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Accessibility
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.\textsuperscript{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.\textsuperscript{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 larger 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 \(\approx8\) 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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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 | ≤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 | ≤27 Cases | 28 to 58 Cases | 59 to 106 Cases | ≥107 Cases | P Value |
|--------------|-----------|----------------|----------------|----------|---------|
| <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) |         |

| Race          | ≤27 Cases | 28 to 58 Cases | 59 to 106 Cases | ≥107 Cases | P Value |
|---------------|-----------|----------------|----------------|----------|---------|
| 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 | ≤27 Cases | 28 to 58 Cases | 59 to 106 Cases | ≥107 Cases | P Value |
|-----------------------|-----------|----------------|----------------|----------|---------|
| 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) | 7668 (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             | 30 68 (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.
Critical 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 \( \leq 27 \) cases (n=133,241), 28 to 58 cases (n=134,464), 59 to 106 cases (n=135,051), and \( \geq 107 \) 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

| Treatment Effects                              | Annual Hospital Volume of Cardiogenic Shock Weighted N (%) | \( P \) 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 (1.0) 232 (1.8) 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**

| Treatment effects within 24 hours              | \( P \) Value |
|------------------------------------------------|---------------|
| 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        |
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 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) | |
Hospital Volume and Cardiogenic Shock Mortality

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

| No. of hospitals, % | Annual Hospital Volume of Cardiogenic Shock |
|---------------------|--------------------------------------------|
|                     | ≤27 Cases | 28 to 58 Cases | 59 to 106 Cases | ≥107 Cases |
| 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 inhospital mortality. When comparing odds of mortality to patients in quartile 4, adjusted 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 inhospital 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 Tandem-Heart devices). The primary therapy that has 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. 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
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.

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) |

Table 5. Continued

| Variables                                      | Odds Ratio (95% CI) |
|------------------------------------------------|---------------------|
| 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                                | 1.00 [Reference]    |
| Rural                                          |                     |
| 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.
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.\textsuperscript{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 treatment, can be 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.\textsuperscript{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: Concept 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. 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
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