



Outcomes of Laparotomy at a Large Referral Center in Rwanda

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ABSTRACT

Background: A large burden of surgical disease is found in low- to middle-income countries, but only 3.5% of the 234 million major operative procedures performed annually in LMICs due to many challenges. Rwanda faces similar challenges observed in many other LMICs. One common major procedure that can give an indication of surgical provision is laparotomy, which has a high mortality rate in many Sub-Saharan African countries. However, little data exists on the outcomes of laparotomies in Rwanda, at all levels of surgical provision.

Methods: This was a retrospective cohort study of patients who had laparotomy at the Centre Hospitalier Universitaire de Kigali (CHUK) between 2011 and 2013. Cases were identified using the operative logs. Patient characteristics and outcomes were collected from charts.

Results: Records of 1276 laparotomy patients were analyzed; 827(65%) from general surgery and 449 (35%) from obstetrics and gynecology. Most patients transferred into CHUK, 1093(86%). The postoperative complication rate (POCR) was 29% (n=376) and the postoperative mortality rate (POMR) was 12% (n=153). Common predictors for POCR were home province, needing ICU care and having generalized peritonitis. General surgery patients had higher POCR if they had a high ASA score (OR 1.30 (95% CI: 1.12, 1.49)), were operated on between 12 and 6am (OR 1.99 (95% CI: 1.15, 3.45)) or had a pediatric congenital condition (OR 2.99 (95% CI: 1.04, 8.55)). ObGyn patients were affected by acuity of presentation (OR 4.47 (95% CI: 1.43, 13.98) and having a perforated organ (OR 5.13 (95% CI: 1.18, 22.23)). ASA score, home province and needing ICU care were significant predictors of high POMR in both groups. Pediatric patients with congenital disorders had an OR of 41.47 (95% CI: 4.47, 384.64)). ObGyn patients with generalized peritonitis had a significantly high OR of 14.90 (95% CI: 1.63, 136.5)).

Discussion: The POCR and POMR observed were consistent with rates observed in previous studies from other sub-Saharan countries, which ranged from 14-33% complications rates and 10-30% mortality rates. POMR and POCR provide reliable and cost-effective metrics that are measurable and traceable, providing vital information about success or failure of implemented policies. Our study suggests hospital-specific and community level socioeconomic influences can be associated with surgical outcomes. Since provision of surgical care at the district hospital level may minimize delays in care provision, addressing district level socioeconomic and hospital factors may facilitate a holistic approach to improvement of surgical care in Rwanda.

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GLOSSARY OF ABBREVIATIONS

ANOVA – Analysis of Variance

CHUB – Centre Hospitalier Universitaire de Butare

CHUK – Centre Hospitalier Universitaire de Kigali

DALYs – Disability-adjusted life years

DH – District Hospital

DHS – Demographic and health survey

GP – General practitioner

HC – Health center

ICU – Intensive care unit

KFH – King Faisal Hospital

LMICs – Low-to- middle-income countries

MDG – Millennium development goal

MOH – Ministry of Health

NOS – Not otherwise specified

ObGyn – Obstetrics and Gynecology

PACU – Post-anesthesia care unit

PMH – Past medical history

POCR – Postoperative complication rate

POMR – Postoperative mortality rate

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INTRODUCTION

Many of the contributors to global morbidity and mortality, which include trauma, cancer, obstetric complications, cataracts and glaucoma, congenital anomalies, acute abdominal conditions, and perinatal conditions, are potentially amenable to operative intervention [29]. A significant burden of surgical conditions, including obstetric problems, account for 11% of the world's disability adjusted life-years (DALYs) and are found in low- to middle-income countries (LMICs) [29, 40]. Despite this reality, only 3.5% of the 234 million major operative procedures performed annually, are performed in low-income countries, which account for one-third of the global population and a majority of the global burden of disease [29, 48]. This leaves millions of people without access to surgical services, with millions more being subjected to poor surgical and anesthetic conditions. As the burden of non-communicable disease, such as cancer, trauma, and obstetric complications, begins to surpass that of communicable diseases, there is an epidemiological shift that has resulted in increased surgical need in low and middle-income countries (LMICs) [29, 48].

Deficiencies in access to and provision of surgical care in LMICs are widely recognized; including but not limited to poor infrastructure, limited human resources, poor institutional funding and many other socioeconomic factors directly influencing patients. All these factors provide avenues for health system strengthening [45, 46]. Nevertheless, despite the awareness and benchmarks generated by the Millennium Development Goals, most sub-Saharan African nations have a negative annual growth rate in the number of physicians compared with their population growth rate [12]. These trends raise concerns about the morbidity, mortality, and DALYs lost due to injury and diseases requiring surgical treatment in sub-Saharan Africa.

Furthermore, with increasing efforts to privatize healthcare costs by introducing fee-for-service procedures in poor countries, surgery is becoming less available for the poor population [15]. Out-of-pocket payments for treatment and for the materials needed during surgical procedures are commonly requested from the patients themselves, thereby limiting their access to necessary medical attention. In some places even vital operations are performed only after a prepayment

for surgical materials. These problems and many more are prevalent in Rwanda, much like they are in many other sub-Saharan African countries.

Country overview

Rwanda is a small, land-locked country in Central Africa, consisting of only 26,338 square kilometers of mountainous terrain [40]. According to the most recent census conducted in 2010 the nation's population is 10,746,311 [38]. Kigali, Rwanda's capital and largest city, is centrally located and has a population of over 1 million people. Since 2006 Rwanda is now comprised of five provinces, from the former 12; named North, South, East, West, and Kigali Provinces, which are further divided into 30 administrative districts.

In 1994 the country suffered from a genocide that left the nation and its infrastructure debilitated. The health care system was not spared, experiencing losses of human resources, funding and physical infrastructure [40]. Political pressures also precipitated changes in the management of the health care sector. In an effort to shift power from a select controlling group to the locally elected representatives in the districts, the government adopted a policy of decentralization and redistricting [40]. Subsequently, the responsibility for health and social services was placed in the hands of the locally elected populations. However, since re-defining the districts in 2006 the health officials also now report to the Republic of Rwanda Ministry of Health

From 2000 to 2010, even up to this day, Rwanda implemented and continues to implement comprehensive health sector reforms to strengthen the public health system, with the aim of reducing maternal and newborn deaths, as well as many other improvements in national health [7, 12]. Although premature mortality rates have fallen precipitously in recent years, and life expectancy has doubled since the mid-1990s [6], Rwanda's mean life expectancy remains low, at 64.5 years. Rwanda's maternal mortality rate is 1,300 per 100,000 and the infant mortality rate is 72 per 1,000 live births. The number of physicians is 0.5 per 10,000 population and the number of hospital beds is 0.0017 per 100,000 population, both significantly lower than that of the Americas and the global mean [40, 49].

Healthcare in Rwanda - Surgery

The country has a total of 48 hospitals (including 1 military/police hospital and 5 referral hospitals – one referral hospital is for mental health), 465 health centers, 15 prison dispensaries, 137 private dispensaries, 252 health posts, 84 private clinics, 15 community-owned health facilities and 20 voluntary counselling and testing centers [31, 32]. The district hospital (DH) is the lowest level, above health centers, with inpatient services. A DH is defined by the Ministry as an institution that includes all of the following components: inpatient and outpatient services, surgery, laboratory, gynecology and obstetrics, and radiology [31-33]. However, the scope of provision of these services is not clearly defined.

Despite major gains in health indicators, Rwanda still suffers from severe deficiencies in surgical care provision [8, 14]. Recent household surveys in Rwanda show that greater than 30% of deaths were associated with surgical conditions; with an estimated operative need at 6.4% of the population, which is twice the HIV prevalence in Rwanda, estimated at 3.0% by the demographic and health survey (DHS) of 2010 [29, 45]. What is further concerning is that nearly 80% of the lifetime operative conditions (and well >80% of the operative conditions in the previous year) noted in individuals younger than 45 years of age, comprising Rwanda's key economic demographic [45, 46].

Despite this situation, Rwanda has only 124 operating rooms, about 50 full-time surgeons and 12 anesthetists, most of whom are located at the referral hospitals in Kigali; on a per-capita basis, there were 0.49 surgeons per 100 000 persons, 0.15 general surgeons per 100 000 and 0.09 orthopedic surgeons per 100 000 and no Rwandan pediatric, cardiothoracic, plastic or oncological surgeons (Table 1) [30, 44, 49]. According to a survey by Petroze et al anesthesia care was primarily provided by anesthesia technicians, of which there were only 13 trained anesthetists [49]. This serious shortage meant that at least six of 44 hospitals had no trained anesthesia provider of any kind. Their survey also noted that only one hospital reported that general doctors provided anesthesia care [49].

Despite these deficiencies, data from the Rwanda ministry of health (MOH) shown in table 2 illustrates that 75 177 surgical procedures (major and minor) were recorded in 2013 in Rwanda,

with 64% of these being gynecological (mostly caesarean sections), followed by hernia repairs, cataracts and osteosynthesis surgeries [32, 33]. Their evaluation of surgical registers and annual hospital reports at the referral hospitals (CHUB Annual Report 2009, KFH and CHUK Annual Report 2010) showed that 82.5% of major surgical procedures were performed at DHs [47, 49].

Provision of safe surgery and anesthesia at DHs requires high-quality trained personnel and infrastructure. However, Notrica et al noted that most hospitals reported lack of continuous access to electricity, water, oxygen, and monitoring equipment for their operating rooms. In fact, all of the hospitals reported a lack of supplies that are important and/or critical for providing surgery [40]. Hospitals that had sufficient equipment reported an inability to use it consistently owing to either lack of training on how to use the equipment safely or how to maintain it [40]. Furthermore, DHs are predominantly staffed by general practitioners (GPs) and nurses. This ultimately leads to provision of limited surgical and anesthetic services, of generally low quality at the DH level. Some surgical services, such as operative trauma and major laparotomies are neglected entirely.

Healthcare in Rwanda - Obstetrics and Gynecology (ObGyn)

Since the 1994 genocide Rwanda has made massive strides in improving its health indicators, especially maternal mortality; being one of eight sub-Saharan African countries to have annual reductions in their maternal mortality ratio (number of maternal deaths per 100 000 live births) of Millennium Development goal (MDG) 5 [26, 57]. However, it still has one of the highest maternal mortality ratios in the world, estimated between 249–584 maternal deaths per 100,000 live births [25]. In a 2012 survey Joharifard et al noted that even though the 2010 DHS shows improvement in virtually all maternal health indicators, highlighted by the 98.0% of women who reported receiving some prenatal care, still only 68.9% of Rwandan women reported delivering in a health facility [25, 50].

Although the absolute numbers of deaths due to abortion, maternal hemorrhage, and hypertensive disorders of pregnancy have decreased in real terms, these causes remain important,

collectively accounting for nearly 50% of all deaths [26, 51]. Given the increasing rates of cesarean delivery, globally and in Rwanda, postoperative complications from cesarean delivery are now a serious concern, particularly postoperative infections, whose rates range from 4.6% for women undergoing elective cesarean to 20%–85% for women undergoing cesarean delivery after labor or rupture of membranes [34].

Obstetric care providers at the point of presentation for patients, at community health centers in Rwanda, are nurses with one or two years of general health training, who refer complicated cases to GPs – with no specialized ObGyn training – at DHs [51]. There are only 20 full-time consultants in ObGyn in the entire country, of which 14 work in Kigali [49]. Puri et al observed significant knowledge gaps by the care providers at the community health centers and questionable referral patterns [51, 52]. There are severe infrastructural, human resource and financial challenges. Some of these challenges include delays in seeking health care by women and their families, transfer delays and low quality care - shortages of equipment and supplies, inadequately trained staff, no drugs or blood supply, and poor staff motivation [50]. These challenges are particularly concerning as most surgical care in Rwanda is obstetric.

Nonetheless, Rwanda recognized these challenges and began implementing policies to mitigate these obstacles. They integrated the traditional birth attendants into the village community health system, regulated the ambulance system – for example they subsidized 90% of the ambulance cost through their community health insurance plan – and they improved quality of care by training staff on hygiene and professionalism [50]. The process to improve ObGyn care in Rwanda is an ongoing long-term process.

Motivation for study

One common procedure that frequently necessitates transfer from DHs to referral hospitals is laparotomy. A number of problems can be encountered intra-operatively and post-operatively that can contribute to adverse events, which range from wound infections to death [37]. Although these adverse outcomes are generally related to underlying pathology,[9, 20, 27] the co-morbid conditions, technique or surgical expertise and post-operative care also contribute [37].

Furthermore, in emergency settings laparotomy can be associated with high mortality rates [11,

35, 42, 56, 58, 59]. Previous studies indicated that mortality following emergent laparotomy ranges from 10-30% for all patients [5, 23, 35, 41, 53, 56, 59], and even higher mortality rates of 42% in octogenarians [11].

To date no studies have described the mortality and complication rates following laparotomy in Rwanda. This study was part of a larger, on-going, study looking at surgical provision throughout the different levels of care in Rwanda's referral system. It aimed to quantify the postoperative mortality rates (POMR) and postoperative complication rates (POCR) of laparotomy at one the Rwanda's four national referral hospitals, CHUK, and identify the patient and hospital factors that contribute to these adverse events. Furthermore, the study aimed to characterize regions and districts according to publicly available demographic and economic data to determine if clinical factors related to transfer can be correlated with these general statistics. The objective was to identify actionable information that will be useful in improving surgical care in Rwanda, not only at national referral hospital level, but at the DH level as well.

METHODS

Design

This study was a retrospective cohort study of patients undergoing laparotomy at Centre Hospitalier Universitaire de Kigali (CHUK) over a 2- year period (September 2011 through August 2013).

Setting

Rwanda's healthcare system is decentralized and multi-tiered, comprising of 18 dispensaries, 16 prison dispensaries, 34 health posts, 430+ health centers, 39 district hospitals (lowest level with inpatient services) and 5 national referral hospitals (specialized inpatient and outpatient services) [54]. The study was conducted at CHUK one of Rwanda's four national referral hospitals. CHUK is a 560 bed, public hospital affiliated with the National University of Rwanda. It is one of the biggest hospitals in Rwanda. It is located in Kigali the capital of Rwanda. Of the 5 referral hospitals in Rwanda, only one other national referral hospital is located outside Kigali, Centre Hospitalier Universitaire de Butare (CHUB) in the Southern Province.

Data extraction and management

Patients were identified from the operative logs and a review of their medical records at CHUK was conducted. All patients who underwent a laparotomy from September 2011 to August 2013 were included in the study. This included both the general surgery patients and the obstetrics and gynecology (ObGyn) patients. Patients with missing charts were excluded from the final analysis. If a patient had more than one laparotomy only the first laparotomy at CHUK was analyzed. Study data were collected and managed using REDCap (Research Electronic Data Capture) electronic data capture tools.[22]

Variables

Information collected from the patients' charts included demographic information (including gender, age, insurance status, occupation and home province, district and sector), transfer information and clinical data. The clinical data collected included past medical history, past surgical history, clinical course at district for transferred patients and clinical course at CHUK.

Outcome measures

The primary outcomes were in-hospital postoperative complication rate (POCR) and in-hospital postoperative mortality rate (POMR). Length of stay was a secondary outcome measure.

Complications were defined as any negative clinical outcome according to the surgeon or patient [37]. Issues that generally led to deviation from a normal postoperative course, requiring further diagnostics, treatment or procedures not otherwise indicated at presentation.

Statistical Analysis

Given that CHUK is a referral center, approximately two-thirds of patients undergoing laparotomy have transferred from other hospitals. A 10% mortality rate for all laparotomy patients was estimated in keeping with the data cited previously [5, 56]. To detect a 15% difference in mortality rate between transferred and non-transferred patients, with 90% power, the study was estimated to require a total of 516 patients.

Postoperative complication and in-hospital mortality frequencies, as well as median and mean length of stay (excluding deaths) for the entire cohort were calculated and analyzed, stratified by transfer status, acuity of presentation, operative service, age group, home province, level of training of surgeon, time of day of operation and whether they require ICU care postoperatively. Student t-test and one-way ANOVA were performed to note for any differences within groups.

Multivariate logistic regression was performed using a model that included these variables, as well as prior surgical status, ASA class, gender, primary diagnosis and estimated time to presentation. The variables contained in the model were selected a priori before initiation of analysis since they represented elements in the health system of Rwanda that could provide actionable information. General surgery patients were analyzed separately in the multivariate logistic analysis from the ObGyn patients since initial analysis revealed significant confounding based on the operative service.

Backwards, stepwise generalized linear mixed (GLM) regression was performed to identify the best-fit model for length of stay. The initial model included the same variables as those used in the complications and mortality logistic regression.

Using publicly available data from the Rwanda MOH and National Statistics office, district specific characteristics were identified from the 2012 DHS. A backwards, stepwise GLM regression analysis of these characteristics with POMR and POCR as dependent variables was performed for all the 30 districts.

All analyses were conducted using STATA 13.0 statistical package. Mapping was performed with QGIS 2.6.

RESULTS

Clinical characteristics

The operative log review identified 1542 laparotomy cases over the two-year period, 1071 (69%) general surgery patients and 471 (31%) ObGyn patients. 1276 (83% of 1542) had charts available for data extraction, of which 827 (65% of 1276) were general surgery patients and 394 (35% of 1276) were ObGyn patients (Table 1). The mean age was 32.1 years. 516 (62% of 827) of the general surgery patients were male, making it 40% male for the entire cohort of 1276 patients. 1209 (95%) of the cohort was insured predominantly with the community insurance, especially since the most of the patients were poor peasant farmers, 495 (39%) individuals. 972 patients (77% of the cohort) were deemed emergency cases, with a mean ASA class of 1.80.

DH Surgical care

Table 1 further shows that 1093 (86%) of the cohort came as transfers/referrals to CHUK. These transferred/referred patients mostly came without documentation – only 381 (35%) overall had a transfer document and 313 (30%) had their DH medical history properly recorded in their charts at CHUK. Furthermore, only 120 (11%) of the 1093 transferred/referred patients had received any surgery at the DH level, 93% of whom had been transferred due to postoperative complications.

The spectrum of surgical care provided for the patients transferred is shown in figure 1. Most of the procedures performed were ObGyn operations, mostly caesarean sections. Consequently, most of the complications observed in this group were ObGyn related (figure 2).

Pattern of transfer/referral

The major proportion of patients that came to CHUK for laparotomy came from the Eastern and Northern provinces and some from DHs in the Kigali area (figure 3). Smaller proportions came from the Western and Southern provinces since CHUB caters to some of this catchment area. However, the patients who developed the most postoperative complications had been transferred from the Western and Southern provinces (figure 4). Although, the Western and Southern provinces have some DHs which transferred high POMR patients, most of the high POMR transfers came from the Eastern province and some from Kigali (figure 5).

Spectrum of operations performed at CHUK

Lavages/Washouts were the most common procedures performed, since in many cases no obvious pathology was identified (figure 6). The majority of the cases were performed by general surgery residents as the primary surgeon. For all general surgery cases performed, residents performed more cases than the consultant (attending) surgeons. A similar trend was observed for the ObGyn cases where the residents performed most of the cases as the primary surgeon.

Overall complications and Mortality

The overall POCR for the study was 29.47% (n=376), while the POMR was 12% (n=153). Of the 153 patients that died 90% (n=138) died within 30 days; the mean survival time was 12 days, while the median was 6 days. Figure 7 illustrates the various complications noted in the study as percentages of the entire cohort. The most common complication was unplanned reoperation, 14% (n=183).

As illustrated in figure 8 the complication rate and mortality varied with the variables selected a priori for analysis. The general surgery patients had significantly higher POCR and POMR, 34.7% and 15% respectively (p-value<<0.05 for both). Overall figure 8 shows that referred/transferred patients (13% mortality), emergency patients (13.48% mortality), older patients greater than 65years (19.7% mortality), patients from the northern province (15.38% mortality), those that were operated by a general surgeon (16.97% mortality), patients operated between 12am and 6am (15.17% mortality) and patients that needed admission to the ICU (53.64% mortality) had significantly higher mortality rates (p-values<<0.05 for all categories).

The logistic regression models in table 4 illustrate that the patient groups had some similar predictors for developing complications and for mortality, but there were also notable differences. Common predictors for developing complications were home province, needing ICU care and having generalized peritonitis. Besides these common factors general surgery patients were also predisposed to developing complications if they had a high ASA score (OR 1.30 (95% CI: 1.12, 1.49)), were operated on between 12 and 6am (OR 1.99 (95% CI: 1.15, 3.45)) or had a

pediatric congenital condition (OR 2.99 (95% CI: 1.04, 8.55)). ObGyn patients were negatively affected by acuity of presentation (OR 4.47 (95% CI: 1.43, 13.98) and having a perforated organ (OR 5.13 (95% CI: 1.18, 22.23)). There was favorable OR when the primary surgeon was a resident for the general surgery patients with OR of 0.50 (95% CI: 0.35, 0.72).

Similarly with mortality, common factors were present, with some group specific differences. ASA score, home province and needing ICU care were significant predictors of mortality in both groups. Pediatric patients with congenital disorders had an OR of 41.47 (95% CI: 4.47, 384.64)). ObGyn patients with generalized peritonitis had a significantly high OR of 14.90 (95% CI: 1.63, 136.5)).

Length of stay

The mean length of stay was 18.29 days, while the median was 10 days (IQR: 6-22). Figure 9 illustrates the univariate analysis results for length of stay. Very similar trends to those observed with POCR and POMR were observed, especially when median length of stay was the measure used. General surgery patients (median 12 days), referred/transferred patients (median 11.5 days), emergency patients (median 10 days), older patients greater than 65years (median 14 days), patients from the eastern province (median 13 days), those that were operated by a general surgeon (median 13.5 days), patients operated between 6am-12pm (median 12 days), patients who had a surgery at the district hospital prior to admission at CHUK (median 19 days) and patients that needed admission to the ICU (median 23 days) had significantly higher median length of stay (p-values<0.05 for all categories).

The regression analysis shown in table 5 revealed that for the general surgery patients the significant predictive factors for longer length of stay included longer preoperative time with risk ratio (RR) of 1.01 and a history of previous surgery (RR 1.14), while being male (RR 0.88) and operated by a resident (RR 0.89) predicted shorter length of stay. Length of stay for the ObGyn patients was significantly associated with ASA score (RR 1.09), referral/transfer (RR 2.56), preoperative time (RR 1.01) and having had surgery at the district hospital (RR 1.81).

Linking outcomes to districts

The regression analysis using publicly available data from the 2012 DHS shows that for the cohort district level employment (RR 1.06), literacy (RR 1.04) and access to improved water (RR 0.98) were significantly associated with transferring patients that develop complications (Table 6). For the general surgery group the same factors were significant with risk ratios of 1.04, 1.04 and 0.98, respectively. Districts that transferred ObGyn patients that developed complications were characterized by increased access to skilled delivery (RR 1.04), extreme poverty (RR 0.96) and extended times to HCs (RR 1.06).

The groups had some similar predictors for mortality (Table 7). Overall POMR were associated with district level extreme poverty level (RR 0.96), access to improved sanitation (RR 1.03) and time to HC (RR 1.03). Only time to HC was significant for the general surgery group (RR1.03), while extreme poverty (RR 0.92), access to improved water (RR 1.05), access to improved sanitation (RR 1.06) and time to HC (RR 1.08) were associated with POMR in the ObGyn group.

DISCUSSION

For a small country such as Rwanda with very limited surgical capacity the focus continues to be the expansion of surgical care provision. However, before services can be extended it is vital to measure the quality of the current services being provided. A necessary component of this quality measurement process is to identify metrics that can be reliably measured over time [47]. However, there is no single health indicator that describes quality of surgical care. Hence, an appropriate indicator of anesthesia and surgery access and outcome would be an important step forward. POMR has been proposed as measurable and traceable, and may be a best first option for following anesthesia and operative related mortality [29]. We further propose that POCR is another measurable and traceable metric that can be considered to assess surgical care. Both of these measures are reliable and cost-effective. Our study suggests that POMR and POCR are metrics that are measurable in a low-resource settings and that can be used to track surgical outcomes and quality.

Postoperative complication rate and Postoperative mortality rate

The POCR and POMR observed in our study were consistent with rates observed in previous disease-specific studies from other sub-Saharan countries, which ranged from 14-33% complications rates and 10-30% mortality rates [1-5, 23, 35, 37, 41, 42, 53, 56, 59]. Although there was a wide spectrum of complications observed, the major complications involved reoperation. Reoperations have been shown to be associated with increased mortality [18]. They can also further strain already limited resources, reducing care that would have been otherwise provided to other patients. Increasing the quality of care to minimize reoperations is essential. Further investigation is necessary into elucidating the factors contributing to this high rate of reoperations.

Although the pathology and patient presentation plays a pivotal role in development of complications, other factors such as surgical technique, postoperative care and coming from a rural area can play significant roles as well [28, 59]. Several factors were identified that significantly contributed to adverse events. Factors, such as the home province, suggest that complications and mortality rates are directly influenced by patient transfer and referral. For each group it was possible to identify the worst affected provinces, such as the Southern province that

has the highest odds ratios for complication rates (3.14 and 3.61 for general surgery and ObGyn, respectively).

Since the Southern province is the only province outside Kigali that has a national referral center, Centre Hospitalier Universitaire, Butare (CHUB), these results could present a deviation in transfer practice, perhaps necessitated by CHUB's limited capacity (420 beds) [36]. However, on February 20, 2014 the MOH issued a new directive that delineates where the DHs should transfer their patients (internal communication). This directive saw more DHs being mandated to transfer to CHUB, which will in effect increase surgical volume at CHUB. Hence, there is a need to re-assess CHUB's readiness for the increased volume in the light of our results.

Furthermore, the patients' status on presentation, such as emergency status, ASA class and underlying pathology, were significant factors in determining complication rates and mortality. Previous studies have shown that emergency major gastrointestinal surgery is associated with significant morbidity and mortality, relative to elective surgeries.[19, 37, 55, 56, 59] ICU admission, a factor that can be attributed to patient presentation, has also been observed in prior studies to influence patient outcome after emergency GI surgery.[19, 59] Hence, as would be expected, the severity of illness at presentation is a substantial contributor to adverse outcomes. Although general surgery had a higher POCR and POMR, it should also be noted that these patients had higher ASA scores and they mostly presented as emergency cases. Emergency cases had a preoperative time of, as many as, 2.5 days. Sometimes at CHUK the patients, even emergency patients, do not go the operating room because of limited space to accommodate them postoperatively in the ward, PACU or the ICU.

The effect of surgical training at CHUK

Surgical experience is vital in providing high quality care. Fully trained surgeons have the skills to treat more complicated and sicker patients, while trainees may not yet possess such abilities. As such, patients had more adverse events if their operation occurred between 12am and 6am, a time when the resident physicians predominantly operated. 29% of the resident cases were performed during this timeframe. As a key teaching hospital for Rwanda's surgical residency program further investigation is necessary to elucidate the factors at play. Possible issues could

be resident fatigue, limited supervision or limited operating room staff and equipment during this timeframe. The challenge faced at CHUK, is something many teaching programs face – how to give the trainees adequate autonomy and exposure without compromising patient safety and quality. As the program matures and evolves we strongly recommend implementation of measures to improve and maintain high quality healthcare provision without necessarily compromising surgical training.

Length of stay

Female gender, prior abdominal surgery, needing surgical care by a surgeon and having a longer preoperative time were associated with longer lengths of stay in general surgery patients, while high ASA score, being a transfer/referred patient, delays in presentation and getting surgery at the district hospital influenced length of stay in the ObGyn group. Prior abdominal surgery presents difficulties during subsequent surgeries, for example due to adhesions, contributing to more sequelae postoperatively. This may explain why patients with prior surgeries required more advanced care by a qualified surgeon and stayed longer in the hospital. As would be expected sicker patients (with high ASA scores, who come in as transfers and delayed care) had a protracted stay in the hospital. However, it is more concerning that preoperative time was a significant factor for both groups. Preoperative delays for various reasons continue to negatively impact patient outcomes at CHUK. Increased hospital stays have been associated with development of hospital-acquired infections in some groups of patients such as trauma patients [43]. Longer stays also create space and resource shortages, leading to backlogs and delays in provision of care to new patients.

Community level influences

The community-level analysis supports widely recognized evidence that employment, literacy, water and sanitation provision, access to healthcare facilities and poverty all influence the quality of health care and health outcomes. This has been demonstrated with many other disease processes such as HIV. Our study supports the fact that not only do factors at individual institutions influence outcomes, but broader, community-wide, socioeconomic influences can be associated with surgical outcomes. It is necessary to investigate any causative relationships these factors may have on surgical outcomes. By identifying the community level influences it will be

easier to implement targeted programs that can have far-reaching benefits within the health sector.

Decentralizing surgical care

There was evidence for significant delay in provision of surgical care from the time of their presentation. Only 2% of the general surgery patients had undergone surgery at the district hospital level, compared to 23% for the ObGyn patients. Previous studies have demonstrated significant deficits in provision of surgical care at the district hospital level [16, 21, 39].

Although there is some indication Rwanda has some capacity for surgical provision at the DH level, the quality and scope of service provision remains unassessed and unmeasured. Increased provision of surgical care at the district hospital level where most patients present would mitigate delays in care provision and reduce surgical need at the referral hospitals.

Provision of surgical care at the district hospital level would provide much needed care at an earlier point in the disease course for many of these patients. In addition, the WHO and other groups have offered international recommendations that district level hospitals provide emergency and some essential surgery and that such hospitals follow guidelines for the provision of safe surgery and anesthesia [29, 40]. Rwanda needs to ensure consistent provision of basic surgical resources, including, without limitation, reliable anesthesia equipment for each operating room, dedicated post-surgery recovery areas and surgical intensive care units with dedicated personnel and monitoring equipment.

Surgical provision at DH level also requires improved human resources at these sites. At present district hospitals are staffed mostly by general practitioners, whose surgical skillset is limited. As Rwanda trains more surgeons it may be prudent to encourage these surgeons to work at the DH level to widen the spectrum of pathologies managed at this level. This approach will further minimize pressure on the referral hospitals, allowing them to focus on smaller populations with more complex issues.

Highest impact programs for increasing surgical capacity will be based on long-term partnerships focused on training of local physicians, thereby increasing information retention and sustain

ability. As noted by Denkelbaum et al, for the implementation of productive programs, there are several important principles: local motivation and accountability, establishment of strong partnerships, understanding the local environment, curriculum development based on local needs and not on western models, early program assessment, and substantial involvement of local partners for program development [12]. They further argue that mature, in-country postgraduate training programs are more likely to reduce the need for foreign training while also generating locally relevant skill sets, augmenting the social accountability of trainees and providing potential hiring opportunities in education [13].

In the meantime to help overcome some of these limitations, task-shifting to non-physicians for some procedures such as caesarean delivery, trauma-related procedures, and emergency disorders has been shown to be feasible, cost-reducing, and well received by physicians in some settings [10]. This could be a viable temporizing measure for Rwanda as it grows and matures its residency programs in the coming years. The Rwanda healthcare system is already structured with mid-level providers at the points of presentation such that task-shifting would not be a drastic shift in practice.

The most obvious strategy is to strengthen existing systems. While human resource challenges receive most attention from governments, efforts to address these should be implemented in tandem with systems-level changes like investment in facilities, establishment of quality systems and determination of processes of care (e.g. equipment repair and maintenance; storage of medicines; infection control) [17, 24]. A major commitment from the Ministry, the National University, the WHO and the international medical community is necessary to facilitate district hospital growth.

LIMITATIONS

This project is observational only; no intervention is tested. Additionally, it relies on descriptive statistics, and can identify correlation between various factors, but cannot identify the causes of patient outcomes. As a retrospective study it relies on pre-collected data, limiting the elements of information that were collected for this study. Nonetheless, we feel that it can help “lay the groundwork” for potential interventions in the future, by providing a clear description of some areas of strength and weakness in the Rwandan surgical care system.

CONCLUSION

As a national referral hospital CHUK treats patients from all over Rwanda. However, it has significant resource limitations such as only having 14 operating rooms, small ICU, limited manpower and limited anesthesia care. This means that appropriate risk stratification of patients is necessary in order to effectively apportion these scarce resources if outcomes for transferred/referred patients are going to improve. Properly identifying sicker patients and those whose care has been significantly delayed before their arrival to CHUK is vital in order to mitigate further delays in their care. Not only will implementation of appropriate risk stratification be to the benefit of the patients, but it will mean efficient and cost-effective appropriation of limited resources leading to higher quality care provision. The delay in provision of surgical care once patients arrived at CHUK influenced POCR, POMR and length of stay. Facilitating expedient door-to-operating room time could mitigate longer hospital stays and minimize complications and deaths.

Rwanda has made strategic moves to improve its surgical capacity by training more surgeons. However, as it moves to decentralize surgical care from the four referral hospitals to the DHs there is a need for concerted efforts to implement a holistic approach that will ensure consistent, reliable surgical care provision. This approach involves strengthening support services, physical infrastructure, supply chains and financing. In addition, execution of community-wide socioeconomic programs in tandem with healthcare-specific programs will provide significant gains across multiple disease burdens. Coupling surgical capacity-building with socioeconomic development will convert the process from a vertical approach to a diagonal approach that benefits numerous elements of the health care sector.

As Rwanda and the global surgery community move towards systems strengthening simple metrics will be necessary to quantify the gains or shortcomings of programs. It is vital to assess the state of surgical provision at the DH level and continue to measure progress. POMR and POCR provide reliable and cost-effective metrics that are measurable and traceable, providing vital information about success or failure of implemented policies.

FUTURE DIRECTION

This surgical outcomes study was intended to build a foundation for ongoing research projects in Rwanda. We hope that it will illustrate ways in which initiatives for surgical outcomes improvement may be pursued over a longer term. We believe that the knowledge produced by this project can help local stakeholders to build on the existing strengths of the Rwandan surgical care delivery system, and design improvements in that system.

Specifically we hope this study can be useful in helping develop and clarify country-level and hospital-level transfer policy for surgical patients. Information obtained in this study can be useful in assisting surgical providers to effectively triage and manage patients needing major surgery at CHUK. Therefore, research into key areas such as emergency and transfer services to get causation data would be a necessary next step. Also, more information is needed to understand the best way forward in improving surgical care delivery, while strengthening surgical training in Rwanda.

Our study suggests significant differences between regions exist. Further research is needed to adequately delineate district level causative factors. This will allow development of strategies to address needs of individual districts with less robust transfer outcomes. It is essential to also pursue further research into the successful transfer strategies of districts with superior transfer outcomes, in order to apply them to other districts

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TABLES AND FIGURES

Table 1: Rwandan government hospital profile [49].

	<i>n</i>	Mean distance to furthest health centre (km)	Population served	Hospital beds	Operating rooms	Operating rooms per 100 000
District hospitals	41	44	9 710 108*	6534	101	1.04
Kigali City	4	27	882 011	640	15	1.70
Northern Province	6	54	1 852 517	1129	16	0.86
Southern Province	10	39	2 355 891	1576	25	1.06
Eastern Province	9	48	2 168 518	1250	17	0.78
Western Province	12	50	2 451 171	1939	28	1.14
Referral hospitals			10 117 029†	1063	23	0.22
CHUK (Kigali City)			6 238 736‡	513	14	0.22
KFH (Kigali City)			10 117 029†	130	5	0.04
CHUB (Southern Province)			3 471 372‡	420	4	0.11
National total			10 117 029†	7597	124	1.22

Table 2: Surgeries performed as per 2013 MOH report [32].

2012	Planned	Urgent	Total
Major Surgery	14613	35050	49663
Minor Surgery	24580	15629	40209
Total Surgeries	39193	50679	89872

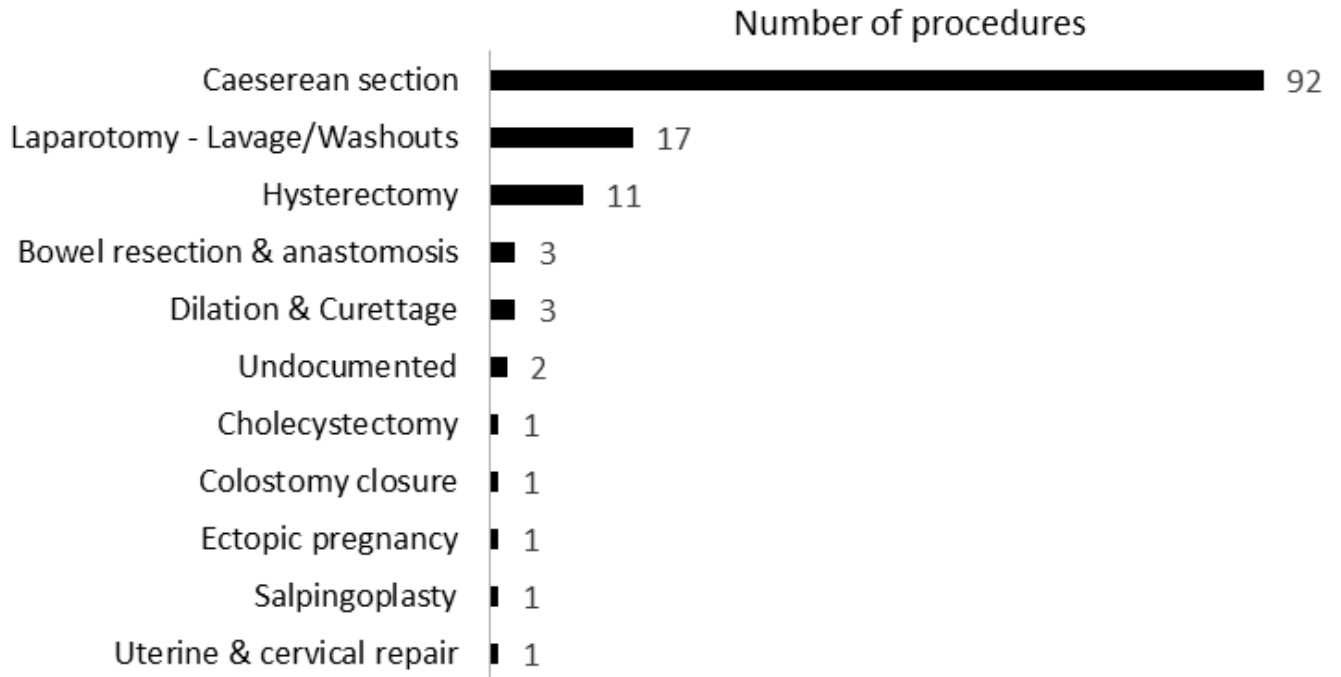
Type of Surgery	2013						%
	District Hospital	Medical Clinic	Military Hospital	Provincial Hospital	Referral Hospital	Total	
Planned interventions							
Major surgery	7349	842	428	3729	7735	20083	39.73
Minor surgery	12132	208	28	4792	3607	20767	
Sub Total	19481	1050	456	8521	11342	40850	
Urgent interventions							
Major surgery	27963	1375	1348	6678	3906	41270	60.27
Minor surgery	8349	353	77	5877	6036	20692	
Sub Total	36312	1728	1425	12555	9942	61962	
Grand Total	55793	2778	1881	21076	21284	102812	100.00

Selected Surgical	2012			2013				%
	Planned	Urgent	Total	Planned	Urgent	Total		
General Surgery	13,047	4,051	17,098	12,609	6,432	19,041	100.00	25.33
Appendectomy	72	74	146	81	113	194	1.02	0.26
Hernia	1913	147	2060	1955	166	2121	11.14	2.82
Laparotomy	246	383	629	613	925	1,538	8.08	2.05
Thyroidectomy	191	5	196	288	3	291	1.53	0.39
Cataract	2,106	0	2,106	2,075	37	2,112	11.09	2.81
Adenomectomy	103	2	105	94	2	96	0.50	0.13
Glaucoma	340	1	341	1	0	1	0.01	0.00
Trachoma	1	1	2	189	0	189	0.99	0.25
Others	8,075	3,438	11,513	7,313	5,186	12,499	65.64	16.63
Gyneco-obstetrical (G-O) Surgery	4,164	37,751	41,915	6,513	41,338	47,851	100.00	63.65
Caesarean Section	2,796	35,617	38,413	4,869	39,452	44,321	92.62	58.96
Hysterectomy	421	341	762	585	181	766	1.60	1.02
Ectopic Pregnancy	49	219	268				0.00	0.00
Other Laparotomies (G-O)	256	356	612	452	472	924	1.93	1.23
Myomectomy	313	48	361	441	38	479	1.00	0.64
Curettage	157	1126	1283	108	1178	1286	2.69	1.71
Fistula Repair	172	44	216	58	17	75	0.16	0.10
Orthopedic Surgery	2,216	3,140	5,356	4,036	4,249	8,285	100.00	11.02
Amputations	153	28	181	167	82	249	3.01	0.33
Osteosynthesis	582	288	870	1,558	692	2,250	27.16	2.99
Other	1481	2824	4305	2311	3475	5786	69.84	7.70
total	19427	44942	64369	23158	52019	75177	100.00	100.00

Table 3: Clinical characteristics of study cohort.

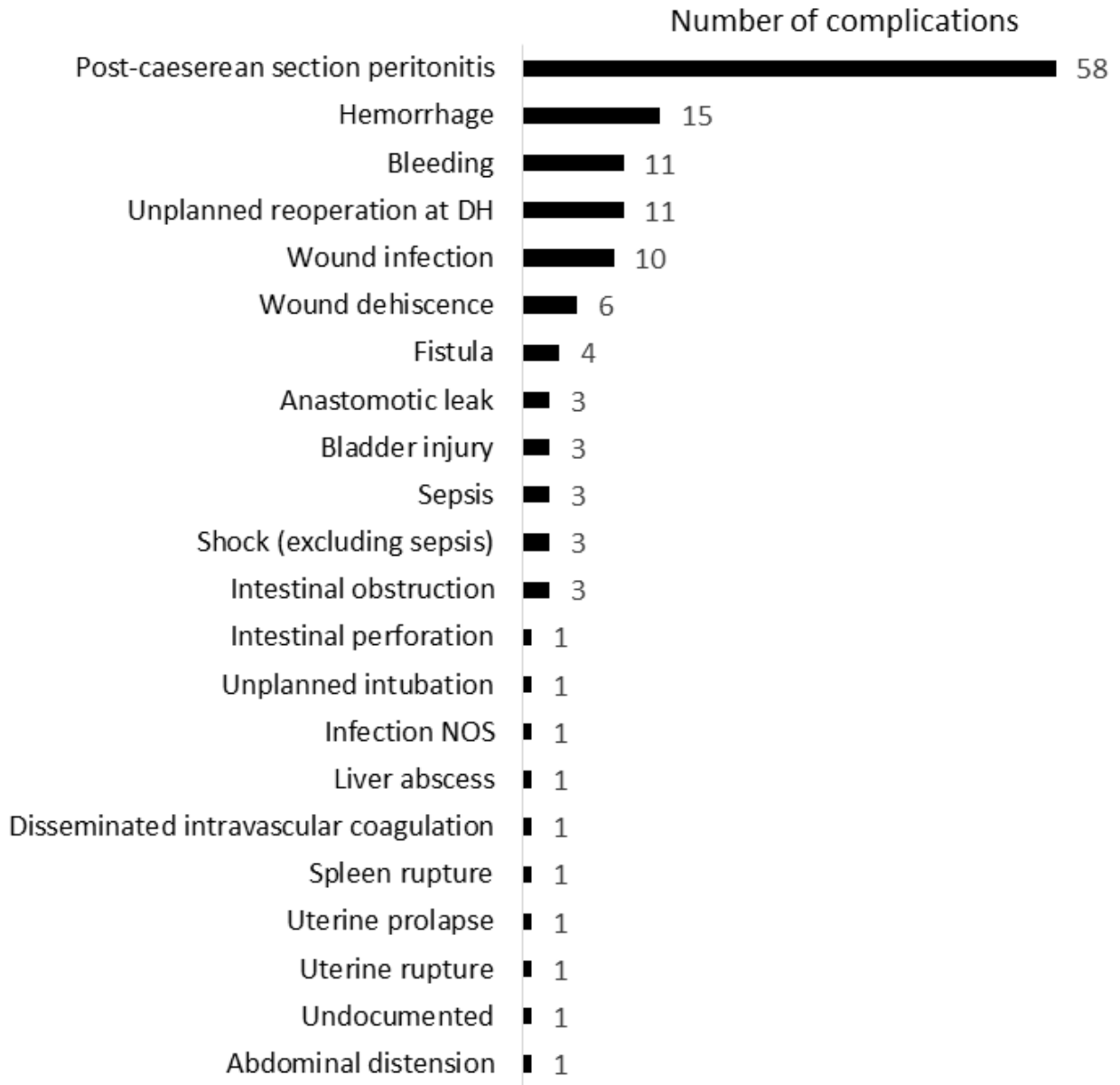
Category		General Surgery	ObGyn	Total
		% (n)	% (n)	% (n)
Number of patients		64.81 (827)	35.19 (449)	100 (1276)
Gender	Male	62.39 (516)	0 (0)	40.44 (516)
	Female	37.60 (311)	100 (449)	59.56 (760)
Mean Age (years)		32.73	31.15	32.1
Insured		92.99 (769)	97.97 (386)	94.75 (1209)
Employment (Farmers)		35.32 (291)	43.77 (172)	38.92 (495)
PMHT of Surgery		10.64 (88)	23.61 (106)	15.20 (194)
Transfers/Referrals		85.13 (704)	86.64 (389)	85.66 (1093)
	Transfer document	12.38 (87)	75.58 (294)	34.89 (381)
	Surgery at District Hospital	2.41 (17)	22.94 (103)	10.98 (120)
	Complications at District	70.59 (12)	96.12 (99)	92.50 (111)
	Prior care documented	19.90 (122)	42.92 (191)	29.58 (313)
Emergency		77.83 (639)	74.16 (333)	76.9 (972)
Mean ASA class		1.96	1.59	1.80
ICU care	MD requested	10.18 (84)	8.28 (37)	9.51 (121)
	Admitted to ICU	9.31 (77)	7.35 (33)	8.62 (110)
	Mean ICU time (days)	8.15	6.07	7.54

Figure 1: Surgical procedures performed at the district hospitals.



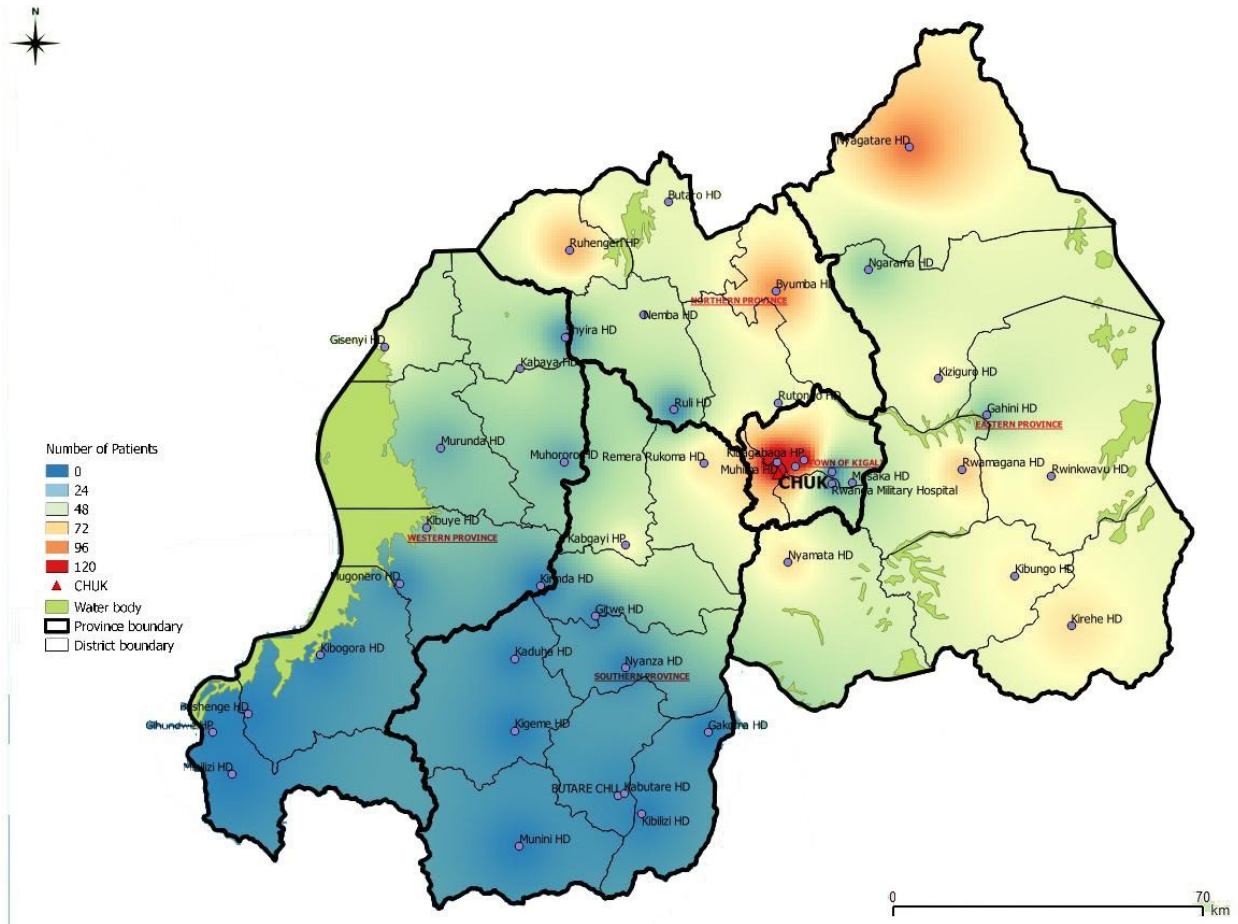
120 patients underwent surgery at the DH level before transfer to CHUK. These 120 patients had at least one procedure each, with some undergoing more. The graph shows the various procedures performed.

Figure 2: **Complications at the district hospitals.**



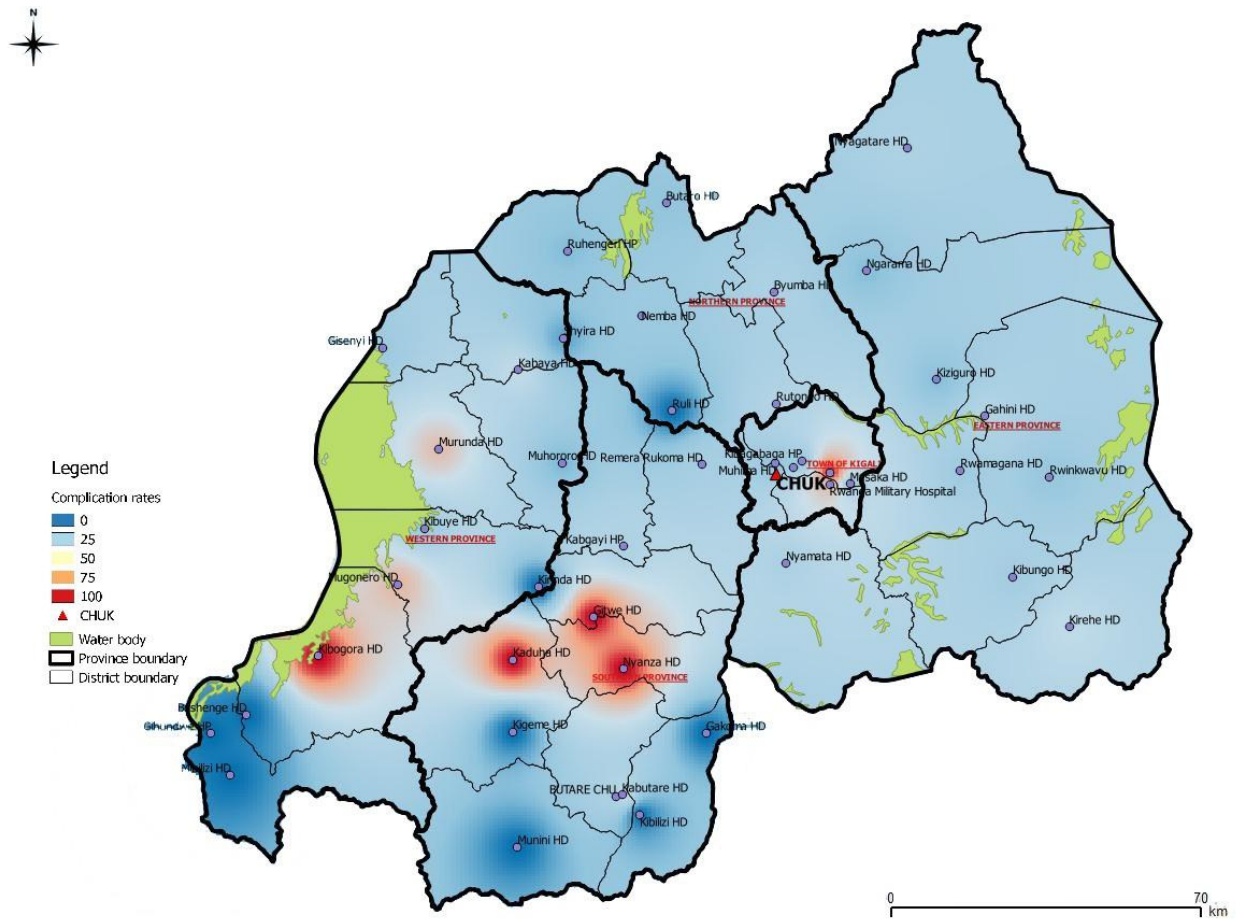
Of the 120 patients who underwent surgery at the DH level before transfer to CHUK, 111 developed at least one postoperative complications. The graph shows the complications recorded in the cohort.

Figure 3: Distribution of patients coming to CHUK for surgical care.



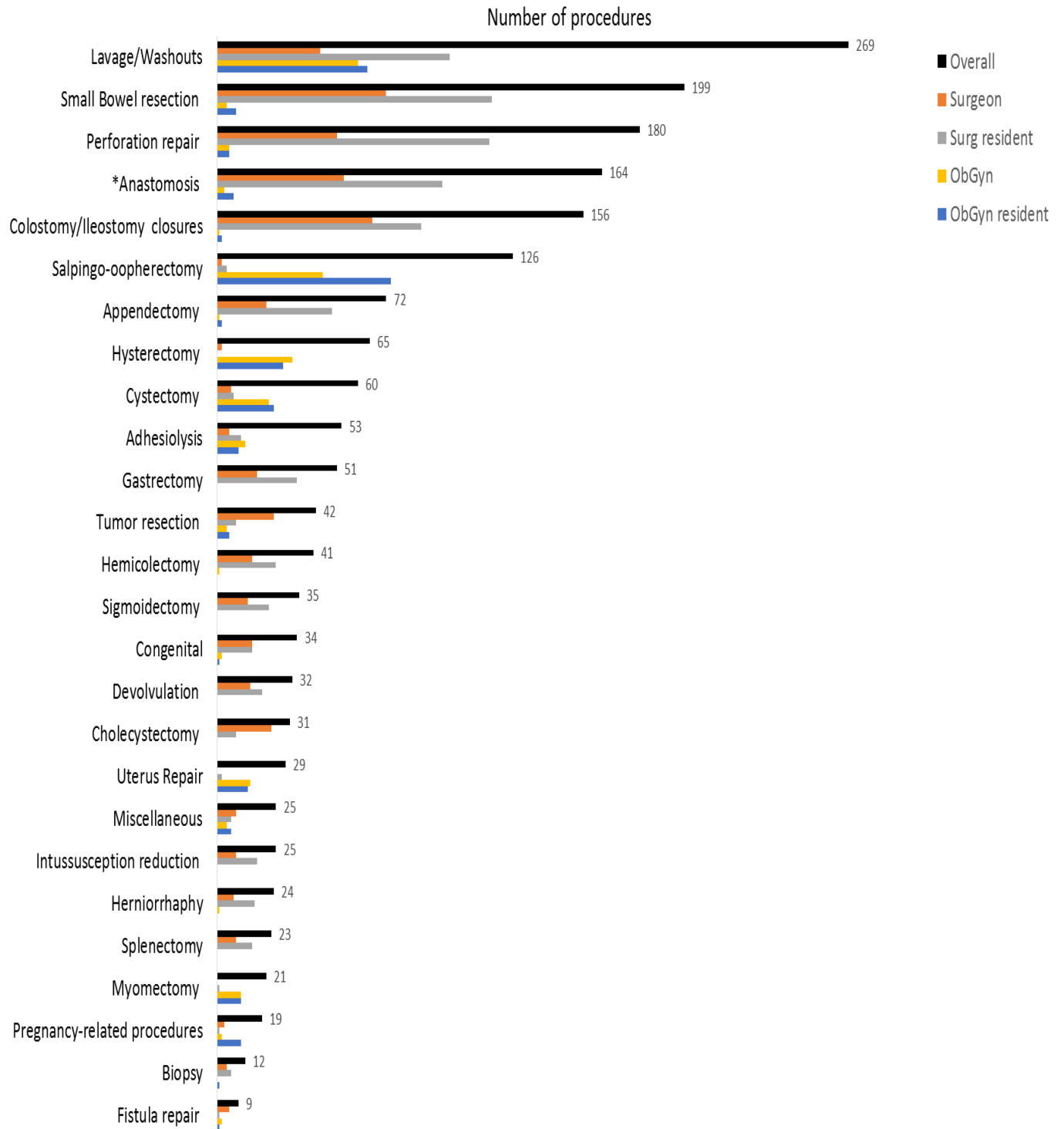
Most of the patients that presented to CHUK came from Kigali, Northern and Eastern provinces. The only other referral hospital outside Kigali was CHUB in the Southern province, at the time of this study.

Figure 4: Distribution of patients, by POCR, coming to CHUK for surgical care.



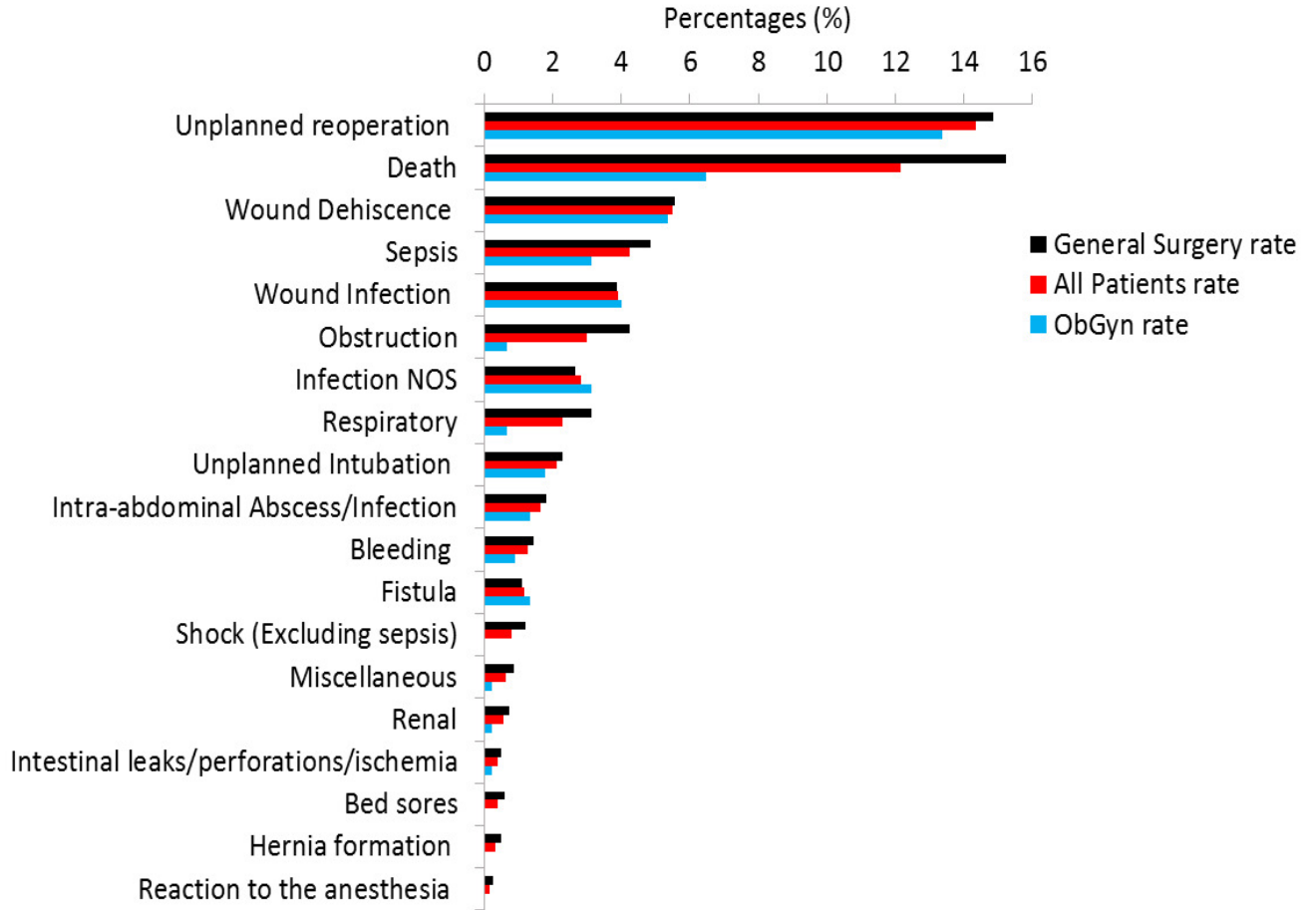
The map illustrates composite complication rates based on the district the patients were transferred from. These complication rates were not normalized to district population, catchment area, patients admitted at DH or district surgical need. Complication rates per district were calculated as number of patients who developed complications as a percentage of total transferred patients. Major lines in the map illustrate provincial borders.

Figure 6: **Procedures performed at CHUK.**



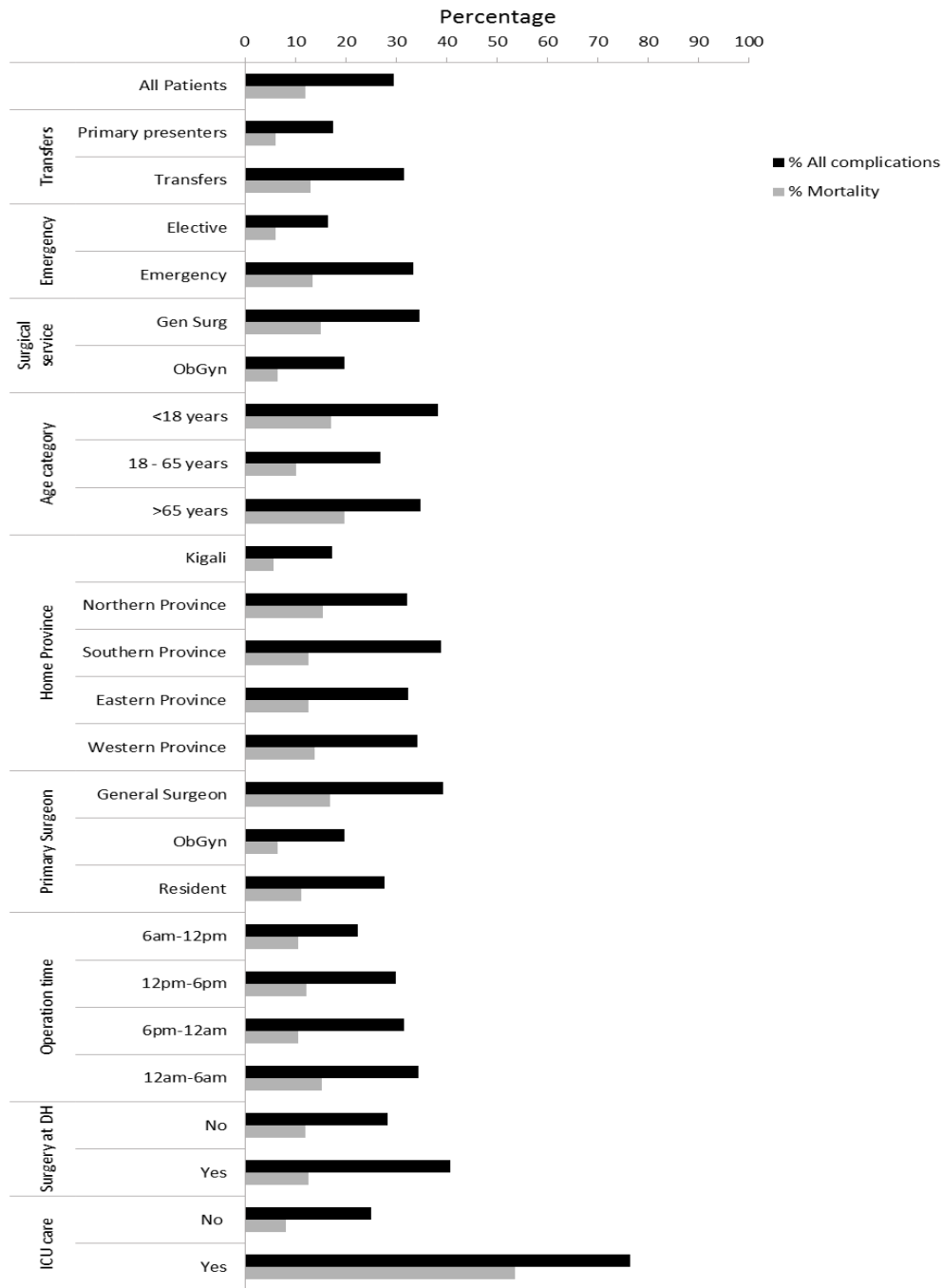
All patients had at least one laparotomy each, with some undergoing further procedures. The procedures are categorized according to primary surgeon.

Figure 7: Spectrum of complications.



Percentage complications as a function of the total cohort of 1276 patients, where 376 (29.5 %) of the patients developed at least one complication. Both surgical services illustrate a similar pattern in the complications observed. The values at the end of the bars represent composite complication rates for all patients, for individual complication types.

Figure 8: Overall complications and mortality.

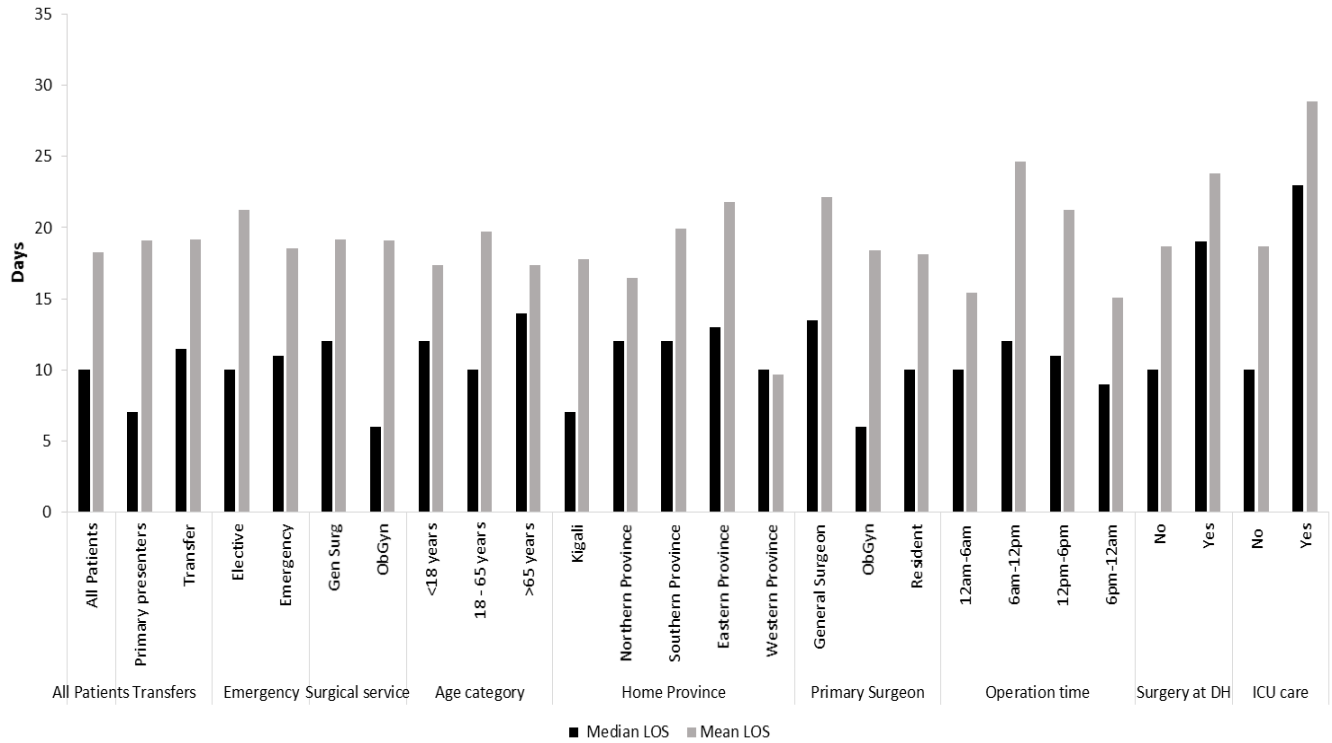


The overall complication rates and mortality rates of the transfers, emergency patients, the two surgical services, different age groups, home provinces, surgical providers, different operative time periods, those who received surgery at the district hospital (DH) and those that received ICU care showed variation between groups. All categories had significant (p -value < 0.05) between group differences except for operative time and surgery at DH mortality rates.

Table 4: Logistic regression analysis of general surgery patients (n=721) and Obstetrics and gynecology patients (n=394). ***p<0.001, **p<0.01, *p<0.05 when compared to the reference group.

Factor	General Surgery		Obstetrics and Gynecology	
	Complications OR (95% CI)	Mortality OR (95% CI)	Complications OR (95% CI)	Mortality OR (95% CI)
Transfer	1.15 (0.65, 2.03)	1.22 (0.53, 2.78)	1.28 (0.26, 6.43)	0.38 (0.06, 2.33)
Prior surgery	1.44 (0.80, 2.62)	0.98 (0.43, 2.23)	1.02 (0.48, 2.14)	1.32 (0.42, 4.11)
Emergency	1.03 (0.58, 1.84)	1.31 (0.58, 2.93)	4.47 (1.43, 13.98)**	2.34 (0.53, 10.34)
ASA Class	1.30 (1.12, 1.49)***	1.55 (1.28, 1.88)***	1.24 (0.94, 1.65)	1.55 (0.99, 2.41)*
Male	0.81 (0.57, 1.15)	0.86 (0.54, 1.36)	-	-
Age				
<18 years	Reference	Reference	Reference	Reference
18 - 65 years	1.12 (0.75, 1.66)	1.13 (0.66, 1.94)	0.27 (0.05, 1.58)	0.36 (0.05, 2.52)
>65 years	1.10 (0.52, 2.35)	1.62 (0.64, 4.06)	0.86 (0.09, 8.19)	1.69 (0.13, 21.16)
Home Province				
Kigali Province	Reference	Reference	Reference	Reference
Northern Province	1.85 (1.07, 3.20)*	2.03 (0.94, 4.39)	0.88 (0.26, 2.92)	1.45 (0.29, 7.18)
Southern Province	3.14 (1.57, 6.30)***	2.42 (0.94, 6.21)	3.61 (1.37, 9.55)**	1.54 (0.31, 7.71)
Eastern Province	2.06 (1.24, 3.41)**	2.13 (1.03, 4.40)*	2.08 (0.99, 4.37)*	1.85 (0.59, 5.86)
Western Province	2.03 (1.11, 3.70)*	1.93 (0.82, 4.58)	3.70 (1.05, 13.02)*	6.29 (1.22, 32.52)*
Surgeon				
General Surgeon	Reference	Reference	1.03 (0.24, 4.53)	2.43 (0.46, 12.88)
Resident	0.50 (0.35, 0.72)***	0.59 (0.37, 0.93)*	0.97 (0.50, 1.88)	11.28 (0.67, 189.03)
ObGyn	-	-	Reference	Reference
Time of procedure				
12am - 6am	1.99 (1.15, 3.45)**	1.50 (0.72, 3.12)	0.94 (0.37, 2.38)	0.48 (0.13, 1.76)
6am - 12pm	Reference	Reference	Reference	Reference
12pm - 6pm	1.55 (0.93, 2.59)	1.53 (0.77, 3.01)	0.77 (0.32, 1.88)	0.51 (0.15, 1.77)
6pm - 12am	1.64 (0.92, 2.92)	1.17 (0.53, 2.55)	0.76 (0.28, 2.05)	0.42 (0.10, 1.82)
Primary Diagnosis				
Appy/Chole	Reference	Reference		
Benign GYN	-	-	Reference	Reference
Peritonitis NOS	3.49 (1.50, 8.19)**	7.60 (0.86, 66.92)	13.53 (4.52, 40.51)***	14.90 (1.63, 136.5)**
Congenital-Peds	2.99 (1.04, 8.55)*	41.47 (4.47, 384.64)***	-	-
Malignancy	1.04 (0.42, 2.57)	8.54 (0.95, 76.99)	2.73 (0.42, 17.57)	5.38 (0.28, 104.24)
Miscellaneous	0.70 (0.21, 2.27)	7.25 (0.70, 75.22)	33.41 (5.96, 187.1)***	0.00 (0.00, 0.00)
Obstruction	1.26 (0.60, 2.65)	7.09 (0.88, 57.25)	-	-
Trauma	1.42 (0.60, 3.37)	2.38 (0.25, 22.67)	1.95 (0.14, 28.06)	5.53 (0.21, 146.33)
Viscus perforation	1.55 (0.71, 3.37)	7.42 (0.90, 61.10)	5.13 (1.18, 22.23)*	8.17 (0.55, 122.08)
Pregnancy	-	-	2.90 (0.70, 12.11)	8.18 (0.70, 95.51)
Time to Presentation	0.99 (0.99, 0.99)**	0.99 (0.99, 1.00)	0.99 (0.99, 1.00)	0.99 (0.99, 1.00)
ICU care	14.5 (6.42, 32.5)***	15.42 (7.88, 30.16)***	2.82 (1.05, 7.58)*	6.80 (2.21, 20.93)***
Surgery at DH	1.20 (0.30, 4.77)	0.61 (0.09, 4.07)	1.39 (0.66, 2.96)	1.12 (0.33, 3.82)

Figure 9: Univariate analysis of median and mean length of stay.



The median length of stay of the transfers, emergency patients, the two surgical services, different age groups, home provinces, surgical providers, different operative time periods, patients who received surgery at the district hospital (DH) and patients that received ICU care exhibited some between group differences. Between-group p-values were <0.05 for all categories except for elective vs emergency.

Table 5: Multivariate regression analysis of LOS for general surgery patients (n=802, r-squared = 0.04) and Obstetrics and Gynecology patients (n=403, r-squared = 0.51). ***p<0.001, **p<0.01, *p<0.05.

Equation	General Surgery		Obstetrics and Gynecology	
	RR	(95% CI)	RR	(95% CI)
Male (vs Female)	0.88	(0.85 – 0.91)*	-	
Prior surgery (Yes vs No)	1.14	(1.09 – 1.21)*	-	
Resident (vs Consultant)	0.89	(0.86 – 0.92)*	-	
Preoperative time	1.01	(1.01 – 1.02)***	1.01	(1.01 – 1.02)***
ASA class	-		1.09	(1.07 – 1.11)***
Transfer (vs Primary Presenters)	-		2.56	(2.33 – 2.80)*
Estimated time to presentation	-		1.00	(1.00 – 1.00)
Surgery at DH	1.18	(1.06 – 1.31)	1.81	(1.71 – 1.91)**

Table 6: Multiple linear regression analysis of POCHR by DHS characteristics, of the 30 districts, for all patients (n=1276, r-squared = 0.34, general surgery patients (n=831, r-squared = 0.30) and Obstetrics and Gynecology patients (n=445, r-squared = 0.44). ***p<0.001, **p<0.01, *p<0.05.

	All Patients		General Surgery		Obstetrics and Gynecology	
Equation	RR	(95% CI)	RR	(95% CI)	RR	(95% CI)
Literacy	1.04	(1.02, 1.05)***	1.04	(1.03, 1.06)***	-	
Access to improved water	0.98	(0.97, 0.99)***	0.98	(0.97, 0.99)***	-	
Total district population	-		-		1.00	(1.00, 1.00)
Access to skilled delivery	-		-		1.04	(1.02, 1.05)*
Extreme poverty	-		-		0.96	(0.94, 0.97)*
Access to improved sanitation	-		-		1.03	(1.01, 1.04)
Time to HC	-		1.01	(1.00, 1.02)	1.06	(1.04, 1.07)**

Table 7: Multiple linear regression analysis of POMR by DHS characteristics, of the 30 districts, for all patients (n=1276, r-squared = 0.37, general surgery patients (n=831, r-squared = 0.20) and Obstetrics and Gynecology patients (n=445, r-squared = 0.52). ***p<0.001, **p<0.01, *p<0.05.

	All Patients		General Surgery		Obstetrics and Gynecology	
Equation	RR	(95% CI)	RR	(95% CI)	RR	(95% CI)
Employment	1.06	(1.02, 1.09)	-		-	
Extreme poverty	0.96	(0.94, 0.97)*	0.97	(0.95, 0.98)	0.92	(0.90, 0.94)***
Access to improved water	1.02	(1.01, 1.04)	1.01	(1.00, 1.02)	1.05	(1.03, 1.07)**
Access to improved sanitation	1.03	(1.01, 1.04)*	1.02	(1.00, 1.03)	1.06	(1.04, 1.08)**
Time to HC	1.03	(1.02, 1.04)*	1.03	(1.02, 1.04)*	1.08	(1.06, 1.10)***