Effect of Cardiogenic Shock Hospital Volume on Mortality in Patients With Cardiogenic Shock

ORIGINAL RESEARCH

Effect of Cardiogenic Shock Hospital Volume on Mortality in Patients With Cardiogenic Shock

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***Background*—**Cardiogenic shock (CS) is associated with significant morbidity, and mortality rates approach 40% to 60%. Treatment for CS requires an aggressive, sophisticated, complex, goal-oriented, therapeutic regimen focused on early revascularization and adjunctive supportive therapies, suggesting that hospitals with greater CS volume may provide better care. The association between CS hospital volume and inpatient mortality for CS is unclear.

***Methods and Results*—**We used the Nationwide Inpatient Sample to examine 533 179 weighted patient discharges from 2675 hospitals with CS from 2004 to 2011 and divided them into quartiles of mean annual hospital CS case volume. The primary outcome was in-hospital mortality. Multivariate adjustments were performed to account for severity of illness, relevant comorbidities, hospital characteristics, and differences in treatment. Compared with the highest volume quartile, the adjusted odds ratio for inpatient mortality for persons admitted to hospitals in the lowest-volume quartile (≤27 weighted cases per year) was 1.27 (95% CI 1.15 to 1.40), whereas for admission to hospitals in the low-volume and medium-volume quartiles, the odds ratios were 1.20 (95% CI 1.08 to 1.32) and 1.12 (95% CI 1.01 to 1.24), respectively. Similarly, improved survival was observed across quartiles, with an adjusted inpatient mortality incidence of 41.97% (95% CI 40.87 to 43.08) for hospitals with the lowest volume of CS cases and a drop to 37.01% (95% CI 35.11 to 38.96) for hospitals with the highest volume of CS cases. Analysis of treatments offered between hospital quartiles revealed that the centers with volumes in the highest quartile demonstrated significantly higher numbers of patients undergoing coronary artery bypass grafting, percutaneous coronary intervention, or intra-aortic balloon pump counterpulsation. A similar relationship was demonstrated with the use of mechanical circulatory support (ventricular assist devices and extracorporeal membrane oxygenation), for which there was significantly higher use in the higher volume quartiles.

***Conclusions*—**We demonstrated an association between lower CS case volume and higher mortality. There is more frequent use of both standard supportive and revascularization techniques at the higher volume centers. Future directions may include examining whether early stabilization and transfer improve outcomes of patients with CS who are admitted to lower volume centers. **(*J Am Heart Assoc*. 2015;4:e001462 doi: 10.1161/JAHA.114.001462)**

Key Words: acute coronary syndromes • cardiogenic shock • hospital volume

Cardiogenic shock (CS) is a highly morbid, often fatal condition for which timely advanced therapy is critical. This syndrome, the hallmark of which is acute myocardial contractile dysfunction with resultant systemic hypoperfusion, is most commonly the result of acute myocardial infarction, decompensated heart failure, postcardiotomy shock, or acute myocarditis. The mortality associated with CS approaches 40% to 60%.[1–4] The current standard of care in CS management includes timely aggressive medical management, revascularization with percutaneous coronary intervention (PCI)[5,6] or coronary artery bypass grafting (CABG),[7] and adjunctive use of mechanical circulatory devices including intra-aortic balloon pump counterpulsation (IABP) and ventricular assist devices.[8–10] A recent database review of the temporal trends in the management of CS complicating ST-segment elevation myocardial infarction from 2003 to 2010 revealed an increase in overall incidence of roughly 55% but with significantly decreased in-hospital mortality, which could be explained by a concomitant increase in the use of early mechanical revascularization and IABP.[11]

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Despite the high morbidity and mortality associated with CS, little is known about why some hospitals may have better outcomes than others for this condition. A possibility is that CS case volume may play a role. An expansive body of literature demonstrates the volume–outcome relationship in a number of medical conditions, operations, and procedures.[6,12–20] Consensus guidelines exist regarding threshold numbers for institutional competency of both total and primary PCI, pointing toward worse outcomes below these recommended thresholds.[14,21,22] This relationship has not been explored for patients with CS.

In this study, we first set out to examine whether larger centers were more likely to use current standard of care therapies and advanced circulatory support devices. Second, we sought to determine whether higher annual hospital CS volume was associated with lower mortality from CS. Finally, we sought to determine whether the volume–outcome relationship for CS was independent of other patient, institutional, and geographic characteristics that are predictive of increased survival.

Methods

Data Source

The Nationwide Inpatient Sample (NIS) was the administrative database used in this study. The NIS is a nationally representative database created by the Agency for Healthcare Research and Quality that provides annual data on ≈8 million hospital stays. It contains discharge data from a 20% stratified sample of 1000 US nonfederal specialty and public hospitals and academic medical centers that, when weighted, encompasses 97% of all hospital discharges in the United States.[23] The NIS data set includes data regarding patient demographics and comorbidities, hospital characteristics, inpatient mortality rates, and patient disposition, with each hospitalization considered as an individual entry to the database. Because the NIS has no patient-level identifiers, the Institutional Review Board at Beth Israel Deaconess Medical Center granted this study exempt status.

The NIS validates the data by performing annual external and internal quality assessments. Validations of the NIS data set have performed well when compared against the American Hospital Association Annual Survey database, the National Hospital Discharge Survey from the National Center for Health Statistics, and the Medicare Provider Analysis and Review (MEDPAR) inpatient data from the Centers for Medicare and Medicaid Services.[24]

Study Population

The study population included all patients in the NIS with a diagnosis of CS from 2004 through 2011. NIS data can be weighted to produce national-level estimates by using standard stratum-specific discharge weights provided by the Healthcare Cost and Utilization Project. Weighting is used to produce accurate unbiased estimates. Patients diagnosed with CS were identified by the presence of International Classification of Diseases, ninth revision, clinical modification (ICD-9-CM) code 78551 in the list of diagnoses generated during the course of their hospital stay. Validation studies based on this definition have demonstrated very high specificity (99.3%), moderate sensitivity (59.8%), and very high positive (78.8%) and negative (98.1%) predictive value when used to identify the diagnosis of CS.[25]

Exposure, Outcome, and Covariates

The exposure of interest was the mean yearly CS case volume per hospital divided into quartiles. The primary outcome was inpatient mortality. Those patients who died in skilled nursing care and intermediate-care facilities or free-standing hospice care were excluded from the analysis. Potential confounders such as age, severity of illness, race, hospital teaching status, hospital region, and mechanical ventilation were identified and adjusted for in our final analysis. Comorbid conditions that could potentially influence patient outcome were identified using the Elixhauser Comorbidity Index, which has been shown to possess excellent discriminative power for predicting in-hospital mortality when analyzing administrative databases.[26] Elixhauser comorbidities were developed by the Agency for Healthcare Research and Quality using ICD-9 coding for comorbidity identification at patient discharge. These comorbidities are present on admission but are not directly related to the main reason for hospitalization. Commonly performed procedures that could influence patient outcome (eg, PCI and CABG for early revascularization) were identified using ICD-9-CM procedure codes and adjusted for in the final analysis. Early revascularization was defined as CABG or PCI within 24 hours of admission. To address transfer to a high-volume center as a potentially competing outcome, we excluded patients transferred to any acute-care facility.

Statistical Analysis

All analyses were performed using SAS 9.3 (SAS Institute) and SUDAAN 10.0 (Research Triangle Institute) to account for the complex survey design of the NIS. Frequencies and percentages were calculated and weighted to reflect national estimates. Weighted estimates were used for the analyses to produce accurate unbiased estimates. Categor-

Table 1. Patient Characteristics at Presentation

	Annual Hospital Volume of Cardiogenic Shock Weighted N (%)				
	≤27 Cases	28 to 58 Cases	59 to 106 Cases	≥107 Cases	*P* Value
No. of hospitals	2046 (76.49)	366 (13.68)	177 (6.62)	86 (3.21)	
No. of discharges	133 241 (24.99)	134 464 (25.22)	135 051 (25.33)	130 423 (24.46)	
Patient characteristics					
Age group, y					
<18	5052 (4.05)	6296 (5.19)	6775 (5.64)	10 265 (8.41)	<0.001
18 to 44	32 369 (25.96)	38 660 (31.85)	38 311 (31.91)	44 989 (36.87)	
45 to 64	63 094 (50.61)	61 139 (50.36)	61 198 (50.97)	57 035 (46.74)	
65 to 84	24 062 (19.30)	15 246 (12.56)	13 733 (11.44)	9712 (7.96)	
≥85	97 (0.08)	59 (0.05)	58 (0.05)	24 (0.02)	
Female sex	59 746 (44.80)	52 187 (40.72)	50 958 (39.87)	50 311 (38.57)	<0.001
Race					
White	81 962 (75.29)	77 492 (72.48)	80 974 (76.13)	73 755 (68.84)	0.003
Black	10 511 (9.66)	11 606 (10.85)	9776 (9.19)	16 999 (15.87)	
Hispanic	9391 (8.63)	10 163 (9.51)	6727 (6.33)	7864 (7.34)	
Asian or Pacific Islander	3074 (2.82)	3248 (3.04)	4054 (3.81)	2288 (2.14)	
Native American	752 (0.69)	943 (0.88)	440 (0.41)	621 (0.58)	
Other	3174 (2.92)	3466 (3.24)	4388 (4.13)	5610 (5.24)	
Patient comorbidities					
Anterior STEMI	15 990 (11.91)	20 178 (15.65)	19 118 (14.83)	15 318 (11.58)	<0.001
Inferior STEMI	14 626 (10.89)	18 480 (14.33)	17 335 (13.44)	11 751 (8.88)	<0.001
Other STEMI	16 959 (12.63)	12 827 (9.95)	11 154 (8.65)	7593 (5.74)	<0.001
NSTEMI	31 575 (23.51)	28 767 (22.31)	29 876 (23.17)	26 668 (20.16)	0.003
Old MI	8810 (6.61)	9217 (7.19)	8975 (7.02)	10 531 (8.07)	0.06
Coronary artery disease	56 564 (42.12)	66 789 (51.80)	69 449 (53.86)	64 805 (48.99)	<0.001
Cardiac arrest	23 339 (17.50)	24 059 (18.77)	22 173 (17.35)	19 768 (15.15)	<0.001
Congestive heart failure	44 079 (33.05)	39 711 (29.58)	36 888 (28.86)	31 535 (24.17)	<0.001
Pulmonary circulation disease	4945 (3.71)	4430 (3.46)	4698 (3.68)	5085 (3.90)	0.41
Valvular heart disease	12 820 (9.61)	12 164 (9.49)	13 786 (10.79)	9696 (7.43)	0.02
Peripheral vascular disease	10 240 (7.68)	10 919 (8.52)	11 160 (8.73)	11 599 (8.89)	0.001
Hypertension	56 539 (42.40)	54 673 (42.66)	53 656 (41.98)	52 159 (39.98)	0.35
Diabetes without chronic complications	27 085 (20.31)	25 235 (19.69)	25 119 (19.65)	23 803 (18.25)	0.05
Diabetes with chronic complications	6526 (4.89)	5896 (4.60)	5730 (4.48)	4946 (3.79)	0.002
Renal failure	28 985 (21.73)	25 520 (19.91)	26 046 (20.38)	27 068 (20.75)	0.004
Coagulopathy	13 202 (9.90)	16 511 (12.88)	20 130 (15.75)	26 819 (20.56)	<0.001
Obesity	6485 (4.86)	6938 (5.41)	7666 (6.00)	7766 (5.95)	0.001
Mitral disease	10 613 (7.96)	13 407 (10.46)	16 740 (13.10)	15 960 (12.23)	<0.001
Aortic disease	6340 (4.75)	6498 (5.07)	7395 (5.79)	8731 (6.69)	<0.001
Chronic pulmonary disease	30 646 (22.98)	26 517 (20.69)	26 772 (20.94)	20 975 (16.08)	<0.001
Paralysis	3068 (2.30)	2885 (2.25)	2715 (2.12)	2839 (2.18)	0.66

MI indicates myocardial infarction; NSTEMI, non–ST-segment elevation myocardial infarction; STEMI, ST-segment elevation myocardial infarction.

ical variables are presented as frequencies or proportions and were compared using the chi-square test. Inpatient mortality differences between hospital quartiles were analyzed by fitting multivariate logistic regression models sequentially to calculate odds ratios (ORs) and 95% CIs. An unadjusted logistic regression model was used to estimate the OR for inpatient mortality among patients with CS relative to quartiles of volume for CS. We then used a multivariate adjusted model, adjusting for patient age group, sex, Elixhauser Comorbidity Index, race, hospital location, and early revascularization. To account for in-hospital clustering, we used generalized estimating equations with robust variance estimates. All tests were 2-sided, and *P* values <0.05 were considered statistically significant.

Results

Demographics and Clinical Patient Characteristics

We identified 533 179 weighted patient discharges with CS. Demographics and clinical characteristics are shown in Tables 1 and 2. Women accounted for 41% of cases, and the majority of the patients were white (73.2%). The median yearly CS volume was 58 cases per year. When grouped into quartiles, the mean yearly CS volume was distributed into groups of hospitals treating ≤27 cases (n=133 241), 28 to 58 cases (n=134 464), 59 to 106 cases (n=135 051), and ≥107 cases (n=130 423) per year. Hospitals in the higher volume quartiles treated a significantly higher percentage of patients with coronary artery disease (49.0% versus 42.1%), mitral valvular disease (12.2% versus 8.0%), aortic valvular disease (6.7% versus 4.8%), obesity (6.0% versus 4.9%), and coagulopathy (20.6% versus 9.9%) compared with the lower volume centers.

Hospital and Regional Characteristics

Hospitals with the highest CS volumes were more likely to be urban, large, academic centers (Table 3). Among hospitals with <59 cases, rural and urban nonteaching hospitals accounted for the highest proportion of discharges (76.9% and 52.5% for quartiles 1 and 2, respectively). In contrast, these hospitals represented only 6.0% of discharges at the highest volume centers.

Clinical Management and Quality of Care

Patients at the higher volume hospitals were significantly more likely to receive certain treatments both in terms of supportive therapy in the setting of organ dysfunction (ie, hemodialysis) and modalities for definitive revascularization (Table 2). Patients in the highest volume quartiles were significantly more likely to receive early revascularization within 24 hours of admission (34.1% versus 17.1%) than

Table 2. Treatment Effects

	Annual Hospital Volume of Cardiogenic Shock Weighted N (%)				
	≤27 Cases	28 to 58 Cases	59 to 106 Cases	≥107 Cases	*P* Value
Early revascularization (total)	27 664 (20.60)	50 905 (39.48)	53 992 (41.88)	48 143 (36.39)	<0.001
Thrombolysis	2034 (1.53)	1783 (1.39)	1982 (1.55)	1416 (1.09)	0.002
Percutaneous coronary intervention	22 343 (16.64)	37 537 (29.11)	35 212 (27.31)	24 931 (18.85)	<0.001
Coronary artery bypass graft (total)	6663 (4.96)	16 403 (12.72)	21 882 (16.97)	25 614 (19.36)	<0.001
Valvular surgery	1694 (1.26)	5047 (3.91)	8368 (6.49)	12 957 (9.79)	<0.001
Intra-aortic balloon pump	22 382 (16.78)	40 587 (31.67)	42 070 (32.91)	35 495 (27.21)	<0.001
Ventricular assist device	82 (0.06)	320 (0.25)	1577 (1.23)	4350 (3.33)	<0.001
Biventricular assist device	29 (0.02)	19 (0.02)	140 (0.11)	285 (0.22)	<0.001
TandemHeart device	49 (0.04)	132 (0.10)	232 (0.18)	644 (0.49)	<0.001
Extracorporeal membrane oxygenation	403 (0.30)	324 (0.25)	760 (0.59)	2878 (2.21)	<0.001
Mechanical ventilation	71 760 (53.81)	70 556 (55.05)	71 591 (56.01)	69 082 (52.95)	0.14
Hemodialysis	9246 (6.93)	11 358 (8.86)	12 238 (9.57)	14 631 (11.22)	<0.001
Treatment effects within 24 hours					
Early revascularization within 24 hours	2623 (17.13)	5259 (34.49)	6406 (39.73)	5922 (34.14)	<0.001
Valvular surgery within 24 hours	259 (1.69)	693 (4.54)	1079 (6.69)	1685 (9.72)	<0.001

Table 3. Hospital Characteristics

	Annual Hospital Volume of Cardiogenic Shock Weighted N (%)				
	≤27 Cases	28 to 58 Cases	59 to 106 Cases	≥107 Cases	*P* Value
Transfer into the hospital					
Not transferred in	69 887 (90.94)	64 075 (83.28)	62 907 (76.81)	64 223 (64.42)	<0.001
Transferred from another acute care hospital	4350 (5.66)	10 118 (13.15)	15 990 (19.52)	32 009 (32.11)	
Transferred from another health facility	2611 (3.40)	2750 (3.57)	3000 (3.66)	3456 (3.47)	
Transfer out of the hospital					
Not a transfer	27 156 (66.35)	31 642 (70.37)	28 252 (71.13)	42 322 (74.40)	<0.001
Transferred out to a different acute care hospital	5113 (12.49)	3133 (6.97)	1685 (4.24)	1463 (2.57)	
Transferred out to another type of health facility	8660 (21.16)	10 193 (22.67)	9779 (24.62)	13 098 (23.03)	
Admission source					
Emergency department	53 285 (73.05)	44 109 (61.83)	33 581 (53.59)	17 702 (42.23)	<0.001
Another hospital	4102 (5.62)	8389 (11.76)	13 303 (21.23)	11 309 (26.98)	
Another health facility	1663 (2.28)	1994 (2.80)	2438 (3.89)	993 (2.37)	
Teaching status					
Urban nonteaching	76 154 (57.64)	62 556 (49.02)	50 534 (39.96)	7842 (6.04)	<0.001
Urban teaching	30 545 (23.12)	60 678 (47.55)	72 436 (57.29)	122 067 (93.96)	
Bed size of hospital					
Small	29 245 (22.14)	7141 (5.60)	5664 (4.48)	1118 (0.86)	<0.001
Medium	47 140 (35.68)	32 333 (25.34)	22 587 (17.86)	3089 (2.38)	
Large	55 729 (42.18)	88 136 (69.07)	98 195 (77.66)	125 701 (96.76)	
Hospital region					
Northeast	24 424 (18.31)	17 974 (14.02)	21 624 (16.92)	30 132 (23.10)	0.02
Midwest	32 356 (24.26)	27 664 (21.58)	31 578 (24.70)	27 133 (20.80)	
South	51 182 (38.38)	48 500 (37.84)	35 708 (27.94)	52 304 (40.09)	
West	25 396 (19.04)	34 032 (26.55)	38 912 (30.44)	20 887 (16.01)	
Median household income for the patient's ZIP code					
0 to 25th percentile	37 608 (28.97)	33 609 (26.86)	31 385 (25.17)	37 514 (29.50)	0.01
26th to 50th percentile	37 239 (28.69)	31 260 (24.98)	32 795 (26.30)	31 285 (24.60)	
51st to 75th percentile	29 511 (22.73)	31 801 (25.41)	31 235 (25.05)	31 263 (24.59)	
76th to 100th percentile	25 457 (19.61)	28 469 (22.75)	29 280 (23.48)	27 099 (21.31)	

patients in the lowest volume quartile. In terms of contemporary specific revascularization options, the 2 centers with volumes in the higher quartile demonstrated significantly higher numbers of patients undergoing CABG or PCI. A similar relationship was demonstrated with the use of mechanical circulatory support including IABP, extracorporeal membrane oxygenation, the TandemHeart device (CardiacAssist, Inc), ventricular assist devices, and biventricular assist devices, all of which were used more often at the higher volume centers. In contrast, the lowest quartile hospitals used thrombolysis more than the centers in higher volume quartiles; this therapy confers less of a mortality benefit than contemporary revascularization strategies.[27]

Inpatient Mortality

The crude inpatient mortality was 38.9%. Decreased survival was seen across the strata as mean annual hospital volume decreased from the highest quartile (>106 weighted cases per year) to the lowest quartile (<28 weighted cases per year). Compared with the highest quartile of CS volume (quartile 4), patients cared for in hospital quartiles 1, 2, and 3 had increased unadjusted odds of inpatient mortality by 58% (OR

Table 4. Association Between Hospital Volume and Risk-Adjusted Mortality

	Annual Hospital Volume of Cardiogenic Shock			
	≤27 Cases	28 to 58 Cases	59 to 106 Cases	≥107 Cases
No. of hospitals, %	2046 (76.49)	366 (13.68)	177 (6.62)	86 (3.21)
Odds ratio, 95% CI				
Unadjusted model	1.58 (1.45 to 1.73)	1.29 (1.17 to 1.41)	1.17 (1.06 to 1.29)	1.00 [Reference]
Multivariate model*	1.27 (1.15 to 1.40)	1.20 (1.08 to 1.32)	1.12 (1.01 to 1.24)	1.00 [Reference]
Mortality incidence, 95% CI				
Unadjusted model	45.32 (44.53 to 46.11)	40.27 (39.25 to 41.29)	37.96 (36.66 to 39.28)	34.40 (32.53 to 36.32)
Multivariate model*	41.97 (40.87 to 43.08)	40.72 (39.52 to 41.93)	39.31 (37.91 to 40.72)	37.01 (35.11 to 38.96)

MI indicates myocardial infarction.

*Adjusted for age group, sex, race, acute MI, early revascularization, hemodialysis, teaching status of the hospital, hospital region, median household income for the patient's ZIP code, mechanical ventilation, valvular disease, pulmonary circulation disease, peripheral vascular disease, hypertension, paralysis, neurological disorders, chronic pulmonary disease, diabetes with and without chronic complications, hypothyroidism, renal failure, liver disease, peptic ulcer disease, AIDS, lymphoma, metastatic cancer, solid tumor without metastasis, rheumatoid arthritis, coagulopathy, obesity, weight loss, fluid and electrolyte disorders, chronic blood loss anemia, deficiency anemias, alcohol abuse, drug abuse, psychoses, depression.

1.58; 95% CI 1.45 to 1.73), 29% (OR 1.29; 95% CI 1.17 to 1.41), and 17% (OR 1.17; 95% CI 1.06 to 1.29), respectively (Table 4).

After adjustment for Elixhauser comorbidities, hospital location and teaching status, sex, race or ethnicity, and age, a lower mean annual hospital case volume for the treatment of CS was associated with significantly increased odds of in-hospital mortality. When comparing odds of mortality to patients in quartile 4, adjusting demonstrated increases in the odds of 27% (OR 1.27; 95% CI 1.15 to 1.40), 20% (OR 1.20; 95% CI 1.08 to 1.32), and 12% (OR 1.12; 95% CI 1.01 to 1.24), respectively (Table 4). Although the odds of mortality remain significant, the unadjusted model yielded a wider range of ORs than the adjusted model. In addition, a statistically significant decrease in incidence of overall adjusted mortality was seen in comparison of hospital quartiles 1 through 4 (42.0%, 40.7%, 39.3%, and 37.0%, respectively) (Table 4).

Discussion

In this study, we demonstrated that an increase in hospital volume of patients with CS was associated with improved in-hospital mortality. We further demonstrated that lower volume hospitals were less likely to offer aggressive and specific treatments for CS, and that may partially explain these differences in mortality. These findings remained robust after multivariate adjustment for relevant confounders.

There are a number of potential reasons why hospitals with high volumes of CS cases had lower mortality rates for CS. A more central factor that may contribute to this inverse relationship between hospital volume and outcome in CS is significant difference in the use of currently recommended therapies between the hospital quartiles (Table 2). Of particular note are the significant differences in the incidence of definitive revascularization therapies (PCI and CABG) and temporizing therapeutic measures (IABP, biventricular assist devices, extracorporeal membrane oxygenation, and TandemHeart devices). The primary therapy that has a demonstrated mortality benefit for patients with acute myocardial infarction and CS is early revascularization. Previous work has demonstrated a 13% increase in survival among patients who received early revascularization.[28] This survival benefit conferred by early revascularization was found to be independent of revascularization technique (whether PCI or CABG) and was consistent across age groups. Interestingly, despite controlling for early revascularization, center volume remained independently associated with inpatient mortality. This may be partially explained by the more frequent use of supportive therapies for multiple organ dysfunction such as hemodialysis in the higher volume centers. Of note, the highest volume centers exhibited a lower rate of PCI and IABP use than the centers in the second-highest volume quartile. The highest volume centers, however, displayed higher rates of surgical revascularization and valvular surgical intervention. This raises a question of whether recognition of etiological factors of CS, particularly with regard to valvular pathology, is somewhat evident or, most likely, whether referral to the highest volume centers is often for advanced therapies not offered at small or medium-sized hospitals. We also report significant differences in commonly practiced but adjunctive mechanical supportive therapies such as IABP or mechanical circulatory support among quartiles 1 through 4. These devices serve as a bridge lending support, viability, and time, often after revascularization or supporting the CS patient through to recovery.

Our study broadens the existing body of literature on the relationship between hospital volume and outcome in patients receiving cardiovascular care. Previous work has

Table 5. Multivariate Model

Variables	Odds Ratio (95% CI)
Cardiogenic shock quartiles	
>106 cases	1.00 [Reference]
59 to 106 cases	1.12 (1.01 to 1.24)
28 to 58 cases	1.20 (1.08 to 1.32)
<28 cases	1.27 (1.15 to 1.40)
Age group, y	
<18	1.00 [Reference]
18 to 44	1.07 (0.99 to 1.16)
45 to 64	1.67 (1.55 to 1.81)
65 to 84	3.12 (2.86 to 3.40)
>85	4.14 (2.03 to 8.44)
Race	
White	1.00 [Reference]
Black	0.97 (0.91 to 1.02)
Hispanic	1.02 (0.95 to 1.09)
Asian or Pacific Islander	1.01 (0.91 to 1.11)
Native American	1.08 (0.86 to 1.35)
Other	1.03 (0.94 to 1.12)
Female sex	1.05 (1.02 to 1.09)
Valvular disease	1.06 (1.00 to 1.13)
Acute MI	1.23 (1.18 to 1.28)
Pulmonary circulation disease	1.13 (1.03 to 1.24)
Peripheral vascular disease	1.29 (1.22 to 1.36)
Hypertension	1.04 (1.00 to 1.08)
Paralysis	0.96 (0.87 to 1.07)
Other neurological disorders	1.41 (1.32 to 1.50)
Chronic pulmonary disease	0.87 (0.83 to 0.90)
Diabetes without chronic complications	1.09 (1.05 to 1.14)
Diabetes with chronic complications	0.93 (0.86 to 1.00)
Hyperthyroidism	1.00 (0.94 to 1.07)
Renal failure	1.03 (0.98 to 1.07)
Liver disease	1.55 (1.41 to 1.72)
Peptic ulcer disease	0.71 (0.32 to 1.56)
AIDS	1.30 (0.90 to 1.89)
Lymphoma	1.44 (1.21 to 1.72)
Metastatic cancer	2.05 (1.81 to 2.31)
Solid tumor without metastasis	1.50 (1.33 to 1.69)
Rheumatoid arthritis	1.19 (1.06 to 1.35)
Coagulopathy	1.13 (1.06 to 1.20)
Obesity	0.87 (0.80 to 0.93)
Weight loss	0.59 (0.55 to 0.63)
Fluid and electrolyte disorders	1.19 (1.15 to 1.23)
Chronic blood loss anemia	0.63 (0.55 to 0.73)
Deficiency anemias	0.77 (0.73 to 0.81)
Alcohol abuse	0.88 (0.80 to 0.96)
Drug abuse	0.84 (0.75 to 0.95)
Psychoses	0.77 (0.68 to 0.87)
Depression	0.86 (0.78 to 0.94)
Teaching status	
Rural	1.00 [Reference]
Urban nonteaching	0.94 (0.85 to 1.03)
Urban teaching	0.97 (0.88 to 1.08)
Hospital region	
Northeast	1.00 [Reference]
Midwest	0.96 (0.88 to 1.05)
South	0.99 (0.92 to 1.06)
West	0.94 (0.86 to 1.02)
Median household income for patient's ZIP code	
0 to 25th percentile	1.00 [Reference]
26th to 50th percentile	0.97 (0.93 to 1.01)
51st to 75th percentile	0.97 (0.92 to 1.02)
76th to 100th percentile	0.95 (0.90 to 1.00)
Mechanical ventilation	2.75 (2.63 to 2.88)
Hemodialysis	1.33 (1.24 to 1.42)
No early revascularization	2.23 (2.14 to 2.33)

MI indicates myocardial infarction.

demonstrated a mortality benefit in higher-volume centers in the treatment of certain etiologies of CS including acute myocardial infarction and heart failure.[29,30] To our knowledge, this study is the first to define this relationship for the specific diagnosis of CS.

Interestingly, in the multivariate analysis (Table 5), we found certain risk factors (ie, anemia and obesity) known to portend poor prognosis in coronary artery disease to have a protective effective in CS. Chronic anemia, after multivariate adjustment for confounding, was found to be associated with decreased mortality. This result compares well with Sherwood et al, who demonstrated increased mortality associated with blood transfusions in anemic patients with acute coronary syndrome.[31] Obesity also conferred a protective effect on multivariate adjustment. This effect with obesity has been demonstrated previously in patients with other critical illnesses including septic shock and heart failure.[32,33] The likely mechanism that confers this protection is a blunted inflammatory cytokine response in obese patients.

Because the in-hospital mortality associated with CS is almost 5% higher in the lowest quartile hospitals than the highest quartile hospitals, early aggressive measures, including transfer to a higher volume center, could be considered by lower volume hospitals when managing this cohort of severely ill patients. This approach would be consistent with current American College of Cardiology recommendations for triage and immediate transfer to a PCI-capable facility with surgical backup for patients with acute coronary syndromes because revascularization has demonstrated a mortality benefit at both 6 and 12 months when compared with medical stabilization.[28,34]

Our study has certain limitations. Although billing diagnoses are captured by these types of administrative databases, the lack of laboratory data does not permit the severity of metabolic disarray to be quantified. Consequently, although some conditions may be denoted, the significance of those conditions cannot be determined. Furthermore, despite the wide scope and established validity of this database, coding accuracy and consistency of data collected are dependent on coding expertise and experience. Although the sensitivity of the ICD-9 code for CS is only moderate, the large sample size and high specificity make this cohort appropriate for this study. In addition, the temporal relationship of interventions and presence of pathology on admission, as opposed to development during hospitalization, is difficult to discern from the database alone. Many cases of CS may evolve during the hospital course, and etiology may be endogenous or iatrogenic. Discrimination of these variables is unachievable within the present methodology and would rely on previous standards such as a retrospective chart review. Mortality of patients within 24 hours of admission may reflect inherent severity of disease on presentation rather than treatment discrepancies between different volume hospitals. Because data regarding timing of mortality are unavailable in this administrative database, it is admittedly impossible to exclude this potential confounder. Despite our mortality being similar to a recently published randomized control trial involving patients with CS, caution should be used when comparing trial mortalities with observational data.[9] We excluded patients transferred to any acute-care facility because transfer to a high-volume center may represent a competing outcome. We acknowledge that this sound methodology does not allow investigation of the types of patients who are transferred and is an avenue worthy of further examination.

In conclusion, our study demonstrated an association between mean annual CS volume and inpatient mortality with more frequent use of both standard supportive and revascularization techniques in the higher volume centers. Future directions may include examining whether early stabilization and transfer improve outcomes of patients with CS who are admitted to lower volume centers.

Author Contributions

Shaefi: Conception and design, acquisition of data, analysis and interpretation of data; drafting the article; approving final version of article. O'Gara: Acquisition of data, analysis and interpretation of data; drafting the article; approving final version of article. Kociol: Analysis and interpretation of data; critically revising the article; approving final version of article. Joynt: Analysis and interpretation of data; critically revising the article; approving final version of article. Mueller: Acquisition of data, analysis and interpretation of data; drafting the article; approving final version of article. Nizamuddin: Analysis and interpretation of data; critically revising the article; approving final version of article. Mahmood: Acquisition of data, analysis and interpretation of data; drafting the article; approving final version of article. Talmor: Conception and design, acquisition of data, analysis and interpretation of data; drafting the article; approving final version of article. Shahul: Conception and design, acquisition of data, analysis and interpretation of data; drafting the article; approving final version of article.

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Disclosures

None.

References

1. Sayer GT, Baker JN, Parks KA. Heart rescue: the role of mechanical circulatory support in the management of severe refractory cardiogenic shock. *Curr Opin Crit Care*. 2012;18:409–416.
2. Paden ML, Conrad SA, Rycus PT, Thiagarajan RR; ELSO Registry. Extracorporeal life support organization registry report 2012. *ASAIO J*. 2013;59:202–210. doi: 10.1097/MAT.0b013e3182904a52.
3. Cooper HA, Panza JA. Cardiogenic shock. *Cardiol Clin*. 2013;31:567–580.
4. Fuernau G, Thiele H. Intra-Aortic Balloon Pump (IABP) in cardiogenic shock. *Curr Opin Crit Care*. 2013;19:404–409. doi: 10.1097/MCC.0b013e328364d78d.
5. McNamara RL, Wang Y, Herrin J, Curtis JP, Bradley EH, Magid DJ, Peterson ED, Blaney M, Frederick PD, Krumholz HM. Effect of door-to-balloon time on mortality in patients with ST-segment elevation myocardial infarction. *J Am Coll Cardiol*. 2006;47:2180–2186.
6. Cannon CP, Gibson CM, Lambrew CT, Shoultz DA, Levy D, French WJ, Gore JM, Weaver WD, Rogers WJ, Tiefenbrunn AJ. Relationship of symptom-onset-to-balloon time and door-to-balloon time with mortality in patients undergoing angioplasty for acute myocardial infarction. *JAMA*. 2000;283:2941–2947.
7. Babaev A, Frederick PD, Pasta DJ, Every N, Sichrovsky T, Hochman JS; NRMI Investigators. Trends in management and outcomes of patients with acute myocardial infarction complicated by cardiogenic shock. *JAMA*. 2005;294:448–454.
8. Buerke M, Prondzinsky R, Lemm H, Dietz S, Buerke U, Ebelt H, Bushnaq H, Silber RE, Werdan K. Intra-aortic balloon counterpulsation in the treatment of

infarction-related cardiogenic shock–review of the current evidence. *Artif Organs*. 2012;36:505–511.

9. Thiele H, Zeymer U, Neumann FJ, Ferenc M, Olbrich HG, Hausleiter J, Richardt G, Hennersdorf M, Empen K, Fuernau G, Desch S, Eitel I, Hambrecht R, Fuhrmann J, Bohm M, Ebelt H, Schneider S, Schuler G, Werdan K. Intraaortic balloon support for myocardial infarction with cardiogenic shock. *N Engl J Med*. 2012;367:1287–1296.
10. Kapur N, Jumean M. Defining the role for percutaneous mechanical circulatory support devices for medically refractory heart failure. *Curr Heart Fail Rep*. 2013;10:177–184.
11. Kolte D, Khera S, Aronow WS, Mujib M, Palaniswamy C, Sule S, Jain D, Gotsis W, Ahmed A, Fishman WH, Fonarow GC. Trends in incidence, management, and outcomes of cardiogenic shock complicating ST elevation myocardial infarction in the United States. *J Am Heart Assoc*. 2014;3:e000590 doi: 10.1161/JAHA.113.000590.
12. Walkey AJ, Wiener RS. Hospital case volume and outcomes among patients hospitalized with severe sepsis. *Am J Respir Crit Care Med*. 2014;189:548–555.
13. Shahin J, Harrison DA, Rowan KM. Is the volume of mechanically ventilated admissions to UK critical care units associated with improved outcomes? *Intensive Care Med*. 2014;40:353–360.
14. Kontos MC, Wang Y, Chaudhry SI, Vetrovec GW, Curtis J, Messenger J. Lower hospital volume is associated with higher in-hospital mortality in patients undergoing primary percutaneous coronary intervention for ST-segment-elevation myocardial infarction: a report from the NCDR. *Circ Cardiovasc Qual Outcomes*. 2013;6:659–667.
15. Fernandez R, Altaba S, Cabre L, Lacueva V, Santos A, Solsona JF, Anon JM, Catalan RM, Gutierrez MJ, Fernandez-Cid R, Gomez-Tello V, Curiel E, Fernandez-Mondejar E, Oliva JC, Tizon AI, Gonzalez J, Monedero P, Sanchez MG, de la Torre MV, Ibanez P, Frutos F, Del Nogal F, Gomez MJ, Marcos A, Vera P, Serrano JM, Umaran I, Carrillo A, Lopez-Pueyo MJ, Rascado P, Balerdi B, Suberviola B, Hernandez G. Relationship between volume and survival in closed intensive care units is weak and apparent only in mechanically ventilated patients. *Anesthesiology*. 2013;119:871–879.
16. Kanhere MH, Kanhere HA, Cameron A, Maddern GJ. Does patient volume affect clinical outcomes in adult intensive care units? *Intensive Care Med*. 2012;38:741–751.
17. Anderson O, Ni Z, Moller H, Coupland VH, Davies EA, Allum WH, Hanna GB. Hospital volume and survival in oesophagectomy and gastrectomy for cancer. *Eur J Cancer*. 2011;47:2408–2414.
18. Ross JS, Normand SL, Wang Y, Ko DT, Chen J, Drye EE, Keenan PS, Lichtman JH, Bueno H, Schreiner GC, Krumholz HM. Hospital volume and 30-day mortality for three common medical conditions. *N Engl J Med*. 2010;362:1110–1118.
19. Needham DM, Bronskill SE, Rothwell DM, Sibbald WJ, Pronovost PJ, Laupacis A, Stukel TA. Hospital volume and mortality for mechanical ventilation of medical and surgical patients: a population-based analysis using administrative data. *Crit Care Med*. 2006;34:2349–2354.
20. Kahn JM, Goss CH, Heagerty PJ, Kramer AA, O'Brien CR, Rubenfeld GD. Hospital volume and the outcomes of mechanical ventilation. *N Engl J Med*. 2006;355:41–50.
21. Dehmer GJ, Blankenship JC, Cilingiroglu M, Dwyer JG, Feldman DN, Gardner TJ, Grines CL, Singh M. SCAI/ACC/AHA expert consensus document. *Catheter Cardiovasc Interv*. 2014;84:169–187.
22. Harold JG, Bass TA, Bashore TM, Brush JE Jr, Burke JA, Dehmer GJ, Deychak YA, Jneid H, Hollis JG, Landzberg JS, Levine GN, McClurken JB, Meesenger JC, Moussa ID, Muhlestein JB, Pomerantz RM, Sanborn TA, Sivaram CA, White CJ, Willams ES. ACCF/AHA/SCAI 2013 update of the clinical competence statement on coronary artery interventional procedures. *J Am Coll Cardiol*. 2013;62:357–396. doi: 10.1016/j.jacc.2013.05.002.
23. HCUP. HCUP Nationwide Inpatient Sample (NIS). Healthcare Cost and Utilization Project (HCUP). Agency for Healthcare Research and Quality; 2011. Available at: www.hcup-us.ahrq.gov/nisoverview.jsp. Accessed September 22, 2014.
24. Barrett M, Wilson E, Whalen D. 2007 HCUP Nationwide Inpatient Sample (NIS) comparison report. HCUP Methods Series Report # 2010-03. U.S. Agency for Healthcare Research and Quality; 2010. Available at: www.hcup-us.ahrq.gov/reports/methods.jsp. Accessed September 22, 2014.
25. Lambert L, Blais C, Hamel D, Brown K, Rinfret S, Cartier R, Giguère M, Carroll C, Beauchamp C, Bogaty P. Evaluation of care and surveillance of cardiovascular disease: can we trust medico-administrative hospital data? *Can J Cardiol*. 2012;28:162–168.
26. Chu Y-T, Ng Y-Y, Wu S-C. Comparison of different comorbidity measures for use with administrative data in predicting short- and long-term mortality. *BMC Health Serv Res*. 2010;10:140.
27. Huynh T, Perron S, O'Loughlin J, Joseph L, Labrecque M, Tu JV, Théroux P. Comparison of primary percutaneous coronary intervention and fibrinolytic therapy in ST-segment-elevation myocardial infarction: Bayesian hierarchical meta-analyses of randomized controlled trials and observational studies. *Circulation*. 2009;119:3101–3109.
28. Hochman JS, Sleeper LA, Webb JG, Sanborn TA, White HD, Talley JD, Buller CE, Jacobs AK, Slater JN, Col J, McKinlay SM, Picard MH, Menegus MA, Boland J, Dzavik V, Thompson CR, Wong SC, Steingart R, Forman R, Aylward PE, Godfrey E, Desvigne-Nickens P, LeJemtel TH. Early revascularization in acute myocardial infarction complicated by cardiogenic shock. *N Engl J Med*. 1999;341:625–634.
29. Canto JG, Every NR, Magid DJ, Rogers WJ, Malmgren JA, Frederick PD, French WJ, Tiefenbrunn AJ, Misra VK, Kiefe CI, Barron HV. The volume of primary angioplasty procedures and survival after acute myocardial infarction. National Registry of Myocardial Infarction 2 Investigators. *N Engl J Med*. 2000;342:1573–1580.
30. Joynt KE, Orav EJ, Jha AK. The association between hospital volume and processes, outcomes, and costs of care for congestive heart failure. *Ann Intern Med*. 2011;154:94–102.
31. Sherwood MW, Rao SV. Acute coronary syndromes: blood transfusion in patients with acute MI and anaemia. *Nat Rev Cardiol*. 2013;10:186–187.
32. Arabi YM, Dara S, Tamim HM, Rishu AH, Bouchama A, Khedr MK, Feinstein D, Parillo JE, Wood KE, Keenan SP, Zanotti S, Martinka G, Kumar A; The Cooperative Antimicrobial Therapy of Septic Shock (CATSS) Database Research Group. Clinical characteristics, sepsis interventions and outcomes in the obese patients with septic shock: an international multicenter cohort study. *Crit Care*. 2013;17:R72.
33. Curtis JP, Selter JG, Wang Y, Rathore SS, Jovin IS, Jadbabaie F, Kosiborod M, Portnay EL, Sokol SI, Bader F, Krumholz HM. The obesity paradox: body mass index and outcomes in patients with heart failure. *Arch Intern Med*. 2005;165:55–61.
34. Harold JG, Bass TA, Bashore TM, Brindiss RG, Brush JE, Burke JA, Dehmers GJ, Deychak YA, Jneids H, Jolliss JG, Landzberg JS, Levine GN, McClurken JB, Messengers JC, Moussas ID, Muhlestein JB, Pomerantz RM, Sanborn TA, Sivaram CA, Whites CJ, Williamss ES; ACCF/AHA/ACP Task Force On Clinical C, Training, Halperin JL, Beckman JA, Bolger A, Byrne JG, Lester SJ, Merli GJ, Muhlestein JB, Pina IL, Wang A, Weitz HH. ACCF/AHA/SCAI 2013 update of the clinical competence statement on coronary artery interventional procedures. *Catheter Cardiovasc Interv*. 2013;82:E69–E111.