychiatry unit on the allocation of ICU beds

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Introduction Many patients with drug overdose are sedated, but do not have medical reasons to warrant ICU admission. Historically, monitoring behavior and suicide risk was done in the ICU, until the patient was awake enough for psychiatric consultation.
Methods A medical psychiatry unit (MPU) was instituted as part of the Department of Clinical Psychiatry. For all patients with drug overdose in the emergency department, a risk assessment was made by the intensivist. Those without ICU indication (such as cardiac or respiratory monitoring) were admitted to the MPU. Alternatively, when awake enough, they were seen by the psychiatrist immediately. We performed an analysis of all patients with drug overdose, admitted to our ICU (before MPU $n = 88$, after MPU $n = 191$). We used the Welch t test for comparisons.
Results After institution of the MPU, there was a 28% reduction in the number of patients with drug overdose per month, admitted to the ICU. Also, patients admitted to the ICU were sicker and stayed longer (see Table 1). There were no patients admitted to the ICU after initial MPU admission.

Table 1 (abstract P513). Patient numbers and disease severity before and after introduction of MPU

	Before MPU (18 months)	Since MPU (51 months)	Difference	95% CI	*P* value
Admissions per month	4.9	3.5	−1.4	−2.7 to −0.1	0.04
APACHE II score	8.4	12.5	+4.0	+1.8 to +6.2	0.0004
APACHE III score	30.9	40.3	+ 9.4	+2.6 to +16.2	0.0069
Length of stay	0.8	1.3	+ 0.5	−0.0 to +1.0	0.05

Conclusion Introduction of an MPU was associated with reduced numbers of patients with drug overdose admitted to the ICU. Those admitted to the ICU after the institution of the MPU were sicker, probably indicating more appropriate use of ICU beds.

P514

Prospective controlled study to compare the effects of a basic patient safety course on healthcare worker patient safety culture

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Introduction It is estimated that about one in 10 patients may be harmed by adverse events during their hospital stay [1]. Transforming organizational culture to improve patient safety culture is considered important. We conducted a prospective, controlled study to assess the impact of a standardized patient safety course on an ICU's patient safety culture, using a validated patient safety culture assessment tool.
Methods Staff from two ICUs – ICU1 (tertiary referral hospital) and ICU2 (district hospital) – in Hong Kong were recruited to compare changes in the measured safety culture before and after a patient safety course. The BASIC Patient Safety course was only administered to staff from ICU1, and safety culture was assessed in both units before and after, using a survey based on the Hospital Survey on Patient Safety Culture [2]. Relative risk (95% CI) of improvement: baseline to follow-up in hospitals in patient safety domains, adjusted for duration of work in the unit (≤10 years vs. >10 years), was calculated. Responses were coded according to the Survey User's Guide, and positive response percentages for each patient safety domain were compared with the 2012 Agency for Healthcare Research and Quality (AHRQ) ICU sample of 36,120 respondents.
Results Preintervention and postintervention period response rates for ICU1 were 88.1% (37/42) and 79.3% (23/29); and for ICU2 63% (20/32) and 63% (15/24). Post intervention, compared with ICU2, ICU1 showed significantly improved perceptions of teamwork within the hospital unit, RR (95% CI for difference between ICUs) 1.55 (1.10 to 2.19, $P = 0.01$); and overall perception of safety, 1.94 (1.11 to 3.37, $P = 0.02$); but not increased frequency of reporting mistakes, 0.90 (0.33 to 2.49, $P = 0.84$). Overall, ICU1 demonstrated a greater improvement in positive responses in five safety culture domains than staff from ICU2. Patient safety culture indices were generally poorer in the two ICUs than the average ICU in the AHRQ database.
Conclusion The study provides supportive evidence that a structured, reproducible short course on patient safety is associated with a general improvement in the ICU's patient safety culture, measured with a validated safety culture assessment tool.
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P515

Audit of imaging documentation on an ICU

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Introduction The Ionising Radiation (Medical Exposure) Regulations 2001 recommend to 'ensure that a clinical evaluation of the outcome of each medical exposure is recorded' [1]. This audit looked at whether ICU documentation of investigations involving ionising radiation could be improved. Anticipated benefits would be improved communication between the multidisciplinary team and better-informed decision-making.
Methods Patients admitted to the ICU between 21 September 2014 and 2 October 2014 were included. If an investigation did not involve ionising radiation or was not requested by intensive care clinicians it was excluded. The indication for imaging was noted, and patient notes were analysed no less than 48 hours after the imaging was reported.

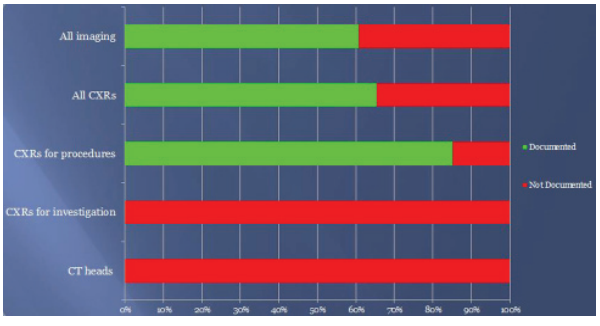


Figure 1 (abstract P515).

Results As shown in Figure 1, imaging requests were generally poorly documented (61%). In total, 17/26 (65%) chest X-rays (CXRs) were documented. A total of 0/2 CT scans were documented, despite one showing acute changes. In total, 17/20 (85%) CXRs requested following procedures carried out on ITU (such as insertion of central venous catheters) were documented, and the three not documented had no significant findings. The six other CXRs were requested to investigate worsening respiratory function. None were documented. Five had significant findings.
Conclusion Investigations following procedures were generally well documented, but investigations seeking pathology were not documented at all, regardless of the findings. This may have influenced the management of the patient and compromised patient safety. As such, the audit was presented at a departmental meeting to emphasise the importance of imaging documentation. A place for investigations was added to the ICU patient list to improve communication between the team, and a second audit is planned to assess the impact of this.
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P516

Barriers to the implementation of checklists in the ICU: a survey on the perceptions of 314 Brazilian critical care nurses and physicians

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Introduction Checklists have been used increasingly in the ICU aiming at mitigating avoidable adverse events, but their content is variable and little is known about barriers to their full implementation. This survey reported practices on the use of checklists and perceptions regarding barriers on its implementation.
Methods A web-based survey was conducted among a convenience sample of Brazilian ICU nurses and physicians between August and October 2014. Standard descriptive statistics were used.
Results A total of 314 professionals, 104 nurses (33.1%) and 210 physicians (66.9%), responded. The majority (82.4%) had more than 5 years of experience in intensive care. Checklists were applied every day, including weekends, in only 49.8% (n = 227). When we compared the barriers perceived by those working in smaller versus larger ICUs (<10 beds vs. >20 beds), the absence of a more comprehensive checklist content (93.6% vs. 81.9%, P = 0.026), the absence of specialized software or app (80.8% vs. 63.8%, P = 0.014), low availability of mobile devices (87.2% vs. 72.4%, P = 0.019), Internet unavailability (83.3% vs. 67.6%, P = 0.017), and the limited number of computers (88.5% vs. 76.2%, P = 0.0366) were the most often barriers to implementation. Checklists were applied with similar frequencies (<3 times a week, three to five times a week, and every day, including on weekends, P >0.05) regardless of the ICU size. When the type of tool used (paper vs. electronic) was considered, the main barrier highlighted was the lack of 100% Internet availability in the ICU (64.8% vs. 100%, P = 0.009). Users of paper form had higher demands for more comprehensive checklist content (84.3% vs. 63.6%, respectively, P = 0.037) and experienced more barriers to team adherence (98.1% vs. 86.4%, respectively, P = 0.034) as compared with those using specialized software.
Conclusion Although checklists are recognized as valuable tools for the adherence to best practice in the ICU, it is difficult to ensure the uniformity of their daily use. Resource limitations in smaller ICUs and the absence of comprehensive digital tools, mobile devices and Internet availability preclude full compliance at the bedside.

P517

After Round Comprehensive Plan Summary tool: an efficiency approach for the ICU

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Introduction ICU workflow for physicians, nurses and other healthcare providers is often complicated by distractions, interruptions, difficulties to concentrate, multitasking and the need to frequently change priorities in patient care-related procedures. It is therefore a continuous challenge to communicate and implement plans in an early, efficient and reliable way within the team and to constantly keep track about tasks that are completed, postponed or that are about to be forgotten. To facilitate every caregiver's workflow and to early and efficiently communicate, we implemented the After Round Comprehensive Plan Summary (ARCoPS) tool.
Methods Most of our patient care-related therapeutic and diagnostic decisions are made during the morning round consisting of intensivists, nursing team, surgeons, respiratory therapists, dieticians, clinical pharmacists and physiotherapists. Immediately thereafter, all plans for the next 24-hour period are again discussed, summarized, confirmed, prioritized and organized by the multidisciplinary team under aspects of optimal patient care and workflow efficiency by entering the plan data into a flat screen visualized template connected to our intranet immediately accessible at every physician and nursing caregiver workstation.
Results Twelve months after implementation of the ARCoPS tool we conducted caregiver interviews and identified the following effects: increase in treatment confidence through standardized multidisciplinary decision-making; reduced loss of information through immediate plan summarization by the whole team; reduction of ambiguity and misunderstanding about care plans through early written documentation; higher level of security not to forget procedures or tasks; positive acceptance of the tool to flexibly change priorities of care procedures; positive acceptance of the tool to mark accomplished tasks providing visual feedback about the care plan status; individual caregiver workflow economization through permanent treatment plan availability; and higher job satisfaction throughout the caregiver team.
Conclusion ARCoPS tool utilization has become a daily routine in our ICU. It functions as an effective communication and workflow tool and has helped us to reduce patient care-related misunderstandings and delays. It also enhanced the economics of our work sequence, which also highly contributes to a better level of patient safety. Furthermore, it has markedly contributed to an improved level of quality of work for caregivers.

P518

Multicenter Thai university-based surgical ICU study (Thai-SICU study): adverse events and outcome in the SICU

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Introduction The aim of this Thai-SICU was to study the incidence and outcome of adverse events in nine SICU university-based hospitals in Thailand.
Methods This multicenter prospective observational study was done in >18 years old, admission >6 hours surgical patients admitted to the large, postgraduate medical training university-based SICU during April 2011 to January 2012. Patient data were divided into three main phases as admission, discharge data and daily CRFs during the ICU stay. The patients were followed until they were discharged from the ICU or up to 28 days of their ICU admission and up to 28 days following discharge from the ICU if they survived.
Results Following a 19.7-month recruitment period, a total of 4,654 patients (17,579 ICU-days) were included in the analysis process. Admitted patients had the median age of 64 years. Most of the patients were admitted directly from the OR for postoperative monitoring with median APACHE II score 10, 23% were admitted with priority I who needed aggressive hemodynamic resuscitation and respiratory support. ICU mortality and 28-day mortality were 9.61% and 13.80%. Each day of ICU increment was associated with a 1.38-day increase of hospital stay (95% CI, 1.24 to 1.53; P <0.01). On the surveillance periods, the six most common adverse events were sepsis (19.5%), AKI (16.9%), new cardiac arrhythmias (6.17%), respiratory failure (5.83%), cardiac arrest (4.86%) and delirium (3.5%) respectively. The other events including reintubation within 72 hours, intraabdominal hypertension, acute MI, unplanned extubation, upper GI hemorrhage, pneumohemothorax, seizure, drug error and pulmonary aspiration were <3% each. The risk

of adverse events on 28-day mortality were significant on cardiac arrest (RR = 9.45; *P* <0.01), ARDS (RR = 4.58; *P* <0.01), AKI (RR = 4.18; *P* <0.01), sepsis (RR = 3.62; *P* <0.01), iatrogenic pneumohemothorax (RR = 3.23; *P* <0.01), seizure (RR = 3.12; *P* <0.01), upper GI hemorrhage (RR = 2.97; *P* <0.01), cardiac arrhythmia (RR = 2.91; *P* <0.01), ALI (RR = 2.71; *P* <0.01), delirium (RR = 2.13; *P* <0.01), MI (RR = 2.12; *P* <0.01), unplanned extubation (RR = 2.06; *P* <0.01), abdominal hypertension (RR = 1.75; *P* <0.01) and reintubation within 72 hours (RR = 1.51; *P* = 0.02).
Conclusion This is the largest systemic surveillance observation in the SICU. The study results are the reference for future research and also provide information for patient and relative advice when confronted with adverse events during SICU admission.

P519

Retrospective observational cohort study of mortality and length of stay for surgical ICU admissions

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Introduction A significant number require a postoperative ICU stay which may be prolonged [1]. Very limited data exist to characterise mortality and ICU length of stay (LOS) in different surgical specialties [2,3]. We aim to describe this relationship in a large cohort of surgical patients.
Methods We performed a retrospective observational cohort study of adult surgical admissions to the ICU of a large academic tertiary medical centre. The primary endpoint was 28-day mortality. We used simple descriptive statistics to characterise the population. The Wilcoxon rank-sum test or Kruskall–Wallis test was used, as appropriate, for tests of continuous data.
Results There were 6,203 surgical admissions during the 8-year study period. For both ICU and in-hospital mortality; the median LOS in days for survivors was 2.2 (IQR: 1.2 to 4.9) and that of nonsurvivors was 3.2 (IQR: 1.5 to 7.9). At 28 days, 1 year, and 2 years, the respective values were 2.2 (1.2 to 4.9) and 3.3 (1.5 to 6.7); 2.1 (1.2 to 4.7) and 3.1 (1.5 to 7.3); and 2.1 (1.2 to 4.6) and 3.0 (1.5 to 7.0), all *P* <0.0001. The greatest median LOS was found in neurosurgery and cardiothoracic surgery; 3.3 days (IQR: 1.7 to 9.5) and 3.1 days (IQR: 1.5 to 8.0) respectively. They corresponded to the specialities with the greatest percentage ICU (9.7% and 10.2%) and 2-year mortality (27.9%, and 35%). The greatest mortality and median LOS was found in ventriculostomy cases; 40.8% at 2 years and 10.6 days (IQR: 4.8 to 18.2).
Conclusion There is an association between postoperative ICU LOS and mortality that persists for at least 2 years after admission. Neurosurgery and cardiothoracic surgery patients appear to have a worse prognosis and also a more prolonged LOS. Our results may provide a more objective basis for clinical decisions, the use of limited resources, and inform on appropriate expectations of treatment.
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P520

Implementation of a horizontal intensive care team can impact efficiency in an emergency observation unit in Brazil

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Critical Care 2015, **19(Suppl 1):**P520 (doi: 10.1186/cc14600)

Introduction Emergency department observation units are often used to monitor critical patients in a situation of constant emergency department overcrowding and lack of intensive care beds. However, those units are often understaffed and might not have enough personnel and equipment to provide the same quality of care as a conventional ICU.
Methods We performed an observational study in a 17-bed, mixed clinical and surgical emergency department observation. Before the year 2012, the staff were composed of first-year internal medicine and surgical residents. There were no senior physicians specifically assigned to this unit, and residents were supervised by the members of the emergency department team, who changed shifts on a daily basis. In February 2012, two senior physicians (one cardiologist and one intensive care doctor) were specifically assigned to supervise the internal medicine residents and provide horizontal care for medical patients during the day, from Monday to Friday. There was no change in assistance for surgical patients. The schedule for nights and weekends remained unchanged. Mortality and length of stay for medical and surgical patients were measured in 2011, 2012 and 2013.
Results In the first year after the implementation of the clinic intensive care team, mortality in internal medicine patients decreased from 47% to 34% in 2012 and 33% in 2013. Although other changes happened in this period (the number of beds decreased from 24 to 17, nurses and physical therapists were hired and trained specifically for this unit), we believe the horizontal staff was critical, because mortality between surgical patients remained almost unchanged in the same period of time (23% in 2011, 22% in 2012 and 23% in 2013), in spite of the structural improvements that equally affected those patients. Length of stay decreased from 6.35 days in 2011 to 3.43 in 2012 and 3.15 in 2013 in medical patients and from 3.9 days on average in 2011 to 3.2 in 2012 and 2.8 in 2013 in surgical patients.
Conclusion Emergency department observation units are an alternative to alleviate emergency room overcrowding when there are no intensive care beds available. However, patients end up staying in those units for days and horizontal care by senior doctors may improve outcomes.
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P521

Rejection for ICU admission: analysis and results of this modality of limitation of therapeutic effort

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Introduction The aim was to know the frequency, criteria and implications of rejection for ICU admission to our ICU unit, a second-level hospital (18 beds).
Methods An observational retrospective study in a time interval of 6 months (January to June 2013). We retrospectively registered all patients rejected for admission to our unit, analyzing the clinical rejection report used in our hospital. From this report we extracted different variables: demographical (age, sex), provenance (emergency room, hospital), clinical (comorbidity, functional situation, diagnosis, reason of requesting admission), rejection motive ('too good', 'too bad', futility, lack of beds, patient rejection), whether it was definitive or conditional, whether the patient was admitted afterwards, and the state at hospital discharge. We realized a descriptive analysis (frequencies) and multivariant analysis of the factors related to futility rejection.
Results There were 165 rejections, which represents 25% of total ICU patients evaluated for admission. A total of 59.4% were male. Mean age was 69 ± 7 years (19 to 98). In total, 53.9% had more than two comorbidities (pluripathological) and 31.5% moderate to severe functional disability. The cause of rejection was in 55.2% of situations that the patient was 'too good', 37.6% related to qualitative futility, 4.8% was 'too bad' and in 1.2% a mix of lack of space (beds) and patient rejection. In the multivariant analysis the significant variables related to futility rejection were age (by years) with an OR of 1.05 (1.02 to 1.08), severe functional disability, OR of 4.35 (2.09 to 9.06), and the hospital provenance with an OR of 2.82 (1.1 to 7.2).
Conclusion Rejection for admission to ICU units is a frequent medical activity in our day-to-day job. The type of patient most rejected is cardiologic, mostly evaluated for thoracic pain probably ischemic but with low risk. In second place we found patients for which we decide rejection based on subjective qualitative futility, related mostly to age, prior functional disability and provenance.

P522

Impact of age, physiological status and APACHE score on acceptance of patients to the ICU

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Introduction Evidence suggests that age, chronic health status and acute illness severity affect the decision-making of clinicians regarding admission to the ICU (ITU) [1-3]. This prospective service review assesses the impact of age, APACHE II score and WHO functional score towards admission acceptance or refusal to ITU in a tertiary-level facility.
Methods Design: a planned prospective review of all referrals over a 14-day period. Data collection: review (LT, DP, SP) of case notes of patients referred to ITU with the following variables collected: age, sex, APACHE II scores, WHO functional status score, grade of referrer and source of referral. Data were collected on 37 patients: 22 accepted to ITU and 15 refused admission. Statistics: data were analyzed using GraphPad 6.05. Categorical variables were expressed as mean and standard error of mean. For unpaired variables, statistical significance is determined using unpaired *t* test. $P < 0.05$ is considered statistically significant.
Results The WHO functional status was the most significant variable affecting admission ($P < 0.001$). The APACHE score of patients admitted to ITU was significantly lower than refused patients ($P = 0.039$). Patient age did not affect admission status ($P = 0.15$). See Table 1.

Table 1 (abstract P522)

	Accepted	Refused	*P* value
Mean age	56.5 ± 4.4	65.3 ± 3.6	0.15
Sex	73% male	56% male	N/A
WHO	0.45 ± 0.2	2.21 ± 0.3	<0.001
APACHE	13.5 ± 1.6	18.8 ± 2.0	0.039

Conclusion This study was performed to assess decision-making for admission to the ITU in times of increased demand and limited availability. We want to validate our findings from this short pilot study in a larger prospective study. Multivariate regression analysis will be used to identify significant features that affect clinician decision-making in critical care admission.
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P523

Lean Six Sigma handoff process between operating room and pediatric ICU: improvement in patient safety, efficiency and effectiveness

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Introduction This Six Sigma project was initiated to evaluate and improve the transfer of care of patients from the OR to the ICU. Medical errors are responsible for billions of dollars in increased healthcare spending. Miscommunication among healthcare providers is a major contributor to these errors, with handoffs a particularly vulnerable period in the care process. At our institution, surgical patients with scheduled admissions to the ICU are first recovered in the postanesthesia care unit (PACU). With this process, multiple, unstructured, and individual handoffs occur in parallel between providers, which may lead to communication errors, differential information sharing, content variability, care delays, and inefficiency.
Methods A multidisciplinary QI project was initiated with input from the ICU, anesthesia and surgical services. A series of PDSA cycles were conducted, which began by defining the current process via direct observation and value stream mapping of orthopedic and neurosurgical patients. A new process was then introduced, including direct transfer of the patient to the ICU and a single, structured, bedside report between all care providers. A standardized handoff tool was implemented. We used process times, wait times and information content as process measures and handoff errors as outcome measures. A 10-point satisfaction score was also measured.
Results Following implementation of the new transfer process, the average wait time decreased by 58 minutes, process time decreased by 9 minutes, and lead time decreased by 66.5 minutes. The handoff error rate decreased by 1.3 errors/patient and first-time quality rate increased by 67%. Staff satisfaction improved from 48% to 73%. By elimination of the PACU stay, the costs involved in admission to the PACU were deferred.
Conclusion A single, multidisciplinary bedside handoff process between the OR and ICU leads to cost and time savings. By elimination of redundant, nonvalue-added processes, less opportunity for medical errors occurred, with substantial improvements in first-time quality. Such a process can be successfully attained while affecting staff satisfaction positively.

P524

Improved interprofessional communication, handover and ward rounds in critical care (ICARUS)

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Introduction There is growing evidence that optimising communication and patient assessment practices including ward rounds and handoffs can improve clinical, safety and operational outcomes, particularly in the critical care setting [1,2]. Here we describe the design and baseline phases of a 5-year project utilising improvement sciences to optimise the quality of interprofessional communication, handoffs and rounding in one of the largest critical care units in the UK.
Methods We obtained institutional ethical and research approvals. We used mixed methods including interviews of opinion leaders and a representative cross-section of staff, roundtables, a survey targeting the whole critical care team ($n = 546$) and a Delphi exercise to generate a baseline consensus for the need to improve and a set of novel quality improvement interventions and tools. We tested two of these in a pilot plan–do–study–act (PDSA) cycle.
Results Baseline consensus for the need and potential to improve was obtained (97.4% and 94.5%). Despite a large degree of heterogeneity of perceptions around current communication and rounding practices, it was possible to develop a set of interventions based on consensus that could be applied in this complex setting. These included a handoff bundle, an operational touch-base, a unit-level safety briefing, a unit-level safety check, a lean rounding bundle and board rounds. These core interventions were supported by several more detailed resources describing the evidence base around best handoff and rounding practices; and a feedback document that described all outputs and recommendations from the ICARUS project. A pilot PDSA cycle demonstrated a 55.3% and 76.3% improvement in key information transfer using a safety briefing and board round summary.
Conclusion Despite wide heterogeneity in baseline beliefs, opinions and perceptions around inter-professional communication, rounding and handoffs, we were able to develop a novel set of feasible quality improvement interventions, targeting these areas, that can be applied in a large complex critical care setting. Furthermore, they can be driven by improvement science methodology and tested for effectiveness using qualitative and quantitative measures. We now plan to use these interventions to deliver quality improvements in communication practices in parallel with the planning and implementation phases of a new critical care facility and electronic clinical information system.
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P525

Adverse events in patients in a Brazilian intensive care unit according to readmission

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Introduction Security policies for the patient are of interest to any health professional. The rates of adverse events in hospitals reach values ranging between 3.7 and 16.6%, being the highest range (40 to 70%) considered preventable or avoidable [1]. The objective of this study is to assess the prevalence and types of adverse effects in intensive care patients according to readmission.
Methods During 4 years the data from 2,582 patients admitted to the coronary ICU (CICU) were analyzed in the coronary care unit of the city of Presidente Prudente, Brazil. We analyzed the rate of readmissions, length of stay and the mainly detected adverse events. We considered significant P <0.05 two-tailed and confidence intervals at 95% (CI).
Results The readmission rate was 15% (n = 392), particularly among males (55% (n = 214)). A 14.3% adverse event rate was observed among the readmitted patients (9.5% among those who were not readmitted). The readmitted patients were older (median (md): 68.0 (95% CI: 65.7 to 67.3) vs. md: 71.0 (95% CI: 67.1 to 71.3); P <0.05) and remained hospitalized for a longer period of time (md: 5.0 (95% CI: 13.2 to 20.7) vs. md: 11.0 (95% CI: 17.0 to 33.2); P <0.05), but not necessarily in the CICU (P = 106).The most prevalent adverse events in readmitted patients were pressure ulcers (n = 16 (4.1%)), drug administration error (n = 13 (3.3%)) and enteral feeding tube (n = 10 (2.6%)). Meanwhile, among the nonreadmitted, phlebitis due to peripheral vein access and pressure ulcers (n = 42 (1.9%)), drug administration error (n = 41 (1.9%)) and enteral feeding tube (n = 31 (1.4%)). There was a tendency (P = 0.71) that readmitted patients were presented with higher prevalence of pressure ulcers (n = 16 (4.1%) vs. n = 42 (1.9%)).
Conclusion There is a higher prevalence of adverse events in readmitted patients with similarity in the type of adverse effects despite readmission.
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P526

Out-of-hours discharge from critical care: does it matter?

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Introduction The aim of this audit was to assess the clinical impact of out-of-hours (OOH) discharge from the adult critical care unit (ACCU) in a tertiary care hospital. Discharging patients from critical care OOH has been associated with both higher mortality and increased rate of readmissions [1,2]. As a result, national guidance stipulates that OOH discharges from critical care should be avoided [3].
Methods A retrospective snapshot analysis of patients was conducted at least 48 hours after discharge from the ACCU in October 2014. Patients discharged OOH (20:00 to 07:59) were compared with those discharged in hours (IH; 08:00 to 19:59). Analysis included: patient demographics, APACHE II score, handover procedure prior to discharge, follow-up by the receiving team, appropriate and timely drug prescribing, recognising and acting upon clinical deterioration and readmission rates.
Results A total of 161 patients were discharged from the ACCU in October 2014. Of these, 46% of the patients were discharged OOH. Forty-one (of 74) OOH and 19 (of 87) IH discharges were sampled for further analysis. The baseline demographics and APACHE II score were similar between both groups. The majority of discharges were delayed (>4 hours, 90% IH vs. 93% OOH). More patients had nursing handover completed if discharged IH (88% IH vs. 61% OOH) and doctors' summaries were less frequently completed OOH (83% OOH vs. 94.4% IH). A management plan for the ward was outlined in 94% of IH versus 65.% of OOH discharges. Seventy-eight per cent OOH versus 95% IH patients discharged were reviewed by a doctor within 24 hours. Twenty-nine per cent OOH versus 67% IH patients discharged were reviewed by a consultant within 24 hours. Following discharge a management plan was followed in 94% of IH patients versus 44% OOH, patients had drug charts correctly charted in 100% of IH cases versus 66% OOH and missed/delayed doses were documented in 11.1% of IH cases versus 61% OOH. There was no difference between the groups in incidence of clinical deterioration and recognition and follow-up of clinical deterioration. Two patients were readmitted within 48 hours from the OOH group.
Conclusion This audit compares with current evidence suggesting harm from OOH discharge despite most discharges being delayed. Discharging patients is a complex hospital process, but focus needs to be on discharging patients IH. Therefore, areas for improvement include targeting forward flow of patients throughout the hospital, completion of handover documents IH and publication of guidance for receiving teams.
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P527

Pre-ICU length of hospital stay is a predictor of hospital but not ICU mortality

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Introduction Prolonged hospital stay prior to admission to the ICU was previously shown to be independently associated with poorer outcome [1,2]. This is probably due to slow deterioration of physiological function in hospital and influenced by processes leading to critical care admission [2]. We investigated whether commonly measured severity scoring systems (Acute Physiology and Chronic Health Evaluation (APACHE) II, Intensive Care National Audit and Research Centre (ICNARC) and Sequential Organ Failure Assessment (SOFA) scores) are significantly different in patients admitted with prolonged pre-ICU hospital length of stay, and describe mortality and hospital length of stay.
Methods A retrospective analysis of prospectively collected data of all emergency admissions in the ICNARC database of a 44-bed adult critical care unit within a major trauma centre over a 2-year period. Demographic data, APACHE II score, SOFA score, ICNARC model score, mortality, and length of hospital stay prior to and after ICU admission were collected. Five groups of patients were defined as follows: those admitted to ICU within 1 week of hospitalization (group 1), within 8 to 14 days (group 2), within 15 to 21 days (group 3), within 22 to 28 days (group 4), and more than 28 days (group 5). Chi-squared and ANOVA tests were performed using the SOFA statistics package.
Results A total of 2,248 emergency admissions were analysed. The majority of patients were admitted within 1 week of hospital admission (n = 1,897). They were younger and had lower APACHE II scores (15 vs. 19; P <0.001). APACHE II scores were the same in all other groups (groups 2 to 5). Patients admitted to the ICU 3 weeks following hospital admission had significantly higher hospital mortality (up to 50%; P <0.001) and ICU length of stay (12 ± 15 vs. 8 ± 10 days; P <0.001). ICU mortality remained the same in all groups (20 to 28%). ICNARC and SOFA scores were equal between the groups. The post-ICU lengths of stay were significantly longer in groups 3 to 5. In-hospital CPR prior to admission to ICU was lower in patients from groups 4 and 5, probably signifying appropriate DNAR decisions made on the ward.
Conclusion Prolonged pre-ICU hospital admission is associated with higher hospital but not ICU mortality. Commonly measured scores do not reflect this higher mortality in patients admitted after prolonged stay in hospital. Further research into parameters that may reflect changes in physiological reserves may strengthen these scores for such patients.
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P528

Study of the costs of an ICU according to age groups relating to SAPS 3 gravity, stay and outcomes

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Introduction Hospital costs are a constant concern within health, especially in the ICU. Hospital admissions and average life expectancy have been growing gradually mainly in older and critical patients. This study is aimed to observe the direct costs of patients admitted to an ICU and their relation to the SAPS 3, length of stay in the ICU and final outcome.
Methods A retrospective observational study in which the direct costs were studied (materials, medicines, oxygen therapy and hospital fees) for 1,790 ICU patients from November 2013 to November 2014. The readmissions within 48 hours were excluded and also 10% of patients who had the highest and lowest costs. The remaining 1,401 patients were divided by age groups.
Results Of the patients studied, 54.6% were male. Average age was 57.8 years (18 to 105 years). The biggest ICU average cost was in the group of patients 81 to 90 years old (US$793.00), as well as longest ICU stay (9.25 days), highest SAPS 3 (53.96) and higher ICU and in-hospital mortality (14.29% and 19.25% respectively). This study shows that the direct cost of the ICU stay for older patients was higher than for younger patients. The difference was explained by the higher severity measured by SAPS 3 in the older age groups (Figure 1), and the required greater length of stay in the ICU (Figure 2). As might be expected, the mortality in the group of older patients was also significantly higher.
Conclusion This study showed that greater age is associated with higher severity measured by SAPS 3, higher direct costs, and higher mortality both in the ICU and in-hospital environment.

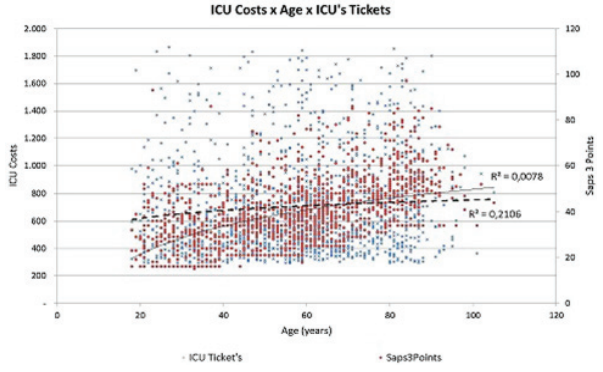


Figure 1 (abstract P528).

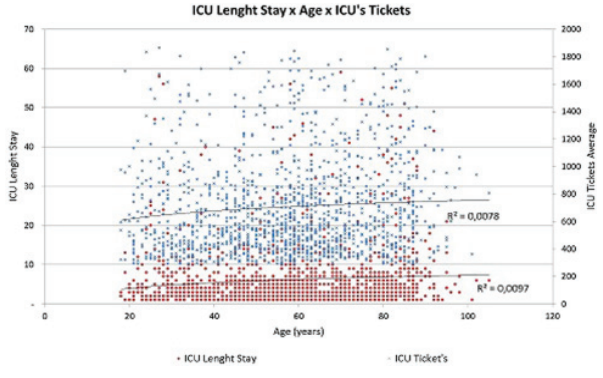


Figure 2 (abstract P528).

P530

Critical care in a maternity hospital: a retrospective observational study

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Introduction Pregnancy and labour usually progress uneventfully; however, serious complications can occur and develop rapidly, necessitating critical care admission and support. Successive confidential enquires have highlighted deficiencies in this area and suboptimal care leading to increased morbidity and mortality [1]. The National Maternity Hospital is the largest maternity hospital in the Republic of Ireland where a total of 8,954 babies were delivered in 2013. It is a stand-alone institution and onsite facilities include a two-bed dedicated anaesthesia lead high-dependency unit.
Methods A retrospective observational study was carried out from January 2011 to January 2014 especially looking at the following parameters: admitting diagnosis, demographics, length of stay and the number of admissions requiring transfer for tertiary-level care.
Results In total, 29,344 deliveries occurred. A total of 376 HDU admissions were recorded in this period, representing 1.28% of all admissions. The average age of patients admitted to the HDU was 34 years. The predominant reasons for admission were hypertensive disease of pregnancy (49.7%), haemorrhage (antepartum/postpartum) (36.4%), sepsis (4.2%) and other reasons (11.1%) including cardiac rhythm disturbances, neurological complications and pre-existing medical disease. In 2013 the average length of stay was 2 days. A total 6.1% of those admitted to HDU required transfer for tertiary-level ICU care in other centres during the study period, this represented 0.07% of all deliveries.
Conclusion There is significant demand within our institution for HDU care for our patients, with the number of admissions increasing in 2013. The main admitting diagnoses are hypertensive disease of pregnancy and haemorrhage with an increase in the number of patients being admitted for management of sepsis in 2013. This highlights the increasing awareness, recognition and management of this condition in pregnancy. The increased number of HDU admissions in 2013 could also be explained by the recent introduction of an early warning score for the deteriorating patient in our hospital but this would require further evaluation. The low number of transfers of patients to other tertiary centres underpins the importance of an anaesthesia lead service.

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P531

Post-traumatic stress symptoms in intensive care staff working in adult and paediatric settings

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Introduction The objectives of this survey were to establish the prevalence of symptoms of post-traumatic stress in mixed staff groups working in adult and paediatric intensive care settings and to examine the main themes in staff descriptions of the most traumatic event they had experienced at work.
Methods A total of 355 health professionals working on three adult and four paediatric units at two centres were asked to rate their current level of post-traumatic stress symptoms on the Trauma Screening Questionnaire (TSQ).
Results Paediatric/neonatal intensive care staff were more likely to score above the clinical cutoff point for post-traumatic stress symptoms on the TSQ in relation to an incident at work than adult intensive care staff in this sample (PICU n = 33/193 (17%) vs. AICU n = 13/162 (8%), P <0.001). For the 172 staff who provided a description of the most traumatic event they had experienced, the following themes were

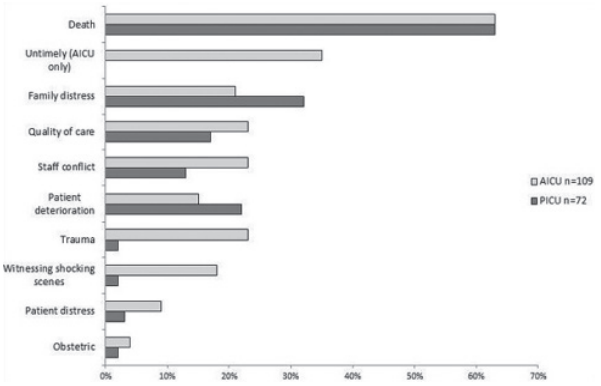


Figure 1 (abstract P531). Main themes of staff descriptions of traumatic events on ICU.

most commonly endorsed: patient death (and particularly untimely deaths on adult units); handling distressed families; and concerns about the quality of care and dealing with staff conflict (see Figure 1).
Conclusion A significant minority of staff reported clinically significant levels of post-traumatic stress related to their work. The facts that post-traumatic stress levels were higher on paediatric units despite their lower rates of mortality and that untimely deaths were frequently mentioned by adult unit staff suggest it may be that untimely deaths are particularly hard to deal with. More research is needed on the prevalence of distress in staff working in these settings.

P532

Distribution and mortality factors of cases with traumatic and nontraumatic brain damage treated in ICU

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Introduction Cases of traumatic and nontraumatic brain damage have high rates of morbidity and mortality. In this study of cases being treated in the ICU for a diagnosis of brain damage, it was aimed to evaluate the relationship between mortality and the distribution of reason for and resulting type of brain damage and to determine other factors affecting mortality.
Methods After local ethics committee approval, a total of 1,004 patients (2012, $n = 492$; 2013, $n = 454$; 2014, $n = 58$) treated in the ICU in a 2-year period were reviewed. This study included for evaluation 135 patients determined with traumatic or nontraumatic brain damage, with a more than 24-hour stay in the ICU. Reasons for brain damage were determined as brain damage associated with head trauma (Group HT), head trauma accompanying general body trauma (Group HT + GBT) and spontaneous haemorrhage (Group SH). The type of brain damage was defined from the radiological diagnosis (CT and/or MRI) as subarachnoid haemorrhage, intracranial haemorrhage (ICH), subdural haematoma (SDH), epidural haematoma (EDH), skull fracture, brain contusion or a combination of these (COM). Operations were evaluated as performed by the brain surgery department.
Results The patients comprised 73.3% males and 26.7% females with a mean age of 40.58 ± 24.14 years (range, 1 to 87 years), mean APACHE II score of 19.07 ± 10.19 (range, 2 to 41), mean GCS of 9.17 ± 4.42 (range, 3 to 15) and 68.1% of whom were discharged and 31.9% were exitus. When the causes of brain damage were evaluated according to the type, the most frequently seen in the HT and HT + GBT groups were COM (37.3%, 42.9%), followed by EDH (13.6%, 28.6%). In the SH group, the most common reason was ICH (43.9%) followed by SDH (24.4%). Directly proportionally, only an increase in APACHE II score increased the mortality risk 1.3-fold (logistic regression analyses, coefficient 0.658) but the duration of intubation and ICH ratio was statistically significantly high and GCS was low in the exitus cases, and rates of EDH were determined as high in discharged cases compared with exitus ($P < 0.01$). No statistical difference was determined in mortality in terms of age, gender, duration in ICU, surgical treatment or not, or reasons for brain damage ($P > 0.05$).
Conclusion There is considerable variation in causes of head injury. From this retrospective study it can be suggested that mortality of neurological/neurosurgical patients, regardless of management method, depends on APACHE II, arrival GCS, number of ventilator-days and type of brain damage.

P533

Association with amount of registration and outcome in pediatric severe trauma patients

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Introduction Unexpected trauma is a one of the most major causes of death for children in the world. However, pediatric severe trauma patients are rare and scattered. Although there is a strong association between patient's volume of trauma center volume and outcomes in adults, such a report is less in children. In this study, we aimed to clarify the relationship of the amount of registration and outcome in pediatric trauma patients.
Methods This retrospective study analyzed data of the Japan Trauma Data Bank from 2004 to 2012. We registered pediatric patients aged younger than 12 years with severe multiple or torso trauma (maximum Abbreviated Injury Scale score ≥3 or Injury Severity Score ≥9, and excluded patients with cardiopulmonary arrest on arrival, burn, isolated head or limb injury, lack of data). We divided the facilities into six groups according to every 10 patients registered and compared mortality between each group.
Results A total of 1,015 patients from 105 facilities were included in the study. Number of registrations: 0 to 10 patients: 673 patients/68 facilities, 11 to 20: 381/28, 21 to 30: 141/6, 31 to 40: 101/3, 41 to 50: 45/1, 51 to 60: 58/1. Victims of blunt trauma accounted for 98.1%. Median age was 7 (interquartile range: 5 to 10) years, median injury severity score (ISS) was 17 (10 to 26). Multivariate analysis adjusted for age, revised trauma score and ISS revealed that the amount of registration (every 10 patients) was independently associated with survival (odds ratio: 1.55, 95% confidence interval: 1.06 to 2.26, $P = 0.023$).
Conclusion There was a strong association between amount of registration and outcome.

P534

Mortality in a French military burn centre: a 12-year retrospective study analysing seasonal variations

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Introduction Factors associated with mortality in severely burned patients are well known. We aimed to assess the seasonal variations of the mortality of patients admitted to the main French military intensive care burn unit (ICBU) and to determine their relations to seasonal variations of severity or other factors (for example, staffing).
Methods We performed a retrospective study analysing the medical records of all patients admitted to the ICBU of Percy Military Hospital (France) between January 2000 and December 2011. Statistical analysis was performed with R version 3.1.2. We first conducted univariate analyses with simple logistic regression, then a simple periodic regression for seasonal variations (with and without harmonics for robustness), and finally a multivariate logistic regression with periodic terms in order to adjust seasonal variations for known severity factors.
Results A total of 1,913 patients were admitted for acute burn injury during the study period, with a male to female ratio of 2.34. Mean total body surface area burned (TBSA) was 23.2% (IQR: 10 to 30) and mean full thickness total body surface area burned (FTBSA) was 13.4% (IQR: 0 to 15). Inhalation injury was present in 441 (23.1%) cases, intoxication (CO, CN) was present in 88 (4.6%) cases, and associated traumatisms also

in 88 (4.6%) cases. The mortality rate was 10.9%. The following factors were associated with mortality in univariate logistic regression: age, body mass index, past medical history, TBSA, FTBSA, intoxication (CO, CN), inhalation injury, flame burns, self-inflicted burns (all P <0.0001), sex (P <0.001), and admission date (P <0.01). Simple periodic regression showed a biannual seasonal effect on mortality, documented with a 1-year periodic (P <0.01) and a 6-month periodic (P = 0.01) dependency. Multivariate analysis with or without periodic terms identified age, past medical history, TBSA, FTBSA, inhalation, intoxication and admission date as the only factors independently associated with mortality.
Conclusion Predictive factors for mortality in our ICBU are in line with the literature. The documented seasonal variations in mortality are fully explained by variations in these severity factors. Complementary analyses are under way to further study a nonlinear age effect.

P535

ICU outcomes in patients suffering granulomatosis with polyangitis

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Introduction This study aims to describe both the clinical course and prognostic factors of patients suffering granulomatosis with polyangitis (Wegener granulomatosis) (GP) who were admitted to the Salvador Zubirán National Medical Sciences and Nutrition ICU.
Methods Twenty-two patients suffering GP admitted to the ICU, between January 2002 and December 2012, were included. The Acute Physiology and Chronic Health Evaluation (APACHE) II prognostic score scale was used in order to assess the severity of illness on the first ICU day. The Sequential Organ Failure Assessment (SOFA) score was used to measure organ dysfunction, and the Birmingham vasculitis activity score for Wegener granulomatosis (BVAS/WG) was used to assess vasculitis activity. The outcome measurements taken into account were ICU mortality and ICU length of stay.
Results One patient was admitted twice during this period. The sample comprised 11 males and 11 females (50%, respectively). Featuring an average age of 52 years, 78% of them were admitted to the ICU because of respiratory failure, 50% were due to diffuse alveoli hemorrhage, 36% due to sepsis, 4% hypovolemic shock and finally 4% because of tuberculosis. According to the BVAS/WG, 20 patients corresponded to severe disease, one to limited diseases and one to persistent disease. The average ICU length of stay was 20.6 days and as inpatients 43 days. While comparing the SOFA score between alive and deceased patients there was a 0.5-point difference (P = 0.077), 63% of the alive patients were diagnosed while they were in the ICU. Plasmapheresis was found to be a protector factor (P <0.05).
Conclusion The BVAS/WG score was significantly different between alive and deceased patients. Plasmapheresis was found to be a survival predictor. This study has shown that both SOFA and APACHE II scores have no prognostic value in these patients.

P536

Liver dysfunction is associated with long-term mortality in septic shock

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Introduction Knowledge of the impact of liver dysfunction on mortality during septic shock is limited. However, the liver appears to play a key role during septic illness. To better explore this issue, we investigated the data collected during the Prospective Recombinant Human Activated Protein C Worldwide Evaluation in Severe Sepsis and Septic Shock (PROWESS-SHOCK) trial in which a cohort of 1,697 septic shock patients were constituted [1]. The study aimed to assess the relationship of liver dysfunction at the onset and during the course of septic shock on short-term and long-term mortality.
Methods All of the patients enrolled in the PROWESS-SHOCK were included. Liver dysfunction at baseline was defined by a liver Sequential Organ Function Assessment (SOFA) score >0. The onset of a liver dysfunction post baseline was defined as any post-baseline increase of the hepatic SOFA score from 0. The worsening of liver dysfunction post baseline was defined as any increase of the hepatic SOFA score from the baseline assessment. The post-baseline period studied extended from study drug infusion to day 28. The main outcome was the mortality at day 180, and the secondary outcomes were the mortality at day 28 and at day 90. Cox proportional hazard models were used to estimate the hazard ratio of death.
Results Baseline liver function was assessed in 1,565 patients. Of those, 522 (33%) exhibited liver dysfunction at baseline. No relationship was found with mortality according to baseline liver dysfunction status at day 28 (HR, 0.847 (95% CI, 0.647 to 1.109); P = 0.2267), day 90 (HR, 0.883 (95% CI, 0.701 to 1.112); P = 0.2892) and day 180 (HR, 0.885 (95% CI, 0.710 to 1.103); P = 0.2761). A total of 403 (26%) patients developed a new liver dysfunction (257/1,043, 25%) or worsened liver dysfunction (146/522, 28%) in the 28-day post-baseline period. The overall median time to develop or to worsen liver dysfunction was 2 (1 to 4) days. Significant relationships between the new onset or the worsening of liver dysfunction post baseline and mortality at day 28 (HR, 1.67 (95% CI, 1.26 to 2.21); P = 0.0004), day 90 (HR, 1.65 (95% CI, 1.30 to 2.09); P <0.0001) and day 180 (HR, 1.57 (95% CI, 1.26 to 1.97); P <0.0001) were found.
Conclusion The new onset or the worsening of liver dysfunction during the course of septic shock impacts strongly on long-term mortality. Septic patients with liver dysfunction need long-term follow-up. Future research should focus on developing specific septic liver therapeutics and new tools for earlier detection of septic liver dysfunction.
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P537

Predictors of 30-day mortality in cancer patients with septic shock

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Introduction In cancer patients, sepsis is the main cause of admission to the ICU and is associated with elevated mortality rates and healthcare costs. In this population, specific factors such as poor functional status and immunosuppression secondary to malignancy and/or antineoplastic treatment contribute to decreased survival. The aim of this study is to identify predictors of mortality in cancer patients admitted to the ICU with septic shock.
Methods This is a retrospective study that analyzed predictors of 30-day mortality in 269 patients admitted to the ICU of the Institute of Cancer of State of São Paulo, Brazil, from February 2012 to November 2014.
Results From 1,250 patients admitted to the ICU, 269 patients had the admission diagnosis of septic shock and were analyzed. The mean age was 62 ± 14 years and 152 patients (56.5%) were male. Most patients had solid cancer (93.6%), and 87 patients (34.5%) had gastrointestinal neoplasm. Upon admission, the median SOFA score was 4 (IQR: 2 to 7), median SAPS 3 score was 55 (IQR: 48 to 68) and median lactate level was 1.88 mmol/l (IQR: 1.22 to 3.21). After 48 hours of ICU admission, acute kidney injury (AKI) was diagnosed according to AKIN classification as follows: 202 patients (75.1%) had grade 0, 49 (18.2%) grade 1, seven (2.6%) grade 2 and 11 (4.1%) had grade 3. The 30-day mortality rate was 24.9%. In the univariate analysis, associated variables with 30-day mortality were age, urea and creatinine levels at admission, SOFA score at admission, SAPS 3 score and 48-hour AKI. In multivariate analysis, the predictive factors for 30-day mortality were SOFA score at admission (OR = 1.12; 95% CI: 1.04 to 1.21, P = 0.002) and 48-hour AKI defined as AKIN grades 1, 2 and 3 (OR = 2.69; 95% CI: 1.45 to 4.97, P = 0.002).
Conclusion In cancer patients with septic shock, SOFA score at admission and acute kidney injury at 48 hours of admission were predictors of 30-day mortality. These findings reinforce the needing of early strategies of diagnosis and therapy in this subset of patients.

P538

Is admission of hematologic malignancies in the ICU justified?

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Introduction The admission of malignant hematology patients to the ICU is combined with poor prognosis [1]. A young population on one side and serious prognosis on the other are the main characteristics. Do we help? We are analyzing continuously clinical characteristics, treatment, and outcomes of critically ill patients with hematologic malignancies admitted to the medical ICU to identify predictors of adverse outcome [2].
Methods Demographic characteristics, hematologic diagnosis, reasons for ICU admission, transplant status, the presence of neutropenia, and APACHE II and SOFA scores were analyzed. Predictors of ICU mortality were evaluated using univariate analysis.
Results There was a total of 194 patients (103 male), APACHE II score by admission was 27 ± 8, SOFA 9 ± 3. Acute leukemia (L) in 81 patients (41.8%), chronic L in 19 patients (9.8%), lymphoma in 58 patients (29.9%), and multiple myeloma in 28 patients (14.4%) were the etiology. Respiratory insufficiency, hemodynamic instability, AKI and CNS disturbances were responsible for the admission of 169 patients (87.1%) from the hematology ward to the ICU. In total, 127 patients (59.7%) were mechanically ventilated; 93 required invasive mechanical ventilation (MV). Non-invasive ventilation started in 34 patients and was successful in 14 (6.5%). The ICU mortality rate was 104 patients (53.6%), and the mortality of MV patients was 98 (77.2%). Need for vasopressors at admission, MV, neutropenia, and APACHE II and SOFA scores were identified as independent predictors of fatal outcome. Overall mortality of admitted patients was 53.6% (104 patients), and in ventilated patients was 77.2% (98 patients).
Conclusion The ICU mortality of critically ill patients with HM is high, particularly in the group on MV. Different factors were independent predictors of mortality, but 46.4% of admitted patients survived because of adequate support possibilities and were transferred back to hematology ward. The ICU admission with organ support is according results important for life saving in this extremely high-risk patient group.

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P539

Outcomes of patients with hematologic malignancies admitted to the ICU

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Introduction In recent decades, therapeutic advances resulted in increased survival of patients with hematologic malignancies. These patients are increasingly admitted to the ICU due to infections, treatment toxicity and decompensation of chronic diseases. The aim of this study is to evaluate ICU, hospital and 6-month mortality in patients with hematological malignancies admitted to the ICU and to identify predictors of ICU mortality.
Methods We performed a retrospective study of 277 consecutive patients with hematological malignancies admitted to the ICU of the Institute of Cancer of State of São Paulo, Brazil, from January 2010 to December 2013. Patient clinical and laboratory characteristics, evaluation of organ dysfunctions and need for hemodialysis, mechanical ventilation and vasoactive agents in the ICU were collected. The primary outcome was ICU mortality. Data were analyzed with univariate and multivariate logistic regression.
Results The median age of the population was 57 years and 144 patients (52%) were male. Upon admission, 15 patients (5.4%) had disease remission and 31 (11.2%) had newly diagnosed disease. The ICU mortality rate was 26%, hospital mortality was 35.7% and 6-month mortality was 55.2%. The median number of organ dysfunction was 3 (IQR 2 to 4) and respiratory failure was the leading dysfunction, being present in 209 patients (75.5%). During the ICU stay, 21 patients needed hemodialysis (8%), 69 (25%) needed mechanical ventilation, 162 (58%) used vasoactive agents and 22 (8%) had a decision for limitation of medical treatment. On univariate analysis, risk factors for hospital mortality were acute myeloid leukemia, hospital stay prior to ICU admission >4 days, number of organ dysfunction ≥2, colonization and infection by a multidrug-resistant (MDR) agent, use of mechanical ventilation, use of vasoactive agents and renal replacement therapy. Multivariate analysis revealed that renal replacement therapy (OR = 6.35 (95% CI: 1.5 to 25.92), $P = 0.010$), SOFA score (OR = 1.69 (95% CI: 1.38 to 2.06), $P < 0.001$), RDW (OR = 1.27 (95% CI: 1.11 to 1.46), $P = 0.001$), lactate (OR = 1.04 (95% CI: 1.02 to 1.06), $P < 0.001$), colonization of MDR agent (OR = 10.73 (95% CI: 2.13 to 53.96), $P = 0.004$) and hospital stay prior to ICU admission >4 days (OR = 4.72 (95% CI: 1.8 to 12.3), $P = 0.002$) were predictive factors of ICU mortality.
Conclusion Patients from our institution have survival rates comparable with data from the literature. Our study suggests that mortality is associated with late ICU admission and colonization of MDR bacteria.

P540

Factors associated with short-term and long-term mortality in solid cancer patients admitted to the ICU

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Introduction Despite multiple reports demonstrating an improvement in outcomes of critically ill cancer patients admitted to ICUs over the last two decades [1], there is concern that admission policies for patients with cancer are overly restrictive [2]. The purpose of this study was to identify factors associated with mortality in the 180 days following unplanned ICU admission in patients with nonhaematological malignancy.
Methods We carried out a retrospective analysis of all patients with solid tumours admitted to the Guy's Critical Care Unit (13-bed level 3 ICU) as an emergency between August 2008 and July 2012. Data were collected regarding patient demographics, type of cancer, reason for referral and organ support required during the ICU stay.
Results During the 4-year study period there were 356 unplanned admissions of patients with solid cancer (8.3% of all admissions). Three hundred individual patients were admitted and 180-day survival data were available for 293 of these. Mean age at first admission was 65.2 years, 115 (38.3%) were female. The most frequently present malignancies were lung (42.7%), head and neck (17.3%) and renal (6.7%). ICU, hospital and 180-day mortality were 19.1%, 31.0% and 52.2% respectively. Those factors found to be independently associated (in multivariate analysis) with increased risk of 180-day mortality include: metastases (OR = 4.0, 95% CI = 2.1 to 7.6); sepsis on admission (OR = 2.2, 95% CI = 1.2 to 4.1); APACHE II score on admission (OR = 1.06, 95% CI = 1.004 to 1.12); need for inotropes/vasopressors during admission (OR = 2.3, 95% CI = 1.05 to 4.8); and need for renal replacement therapy during admission (OR = 4.65, 1.7 to 12.8).
Conclusion In our study, ICU and hospital mortality were lower than the pooled mortalities seen in a recent large systematic review [3] – despite our study excluding planned postoperative admissions (who are known to have better outcomes). The 180-day mortality was significantly lower than in a previous study at our own institution [4]. Our study looked at a number of factors that might reasonably be expected to be associated with short-term and long-term outcomes and identified several that were independent predictors of death by 180 days.

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P541

Characteristics and outcomes of lung cancer patients requiring ventilatory support: results from a multinational study

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Introduction The aim was to evaluate clinical characteristics and outcomes of patients with lung cancer requiring ventilatory support.
Methods Secondary analysis of a prospective multicenter study including patients requiring either invasive (IMV) or non-invasive (NIV) mechanical ventilation for >24 hours admitted to 22 ICUs in six countries from Europe and South America during 2011. We used shared frailty models to identify factors associated with 6-month survival.
Results Out of 449 patients admitted to the ICUs, 239 (small-cell (SCLC) = 34; non-SCLC = 205) required ventilatory support (NIV = 104; IMV = 135). Out of NIV patients, 31 (30%) were subsequently intubated for IMV. Main reasons for ventilatory support were sepsis (n = 119; among them, 102 patients had pneumonia), airway involvement by tumor (n = 79), ARDS (n = 47) and coma (n = 18). Mean SAPS II score was 54 ± 20 and median SOFA score was 7 (4 to 12) points. Hospital and 6-month mortality rates were 55% and 67%; 94 (39%) patients received treatment limitations in the ICU. Mortality according to ventilatory strategy was 56% for NIV only, 77% for NIV followed by IMV, and 70% for IMV only. In the multilevel model, adjusting for the hospital size, presence of step-down units, type of admission and treatment limitation, performance status (PS) 3 to 4 (HR = 2.25 (95% CI, 1.52 to 3.34)), metastasis (HR = 1.66 (1.18 to 2.33)) and the ventilatory strategy compared with NIV only (HR = 1.73 (1.02 to 2.92), for NIV followed by IMV; HR = 2.25 (1.51 to 3.35), for IMV only) were associated with increased mortality. Conversely, patients with sepsis had higher survival (HR = 0.67 (0.46 to 0.96)).
Conclusion In a multinational study, 6-month survival in lung cancer patients requiring ventilatory support is better than perceived *a priori*. Palliative care should be preferred in patients with poor PS.
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P542

Admission to intensive care can be reliably predicted using only clinical judgment

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Introduction Not all patients in need of critical care arrive in clinical distress and some deteriorate after arrival. Identifying these patients early in their clinical course could potentially improve outcome. The present study was performed with the aim of assessing whether nursing and physician staff were able to identify patients in need of critical care using only clinical judgment and to compare this with the National Early Warning Score (NEWS).
Methods This was a prospective cohort study of all adult patients with a first-time admission to a medical admission unit at a 450-bed regional teaching hospital over a 3-month period in 2010. All subspecialties of internal medicine are present as well as a level 2 ICU. Upon first contact with the patient after arrival, nursing staff and physicians were asked to report their estimation of the probability of ICU admission (0 to 100%). Survival status was extracted from the Danish Civil Registry. All administrative details (including transfers to other hospitals, wards and ICUs) were extracted from the National Patient Registry, both ensuring complete follow-up. The discriminatory power (ability to identify patients at increased risk) was estimated using area under the receiver-operating characteristics curve. Calibration (accuracy) was assessed using Hosmer–Lemeshow goodness of fit test. Data will be reported as median (range) or proportions (95% confidence interval).
Results A total of 2,769 patients were included, median age 65 (18 to 100) years and 52% female. Thirty-day mortality was 4.5% and 2.2% were admitted to ICU. Median time to ICU admission was 1 (0 to 70) day. Nursing staff assessed 65% and physicians 26% of admissions. NEWS could be calculated for 85%. Nursing staff had a discriminatory power of 0.865 (0.786 to 0.944) with little variation with experience. Calibration was acceptable, except for the least experienced nurses (<5 years). Physicians had a discriminatory power of 0.789 (0.641 to 0.937), with little variation with experience. Calibration was very good, regardless of experience. NEWS had a discriminatory power of 0.809 (0.727 to 0.891) and poor calibration. There was no significant difference in discriminatory power between the three assessments.
Conclusion Both nursing staff and physicians were as good as NEWS at identifying patients at increased risk of ICU admission after admission to a medical admission unit. However, both nursing staff and physicians had better calibration (accuracy) than NEWS.

P543

Clinical characteristics in surviving and nonsurviving older patients admitted to the ICU

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Introduction In recent years the proportion of older people admitted to the ICU has increased. A variety of clinical and physiological factors are associated with outcome in these patients. The aim of this study is to determine the clinical characteristics associated with survival of ICU mechanically ventilated older patients.
Methods We retrospectively studied 74 patients, aged >65 years, admitted to the ICU who underwent mechanical ventilation. Standard demographic, clinical, and physiologic data were recorded. We examined the significant differences in clinical characteristics between survivors and nonsurvivors using the Student t and chi-square tests.
Results The mean age of patients studied (43 men and 31 women) was 79 ± 6.4 years. The type of admission was surgical 18%, trauma 26% and medical 57%. The ICU mortality of these patients was 57% and it was not associated with gender and cause of admission to ICU. Patients who survived had lower Charlson Comorbidity Index (P <0.05) and shorter duration of mechanical ventilation (P <0.01). The episodes of ventilation-associated pneumonia, sepsis and renal failure were less frequently in survivors (P <0.05). Also, in addition serum iron and cholesterol levels were significantly lower in nonsurvivors (P <0.01).
Conclusion The mortality of ICU older patients is high. VAP, sepsis and renal failure are frequent complications in nonsurvivors. Pre-existing comorbidities considerably affect mortality.
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P544

Frailty predicts increased resource use and postoperative care requirements after revision hip surgery

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Introduction There is increasing demand for revision hip surgery in older patients with poor frailty. Our previously submitted work demonstrated that frailty predicts the need for medical review [1]. We reviewed patients for a further 16 months to see whether frailty impacts on care [2]. This is the largest reported study reviewing frailty and the need for organ supports and outcomes in complex orthopaedic surgery.
Methods A retrospective note review of all patients from January 2012 to April 2014 undergoing revision hip surgery. Data collected included frailty, comorbidities, operative blood loss, anaesthetic technique and level of organ supports and patient location at 30 days.

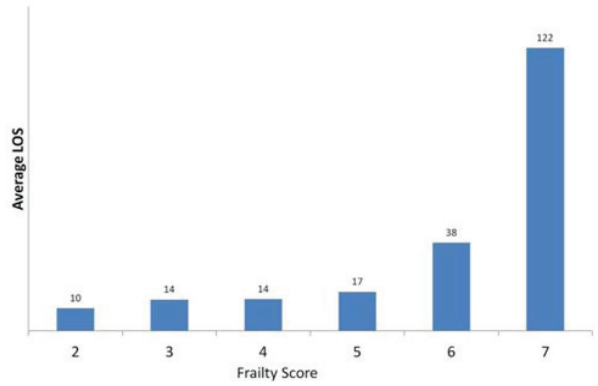


Figure 1 (abstract P544). Frailty versus length of stay.

Results A total of 389 patients with a mean age of 68.7 years were identified. Frail patients were significantly more likely to need vasopressors postoperatively (P = 0.012). Each increase in frailty score was associated with 0.16 increase in length of stay on the HDU (P = 0.025). Analysis of patient location at 30 days shows that frail patients stay in hospital longer (P = 0.00). Frail patients also bleed more intraoperatively (P = 0.00 with a coefficient value of 239; that is, for every point increase in frailty, average blood loss increases by 239 ml). For each increase by unit of blood transfused, the length of stay increased by 5.3 days (P = 0.000). The use of epidural is not associated with increased need for postoperative vasopressors (P = 0.598). See Figure 1.
Conclusion Frailty is associated with increased intraoperative resource use and postoperative care requirements independent of choice of anaesthetic technique. This type of surgery should be subject to health economic analysis as demand amongst the frailer surgical population increases.
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P545

Predicting outcomes in critically ill patients in a resource-poor setting: the Rwanda Mortality Probability Model

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Introduction ICU mortality prediction models provide robust tools for research and benchmarking in the developed world, but an ICU mortality prediction model has not been validated in a resource-poor setting. We sought to validate the Mortality Probability Admission Model, version III (MPMo-III) in two public ICUs in Rwanda and to develop a simplified Rwanda Mortality Probability Model (R-MPM) for use in developing countries.
Methods We prospectively collected data on 339 adult patients admitted to two ICUs in Rwanda between August 2013 and July 2014. We described demographic and presenting characteristics and outcomes. We assessed the discrimination and calibration of the MPMo-III model. Using stepwise selection, we then developed a new logistic model for mortality prediction, the R-MPM.
Results Patient median age was 34 (IQR 26 to 49) years; 48.7% were male. Mortality was 50.3%. The variables most predictive of mortality in univariate analyses were: age, sepsis within 24 hours of ICU admission, hypotension or shock at ICU admission, Glasgow Coma Scale score at ICU admission, and heart rate (beats per minute) at ICU admission. Using these five variables, the R-MPM predicted mortality with area under the curve of 0.829 and Hosmer–Lemeshow chi-square statistic of 8.881. The MPMo-III predicted mortality with area under the curve of 0.720 and Hosmer–Lemeshow chi-square statistic of 16.391, indicating that the predictive risk scores of the MPMo-III were not well calibrated to the Rwandan data.
Conclusion The MPMo-III had modest risk prediction capacity in a population of Rwandan ICU patients. The R-MPM is an alternative severity score with fewer and more accessible variables that provides better predictive power. This model needs to be validated in other ICUs.

P546

Emergency laparotomy clinical outcome according to patient characteristics, level of postoperative care and time of surgery

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Introduction Emergency laparotomies have poor outcomes with variable postoperative critical care provision [1-3]. All patients requiring an emergency laparotomy with an estimated risk of death of >10% should go to critical care. Time of surgery should not affect standard of care [3,4]. In advance of the National Emergency Laparotomy Audit (NELA) results [2], our objective was to see whether the level of postoperative care and time of surgery affect outcome.
Methods Retrospective data were collected across the Imperial NHS trust for all emergency laparotomies over 3 months in 2014: length of stay in days (LOS); mortality; age; ASA; surgery time and postoperative care level, that is ward (L1), high dependency (L2), or ICU (L3). Statistical tests: Mann–Whitney, Pearson correlation (PCC) and multilinear regression analysis.
Results Seventy-one patients underwent surgery. Overall mortality was 13% and 70% of patients went to a L2/3 bed. More ASA 1/2 patients went to L1 and all ASA 4/5 went to L2/3. Median (IQR) for age was 61 (44 to 67) for L1, 65 (48 to 73) for L2/3 (P = 0.11), LOS was 10 (7 to 16) for L1, 19 (12 to 57) for L2/3 (P = 0.002), and mortality (%) was 0 for L1 and 18 for L2/3. For surgery between 08:00 and 17:59, 14 went to L1, 28 to L2/3. Mortality was 5% and LOS 15 (9 to 24). Between 18:00 and 21:59, two went to L1, 10 to L2/3. Mortality was 17% and LOS 22 (8 to 34). Between 22:00 and 07:59, five went to L1, 12 to L2/3. Mortality was 29% and LOS 15 (9 to 36). ASA strongly predicted mortality (P = 0.006, PCC 0.32). There was a negative correlation between postoperative destination and mortality with all deaths happening in those who went to L2/3 (P = 0.038 and PCC –0.25); however, sicker patients may have gone here. There was a strong correlation between mortality and time of surgery, night surgery being a strong predictor of mortality (PCC 0.31, P = 0.008). LOS can be predicted by a combination of ASA, age and care level (P = 0.027); the postoperative care regression coefficient was negative (–18.04, SE 10.41) with prolonged LOS in patients admitted to L2/3, which could also be explained by illness severity.
Conclusion Trust mortality is similar to that in the Emergency Laparotomy Network audit [1]. Higher ASA patients are appropriately going to L2/3 care. Baseline health status and time of surgery are the strongest predictors of mortality in emergency laparotomy patients.
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P547

Developing a laboratory-based score to predict mortality in patients admitted to the ICU

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Introduction Scoring systems can be used to predict mortality in patients admitted to the ICU. They are produced using variables that are associated with an increased risk of mortality such as patient

demographics, physiological measurements and coexisting conditions and can be used to evaluate ICU performance, to stratify patients in clinical trials and to assist in-hospital and healthcare decisions such as resource allocation. The aim of the project was to determine whether a general score derived from routine laboratory parameters could be used to predict mortality rates in patients admitted to the ICU in the UK.

Methods *P* values were calculated using the *t* test, Mann–Whitney U test and chi-squared test, depending on distribution of data, in order to determine which variables were significantly different in the survivors and nonsurvivors of critical illness. Significant variables were categorised into subgroups according to medically relevant landmarks and univariately analysed by assessing the correlation with mortality. Forward logistic regression models were used to choose the parameters to include in our score. ROC curves illustrated the sensitivity and specificity of selected variables via their AUC.

Results Age, platelets, ALT and APACHE II were selected to be included in the new laboratory-based score. The AUC for the score was 0.714, which was higher than each of the individual laboratory parameters. The AUC was increased further to 0.781 by including all 14 variables (age, lactate, FiO_2, urea, creatinine, ALT, APACHE II, platelet, bicarbonate, haemoglobin, pH, ionised Ca, carboxyhaemoglobin and albumin), although this improvement was not considered significant as the confidence intervals of the two scores (4 and 14 variables) overlapped.

Conclusion A laboratory-based score was successfully established in ICU patients, revealing an AUC of 0.714 which is comparable with established scores in a similar population. The compilation of the variables to produce a laboratory-based score showed greater prognostic power than individual variables. Model developers require an AUC of >0.7 to be termed useful; however, in order to be used in a clinical setting the AUC must be at least 0.75. Further research including internal and external validation studies must be performed to optimise the model before clinical implementation.

P548

Patient preferences for outcomes in critical care trials (OPTICS): preliminary results

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Introduction Although patient-centered outcomes are important to inform therapeutic choices for critically ill patients, patient preferences for outcomes in critical care studies are unknown. It is also unknown whether outcome preferences differ between researchers, decision-makers and those who have never been critically ill (citizens). The aim of the OPTICS Program is to investigate these preferences. Herein we report the preliminary results for outcomes preferences in citizens.

Methods We recruited and surveyed lay public members without a history of critical illness as to their preferences for outcomes in critical care trials. After an in-person educational session, citizens were asked to rank 11 potential critical care trial outcomes in order of personal preference. Each outcome was also rated for importance on a 7-point Likert scale. Participants were then asked to indicate their agreement with potential tradeoffs between potential outcomes.

Results The in-person session was attended by 31 citizens whose had a mean age (SD) of 71.6 (5.9) years and 1.5 (1.4) chronic health conditions; 25 (81%) had partially or fully completed post-secondary school education. Of the 11 potential outcomes, the three outcomes ranked of highest importance were: permanent brain dysfunction, quality of life, and requirement for long-term institutional care. The three outcomes ranked of least importance were: duration of hospitalization, death after a prolonged illness, and occurrence of delirium. When rated on a 7-point Likert scale the results were similar. Of the participants, 24/27 (89%) indicated that they would be willing to receive a therapy which was associated with a higher mortality rate but resulted in an improved quality of life in survivors. Conversely, 16/27 (59%) indicated that they would not be willing to receive a therapy which increased the chances of survival but was associated with a reduced quality of life in the survivors.

Conclusion The citizens surveyed valued outcomes associated with quality of life and intact neurological function. Mortality and other indices of duration of critical illness were valued less. These preferences need to be confirmed in larger groups with greater diversity. Future research also needs to further understand these outcome preferences in survivors of critical illness, clinicians, decision-makers, and researchers. Understanding the outcome preferences of pertinent stakeholders and whether these preferences are congruent is imperative to inform the design of future critical care trials.

P549

Disturbed circadian rhythm in ICU patients as indicated by melatonin levels: a prospective pilot study

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Introduction The aim of this prospective pilot study was to test how melatonin levels follow the circadian cycle in ICU patients. There is strong evidence that changes of circadian rhythm are reflected in melatonin levels with peak levels at dawn and low levels during daytime [1]. The ICU stay is accompanied by disturbed circadian rhythm [2], which could potentially be the result of artificial lighting conditions.

Methods Melatonin levels were determined in eight medical ICU patients on mechanical ventilation, without brain injury or infection. Arterial blood samples were taken on the day of admission at 18:00 (TE0) and 03:00 in the morning (TM0), then at the same time points 48 hours later (TE1, TM1). Blood samples were centrifuged at 3,000 rpm for 8 minutes, and then serum samples were stored at –80°C. Measurements were performed using a US-CEA908Ge melatonin ELISA kit. For statistical analysis, a binary (yes/no) variable was created from the pairs for each day, assigning 'Yes' if the TE values were greater than TM (melatonin peak reversion). The proportion of reversals and their 95% confidence intervals were estimated using a GEE model for repeated binary data, assuming a binomial distribution and log link, and accounting for subject as a repetition factor. All calculations were done in SAS 9.4.

Results Melatonin levels were not normally distributed and were ranging between 9.2 and 23.7 pg/ml at T0 and 11.3 and 17.9 pg/ml at T1. The median differences of the morning and evening serum melatonin levels were: TM0 – TE0 = –2.8 (–3.8 – (–0.2)); TM1 – TE1 = –1.2 (–2.5 – (–0.4)) presented as median (IQR). The proportion of subjects with peak reversals was 92.9% (80.8 to 100.0%).

Conclusion Our preliminary data suggest that circadian rhythm disturbances may occur in critically ill patients within 48 hours after admission, and can be detected by inversion of melatonin peaks. Despite the limitations of this study, it may justify the need for larger observational and randomized trials on the effect of light on melatonin levels and on outcomes in ICU patients.

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P550

Trait anxiety mediates stress-related psychopathology after cardiac surgery and ICU stay

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Introduction ICU survivors are at risk for post-traumatic stress disorder (PTSD) and depression. The development of psychopathology depends partially on stable personality factors such as trait anxiety.

Among ICU patients a high level of trait anxiety is relatively common and associated with intrusions, a symptom of PTSD. Independently, childhood trauma and stress exposure throughout life have been associated with depression. In cardiac surgery patients admitted to the ICU postoperatively, the effect of trait anxiety on the relationship between cumulative life stress and stress-related psychopathology remains unknown. Therefore we aimed to assess the mediating or moderating role of trait anxiety in this at-risk patient population.
Methods In this multicenter follow-up study of the Dexamethasone for Cardiac Surgery (DECS) trial, validated self-report questionnaires were sent 1.5 to 4 years after cardiac surgery and ICU treatment to assess symptoms of PTSD and depression, in relation to cumulative life stress (that is, childhood trauma, major stressful life events) and trait anxiety as determinants of psychopathology. Data were available for 1,125 out of 1,244 (90.4%) eligible participants. Mediating and moderating analyses were performed with multivariable linear regression to assess the effect of trait anxiety. Subgroup analyses were performed for both sexes.
Results Trait anxiety partially mediates the relationship between cumulative life stress and PTSD (β-value reduction from 0.325 to 0.068; $P = 0.000$ to $P = 0.003$) and fully mediates the association between cumulative life stress and depression (β-value reduction from 0.282 to 0.015; $P = 0.000$ to $P = 0.507$). Trait anxiety was not a moderating factor between cumulative life stress and psychopathology. Full mediation of trait anxiety was found in female patients ($n = 247$), whereas only partial mediation was seen in male patients ($n = 878$) with regard to PTSD symptoms. As for depression, full mediation was present in both female and male patients.
Conclusion In cardiac ICU patients, trait anxiety mediates the influence of cumulative life stress on the occurrence of PTSD and depression symptoms. Further prospective research is necessary to establish these factors as reliable measures for the early identification of ICU patients at risk for stress-related psychopathology.

P551

Sleep monitoring in ICU patients

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Introduction Sleep disruption and deprivation is a continuing problem in the ICU. Strategies to improve sleep are confounded by difficulties in monitoring and measuring sleep in the ICU; traditional polysomnography cannot be utilized. Practical, non-intrusive diagnostic monitoring of sleep is required. The aims were to test two new ambulatory sleep diagnostic devices to monitor sleep in the ICU, compare sleep data generated by the different devices, and characterize sleep in the ICU.
Methods The devices were: Watch PAT 200 (Itamar), simple wristwatch style, employing peripheral arterial tone and actigraphy to evaluate sleep time and sleep stage by an automatic algorithm (PAT device); and ALICE PDx (Respironics Philips), miniature polysomnographic device utilizing EEG and EMG recordings, requiring post-study sleep technician scoring (PSG device). Nineteen ICU patients provided informed consent (mean age 37 years, two female). Diagnosis of most patients was trauma. Device technical problems terminated one ALICE PDx study and three Watch PAT study; one patient revoked consent. Therefore, 14 patients were recorded successfully in a private room in the ICU, while simultaneously wearing both devices, from 20:00 to 06:00. No patient received sedation. Subjective sleep quality was estimated by the visual analog scale.
Results Both devices calculated total sleep time (TST), but the results were significantly different ($P < 0.05$), with mean TST reported as 443.07 and 270.8 minutes for PAT and PSG devices. VAS correlated tightly with TST calculated by the PSG device ($r = 0.559$, $P < 0.05$). Both devices were able to successfully discern different sleep stages, summarized as light sleep, deep sleep, and REM. Measurements of sleep stage were generally in agreement between the two devices; REM sleep time correlated strongly between PAT and PSG devices ($P < 0.05$). Sleep stage distribution was light sleep 62.2% (PAT) and 74.1% (PSG); REM 13.0% (PAT) and 10.7% (PSG); deep sleep 14.5% (PAT) and 7.9% (PSG).
Conclusion Both wristwatch-style PAT and miniature PSG devices successfully recorded sleep in ICU patients. Although the simple PAT device overestimated TST, sleep stage times were generally in agreement, especially REM time which correlated strongly. Both devices can be used to effectively monitor and characterize sleep in the ICU environment.

P552

Hospital anxiety and depression after ICU survival: results of a post-ICU aftercare program

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Introduction Although the ICU survival rate has increased in the last decade, the negative effects on mental health and related quality of life become more clear. In the literature the prevalence of anxiety and depressive symptoms post ICU ranges from 10 to 43% [1]. Early recognition and treatment of anxiety and depressive symptoms is important because depression caries a risk for suicide, limited quality of life, and delayed return to work. We studied hospital anxiety and depression (HAD) symptoms after ICU discharge.
Methods Patients who were treated in our ICU from 1 January 2013 until 31 December 2013 for more than 5 days were invited to visit our post-ICU aftercare clinic. Six weeks after discharge they received a letter of invitation together with a health-related questionnaire, the Hospital Anxiety and Depression Scale (HADS) questionnaire [2]. Patients were asked to return the questionnaire prior to their visit. All data were analyzed and if the HADS score indicated a clinically significant anxiety or depression, patients were referred to a psychologist for further analyses and treatment. All patient data were analyzed retrospectively.
Results Seventy-nine patients, 54 men and 43 women, mean age 57 years. Median APACHE II and IV was 18 and 60 respectively. Median ICU and hospitals days were 9 and 20 respectively. Seventy-six percent were mechanically ventilated with a median of 5 days. Median time after ICU discharge to aftercare visit was 165 days. Patients were divided into three categories: 1, no HAD (45.4%); 2, possible HAD (9.3%); and 3, clinically significant HAD (45.4%). Women compared with men showed significantly more HAD symptoms (26.8% vs. 18.6%, $P < 0.05$). Patients with subarachnoid hemorrhage, neurotrauma and multitrauma patients showed more HAD symptoms. Pain, fatigue, muscle weakness, impairment of daily activity dyspnea, and hoarseness were significantly associated with clinically significant HAD. No association between age and HAD was found. Diagnosis at ICU admission, length of stay, severity of illness, delirium and use of sedatives were not associated with HAD.
Conclusion Prevalence of clinically significant post-ICU HAD was 45.4%. Female sex and post-ICU physical complaints – pain, fatigue, muscle weakness, impairment in daily activities, hoarseness and dyspnea – were significantly associated with HAD.
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P553

Post-traumatic stress disorder after ICU discharge: results of a post-ICU aftercare program

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Introduction Patients who survive ICU treatment may experience psychological distress for some time after discharge from the ICU. In the literature the reported prevalence of post-traumatic stress disorder (PTSD) ranges from 5 to 64% [1]. We studied PTSD symptoms in relation to ICU factors, demographic data and physical complaints reported by patients 4 to 6 months after ICU discharge.

Methods Patients who were treated in our ICU from 1 January 2013 until 31 December 2013 for more than 5 days were invited to visit our ICU aftercare clinic. Six weeks after discharge a letter of invitation together with a health-related questionnaire, the Hospital Anxiety and Depression Scale questionnaire and Impact of Event Scale (IES-R) questionnaire, was sent to the patient. Patients were asked to return the questionnaires prior to visiting the aftercare clinic. All data were analyzed and if the IES-R score indicated a possible PTSD, patients were referred to a psychologist for further analyses and treatment. All patient data were analyzed retrospectively. The Pearson chi-squared test was used to compare groups and Cramer's V analyses was used to examine strength of the association between groups.
Results Seventy-nine patients, 54 male and 43 women, with mean age 57 years. Median APACHE II and APACHE IV were 18 and 60 respectively. Median ICU days and hospital days were 9 and 20 respectively. Seventy-six percent of patients were mechanically ventilated with a median of 5 days. Median time of ICU discharge to aftercare visit was 165 days. Delirium occurred in 22 (22.7%) patients during ICU treatment. The prevalence of PTSD was 43.3% and was most seen in patients after subarachnoid hemorrhage (SAH) (28.6%). Pain, muscle weakness, fatigue, impairment in daily activity, dyspnea, and hoarseness reported during the ICU aftercare clinic visit were significantly associated with PTSD. There was no significant difference in men and women. Sedation, opiates, benzodiazepine, inotropic medication and delirium during ICU treatment were not associated with higher prevalence of PTSD. None of the other demographic data analyzed were significantly associated with PTSD.
Conclusion Prevalence of PTSD was 43.3% and most seen in patients after SAH, reflecting the majority of patients treated in our ICU. PTSD was associated significantly with pain, muscle weakness, fatigue, dyspnea, hoarseness and impairment of daily activity after a median 165 days post ICU treatment.
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P554

Somatic complaints after ICU survival: results of a post-ICU aftercare program

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Introduction Critical illness today is well recognized as being associated with new or worsening physical impairment, diminished mental health and cognitive dysfunction. We studied the scope of somatic complaints in ICU survivors 4 to 6 months after ICU treatment.
Methods Patients who were treated in our ICU from 1 January 2013 until 31 December 2013, for 5 or more days, were invited to visit our ICU aftercare clinic. Six weeks after ICU discharge a letter of invitation together with a health-related questionnaire, the Hospital Anxiety and Depression Scale questionnaire [1] and Impact of Event Scale Revised questionnaire [2], was sent. Patients were asked to return the questionnaires before visiting our clinic. The main purpose of the post-ICU aftercare was to screen for somatic complaints, mental health and cognitive dysfunction. If necessary, further examination or treatment was advised. All data were retrospectively analyzed.
Results Ninety-seven patients visited our aftercare program in 2013. Median time after ICU discharge and visit to our after care clinic was 165 days. Twenty-five patients died after ICU discharge. Fifty-four patients were excluded because of various reasons; that is, language barrier, psychiatric illness, mental handicap, hospital admittance elsewhere, great distance. Seventy patients (81.4%) had somatic complaints influencing daily performance and quality of life. Fatigue (74.4%), muscle weakness (48.8%), dyspnea (34.9%), impairment of daily activity (81.4%), pain (38.4%) and weight loss (33.3%) were the most frequently reported complaints. Pain was most reported in patients with subarachnoid hemorrhage (27.3%), multitrauma (15.2%) and pneumonia (12.1%). Pain was most localized in the head (15.6%), one or both legs (15.6%), back (10.9%), shoulder (9.3%), hip (9.3%) and thorax (6.3%). Muscle weakness, fatigue, dyspnea, impairment of daily activity, pain and hoarseness were associated significantly with PTSD and HAD. There was no significant difference in somatic complaints between men and women.
Conclusion Somatic complaints after ICU discharge are frequently reported in our post-ICU aftercare patients, influencing daily performance and quality of life. Patient-centered research and treatment focusing on somatic complaints is of great importance.
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P555

Post-traumatic stress disorder prevalence and subtypes among survivors of critical illness

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Introduction Among North American survivors of critical illness, we aim to describe the prevalence of post-traumatic stress disorder (PTSD), and its subtypes of intrusion, avoidance, and hyperarousal.
Methods In this prospective, observational, multicenter cohort study from 2009 to 2010, we screened adults (age ≥18 years) with new-onset respiratory failure, cardiogenic shock, or septic shock, who were admitted to medical and surgical ICUs in four facilities. At 3-month and 12-month follow-ups, high probability of PTSD was defined by 17-symptom PTSD Checklist – Event Specific Version (PCL-S) score ≥50. Also, PCL-S responses were mapped onto DSM-IV criteria for PTSD. To augment PTSD identification, those with a moderate probability of post-ICU PTSD (PCL-S score ≥35) were further confirmed with the Clinician Administered PTSD Scale (CAPS) structured interview. Moderate or greater symptoms for each PTSD subtype of intrusion, avoidance, and hyperarousal were categorized.
Results Of the 180 eligible participants at 3 months, PTSD was identified in 10 (6%) using PCL-S scores and 15 (8%) using DSM-IV mapping of the PCL-S. Of the 160 eligible participants at 12 months, PTSD was identified in two (1%) using PCL-S scores and 10 (6%) using DSM-IV mapping of the PCL-S. Of those eligible for CAPS assessments, at 3 months only 13 of 24 (54%) interviews were completed resulting in three extra PTSD diagnoses, and at 12 months only six of 22 (27%) interviews were completed resulting in two extra PTSD diagnoses. At 3 and 12 months, the intrusion subtype was present in 25 (14%) and in 25 (16%), the avoidance subtype was present in 78 (43%) and 60 (38%), and the hyperarousal subtype was present in 82 (46%) and 71 (44%).
Conclusion Irrespective of definition using PCL-S or DSM-IV mapping, PTSD was identified in no more than one in 10 survivors of critical illness at either 3 or 12 months post ICU, which is still nearly double the US population past-year PTSD prevalence. In ICU survivors with moderate probability PTSD by PCL-S, the CAPS gold-standard interview is challenging to complete and adds only a small number of diagnoses. However, two in five ICU survivors will develop PTSD subtypes of avoidance or hyperarousal, which both occur twice as frequently as the intrusion subtype. Targeting predominant PTSD subtypes may help optimize treatment strategies for the ICU survivor, such as prolonged exposure and eye movement desensitization and reprocessing for those with the avoidance subtype, and pharmacologic antidepressants targeting the sympathetic nervous system to produce anxiolysis for those with the hyperarousal subtype.

P556

Nonpharmacological interventions to reduce short-term or long-term psychological stress in ICU patients: a systematic review

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Introduction A systematic review was performed of studies of nonpharmacological interventions aiming to reduce short-term or long-term stress in intensive care patients, as little is known about the

efficacy of such interventions. Previous work has shown that intensive care patients undergo many stressful experiences, which can affect their long-term psychological well-being. Studies have demonstrated a high prevalence of depression, anxiety or post-traumatic stress disorder after intensive care admissions.
Methods A systematic review was carried out according to the Prisma statement. A search was conducted of Medline, Embase and Psychinfo databases. Inclusion criteria included studies of populations of adult patients in mixed or general ICUs. No study designs were excluded, but studies that focused on specific disease states were excluded. Included studies were assessed for risk of bias, using a quality checklist.
Results A total of 1,743 papers were retrieved, of which 18 studies were eligible for inclusion in the review. Studies had a combined population of 1,970 patients admitted to 38 ICUs from Europe, Asia and North America. Eleven studies were randomized controlled trials (RCTs). Interventions were classified as four groups – music; therapeutic touch; diary and psychotherapeutic interventions. Ten studies found that music interventions were effective in the short term; however, follow-up results were limited and some studies were low quality. There was moderate quality evidence from three studies for the effectiveness of diary interventions, with medium-term follow-up results. There was mixed-quality evidence for therapeutic touch interventions in the short term from three studies. The two psychotherapeutic interventions studied were of moderate quality, and one showed promising results at 12-month follow-up.
Conclusion The evidence for the efficacy of nonpharmacological interventions to reduce short-term or long-term stress in intensive care patients was of low to moderate quality. Studies included mainly short-term and medium-term follow-up. This highlights the need for larger-scale, better-quality RCTs with longer-term outcome measurement. However, the results indicate that nonpharmacological, including psychological, approaches are likely to be beneficial for reducing short-term or long-term stress in intensive care patients.

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Utilisation of existing community rehabilitation services by critical care survivors

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Introduction Patients recovering from critical illness suffer many physical and psychological problems during their recovery, including muscle weakness, fatigue, signs and symptoms of PTSD, anxiety and depression [1]. At present, specialist intensive care follow-up and rehabilitation is inconsistent and in many geographical areas is nonexistent. As a result, many survivors of critical illness will require using existing community rehabilitation services [2]. The aim of this present service evaluation was to understand the utilisation of community rehabilitation services by critical care survivors.
Methods A database of acute referrals to community rehabilitation services was retrospectively analysed from 1 May 2014 to 31 October 2014. Age, referring specialty and reason for referral for rehabilitation were documented. This database was cross-checked with the critical care database in Glasgow Royal Infirmary to identify which individuals had been admitted to critical care during their admission.
Results Over this 6-month period 769 patients were referred from their parent specialty for community rehabilitation in North East Glasgow. Thirty-three of the 769 patients (4.3%) referred had a critical care stay during their admission. Of these, eight patients were referred for rehabilitation by orthopaedics, eight by medicine for the older patients, 11 from acute medicine and the remaining six from other specialties. Six of the 769 patients who had a critical care admission were of working age (<1%). Two individuals were admitted to critical care following trauma whilst four had complex social needs prior to their critical care admission. This included an individual with a high body mass index. None of the individuals of working age were referred as a consequence of their critical care stay.
Conclusion This service evaluation demonstrates that very few critical care survivors are referred to community rehabilitation services, particularly those of working age. More work is required to understand optimal rehabilitation pathways in this patient group.
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P558

Physiotherapy in the ICU: an evidence-based, expert-driven, practical statement

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Introduction Evidence-based, expert-driven, practical statements improve quality and effectiveness of the diagnostic and therapeutic process of patient care. Although the effectiveness of physiotherapy treatment strategies in ICU patients has been described, statements or guidelines of physiotherapy for ICU patients are not available [1]. Guidelines on safety management and on the diagnostic and therapeutic process may support and guide clinical decision-making leading towards evidence-based tailored care. The aim of this study was to develop an evidence-based statement for the physiotherapy treatment of ICU patients with recommendations for effective and safe diagnostic assessment and intervention strategies.
Methods For the development of this evidence statement, we used the EBRO method, as recommended by the Dutch Evidence Based Guideline Development Platform [2]. This method consists of the identification of clinically relevant research questions, followed by a systematic literature search, quality assessment, and summary of the evidence eventually leading to establishing of concept and final recommendations based on feedback from experts. The final recommendations were prepared according to this methodical approach and summarized in figures, flowcharts and appendices.
Results Three expert-based relevant clinical questions were formulated within the physiotherapy clinical reasoning process and were classified according to the International Classification of Functioning, Disability and Health. In a systematic literature search, 129 studies were identified and assessed for methodological quality and classified according to the level of evidence. The final Evidence Statement consisted of recommendations for physiotherapy in ICU patients including safety criteria, a core set of instruments to assess impairments and activity restrictions and effective interventions.
Conclusion The Evidence Statement for physiotherapeutic diagnostics and intervention in ICU patients will contribute to the quality of clinical practice by supporting the clinical decision-making process.
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P559

Early mobilization according to diagnosis in a Brazilian coronary ICU

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Introduction Early mobilization has been advocated to improve muscle function and, consequently, the patient quality of life after discharge. Nevertheless, few studies have explored it in a coronary ICU (CICU). The aims of the present study were to describe the use of an early mobilization protocol in a CICU and to investigate whether different groups of diagnoses respond similarly to this protocol.
Methods This is a retrospective observational study conducted in a medium-sized hospital located in the city of Presidente Prudente,

Brazil. The early mobilization protocol consists of five phases: 1 – passive exercises for the unconscious patient; 2 – active exercises associated with respiratory exercises (patient lying on the bed); 3 – phase 2 exercises with the patient sitting on the bed; 4 – phase 2 exercises with the patient sitting on a chair or in a standing position; 5 – phase 4 exercises plus walking. All hospital records from patients, between September 2013 and August 2014, were included in this study. Data extracted from hospital records were: age, gender, diagnosis (arrhythmia, coronariopathies, congestive heart failure and other pathologies), length of stay, number of discharge and number in each phase of the early mobilization protocol. Pearson chi-square test was used to compare the number of mobilizations (phase 4 and 5) per group of diagnoses. Odds ratios were calculated for those comparisons found to be statistically significant (P <0.05).

Results A total of 697 hospitals records were analyzed. Patients had on average (SD) 67.8 (13.1) years and the majority of them were males (57%). Our results revealed that 65% of patients in the CICU received phase 4 and 43% of patients in the CICU received phase 5 of the early mobilization protocol. No differences in the proportion of patients receiving phase 4 or 5 were found among arrhythmia, coronariopathies and congestive heart failure groups. The only difference found was between congestive heart failure group and other cardiovascular pathologies (P <0.001). The congestive heart failure group was mobilized 5.6 times (95% CI: 2.7 to 11.5) and 3.2 times (95% CI: 1.7 to 5.7) more than the other cardiovascular pathologies group in phase 4 and 5, respectively.

Conclusion A considerable proportion of patients was mobilized without any serious complications in the CICU. Our findings suggest that patients diagnosed with arrhythmia, coronariopathies and congestive heart failure can be equally mobilized in an ICU.

P560

Need for therapeutic interventions as a predictor of mortality in intensive care

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Introduction Various therapeutic interventions needed in critical care may reflect a high risk of death. We evaluated associations between commonly used interventions and hospital mortality in Finnish ICU patients.

Methods We retrieved data on adult patients treated in Finnish ICUs between 2003 and 2013 from the Finnish Intensive Care Consortium database. We used the Therapeutic Intervention Scoring System (TISS-76) for categorizing ICU interventions and the Simplified Acute Physiology Score (SAPS II) for quantifying severity of illness. We excluded readmissions, patients with missing outcome, SAPS II and TISS data. We also excluded very common interventions (arterial line, bolus intravenous medication), very rare ones (prevalence <1%), and interventions only applicable in specific populations (intracranial pressure monitoring, intra-aortic balloon assist). We grouped several TISS categories when applicable. We performed a backward stepwise binary logistic regression analysis with TISS items to assess the impact of each intervention on hospital mortality (expressed as odds ratio (OR) with 95% confidence intervals (CIs)). Age, admission type, and SAPS score (minus age and admission type scores) were adjusted for in the multivariate analysis.

Results We identified 161,134 patients eligible for analysis. The multivariate analysis showed that the highest risk for hospital mortality in all patients was associated with cardiac arrest and/or countershock, OR 2.58 (95% CI = 2.43 to 2.73), SAPS II emergency admission, OR 2.52 (95% CI = 2.32 to 2.74), vasoactive drug infusion (>1 drug), OR 1.66 (95% CI = 1.59 to 1.73) and blood transfusion (a combined TISS item), OR 1.53 (95% CI = 1.44 to 1.63). TISS items associated with the lowest risk of mortality in general population were: active anticoagulation, OR 0.51 (95% CI = 0.49 to 0.53), induced hypothermia, OR 0.68 (95% CI = 0.62 to 0.74) and measurement of cardiac output by any method, OR 0.87 (95% CI = 0.83 to 0.91). All aforementioned associations were statistically significant (P <0.001). There was no notable association with mortality for pulmonary artery catheter, platelet transfusion and vasoactive drug infusion (one drug) (P >0.05).

Conclusion In this large retrospective multicenter study, the TISS item associated with the highest risk of death was cardiac arrest and/or countershock. Unexpectedly, the independent effect of emergency admission was of comparable magnitude in terms of impact on hospital mortality. Of these, in-ICU cardiac arrest might be amenable to preventive measures and should be studied further.

P561

Payment options: do they affect outcome in the critically ill

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Introduction Increasing cost is an important issue in critical care medicine. We tried to analyze in a level 3 care ICU in Kolkata of a tertiary care hospital whether the different payment options (self-paying vs. insurance/corporate paying) do affect the outcome in the critically ill.

Methods Our prospective study included 1,520 patients admitted consecutively to a level 3 care ICU for a period of 20 months. Readmitted patients during the same period were excluded. Payment method was documented for all and divided into two groups as self-paying and insurance/corporate paying. Outcome assessment was done using the APACHE IV model for all cases. Demographic data, number of observed deaths, predicted mortality rate (PMR), standardized mortality ratio (SMR), average length of stay (ALOS), predicted length of stay, and number of discharge against medical advice (DAMA) were documented for each group. Statistical analysis was carried out using unpaired Student t test and P <0.05 was considered significant.

Results Of 1,520 patients, 995 (65.46%) cases were self-paying while 525 (34.54%) cases were insurance/corporate paying. In the self-paying group, mean age was 59.65 years ± 17.26 SD (median 62), APACHE IV score mean was 62.50 ± 33.61 SD (median 57), average LOS 4.67 days ± 4.29 SD (median 3), PMR was 22.71, 226 observed deaths, 85 cases of DAMA, and SMR was 1.00 (CI = 0.87 to 1.14). In the insurance/corporate-paying group, mean age was 61.75 years ± 17.19 SD (median 65), APACHE IV score mean was 58.53 ± 32.94 SD (median 54), average LOS was 5.64 days ± 5.61 SD (median 4), PMR was 21.26, 113 observed deaths, six cases of DAMA, and SMR was 1.01 (CI = 0.83 to 1.21). In the two compared groups, predicted mortality and SMR were not statistically significant (P = 0.2808); however, ALOS in the insurance/corporate paying group was significantly higher than the self-paying group (P = 0.0002), mean age of the insurance/corporate paying group was significantly higher than the self-paying group (P = 0.02), and incidence of DAMA is significantly higher in the self-paying group (8.54%) as compared with insurance/corporate paying group (1.14%). Root-cause analysis showed DAMA cases are mostly financial (>95%).

Conclusion Statistically significant differences in ALOS and DAMA in the two groups are probably due to cost of healthcare not affordable to all.

P562

Source of ICU admission: does it really matter?

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Introduction Source of admission to the ICU is of importance. We tried to identify the different sources of ICU admission to a level 3 ICU of a tertiary care hospital in Kolkata and analyze whether the overall patient outcome is affected by the different sources of admission.

Methods Our prospective study included 2,056 patients admitted to a level 3 care ICU over a period of 2 years. Numbers of readmissions were not considered. ICU outcome was analyzed using the APACHE IV model and source of admission to the ICU was documented as either from emergency (ER), from the floor or from other hospital. Analysis was carried out between different groups based on admission using unpaired Student t test and P <0.05 was considered significant. Number of ventilations and the mortality rate in each group were also documented.

Results Of 2,056 admissions, 1,223 cases (59.48%) were from ER, 809 cases (39.35%) were from floor and 24 cases (1.16%) were from other hospitals. In the ER group, mean APACHE IV was 55.03 ± 31.49 SD (median 50), PMR 16.26, observed deaths 198, ALOS 4.78 days ± 4.83 SD (median 3), SMR 0.995 (CI = 0.86 to 1.14), mean age 60.52 years ± 17.63 SD (median 63), 323 ventilations. In the floor group, mean APACHE IV was 65.17 ± 34.40 SD (median 60), PMR 27.03, observed deaths 234, ALOS 5.23 days ± 5.22 SD (median 3), SMR 1.07 (CI = 0.94 to 1.21), mean age 61.38 years ± 15.72 SD (median 64), 302 ventilations. In the other hospital group, mean APACHE IV was 55.29 ± 29.82 SD (median 50), PMR 18.0, observed deaths 2, ALOS 6 days ± 5.85 SD (median 3), SMR 0.46 (CI: 0.23 to 0.88), mean age 56.08 years ± 17.79 SD (median 56.5), six ventilations. During analysis, the other hospital group was omitted because of inadequate sample size. There was statistically significant differences in APACHE IV (floor >ER, P <0.0001), PMR (floor >ER, P <0.0001), ALOS (floor >ER, P = 0.04) noted between the floor and ER groups. Number of ventilations (37.33% vs. 26.4%), SMR (1.07 vs. 0.995), and mortality rate (28.92% vs. 16.19%) were also significantly higher for patients admitted from the floor. No significant statistical difference was observed in age between two groups (P = 0.26).
Conclusion The severity of illness index in patients admitted to the ICU from floors is significantly higher than emergency admissions. Overall outcome for patients transferred to the ICU from the floor is worse based on mortality rate, SMR, and ALOS when compared with the emergency group.

P563

Readmission to the ICU: is it a big concern? An analysis

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Introduction Readmission to the ICU is an important quality indicator of ICU care. We conducted a prospective study in a level 3 care ICU in Kolkata of a tertiary care hospital to analyze whether there are overall outcome differences when comparing the readmission group with the entire group.
Methods Our prospective study included 2,140 patients admitted to a level 3 care ICU over a period of 1 year. The number of readmissions (n = 85) during the same period was also documented. Readmission was defined as all patients who were transferred back to the ICU prior to hospital death/discharge during the above period. ICU outcome was calculated using the predictive APACHE IV model. Payment methods were documented as either self-paying or corporate/insurance paying. A comparison analysis between the entire group with the readmission group was done using unpaired Student t test and P <0.05 was considered statistically significant.
Results In the entire group (n = 2,140), mean APACHE IV was 50.34 ± 31.54 SD (median 42), PMR 15.49, observed deaths 327, ALOS 4.05 days ± 4.55 SD (median 3), SMR 0.99 (CI = 0.88 to 1.1), mean age 60.55 years ± 15.68 SD (median 63), 490 ventilations, 72.71% of patients were self-paying while 27.29% of patients were corporate/insurance paying. In the readmission group (n = 85), mean APACHE IV was 77.16 ± 33.72 SD (median 73), PMR 38.89, observed deaths 42, ALOS 5.23 days ± 4.18 SD (median 4), SMR 1.27 (CI = 0.95 to 1.67), mean age 64.79 years ± 14.40 SD (median 67), 43 ventilations, 75.3% of patients were self-paying while 24.7% of patients were corporate/insurance paying. During comparison between the two groups there were statistically significant differences, with the readmission group having significantly higher APACHE IV (P <0.0001), PMR (P <0.0001), ALOS (P = 0.002), age (P = 0.005), and SMR (1.27 vs. 0.99) compared with the entire group. Percentage of patients requiring ventilation (50.59% vs. 22.90%) and mortality rate (49.11% vs. 15.28%) were also significantly higher in the readmission group. Readmission was significantly higher in the self-paying group. Root-cause analysis showed most readmissions were due to deteriorating conditions (desaturation, hypotension, sepsis, arrhythmias); however, it was also associated with cases where transfer policy from the ICU was not followed by stakeholders and financial issues were a cause of early transfer.
Conclusion Readmission to the ICU was associated with worse outcome in our study group. Lack of adherence to transfer policy by concerned stakeholders was a concern as well as increasing cost of healthcare.

P564

Association between out-of-hours discharge and mortality in adult patients leaving critical care

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Introduction Out-of-hours (OOH) discharge from critical care is associated with a significantly increased mortality rate in Australasia [1]. In the UK, daytime discharges from critical care are considered a core standard [2]. We sought to assess the impact of OOH discharge from critical care on mortality in a large general ICU, where operational pressures appear to have led to a high rate of OOH discharges.
Methods Retrospective data for all patients admitted to our ICU from April 2007 to September 2014 were recorded, using routinely collected data from our databases. Adult patients (>15 years) discharged from their first ICU admission during each hospital stay (episode) were included. Patients that died on the unit and those discharged for palliative care were excluded. Patients transferred to other centres were no longer subject to discharge within our control and were therefore also excluded. Patients discharged directly home from ICU were excluded. We defined OOH discharges as those occurring between 22:00 and 06:59, a standard definition in UK practice. Mortality status at the time of hospital discharge for each episode was used. We also recorded the readmission rate to ICU. The relative risk (RR) for OOH mortality and readmission was calculated. Statistical significance was accepted at P <0.05.
Results Of 4,476 index cases, 714 died on the unit and 80 were discharged for palliative care. A total of 490 patients were excluded for transfer to other centres and discharge directly home. Data were missing for three patients, which left 3,189 records for analysis. In total, 2,711 patients were discharged during daytime hours, of which 145 (5.35%) died. A total of 478 patients were discharged at night, 40 died (8.37%). The RR for OOH mortality was 1.56 (95% CI = 1.12 to 2.19, P = 0.0091). Readmission rate was 5.2% by day, 6.1% at night. The RR for readmission was 1.17 (95% CI = 0.79 to 1.72, P = 0.436).
Conclusion Our data demonstrate an association between critical care discharge time and mortality, to a statistically significant level. Due to the retrospective observational nature of the study, causation cannot be assumed; however, a number of factors may contribute to the increased risk of harm to patients discharged from the ICU at night. Further work will focus on annual OOH mortality trends, thereby gaining an insight into whether bed occupancy demands impact on the necessity for nighttime discharges.
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P565

Recovery of health-related quality of life in ICU patients: a 5-year prospective cohort study

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Introduction Severe critical illness requiring treatment in the ICU may have a serious impact on patients and their families. However, optimal follow-up periods are not defined and data on health-related quality of life (HRQOL) before ICU admission as well as those beyond 2-year follow-up are limited. The aim of our study was to assess the impact of ICU stay up to 5 years after ICU discharge.
Methods We performed a long-term prospective cohort study in patients admitted >48 hours to a medical–surgical ICU. The Short-Form 36 was used to evaluate HRQOL before admission (by proxy within 48 hours after admission of the patient), at ICU discharge and at 1, 2 and 5 years following ICU discharge (all by patients). Changes in HRQOL were assessed using linear mixed modeling.
Results We included a total of 749 patients (from 2000 to 2007). At 5 years after ICU discharge, 234 patients could be evaluated. After

correction for natural decline in HRQOL, the mean scores of four dimensions – physical functioning (P <0.001), physical role (P <0.001), general health (P <0.001) and social functioning (P = 0.003) – were still significantly lower 5 years after ICU discharge compared with their preadmission levels, although effect sizes were small (<0.5).
Conclusion Five years after ICU discharge, survivors still perceived a significantly lower HRQOL than their preadmission HRQOL (by proxies), and that of an age-matched general population. Importantly however, after correction for natural decline, the effect sizes were small suggesting that patients regain their age-specific HRQOL 5 years after their ICU stay.

P566

Determination of brain death for adult patients with ECMO

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Introduction ECMO support in ARDS is an emerging strategy when conventional treatment modalities fail. ECMO has advantages on oxygenation and circulation but also it has some unfavorable effects. The most serious complication is brain death due to cerebrovascular hemorrhage. An apnea test is the most important component in confirming brain death. For patients supported by ECMO, apnea testing remains challenging. Brain-death diagnosis is often made without an apnea test.
Methods We present two cases who receive V-V ECMO support after progression to ARDS. After initiation of ECMO we used sedation to prevent movement and improve adaptation to mechanical ventilation. Also we used anticoagulation with heparin to prevent thromboembolic events and ECMO circuit occlusion. On daily follow-up we noticed that patients had lost their pupil reactions to light. Their sedation was ceased and a computed brain tomography was performed. Both patients had intracerebral hemorrhage. We decided to determine brain death with apnea tests. We increased ECMO blood flow and fiO_2 and then decreased sweep gas flow and disconnected the patient from mechanical ventilation respectively. In one patient we did not see any spontaneous breathing efforts after carbon dioxide retention. We concluded that the apnea test was successful and confirmed brain death. On the other hand, we confirmed the brain death of the other patient with cerebral angiography due to the occurrence of hypoxia and hypotension during apnea testing.
Results We experienced some challenges while determining brain death in patients under ECMO support for ARDS. It is challenging to conduct the apnea testing during ECMO support. Auxiliary tests are required for patients who cannot tolerate the changes needed to conduct the apnea test. With increasing use of ECMO therapies, clinicians may come face to face with more complicated life-ending decisions.
Conclusion Current guidelines do not include brain death criteria using supportive therapies such as ECMO and therefore should be updated.
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P567

Making it safe to speak up about futile care: a multiperspective survey on leadership, psychological safety and perceived futile care in the ICU

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Introduction Psychological safety (PS), for example safety of speaking up, fosters team learning and prevents treatment errors on the ICU [1]. Since speaking up might also prevent excessive and inappropriate (futile) care for patients, we hypothesized that teams with higher PS report less perceived futile care (PFC). We also expected that attending physicians' inclusive leadership (IL), which invites nurses' and residents' participation [2], would decrease PFC and that PS mediates this relationship.
Methods The hypotheses were tested in a cross-sectional, multicenter paper-and-pencil survey addressing medical staff on participating ICUs. A total of 22 ICUs and four intermediate care units were included in the sample and 73 attendings, 147 residents and 659 nurses participated in the study (52% participation). Psychometric properties were tested by confirmatory factor analysis (CFA), Cronbach's α and intraclass correlations (ICC). A series of hierarchical linear models (HLM) were conducted to test the study hypotheses separately among nurses/residents and attendings. IL and PS were entered as unit-level predictors (mean values per unit). Covariates were demographics, working hours per week, workload and unit size (number of staff). Mediation effects were tested.
Results The CFA showed a good fit indicating factorial validity (CFI: 0.97), reliabilities were from α 0.79 to 0.93 and ICCs were significant (~0.20, P <0.001). HLM revealed that unit-level IL of nurses and residents was positively related to PS (b = 0.34, P <0.001). Being a resident and working in a smaller unit also predicted PS. As expected, unit-level PS was negatively related to individual PFC (b = –0.38, P = 0.025). Further predictors of higher PFC were: being a nurse, having more than 5 years of job experience and higher workload. PS mediated the relationship between unit-level IL and individual PFC (indirect effect: –0.13, P <0.001). Additional analyses revealed that attendings' PFC was negatively related to their perception of residents PS (b = –0.44, P = 0.019).
Conclusion A sense of PS in an ICU team might reduce futile care by increasing the safety of speaking-up behavior of nurses and residents. PS can be enhanced by attending physicians who practice inclusive leadership behavior to foster autonomy and participation of residents and nurses.
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P568

End-of-life decisions: how do patients die in the ICU?

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Introduction One of the main goals of intensive care medicine is to reduce the mortality of critically ill patients. However, it is essential to recognize end-of-life care as an integral component of critical care. Besides survival, the success of intensive care should also include the quality of lives preserved and the quality of dying. The objective of this study was to evaluate the incidence and type of end-of-life decisions (ELD) in critical patients that died in an ICU.
Methods Analysis of all patients included in an ICU running database and who died from 1 November 2013 to 31 October 2014. The following variables were evaluated: age, gender, reason for admission, SAPS II, length of ICU stay and type of ELD. To classify ELD, four concepts were defined: 'Comfort care', a change from curative therapy to comfort care therapy; 'Limited therapy', maintenance of curative therapy but without escalating it (for example, no renal substitution); 'Decision not to resuscitate', not to perform advanced life support if cardiac arrest occurs; and 'Without previous end-of-life decisions', when there was no prior decision regarding the ELD.
Results A total of 507 patients were admitted to the ICU and 132 died (26%). Reasons for admission in those who died were septic shock (47%), post cardiac arrest (13%), cardiogenic shock (8%), and nontraumatic brain bleeding (8%). Fifty-three patients (40%) died after a 'Comfort care' decision, 28 patients (21%) after 'Decision not to resuscitate' and 14 (11%) after a 'Limited therapy' decision. Thirty-seven patients died 'Without previous end-of-life decisions'. However, specifically in this group, when looking for individual records, 32 patients died (86%) in the first 48 hours after the admission and four (11%) had evidence of brain death and were organ donors, which leaves one patient (3%) in whom there was no ELD.
Conclusion In this study, 'Comfort care' was the main ELD, which is in line with the concept that ELD are essential to ensure that care provided is

consistent with quality of life and death. The apparent large proportion of patients 'Without previous end-of-life decisions' was due to patients who died in the first 48 hours after ICU admission corresponding to conditions refractory to treatment. Additionally, this study also draws our attention to better plan ICU admissions and hospital outreach in order to reduce early ICU mortality.

P569

Do intensivists prognosticate patients differently from themselves or their loved ones?

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Introduction There is a paucity of data about whether our treatment philosophy is different for our patients as compared with what we would have wanted for ourselves, or while acting as surrogate decision-makers for our loved ones.
Methods An anonymous survey was sent to all the members of Australia and New Zealand Intensive Care Society and the College of Intensive Care Medicine (CICM). The first section comprised a hypothetical case scenario spanning over 6 weeks of ICU stay for a patient. At four different stages of the ICU stay, responders were requested to answer multiple-choice questions regarding the philosophy of treatment, based on their perceived prognosis of the patient at that particular time. The following two sections contained the same set of questions with the hypothetical scenario of responders acting as surrogate decision-makers for the patient and that of responders being patients themselves, in the same situation. The responses were compared amongst three sections at each stage using the chi-square test.
Results A total of 115 responses were received from the fellows of CICM. The results are presented in Tables 1 and 2.

Table 1 (abstract P569). Respondents advocating withdrawal for the patient

	Withdrawal self (%)	Withdrawal family (%)
Day 3	71	67
Day 7	83	76
Day 28	96	88
Day 42	98	97

Table 2 (abstract P569). Respondents advocating continuing care for the patient

	Withdrawal self (%)	Withdrawal family (%)
Day 3	16	10
Day 7	23	15
Day 14	25	19
Day 42	42	29

Conclusion Of the ICU physicians who would withdraw care for their patient, the majority would also want the same for themselves. The disparity between decision to continue to treat the patients versus treating self or family increased with increasing length of stay.
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P570

Evaluation of screening criteria for palliative care in an emergency department ICU

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Introduction A high percentage of patients admitted to ICUs fulfill one or more criteria for palliative care. There are currently few comprehensive studies in critical care settings that have set out to examine the association of palliative care screening criteria with adverse patient outcomes.
Methods We performed an observational unicentric study on a 12-bed, medical emergency department intensive care unit (EDICU). A three-item palliative care screen was developed from consensus reports. A senior critical care physician screened patients upon admission using these questions during a 10-week period. The questions were: does this patient suffer from a life-limiting disease (end-stage lung, liver, heart or kidney disease, severe neurological disability, extreme frailty, locally advanced or metastatic cancer, advanced-stage AIDS). If the answer to the first question is yes, we proceed to the next one: do you believe this patient will survive to hospital discharge? Answers to those questions were recorded, SAPS III was calculated and all patients were followed until death, discharge or transfer to another center. Differences in mortality and SAPS III score between groups were examined using a Student's *t* test. Proportions were compared using chi-square test. $P < 0.05$ was considered statistically significant.
Results During the period, 191 patients were admitted to the EDICU, from which 151 had complete data and follow-up. A total of 63 patients (41.7%) suffered from a life-limiting disease and were evaluated as having a high probability of death in 1 year. This group was further divided between 35 patients who in the moment of initial screening were expected to die in this hospital admission and 28 patients who were believed to survive to discharge. Comparison between these two groups showed patients believed to die at this hospital admission had higher SAPS III scores (66.9 vs. 59, $P = 0.010$) and hospital mortality (48.6% vs. 10.7%, $P = 0.001$).
Conclusion A high percentage of patients admitted to our EDICU have life-limiting disease and might benefit from palliative care. These patients can be identified using simple screening questions at admission and positive answers to those questions can be associated with worse outcomes.
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P572

Parents' return to the hospital after the death of their children: importance of palliative care after death

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Introduction To analyze the perception of parents regarding their return to the hospital where their children died to participate in a conversation with doctors and to analyze the feelings of parents about their participation in a study evaluating the care provided in the moments leading up to the death of children.
Methods A descriptive exploratory qualitative study. The study sites were the pediatric ICUs of the Hospital São Lucas and Hospital de Clinicas de Porto Alegre. Fifteen parents of children who died in the PICUs studied participated in the study. Data collection occurred in 2010 and was conducted through semistructured interviews. Data were analyzed using thematic content analysis. The research was approved by the research ethics committees of both hospitals.
Results The ability to return to the hospital and talk to medical assistants was considered by parents as a positive and enlightening opportunity. Parents who participated in the study understood this moment as an opportunity to be heard and demonstrated the intention to contribute with their experiences in order to improve care in the hospitals studied.
Conclusion We conclude that there is a need to implement measures to provide palliative care to parents after the death of their children. It is necessary to consider the possibility of providing families with follow-up meetings with the multidisciplinary team after the death of children.
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P573

How readable are our Patient Information Sheets?

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Introduction We often need to obtain consent for clinical studies in the ICU. Participant Information Sheets (PIS) can be difficult to understand. A recent French publication [1] supports our hypothesis that PIS have poor readability scores.
Methods Protocols submitted for ethics approval between 2008 and 2009 were obtained with permission from the Scotland A Ethics Research Committee. Ethical approval was not required for this observational study. All header, footers, diagrams and tables were removed. Readability scoring was performed using the Flesch Reading Ease and Flesch–Kincaid (FK) grades. Statistical analysis using Excel and MiniTab was then performed. The readability of these documents was compared with everyday documents – newspaper articles, politicians' speeches [2] and standard contract agreements.
Results A total of 104 protocols containing 209 PIS were reviewed. Of these, 99 (47%) were written for patients, 56 (27%) for GPs, 26 (12%) for relatives, 17 (8%) for carers, five (2%) for legal representatives and six (3%) were summary sheets only. Sixty-seven (64%) of these protocols were submitted by academic institutions (for example, university or health boards) and 37 (36%) by pharmaceutical companies. Results are expressed as the median and 25th and 75th percentiles. The word count and number of pages were higher for those PIS submitted by pharmaceutical companies compared with academic institutions: 1,561 (471; 5,167) versus 1,177 (626.5; 1,559.8) with P <0.05 and 4 (2; 10) versus 3 (2; 4) with P <0.05 respectively. The Flesch Reading Ease (63 (56; 69) vs. 60 (52.6; 65.4)) and FK grades (3 (5.4; 7.2) vs. 6.8 (6; 7.6)) were similar for both groups. Further subanalysis demonstrated that PIS designed for GPs had a lower word count, lower Flesch and higher FK grade compared with those for patients – the difference in Flesch and FK grade were compared using a Mann–Whitney test and were statistically significant.
Conclusion The FK grade is equivalent to US school grade level. The US government advises all policies produced should have a FK grade of <9. Our study suggests that protocols submitted to the ethics committee are easy to read, comparing favourably with broadsheet journalism and standard contract, for example loan contract. However, the average reading age in the UK is 9 years [3], suggesting participants may struggle with the information provided.
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P574

Stakeholder engagement to identify priorities for improving the quality and value of care provided to critically ill patients

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Introduction Healthcare systems do not make optimal use of evidence, which results in suboptimal patient care. Large amounts of scientific evidence are generated but not implemented into patient care (knowledge to care gap). We sought to identify and prioritize knowledge to care gaps in critical care medicine as opportunities to improve quality and value in care.
Methods Using a modified RAND/UCLA Appropriateness Methodology, a committee of 38 providers and decision-makers representing a population-based clinical network of adult (n = 14) and pediatric (n = 2) medical–surgical ICUs in Alberta, Canada (population 4 million) serially proposed, rated and revised potential knowledge to care gaps as priorities for improvement. The priorities developed by the committee were sent to the network's 1,790 frontline providers to rate their importance. The final list of priorities that were rated as important was disseminated to all network members for feedback.
Results Sixty-eight knowledge to care gaps were proposed, rated and revised by the committee over three rounds of review, resulting in 13 priorities for improvement. Then, 1,103 providers (62% response rate) representing nurses, respiratory therapists, allied health professionals and physicians evaluated the priorities and rated nine as necessary. In multivariable logistic regression analyses, provider (profession, experience and teaching status of ICU) and knowledge to care gap characteristics (strength of supporting evidence, potential to benefit the patient, potential to improve patient/family experience, and potential to decrease costs) were associated with priorities rated as necessary. After disseminating the results to all network members, 627 responded (35% response rate) and indicated that the priorities were reasonable choices for quality improvement initiatives (87%), that they were highly supportive of working on initiatives targeting the priorities (61%) and would be willing to act as local champions for the initiatives (n = 92 individuals).
Conclusion Our research approach engaged a diverse group of stakeholders to identify nine priorities for improving the quality and value of care provided to critically ill patients. This methodology can be used to engage stakeholders and identify priorities for quality improvement in other healthcare systems and domains. Additional work is required to reconcile provider/decision-maker and patient/family priorities.

P575

Using patient researchers to understand patient and family experiences in ICUs

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Introduction With increasing emphasis on patient and family-centred care, it follows that patients and their family members should be included when priorities for improving care are established. We therefore used a novel methodology that employs former patients and family members as researchers to describe the experiences of critically ill patients and their families with ICUs and to identify opportunities for improvement.
Methods Using the patient engagement framework developed by Marlett and Emes, we engaged four former patients and family members trained in qualitative research methods to conduct and analyse semistructured focus groups and interviews with adult patients who had recovered from critical illness and family members of both surviving and deceased patients. Participants were recruited from 13 ICUs in Alberta, Canada. Focus groups and interviews were recorded, transcribed and analysed using phenomenological reduction. Data collection continued until thematic saturation was reached.
Results Thirty-two participants including patients (n = 11) and family members (n = 21) participated in five focus groups (n = 23 participants) and eight interviews (n = 9 participants). Participants articulated themes reflecting important components of care organised across three phases of the ICU experience; admission to ICU, daily care in ICU and after ICU discharge. Admission to ICU comprised three themes: patient and family transition into ICU, patient and family disorientation upon admission to ICU and preferred staff actions to help patients/family adapt to the ICU. The daily care phase of ICU consisted of five themes: honouring patient's voices, needing to know, making decisions, culture in ICU and medical care. The experience after ICU discharge comprised two themes: transition from ICU to a hospital ward and long-term effects of critical illness. Participants identified five

priorities for improvement: provide families with a guide/navigator; educate providers about the fragility of family trust; improve provider communication skills; inform patients about the long-term effects of critical illness; and develop strategies to facilitate continuity of care between providers.
Conclusion Patients and family members are an untapped resource and engaging them as researchers is a viable strategy to identify opportunities for quality improvement that are patient and family centred.

P576

Survey of visiting hours in critical care units in English trauma centres

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Introduction The purpose of this study was to assess the visiting restrictions placed on families visiting adult patients on critical care units within trauma hospitals in England. Whilst it is well recognised that high-quality care for patients is of paramount importance, we should also be aware that supporting patients' families offers long-term benefits for patient, family and hospital. In our own unit we are reviewing whether we could adopt a more flexible attitude to visiting times and assessing how to provide a more welcoming environment to relatives. To inform our own review and in order to develop a best practise approach, we surveyed all of the major trauma centres in England.
Methods A telephone survey on visiting times was conducted in 53 adult critical care units in trauma centres in England. A list of trauma centres was obtained from the NHS England website. All critical care units (other than obstetric high dependency units and coronary care units, unless part of a cardiothoracic critical care unit) within each hospital were surveyed. Each respondent was asked about the visiting hours, whether children were allowed to visit and how many visitors to a bed space.
Results Fifty-three units with between four and 75 beds and covering the whole of England were surveyed: there was a 100% response rate. Visiting hours varied between hospitals and between units within the same hospital. Nine units (17%) had open visiting hours, although most gave advice on times to avoid such as nursing handover. The majority of units (44.83%) operated restricted visiting with a median (range) of 6 (2 to 9) hours. All units allowed a maximum of two visitors to the bedspace. Children were allowed in nine units without restriction, the remaining units advised that it may not be appropriate for children to visit and it was at the discretion of the parents and medical staff.
Conclusion The majority of adult critical care units in England, including our own, have restricted visiting policies. Visiting policies are a source of debate amongst staff in intensive care with concerns about open visiting including increased workload and interruptions to normal routine [1]. This is consistent with the views of staff at our own unit who, in appreciative enquiry, have expressed mixed opinions about extending visiting times. Extending visiting times is only part of a wider project to improve the way relatives experience intensive care whilst ensuring both medical and nursing staff feel supported, creating an environment for optimal communication.
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P577

Evolving outcomes in the ICU: family ward rounds improve satisfaction year on year

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Introduction Patient satisfaction is a crucial part of clinical care and there is now increasing recognition of the importance of family involvement and satisfaction in the provision of care for the critically ill. Since 2012 our unit has introduced a consultant-led family ward round (FWR), to enhance and standardise communication and improve satisfaction. Following introduction of the FWR we have audited family satisfaction using the validated FS-ICU questionnaire [1].
Methods This was a prospective study of relatives' satisfaction for patients completing their critical care episode. The questionnaire was completed anonymously and data collected. This was a pragmatic study, no changes were made to communication strategies.
Results There is a high degree of satisfaction across all domains of the FS-ICU including treatment of family and provision of information (Figure 1). One hundred per cent found FWR to be helpful, only 55% had anticipated this. Fifteen per cent changed their perception of critical care. It enabled 15% to raise new concerns. One hundred per cent were able have questions answered satisfactorily. Linked to the FS-ICU, we have seen marked improvements in decision-making and satisfaction.
Conclusion We have shown progressive improvement over 3 years across all domains. Marked improvement in information provision and decision-making support from 53% to 96% over 3 years since introducing the FWR correlates with the improved overall satisfaction (Figure 1). Interestingly FWR is more helpful than relatives anticipated. The FWR was very well received and our results suggest an unrecognised need is being met. Because this was a pragmatic study, we feel this is a true representation of family satisfaction. It is encouraging that communication, information and decision-making support continue to improve. They have become embedded in the fabric of our critical care practice and lead to marked improvement in satisfaction for families.
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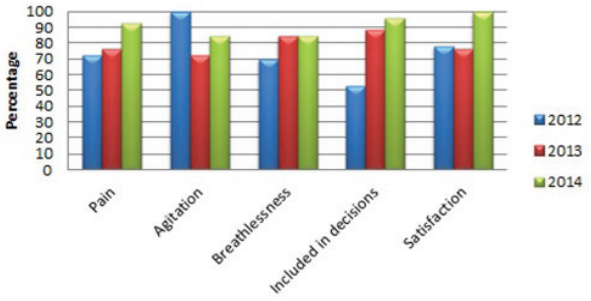


Figure 1 (abstract P577). Trends in family satisfaction.

P578

Bereavement care in UK ICUs: a national survey

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Introduction For the families of critically ill patients, the death of a loved one in the ICU is often an unexpected and traumatic event, characterised by difficult decisions regarding withholding or withdrawing life-sustaining therapy. Increasingly the importance of bereavement care (BC) in the ICU is being acknowledged, although reports continue to highlight the inadequacies around end-of life care in the critical care environment. In 1998, the Intensive Care Society (ICS) published guidelines mapping out BC in the ICU [1]. We aimed to compare BC in ICUs across England against the recommendations set out by the ICS.
Methods All adult ICUs in England were contacted over a 2-week period, using a standardised questionnaire based on the nine domains identified by the ICS. All answers were collected anonymously using SurveyMonkey®. An 80% compliance rate was deemed acceptable.
Results From the 148 ICUs identified, 113 answered the questionnaire (76%). Forty-three per cent of the responders had access to training in BC and in communication skills, and 54% had a named member of staff responsible for training, writing, auditing and developing the

BC policy. When asked about the presence of a written BC policy only 45% responded positively, and even less (19%) had provisions for audit and development of the service. Information to staff about cultural and religious rites around the time of death, and to relatives on what to do after a death was available in 81% and 96% respectively. The general practitioner was informed of the deaths taking place in the ICU in 77% of the cases. In more than 70% of the participating ICUs, efforts were made to ensure privacy of the grieving relatives and to have dedicated follow-up facilities for the bereaved. Even though staff support programmes were recognised as paramount, only 54% of the ICUs had formal ones set up.

Conclusion This is the first national audit of BC in the ICU since the initial ICS guideline publication. Even though most ICUs provided relatives with information around the time of death, training, auditing and adequate facilities do not meet the recommended standards. The lack of adherence is definitely multifactorial and requires further research. In the meantime, vigorous implementation of these guidelines is warranted in order to ensure optimal care for the bereaved families.

Reference

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