tary Appendix 1 (available with the full text of this article at www.nejm.org).

There were negligible differences in age and sex between the patients who received care from low-volume surgeons and those who received care from high-volume surgeons; for some procedures, the prevalence of coexisting conditions varied to a small degree according to surgeon volume (Table 1). Patients receiving care from low-volume surgeons were more likely to be black and to be admitted to the hospital nonelectively. Overall, however, there were no clinically important differences in predicted mortality rates according to surgeon volume.

When surgeon volume was assessed as a con-

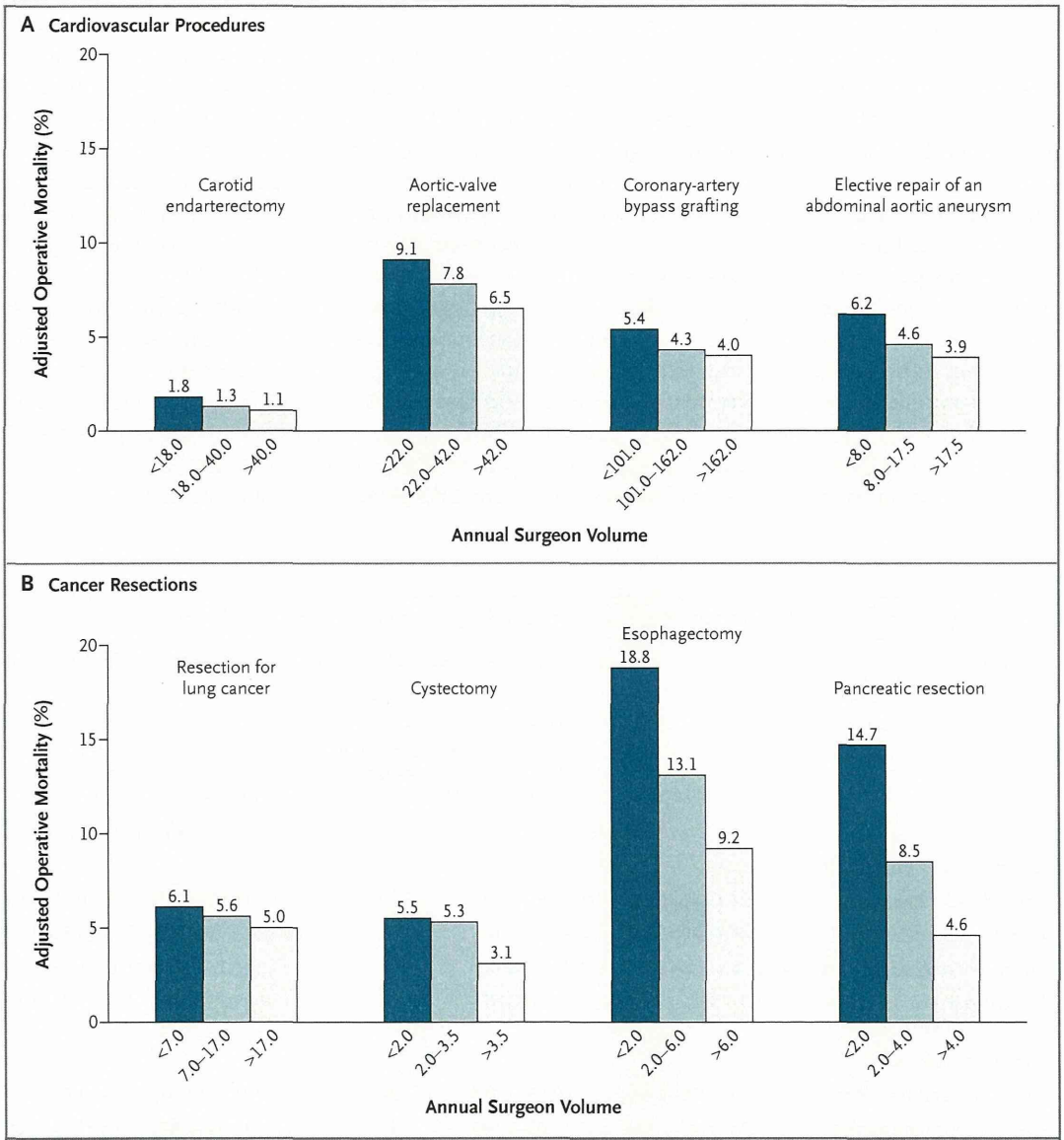

Figure 1. Adjusted Operative Mortality among Medicare Patients in 1998 and 1999, According to Surgeon-Volume Stratum, for Four Cardiovascular Procedures (Panel A) and Four Cancer Resections (Panel B).

Operative mortality was defined as the rate of death before hospital discharge or within 30 days after the index procedure. Surgeon volume was determined on the basis of the total number of procedures performed in both Medicare and non-Medicare patients. P<0.001 for all procedures except resection for lung cancer; P=0.003 for lung resection; P values reflect associations between operative mortality and volume assessed as a continuous variable.

tinuous variable, it was inversely related to operative mortality for all eight procedures (P=0.003 for lung resection, P<0.001 for all other procedures). The strength of the inverse association between surgeon volume and outcome varied markedly according to the procedure in terms of both the absolute operative mortality rate (Fig. 1) and the adjusted odds ratio for operative death (Table 2). The adjusted odds ratios for operative death among patients of low-volume surgeons as compared with patients of high-volume surgeons ranged from 1.24 for lung resection to 3.61 for pancreatic resection. Adjusting for hospital volume attenuated the strength of the associations between surgeon volume and outcome, but the effect of surgeon volume remained statistically significant for seven of the eight procedures.

When hospital volume was assessed as a continuous variable, it was inversely related to operative mortality for seven of the eight procedures (P=0.20 for carotid endarterectomy, P<0.001 for all the other procedures). After adjustment for surgeon volume, however, higher hospital volume remained a significant predictor of decreased mortality for only four procedures (repair of an abdominal aortic aneurysm, cystectomy, lung resection, and pancreatic resection). In fact, after adjustment for surgeon volume, high hospital volume was associated with increased mortality among patients undergoing carotid endarterectomy. For many procedures, surgeon volume accounted for a large proportion of the apparent differences in operative mortality between high-volume hospitals and low-volume hospitals. Among patients undergoing elective repair of an abdominal aortic aneurysm, for example, the adjusted odds ratio for death with surgery performed in a low-volume hospital as compared with that performed in a high-volume hospital decreased from 1.40 to 1.17 after adjustment for surgeon volume. Thus, surgeon volume accounted for 57 percent of the apparent difference in mortality between low-volume and high-volume hospitals ([1.40−1.17]÷[1.40−1.00]). The proportion of the apparent effect of hospital volume that was actually attributable to surgeon volume varied according to the procedure: it was 100 percent for aortic-valve replacement, 54 percent for pancreatic resection, 49 percent for coronary-artery bypass grafting, 46 percent for esophagectomy, 39 percent for cystectomy, and 24 percent for lung resection.

Table 2. Adjusted Odds Ratio for Operative Death, According to Surgeon Volume and Hospital Volume.*

Procedure	Odds of Operative Death with Low Volume as Compared with High Volume					
	Surgeon Volume	Surgeon Volume, Adjusted for Hospital Volume	Proportion of Effect of Surgeon Volume Attributable to Hospital Volume	Hospital Volume	Hospital Volume, Adjusted for Surgeon Volume	Proportion of Effect of Hospital Volume Attributable to Surgeon Volume
	adjusted odds ratio (95% CI)		%	*adjusted odds ratio (95% CI)*		%
Cardiovascular procedures						
Carotid endarterectomy	1.64 (1.47–1.84)	1.70 (1.51–1.91)	0	1.04 (0.92–1.17)	0.89 (0.79–1.01)	—†
Aortic-valve replacement	1.44 (1.29–1.59)	1.45 (1.30–1.63)	0	1.13 (1.00–1.28)	0.97 (0.86–1.10)	100
Coronary-artery bypass grafting	1.36 (1.28–1.45)	1.33 (1.25–1.42)	8	1.26 (1.15–1.37)	1.13 (1.03–1.24)	49
Elective repair of an abdominal aortic aneurysm	1.65 (1.46–1.86)	1.55 (1.36–1.77)	15	1.40 (1.23–1.59)	1.17 (1.02–1.35)	57
Cancer resections						
Resection for lung cancer	1.24 (1.08–1.44)	1.16 (0.99–1.36)	34	1.29 (1.11–1.51)	1.22 (1.04–1.44)	24
Cystectomy of the bladder	1.83 (1.37–2.45)	1.45 (1.03–2.04)	46	2.06 (1.50–2.83)	1.65 (1.14–2.39)	39
Esophagectomy	2.30 (1.54–3.42)	1.80 (1.13–2.87)	38	2.23 (1.47–3.39)	1.67 (1.02–2.73)	46
Pancreatic resection	3.61 (2.44–5.33)	2.31 (1.43–3.72)	50	3.95 (2.55–6.11)	2.34 (1.38–3.99)	54

* Because of rounding, the values given for the proportion of the effect of surgeon volume attributable to hospital volume and the proportion of the effect of hospital volume attributable to surgeon volume may not match the values that can be calculated with the formula given in the text. CI denotes confidence interval.

† There was no statistically significant effect of hospital volume.

Figure 2 shows the relative effects of hospital volume and surgeon volume in terms of adjusted mortality rates. For carotid endarterectomy and aortic-valve replacement, the mortality rates decreased with increasing surgeon volume but did not change substantially with increasing hospital volume. Conversely, for lung resection, the adjusted mortality rates were strongly inversely related to hospital volume, but were less strongly related to surgeon volume. For the remaining five procedures, operative mortality decreased to relatively similar degrees with increasing hospital volume and increasing surgeon volume. Even within the high-volume–hospital stratum, the patients who received their care from low-volume surgeons had considerably higher mortality rates with several procedures than the patients who received care from high-volume surgeons.

We performed similar sensitivity analyses using the hospital-volume criteria that were established by the Leapfrog Group for four of the procedures (Table 3). High-volume hospitals (those with volumes at or above the Leapfrog cutoffs) had lower overall mortality rates than low-volume hospitals, largely because patients at high-volume hospitals were much more likely to be treated by high-volume surgeons than by low-volume surgeons. For coronary-artery bypass grafting, elective repair of an abdominal aortic aneurysm, and esophagectomy, the operative mortality among the patients treated by low-volume surgeons at high-volume hospitals was higher than the overall operative mortality at low-volume hospitals. For pancreatic resection, patients at high-volume hospitals had lower mortality rates than those at low-volume hospitals, regardless of the surgeon volume.

DISCUSSION

By virtue of the large size and generalizability of the national Medicare data base, we were able to examine with precision the associations between surgeon volume and operative mortality for a wide range of cardiovascular procedures and cancer resections. For all eight procedures we studied, the patients treated by high-volume surgeons had lower operative mortality rates than those treated by low-volume surgeons. Surgeon volume accounted for a relatively large proportion of the apparent effect of hospital volume, to a degree that varied according to the procedure. For some procedures, the association between hospital volume and outcome disappeared almost entirely after surgeon volume had been taken into account.

It is not surprising that the relative importance of surgeon volume and hospital volume varies according to the procedure. In the case of carotid endarterectomy, for example, technical skill and the use of specific intraoperative processes (e.g., intraarterial shunt insertion and patch angioplasty)[21] — processes used at the discretion of the operating surgeon — are important determinants of the risk of operative stroke or death. In contrast, other hospital-based services are relatively less important. Most patients undergoing carotid endarterectomy do not require intensive postoperative management, and the length of stay is typically just overnight. For these reasons, the preeminent role of surgeon volume in the outcome of this procedure has strong intuitive validity. In the case of lung resection, in contrast, patients rarely die because of direct technical complications of the procedure itself (e.g., bleeding or leakage from a bronchial stump); they die from cardiac events, pneumonia, and respiratory failure. Hospital-based services (e.g., intensive care, pain management, respiratory care, and nursing care) are very important, and the average length of stay is relatively long. Thus, it is not surprising that hospital volume was more important than surgeon volume in determining the outcome of this procedure. Of course, these two procedures represent the extremes. As suggested by our analysis, factors related to both surgeon volume and hospital volume seem to be important for most high-risk procedures.

Our study has several important limitations. First, because we used Medicare data, our study was restricted to patients 65 years of age or older. However, the elderly constitute the majority of patients undergoing the cardiovascular procedures and cancer resections that we examined in this study. Second, although our study was large, some of our subgroup analyses were based on relatively

Figure 2 (facing page). Adjusted Operative Mortality among Medicare Patients in 1998 and 1999, According to Hospital-Volume Stratum and Surgeon-Volume Stratum for Four Cardiovascular Procedures (Panel A) and Four Cancer Resections (Panel B).

Because of small samples (<20), mortality rates among patients treated by high-volume surgeons in low-volume hospitals are not shown for esophagectomy and pancreatic resection. Mortality rates were adjusted for characteristics of the patients.

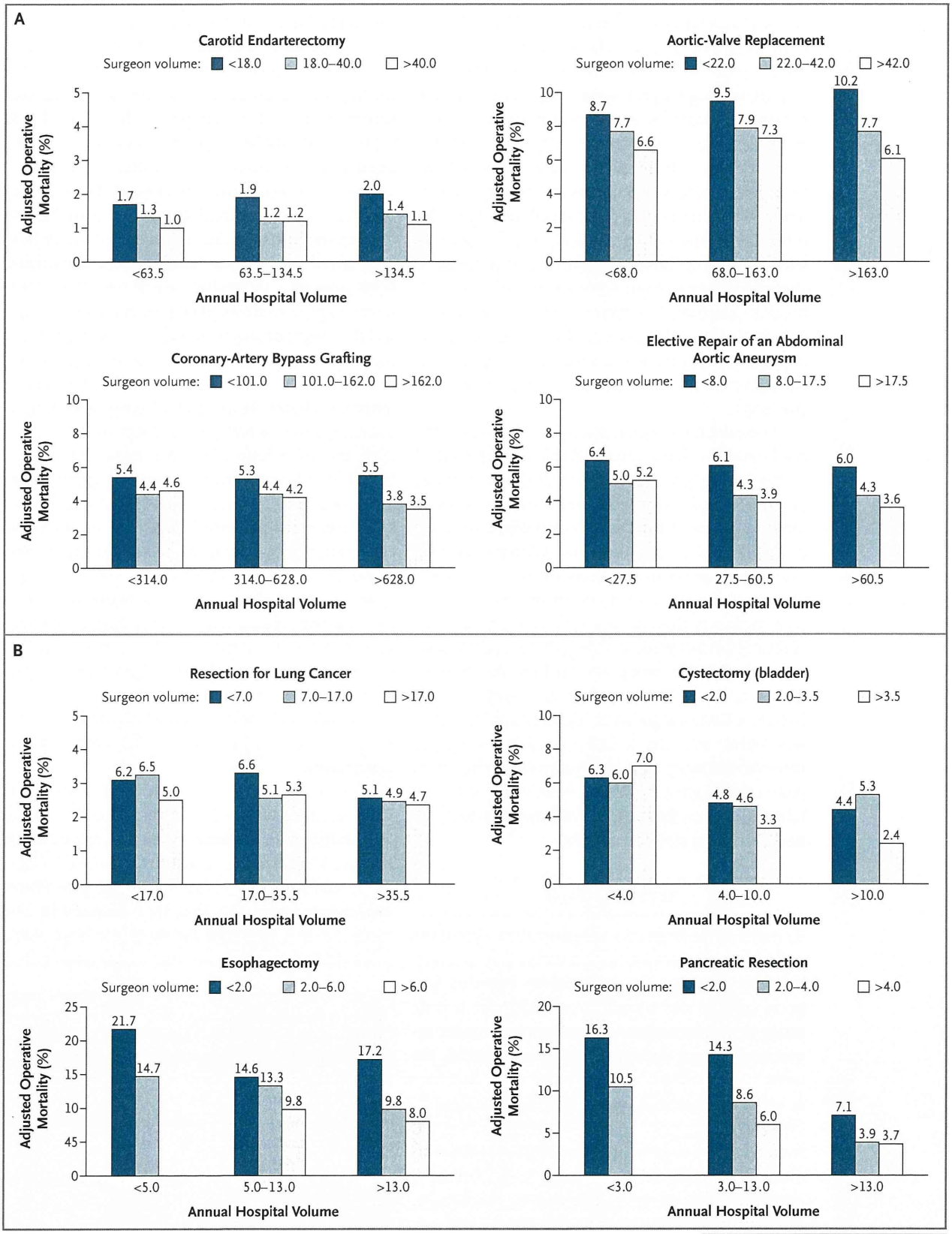

Table 3. Adjusted Operative Mortality Rates among Medicare Patients in 1998 and 1999, According to Total Hospital Volume, Relative to the Leapfrog Group Volume Criteria and Surgeon Volume.*

Procedure	Cutoff	Hospital Volume <Cutoff			Hospital Volume ≥Cutoff		
		Low-Volume Surgeons	High-Volume Surgeons	Overall Hospital Mean	Low-Volume Surgeons	High-Volume Surgeons	Overall Hospital Mean
	no./yr			*percent*			
Coronary-artery bypass grafting	450						
Proportion of patients		47.3	20.1		19.3	46.8	
Mortality		5.4	4.6	5.0	5.4	3.7	4.2
Elective repair of an abdominal aortic aneurysm	50						
Proportion of patients		45.3	18.1		17.8	52.5	
Mortality		6.4	4.3	5.4	5.8	3.6	4.3
Esophagectomy	13						
Proportion of patients		36.0	14.4		9.2	70.0	
Mortality		19.2	11.1	15.3	17.5	8.1	9.5
Pancreatic resection	11						
Proportion of patients		50.5	9.4		6.9	80.5	
Mortality		15.7	6.9	11.9	6.1	3.7	4.5

* Operative mortality was defined as the rate of death before hospital discharge or within 30 days after the index procedure; total hospital volume included procedures in both Medicare and non-Medicare patients.

small numbers of patients. In particular, the number of patients who underwent procedures performed by low-volume surgeons at high-volume hospitals or by high-volume surgeons at low-volume hospitals was relatively low. Thus, estimates of mortality in these subgroups are relatively imprecise. Third, because of errors in the coding and assignment of unique provider identification numbers, we may have incorrectly identified the operating surgeon for some procedures. Such errors, if largely random, would tend to bias our results toward the null hypothesis (no effect of surgeon volume on outcome). However, to reduce any potential bias against low-volume surgeons, we excluded physicians who were not self-designated as surgeons.

Finally, many would question our ability to perform adequate risk adjustment with the use of administrative data.[22,23] Whether risk adjustment is important in studies of surgical volume and outcome is uncertain. Some have noted that analyses based on clinical studies are less likely to report statistically significant associations between volume and outcome than those (the majority) that are based on administrative data.[4] However, clinical studies also tend to be substantially smaller and often lack sufficient statistical power to detect clinically meaningful differences in operative mortality rates. Moreover, there is little evidence from clinical studies that there are important, volume-related differences in case mix (i.e., that low-volume providers care for "sicker" patients). Although we cannot rule out confounding by unmeasured characteristics of the patients in our study, there is no reason to believe that such confounding would affect our analyses of hospital volume and surgeon volume disproportionately. Thus, we do not believe that limitations related to risk adjustment threaten our main conclusions about the relative importance of hospital volume and surgeon volume.

Our findings have direct implications for ongoing initiatives for volume-based referral. Leading the most visible of these initiatives, the Leapfrog Group, a coalition of more than 140 large public and private purchasers, has established "evidence-based hospital referral" standards for several surgical procedures.[24] Although the Leapfrog Group has recently incorporated data on outcomes and selected process measures into its 2003 standards for some procedures, criteria based on minimal hospital volume remain in place for coronary-artery bypass grafting, percutaneous coronary interventions, elective repair of an abdominal aortic aneurysm, esophagectomy, and pancreatic resection. Our analysis confirms that hospitals that exceed the volume criteria set by Leapfrog have lower mortali-

ty rates, on average, than those that do not. However, our findings also suggest that high-volume hospitals have better outcomes in large part because patients at these hospitals are more likely to be treated by high-volume surgeons and that standards based on surgeon volume as well as hospital volume would be more useful in directing patients to the providers who are likely to achieve the best outcomes. Increasing surgeons' volumes would require that administrators and leaders in the field of surgery actively manage the way in which selected operations are distributed within their hospitals — that is, by restricting them to a smaller number of surgeons. Although such efforts would no doubt encounter resistance, they may be more practical and less controversial than policies focusing exclusively on redistributing patients among hospitals.

We should also look for opportunities to improve the quality of surgical care delivered by low-volume surgeons. Determining whether this goal is realistic will require a better understanding of the mechanisms underlying the observed associations between volume and outcome. The key mechanism could simply be "practice" — clinical judgment and technical skill that are achieved only by surgeons who perform a specific procedure with sufficient frequency. Before jumping to this conclusion, however, we must better understand which specific processes of care are most important to the success of various operations and the extent to which they can be exported to other surgeons or hospitals.

Supported by a grant (R01 HS10141-01) from the Agency for Healthcare Research and Quality.

Dr. Birkmeyer reports serving as a paid consultant for the Leapfrog Group and as the chair of its advisory panel on evidence-based hospital referral.

The views expressed in this article are those of the authors and do not necessarily represent those of the Center for Medicare and Medicaid Services or the U.S. government.

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ORIGINAL CONTRIBUTION

Relationship Between Trauma Center Volume and Outcomes

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Context The premise underlying regionalization of trauma care is that larger volumes of trauma patients cared for in fewer institutions will lead to improved outcomes. However, whether a relationship exists between institutional volume and trauma outcomes remains unknown.

Objective To evaluate the association between trauma center volume and outcomes of trauma patients.

Design Retrospective cohort study.

Setting Thirty-one academic level I or level II trauma centers across the United States participating in the University Healthsystem Consortium Trauma Benchmarking Study.

Patients Consecutive patients with penetrating abdominal injury (PAI; n=478) discharged between November 1, 1997, and July 31, 1998, or with multisystem blunt trauma (minimum of head injury and lower-extremity long-bone fractures; n=541) discharged between June 1 and December 31, 1998.

Main Outcome Measures Inpatient mortality and hospital length of stay (LOS), comparing high-volume (>650 trauma admissions/y) and low-volume (≤650 admissions/y) centers.

Results After multivariate adjustment for patient characteristics and injury severity, the relative odds of death was 0.02 (95% confidence interval [CI], 0.002-0.25) for patients with PAI admitted with shock to high-volume centers compared with low-volume centers. No benefit was evident in patients without shock ($P=.50$). The adjusted odds of death in patients with multisystem blunt trauma who presented with coma to a high-volume center was 0.49 (95% CI, 0.26-0.93) vs low-volume centers. No benefit was observed in patients without coma ($P=.05$). Additionally, a shorter LOS was observed in patients with PAI and New Injury Severity Scores of 16 or higher (difference in adjusted mean LOS, 1.6 days [95% CI, −1.5 to 4.7 days]) and in all patients with multisystem blunt trauma admitted to higher-volume centers (difference in adjusted mean LOS, 3.3 days [95% CI, 0.91-5.70 days]).

Conclusions Our results indicate that a strong association exists between trauma center volume and outcomes, with significant improvements in mortality and LOS when volume exceeds 650 cases per year. These benefits are only evident in patients at high risk for adverse outcomes.

JAMA. 2001;285:1164-1171 www.jama.com

THE PREMISE UNDERLYING REgionalization of trauma care is that optimal outcomes can be achieved at greatest efficiency if care is restricted to relatively few dedicated trauma centers. Limitation of the number of trauma centers based on community need has been proposed as a critical component of regional trauma systems and, in a recent evaluation of systems across the country, one of their most frequent deficiencies.[1,2] Implicit in this premise is that higher patient volumes will lead to greater experience and that this experience translates into better outcomes. This relationship appears to hold true for other areas of surgical care, including major oncologic, cardiac, vascular, and neurosurgical procedures.[3-7] In contrast, no such relationship is evident when less complex procedures like cholecystectomy or operative management of hip fractures are considered,[8] suggesting that the association between volume and outcomes is dependent on the complexity of care and the potential for adverse outcomes.

Care of trauma patients poses 2 challenges not encountered in other aspects of surgical care. First, time to definitive care is a critical factor influencing patient survival. The primacy of time renders an ad hoc approach to trauma care inappropriate, potentially increasing the magnitude of the relationship between institutional experience and outcomes. Second, polytrauma patients often require complex, cross-specialty surgical care. The necessity for interdisciplinary surgical management lessens the impact of any particular individual and increases the importance of institutional experience. These challenges suggest that a clear association between volume and outcomes should ex-

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ist. However, unlike in other aspects of surgical care, many institutions caring for trauma patients have already achieved a high level of quality by virtue of the trauma center designation and accreditation process, whereby an outside organization assesses the resources and capabilities of institutions caring for such patients.[9] In the setting in which all institutions have already met quality criteria, it is unclear whether any relationship between experience and outcome should exist. We used 2 distinct cohorts of trauma patients to evaluate whether institutional volume thresholds exist at which optimal outcomes can be achieved. These cohorts included patients with penetrating abdominal injury (PAI) and patients with multisystem blunt trauma with a minimum of a combination of head injury and lower-extremity long-bone fracture.

METHODS

Institutions and Patients

The institutions on which this analysis is based are trauma centers voluntarily participating in the University Healthsystem Consortium (UHC) Trauma Benchmarking Study. The consortium participates in a variety of projects designed to improve clinical and operating efficiencies among its member institutions by pooling resources and by means of benchmarking projects not limited to trauma.[10] Currently, the consortium consists of 84 academic medical centers and associated institutions located throughout the United States. The UHC Trauma Benchmarking Study was designed to compare outcomes and resource utilization among centers in 2 separate and homogeneous cohorts of patients, those with isolated PAI and those with a minimum of a combination of long-bone fracture and head injury (ie, multisystem blunt trauma). This analysis was limited to level I or level II trauma centers that contributed at least 10 patients to the UHC Trauma Benchmarking Study. Not all members of the UHC participated in the Trauma Benchmarking Study and not all centers contributed patients to both cohorts. Trauma center volume was derived from a related UHC operational database containing information on the organizational structure of each institution. Trauma center volume was reported from institutional registries and represented the total number of trauma admissions with an Injury Severity Score (ISS) of greater than 15 who were admitted during 1998. Patients with an ISS of greater than 15 are considered to have experienced major multisystem trauma. Thus, institutional volume refers to the annual number of major trauma admissions to that institution rather than the number of cases with index injuries contributed to the UHC Trauma Benchmarking Study.

Table 1. Study Inclusion and Exclusion Criteria

Multisystem Blunt Injury	Penetrating Abdominal Injury
Inclusion Criteria	
Age >18 y	Age >12 y
Head injury (Abbreviated Injury Scale[11] score ≥2)	Penetrating abdominal injury (highest Abbreviated Injury Scale[11] score in abdominal region)
Lower-extremity long-bone fracture (tibia/femur)	
Exclusion Criteria	
No vital signs on emergency department arrival	No vital signs on emergency department arrival
Burn injury	Burn injury
Pregnancy	Pregnancy
Spinal cord injury with neurologic deficit	Abbreviated Injury Scale[11] score >2 in any other body region
Length of stay >24 h at referring institution	Length of stay >24 h at referring institution

Inclusion and exclusion criteria for the 2 cohorts are shown in TABLE 1. The cohorts include consecutive patients meeting inclusion criteria and discharged from participating institutions during a 7-month period between June 1, 1998, and December 31, 1998 (multisystem blunt trauma), or a 9-month period between November 1, 1997, and July 31, 1998 (PAI). Data were collected by medical record abstraction and then collated by the UHC.

Statistical Analysis

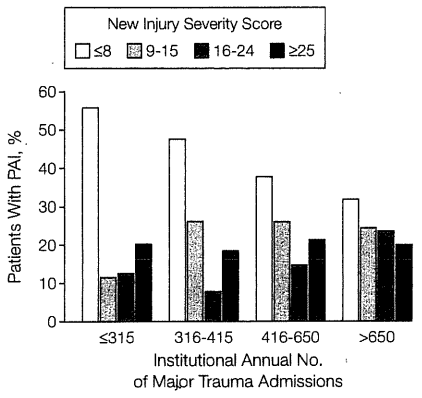
The primary outcomes were inpatient mortality and hospital length of stay (LOS). We considered the possibility that risk factors for mortality and prolonged LOS may not be similarly distributed across centers, thus confounding the effect of institutional volume on outcome. Several such risk factors were considered, including age, sex, mechanism of injury, injury severity, shock (systolic blood pressure <90 mm Hg) on admission to the emergency department, massive blood transfusion (>6 units in the first 24 hours), admission Glasgow Coma Scale score (GCS; 3-8, 9-12, or 13-15), and whether the patient had been transferred from another institution or was transported from the scene of injury. The New Injury Severity Score (NISS), a refinement of the ISS, was used as the summary measure of anatomic injury.[12-14] To adjust for these confounding variables, we constructed logistic (for mortality) and linear (for LOS) regression models separately for both multisystem blunt trauma and PAI. In-hospital deaths were excluded from all LOS analyses. Confounding variables were chosen for inclusion in these models by using a change in estimates approach. Briefly, if the addition of a variable to the model changed the estimate of the main effect (ie, trauma center volume) by greater than 10%, then the variable was considered to be an important confounder and was kept in the model.[15] We used variance estimators that allowed for the possibility that observations within each center might be correlated. To ensure optimal model fit, we used a backward stepwise regression technique using all variables, with the predetermined confounding variables forced into the model. We also considered the possibility that the ef-

Table 2. Characteristics of Patients Admitted With Penetrating Abdominal Injury*

Characteristics	Total Major Trauma Admissions per y				*P* Value
	≤315	316-415	416-650	>650	
No. of institutions	5	6	6	5	
No. of patients	104	103	135	136	
Age, mean (SD), y	31 (10)	31 (11)	32 (11)	32 (11)	.77†
Male sex	87 (84)	92 (83)	112 (83)	121 (89)	.32‡
Mechanism of injury					
Firearm	51 (49)	46 (45)	78 (58)	65 (48)	.50
Stab	51 (49)	53 (51)	53 (39)	66 (49)	
Other	2 (2)	4 (4)	4 (2)	5 (4)	
Transferred from another center	27 (26)	33 (34)	23 (17)	28 (21)	.02‡
Shock§	2 (2)	4 (4)	14 (11)	16 (12)	.007‡
Massive blood transfusion‖	3 (3)	12 (12)	15 (11)	21 (16)	.02‡

*Data are No. (%) of all patients in that volume quartile unless otherwise specified.
†By analysis of variance.
‡By χ^2 test.
§Shock defined as systolic blood pressure <90 mm Hg on admission to hospital.
‖Massive blood transfusion defined as >6 units in the first 24 hours after admission.

Figure 1. Distribution of NISS Across Quartiles of Trauma Center Volume in Patients Admitted With PAI



NISS indicates New Injury Severity Score; PAI, penetrating abdominal injury.

fect of volume on outcomes may be modified by other factors. We tested interactions between markers of injury severity (shock on admission, coma on admission, and NISS) and institutional volume to determine whether the effect of volume on outcomes depended on either anatomical or physiologic injury severity. If the interaction terms were statistically significant ($P<.05$), then the results are presented by severity strata to demonstrate the effect modification. The first GCS recorded at the scene was used if data regarding GCS at the time of admission were unreliable because of intubation or pharmacologic paralysis. If field data were unavailable and the patient was intubated but not paralyzed, we imputed GCS from the motor component using an approach similar to that described by Meredith et al.[16] Patients intubated and paralyzed on admission without a GCS recorded at the scene were excluded from analysis.

Trauma center volume was first modeled as a continuous variable using the fractional polynomial method described by Royston and Altman[17] to demonstrate the relationship between volume and outcome and to help identify volume thresholds at which outcomes appear to change. This method makes no underlying assumptions regarding the relationship between volume and outcome.[18] As a result, the model is not constrained by a simple linear relationship. A significant limitation to this approach is that the comparator is limited to the lowest volume center. Thus, this approach places undue emphasis on the outcomes at a particular center. To provide a second means of assessing any association between trauma center volume and outcome, the variable representing volume was reparametrized to a binary variable such that institutions were categorized as either high- or low-volume centers. The volume threshold used for this stratification was derived graphically from the relationship between volume and outcomes obtained by using the first approach. For mortality, this was the point at which the odds of death began to change with increasing volume. Volume thresholds for LOS were estimated graphically by identifying the inflection point on the LOS-vs-institutional volume curve. As an approximation, this was the point at which increasing volumes yielded no further changes in LOS. Analyses were conducted with Stata statistical software, release 6.0 (Stata Corp, College Station, Tex).

RESULTS

Penetrating Abdominal Injury

A total of 478 patients who met the inclusion criteria for PAI were admitted to 22 academic trauma centers (21 level I and 1 level II). Among these centers, the institutional volume of major trauma ranged from 257 to 1050 per year. There were minimal differences in admission demographics and mechanism of injury of patients with PAI across institutional volume quartiles, with approximately half of all PAI patients admitted following injury from a firearm (TABLE 2). There were significant differences in the proportion of patients transferred from outside centers but no clear, consistent trend across quartiles. If anything, higher-volume centers admitted fewer transfer patients than lower-volume centers. Patients with PAI who were admitted to higher-volume institutions were significantly more likely to present with shock and require massive blood transfusion within 24 hours of admission. The NISS distribution was different across quartiles; admissions to higher-volume institutions had a significantly greater proportion of patients with more severe injuries ($P=.01$ by χ^2 test) (FIGURE 1).

In initial analyses, there was a significant interaction between the terms for shock at admission to the emergency department and trauma center volume. There was no discernible relationship between volume and crude mortality in patients without shock, while the crude risk of death appeared

to decline with increasing volume quartiles in patients with shock (TABLE 3). After adjusting for NISS, age, and need for massive blood transfusion, increasing volume had no effect on mortality in patients without shock (FIGURE 2A). In contrast, the adjusted odds of death in patients with PAI and shock declined dramatically as trauma center volume increased (Figure 2B). When a volume threshold of 650 cases per year was used to discriminate high- vs low-volume institutions, the crude odds ratio for death in high-volume centers was 0.22 (95% confidence interval [CI], 0.05-0.91); 12 (60%) of 20 patients with shock died at low-volume centers while only 4 (25%) of 16 died at high-volume centers. The adjusted relative odds of dying was 0.02 (95% CI, 0.002-0.25) in patients with shock admitted to high-volume institutions compared with similar patients admitted to low-volume centers.

To evaluate whether there was any association between hospital LOS and institutional volume, we used a similar approach except that in-hospital deaths were excluded. Volume was first modeled as a continuous variable in a regression analysis adjusting for NISS, age, presence of shock at admission, mechanism of injury, and need for massive blood transfusion. As shown in FIGURE 3, a reduction in LOS with increasing trauma center volume was only evident in patients with an NISS of more than 15. Hospital LOS declined steadily until institutional volume approached 550 cases per year. At this volume threshold, the crude mean (SD) LOS in patients with an NISS of more than 15 who were admitted to high- and low-volume centers was 10.0 (7.9) and 12.3 (10.6) days, respectively. The adjusted mean LOS was 1.6 (95% CI, 4.7 to −1.5) days shorter among patients with an NISS of more than 15 who were admitted to high-volume centers.

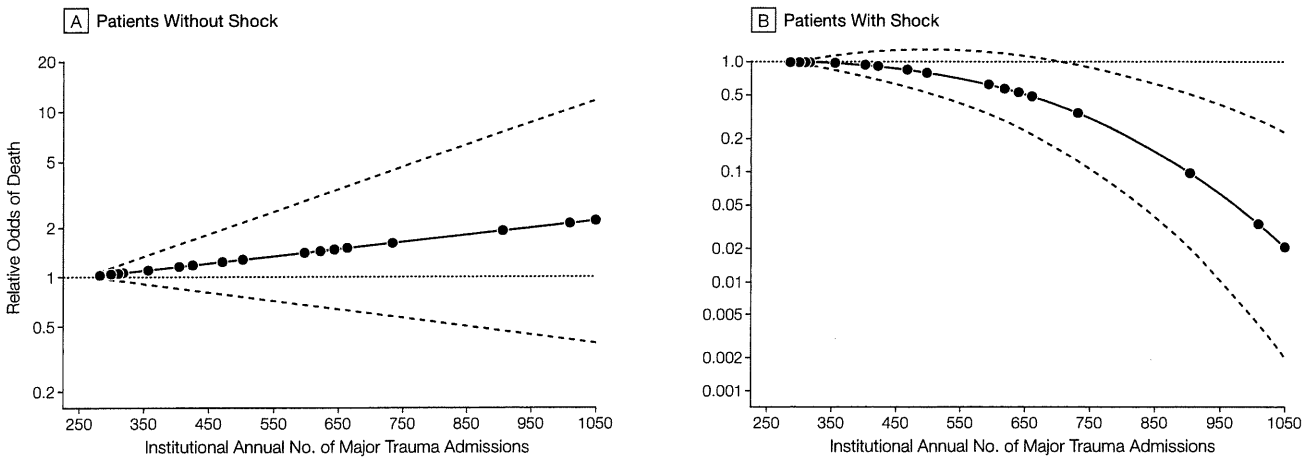
Multisystem Blunt Trauma

A total of 541 patients who met the inclusion criteria for multisystem blunt trauma were admitted to 25 academic level I trauma centers. Although only 16 of these 25 institutions contributed patients to the PAI cohort, the range of institutional volume of trauma admissions was identical for both cohorts. There were minimal differences in age, sex, and mechanism of injury in patients admitted to centers across volume quartiles defined for the PAI cohort (TABLE 4). Approximately 70% of all injuries were due to motor vehicle crashes. Imputation of GCS from the motor component was required in 30 cases (5%) and 12 cases were excluded from analysis because no reliable GCS data were available. Patients admitted to higher-volume centers were similar to those admitted to lower-volume centers in most respects. There was no consistent pattern to the distribution of NISS across volume quartiles; however, these differences in distributions approached statistical significance ($P = .05$) (FIGURE 4). There was no consistent trend in the proportion of patients admitted following transfer from another center, although the differences across quartiles were statistically significant, with

Table 3. Crude Mortality as a Function of Trauma Center Volume in Patients With Penetrating Abdominal Injury

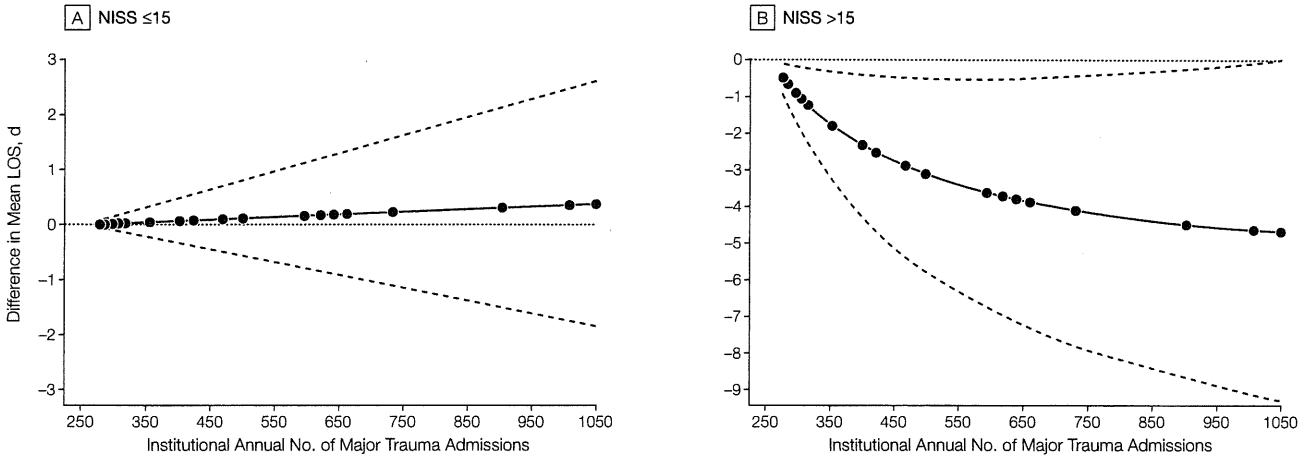
	Total Major Trauma Admissions per y				
No. (%) of Patients	≤315	316-415	416-650	>650	*P* Value
No shock	2/100 (2)	5/96 (5)	3/119 (3)	6/115 (5)	.50
Shock	0/2 (0)	3/4 (75)	9/14 (64)	4/16 (25)	.05

Figure 2. Association Between Adjusted Relative Odds of Death and Trauma Center Volume in Patients With PAI



Relative odds of death compared with the lowest-volume institution are shown for patients admitted (A) without and (B) with shock. These estimates are adjusted for New Injury Severity Score, age, and need for massive blood transfusion. PAI indicates penetrating abdominal injury. Dashed lines represent 95% confidence intervals for estimated odds ratios.

Figure 3. Differences in Mean LOS for Patients Admitted With PAI as a Function of Trauma Center Volume



Data are shown for patients with (A) New Injury Severity Score (NISS) ≤15 and (B) NISS >15. The differences represent the number of days by which the mean hospital length of stay (LOS) differed using the lowest-volume institution as a baseline. These estimates are adjusted for NISS, presence of shock on admission, need for massive blood transfusion, and mechanism of injury. PAI indicates penetrating abdominal injury. Dashed lines represent 95% confidence intervals for differences in mean LOS.

Table 4. Characteristics of Patients Admitted With Multisystem Blunt Trauma*

Characteristics	Total Major Trauma Admissions per y ≤315	316-415	416-650	>650	*P* Value
No. of institutions	5	11	4	5	
No. of patients	80	233	85	143	
Age, mean (SD), y	38 (17)	42 (17)	40 (17)	42 (17)	.95†
Male sex	48 (60)	161 (69)	56 (60)	101 (71)	.37‡
Mechanism of injury					
Motor vehicle crash	60 (75)	143 (61)	69 (81)	100 (70)	.02‡
Pedestrian-motor vehicle crash	9 (11)	51 (22)	11 (13)	20 (14)	
Fall	2 (3)	16 (6)	3 (4)	11 (8)	
Other/unknown	9 (11)	23 (10)	2 (2)	12 (8.4)	
Transferred from another center	28 (35)	79 (34)	44 (52)	28 (20)	<.001‡
Shock§	11 (14)	25 (11)	8 (9)	20 (14)	.67‡
Glasgow Coma Scale score in emergency department					
3-8	23 (29)	58 (26)	15 (18)	46 (33)	.18‡
9-12	5 (6)	22 (10)	7 (8)	16 (11)	
13-15	51 (65)	143 (64)	63 (74)	79 (56)	
Massive blood transfusion‖	18 (23)	39 (17)	14 (16)	27 (19)	.67‡

*Data are No. (%) of all patients in that volume quartile unless otherwise specified.
†By analysis of variance.
‡By χ^2 test.
§Shock defined as systolic blood pressure <90 mm Hg on admission to emergency department.
‖Massive blood transfusion defined as >6 units in the first 24 hours after admission to emergency department.

centers in the highest-volume quartiles admitting the lowest proportion of transfer patients.

The effect of institutional trauma volume on mortality in this second cohort of patients was initially assessed by using a logistic regression model with volume as a continuous variable. There was significant interaction between the terms for coma at admission and trauma center volume. Crude mortality increased in patients without coma in higher-volume quartiles, an effect that approached statistical significance ($P=.05$), while mortality declined in increasing volume quartiles in patients with coma ($P=.02$) (TABLE 5). After adjusting estimates for NISS, age, GCS, and presence of shock at admission, the adjusted odds of death was independent of institutional volume in patients without coma, although there appeared to be a trend toward increasing risk of death in the moderate-volume range (FIGURE 5A). In contrast, the adjusted odds of death were lower in patients with coma presenting to higher-volume institutions (Figure 5B). The volume threshold for this effect was between 650 and 750 cases per year. Using a conservative volume threshold of 650 cases per year, the crude odds ratio for death was 0.31 (95% CI, 0.14-0.68) in institutions whose volume exceeded this threshold compared with lower-volume centers; 48 (50%) of 96 patients presenting with coma died in low-volume centers while only 11 (24%) of 46 (24%) died in high-volume centers. The adjusted relative odds of death in patients admitted with coma to high- vs low-volume centers was 0.49 (95% CI, 0.26-0.93).

The relationship between institutional volume and LOS was not influenced by the degree of anatomical or physiologic injury severity in this cohort of patients. Hospital LOS adjusted for shock, sex, age, GCS, NISS, and need for massive blood transfusion as a function of trauma center vol-

ume is demonstrated in FIGURE 6. Hospital LOS following multisystem blunt trauma declined until institutional volume approached 600 cases per year, at which point no further reduction was evident. Crude LOS tended to be lower in centers above this threshold compared with those below, with a mean (SD) LOS of 13.4 (11.1) days in high-volume centers compared with 15.7 (15.8) days in low-volume centers. The adjusted mean LOS was 3.3 (95% CI, 0.91-5.7) days shorter in high-volume institutions.

COMMENT

This study provides strong evidence of a relationship between trauma center volume and outcome in severely injured persons with penetrating or blunt trauma. This association is only evident in the patient subgroups at highest risk of adverse outcomes. After adjusting for differences in injury severity, centers with total major trauma volume (ISS >15) in excess of 650 cases per year demonstrated measurable improvements in mortality and LOS. The relative odds of death in patients admitted with shock following PAI or coma following multisystem blunt trauma were significantly lower in high-volume centers compared with low-volume centers. Furthermore, patients with complex or severe injuries (NISS >15) following PAI and all patients with multisystem blunt trauma tended to have a shorter LOS if admitted to a high-volume center.

The premise underlying the process of regionalization of trauma care is that the concentration of care in relatively few dedicated centers will increase institutional volume and experience, leading to improved outcome.[1,2,19] Despite its importance to trauma system development, there have been relatively few studies directly evaluating the effect of trauma center volume on outcome. In the studies that have been published, the relationship is far from clear. In 7 trauma centers in Chicago, Ill, there was a 30% reduction in mortality among patients admitted to a high-volume center, defined as more than 200 seriously injured cases per year.[20] Although these data are consistent with the data in the current study, a very crude adjustment for differing case-mix across centers and a relatively arbitrary volume threshold hamper any definitive interpretation. Tepas et al[21] assessed the relationship between volume and mortality among pediatric patients admitted to 37 trauma

Figure 4. Distribution of New Injury Severity Score (NISS) Across Quartiles of Trauma Center Volume in Patients Admitted With Multisystem Blunt Trauma

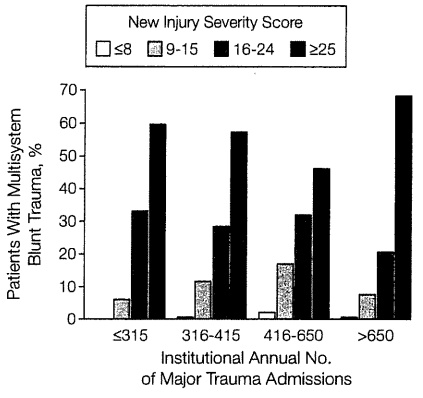
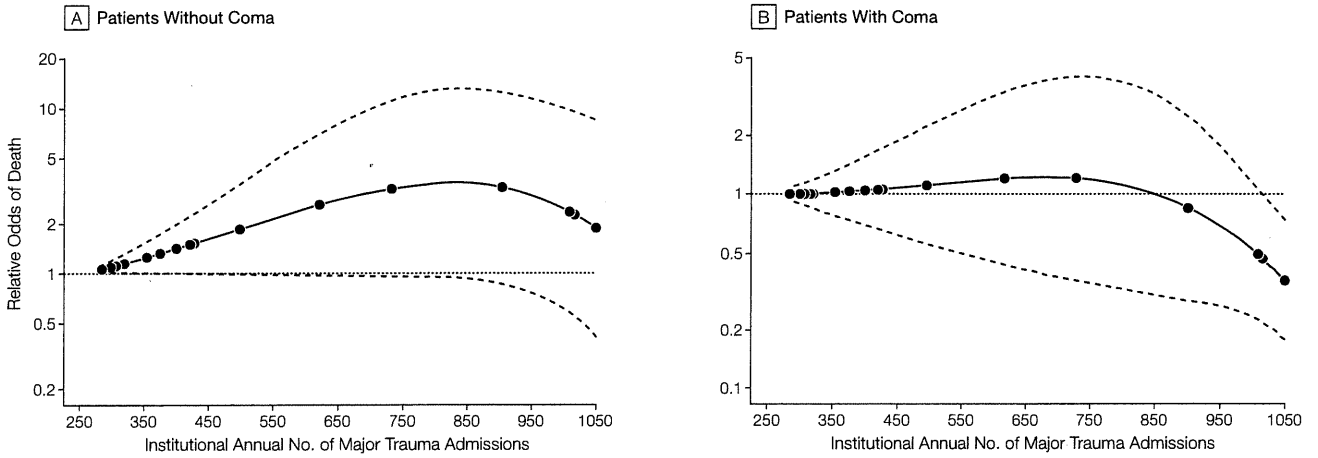


Table 5. Crude Mortality as a Function of Trauma Center Volume in Patients With Multisystem Blunt Trauma Injury

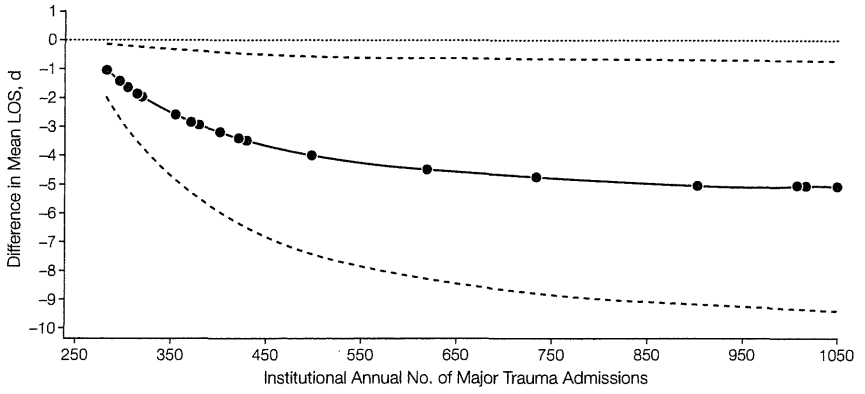
	Total Major Trauma Admissions per y				
No. (%) of Patients	≤315	316-415	416-650	>650	*P* Value
No coma	1/56 (2)	7/163 (4)	4/70 (6)	11/94 (12)	.05
Coma	13/23 (57)	29/58 (50)	6/15 (40)	11/46 (24)	.02

Figure 5. Association Between Adjusted Relative Odds of Death and Trauma Center Volume in Patients Admitted With Multisystem Blunt Trauma



Relative odds of death compared with the lowest-volume institution are shown for patients (A) without and (B) with coma. These estimates are adjusted for New Injury Severity Score, age, Glasgow Coma Scale score, and presence of shock on admission. Dashed lines represent 95% confidence intervals for estimated odds ratios.

Figure 6. Differences in Mean LOS for Patients Admitted With Multisystem Blunt Trauma as a Function of Trauma Center Volume



The differences represent the number of days by which the mean hospital length of stay (LOS) differs using the lowest-volume institution as a baseline. These estimates are adjusted for New Injury Severity Score, age, sex, Glasgow Coma Scale score, need for massive blood transfusion, and presence of shock on admission. Dashed lines represent 95% confidence intervals for differences in mean LOS.

centers participating in the National Pediatric Trauma Registry. In this analysis, risk-adjusted mortality was lowest in the moderate-volume centers. The authors postulated that higher-volume centers functioned at a lower level because of an overwhelming number of admissions with minimal trauma. Finally, there appeared to be no association between trauma center volume and outcomes following an evaluation of trauma centers in Pennsylvania.[22] However, using a survival probability model, these authors demonstrated normative outcomes when individual surgeon volumes approached 35 seriously injured patients per year. Based on these studies and empirical data, the American College of Surgeons Committee on Trauma recommends that level I trauma centers admit a minimum of 1200 trauma patients annually, of which 20% should have an ISS of more than 15. Alternatively, volume per surgeon should exceed 35 patients per year with an ISS of more than 15.[9] However, Cooper et al,[23] in an evaluation of trauma center volume and outcomes in New York State, could not demonstrate any association between this and other volume thresholds and mortality. Unfortunately, the largest-volume center in that study admitted approximately 350 patients per year with an ISS of more than 15, a far lower number than that of most of the centers participating in the current analysis.

The current study offers several methodological strengths and improvements in design compared with prior reports. By first modeling volume as a continuous variable, we avoided the use of arbitrary volume thresholds to categorize trauma centers into volume quartiles. This approach provides an estimate of the relative difference in outcome at any particular volume compared with the lowest-volume center and suggests appropriate volume thresholds for further analysis. In addition, we controlled for differences in injury severity and patient demographics across centers, thus mitigating the effects of potentially confounding variables. We also considered the possibility that the effect of volume on outcomes may relate to the severity of injury. In fact, there is no a priori reason to believe that patients with minimal trauma in whom mortality risk approaches zero would demonstrate a mortality benefit from the resources of a high-volume level I trauma center. The geographic diversity of institutions studied in this analysis provides an additional benefit. Other studies comparing institutions within the same geographic locale may confound the relationship between volume and outcomes in the form of selective referral bias, in which volumes increase at a given center because of improved outcomes, rather than the converse. Due to the urgent nature of trauma care, referrals and transfers across regions from one level I trauma center to another are extraordinarily rare. As a result, the volume of any particular center in this analysis is not higher than the volume in any other because of superior outcomes, because these centers are not competing for the same pool of patients. Finally, the relative consistency in the volume threshold using 2 different (albeit homogeneous) cohorts provides compelling evidence that patients admitted to institutions above this threshold do achieve a mortality benefit from this level of experience.

There are several significant limitations to this study. As volunteer participants in the UHC Trauma Benchmarking Study, all of the centers function as level I or level II academic trauma centers, with a full complement of surgical residents and an active teaching program. Furthermore, because of their participation in the UHC Benchmarking Study, these centers are committed to quality improvement. For these reasons, their performance may exceed those of other trauma centers not participating in the study. Similarly, all of the institutions have reached a predetermined level of quality by virtue of being designated by either the American College of Surgeons or regional authorities. As a result, the volume thresholds reported here might be higher than previously reported to demonstrate benefit in addition to what might already be considered optimal care. Nevertheless, an association between experience and outcomes appears to exist even at this level of quality.

The potential for poor interinstitutional reliability in coding injury severity may represent an additional limitation to this analysis. This phenomenon could have important effects on our ability to adjust for risk differences across centers and might account for the vary-

ing effects of institutional volume on mortality in patients without coma. The GCS is one of the most important predictors of mortality in blunt trauma patients. Unfortunately, it is also the least reliable, particularly in patients who are intubated or paralyzed.[24] It is possible that lower-volume institutions tend to underestimate GCS in patients with minor head injuries. Alternatively, lower-volume institutions may have better outcomes for patients with minor head injuries, an effect due to a lesser demand on resources; however, the downward trend in the highest-volume institutions argues against this possibility.

Additionally, patients were excluded from their respective cohorts if they had no vital signs at admission to the emergency department. The state of presentation may be altered by prehospital care such that a patient whose death is attributed to the care of one center may be considered dead on arrival at another, excluding them from inclusion in the evaluable cohort. Finally, it is possible that patients traveling long distances to receive definitive care at a high-volume center may die en route and, thus, will not be considered a death attributable to these centers while those who survive are self-selected, having already survived a prolonged period of prehospital care. These biases may be problematic if they relate to trauma center volume. The extent to which this may impact our results cannot be assessed given the data available.

In summary, these data provide further support emphasizing the importance of regionalization of trauma care and provide guidelines for estimating the number of trauma centers per unit population. The volume threshold of approximately 650 cases per year with an ISS of more than 15 may be difficult to attain in all but a few large metropolitan areas. In this study, only 6 (20%) of 31 level I or level II trauma centers exceeded this threshold. Although these volumes may not be attainable in most centers, these data support the hypothesis that greater experience leads to better outcomes. Trauma care systems should ensure triage of the most severely injured patients to relatively few dedicated trauma centers. Consideration should be given to consolidation of urban trauma programs to maximize institutional volume. Further work is needed to identify differences in process of care, the impact of individual surgeon volume, the role of fellowship training programs, trauma research activities, and other factors that may contribute to the observed outcome benefit at high-volume trauma centers.

Author Contributions: *Study concept and design:* Nathens, Jurkovich, Maier, Grossman, MacKenzie, Rivara.
Acquisition of data: Grossman, MacKenzie, Moore, Rivara.
Analysis and interpretation of data: Nathens, Jurkovich, Maier, Grossman, MacKenzie, Rivara.
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Obtained funding: Jurkovich, Maier, Grossman, MacKenzie, Rivara.
Administrative, technical, or material support: Jurkovich, Maier, Grossman, Moore, Rivara.
Study supervision: Jurkovich, Maier, Rivara.
Funding/Support: This work was supported by grant R49/CCR002570 from the Centers for Disease Control and Prevention.
Previous Presentation: Presented in part at the annual meeting of the American College of Surgeons Committee on Trauma, Reno, Nev, March 9, 2000.

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Pediatric and Neonatal Extracorporeal Membrane Oxygenation: Does Center Volume Impact Mortality?*

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Objective: Extracorporeal membrane oxygenation, an accepted rescue therapy for refractory cardiopulmonary failure, requires a complex multidisciplinary approach and advanced technology. Little is known about the relationship between a center's case volume and patient mortality. The purpose of this study was to analyze the relationship between hospital extracorporeal membrane oxygenation annual volume and in-hospital mortality and assess if a minimum hospital volume could be recommended.

Design: Retrospective cohort study.

Setting: A retrospective cohort admitted to children's hospitals in the Pediatric Health Information System database from 2004 to 2011 supported with extracorporeal membrane oxygenation was identified. Indications were assigned based on patient age (neonatal vs pediatric), diagnosis, and procedure codes. Average hospital annual volume was defined as 0–19, 20–49, or greater than or equal to 50 cases per year. Maximum likelihood estimates were used to assess minimum annual case volume.

Patients: A total of 7,322 pediatric patients aged 0–18 were supported with extracorporeal membrane oxygenation and had an indication assigned.

Interventions: None.

Measurements and Main Results: Average hospital extracorporeal membrane oxygenation volume ranged from 1 to 58 cases per year. Overall mortality was 43% but differed significantly by indication. After adjustment for case-mix, complexity of cardiac surgery, and year of treatment, patients treated at medium-volume centers (odds ratio, 0.86; 95% CI, 0.75–0.98) and high-volume centers (odds ratio, 0.75; 95% CI, 0.63–0.89) had significantly lower odds of death compared with those treated at low-volume centers. The minimum annual case load most significantly associated with lower mortality was 22 (95% CI, 22–28).

Conclusions: Pediatric centers with low extracorporeal membrane oxygenation average annual case volume had significantly higher mortality and a minimum volume of 22 cases per year was associated with improved mortality. We suggest that this threshold should be evaluated by additional study. (*Crit Care Med* 2014; 42:512–519)

Key Words: cardiopulmonary resuscitation; critical care; extracorporeal membrane oxygenation; low-volume hospitals; pediatrics; risk adjustment

Extracorporeal membrane oxygenation (ECMO) provides prolonged partial cardiopulmonary bypass and has been used for infants and children with severe cardiopulmonary failure unresponsive to conventional therapy since 1975 (1–3). More recently, this complex technology has been successfully used emergently to rescue "failing" ECMO deployment during cardiopulmonary resuscitation (E-CPR) (4–6). Initial successful applications of ECMO were almost exclusively among term neonates with pulmonary hypertension; however, ECMO has increasingly been used to support older children and adults with both cardiorespiratory failure and cardiac arrest (6–8). Practice in the United Kingdom has

*See also p. 726.

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Dr. Freeman is employed by the University of Utah, Graduate Medical Education (fellowship) and disclosed other: 2013 Annual Scientific Award, Society of Critical Care Medicine. Dr. Bennett and his institution received grant support from the National Institutes of Health (NIH)/National Cancer Institute (Mentored Scholars Program in Translational Comparative Effectiveness Research, 11/1/10-10/31/12) and National Institute of Child Health and Human Development (Pediatric Critical Care Scientist Development Program K12, 1/1/13-12/31/17). Dr. Bennett received support for article research from the NIH. Dr. Bennett and his institution received grant support from NIH/NCI (Mentored Scholars Program in Translational Comparative Effectiveness Research) and NICHD (Pediatric Critical Care Scientist Development Program K12). Dr. Bratton serves as the sub-board pediatric critical care medicine chair with the American Board of Pediatrics, is employed by the University of Utah, lectured and received support for travel from the European Pediatric Academic Society, and lectured for Extracorporeal Life Support Organization. The remaining authors have disclosed that they do not have any potential conflicts of interest.

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DOI: 10.1097/01.ccm.0000435674.83682.96

focused on regional ECMO referral centers while development in the United States has not been centralized (7, 9).

There are numerous reports regarding increasing surgical experience and center volume demonstrating lower mortality in many high-risk surgical procedures (10–13). These observations led to recommendations regarding minimum volume standards for some surgical procedures (12). The favorable relationship between increasing volume and improved outcome also exists for infants and children with some complex conditions (14, 15).

Given that pediatric and neonatal ECMO are highly complex medical-surgical endeavors, a reasonable hypothesis is that center experience and volume may be associated with mortality. There are no large multicenter reports addressing pediatric ECMO center volume and survival. We used a large administrative pediatric database to determine if after adjustment for case-mix, center volume was associated with mortality. Our hypothesis was that an inverse relationship existed between ECMO center volume and mortality. Because applications of ECMO are expanding among both children and adults, study of this high-cost rescue therapy is increasingly important.

MATERIALS AND METHODS

Data Source

The Pediatric Health Information System (PHIS) database, a multicenter administrative database with data from over 40 children's hospitals in the United States, was used. Participating hospitals provide data on demographics, outcomes, diagnoses, procedures, and charges using Clinical Transaction Classification (CTC) codes for billed services (16, 17). Data are de-identified centrally which qualified for exemption from human subjects review by the University of Utah Institutional Review Board.

Patients

Patients admitted between January 1, 2004, and December 31, 2011, less than 18 years old, with an *International Classification of Diseases*, Ninth Revision, Clinical Modification (ICD-9-CM), procedure code for ECMO (39.65) or CTC code for ECMO (521181) were evaluated for inclusion.

Diagnosis Groups

Diagnostic categorization emulated categorizations used by the Extracorporeal Life Support Organization (ELSO) ECMO indications (**Fig. 1**). See details of the diagnostic categorization in **Appendix 1** (Supplemental Digital Content 1, http://links.lww.com/CCM/A754). Seven diagnostic categories were defined: congenital diaphragmatic hernia (CDH), neonatal or pediatric respiratory failure, neonatal or pediatric cardiac disease, and neonatal or pediatric cardiac arrest. Available data could not distinguish a cardiac arrest prior to initiation of ECMO from an ongoing arrest when starting ECMO (i.e., E-CPR). All patients with a cardiac arrest were classified as neonatal or pediatric cardiac arrest regardless of other diagnosis codes except for CDH as cardiac arrest in this group is rarely the indication for ECMO (4).

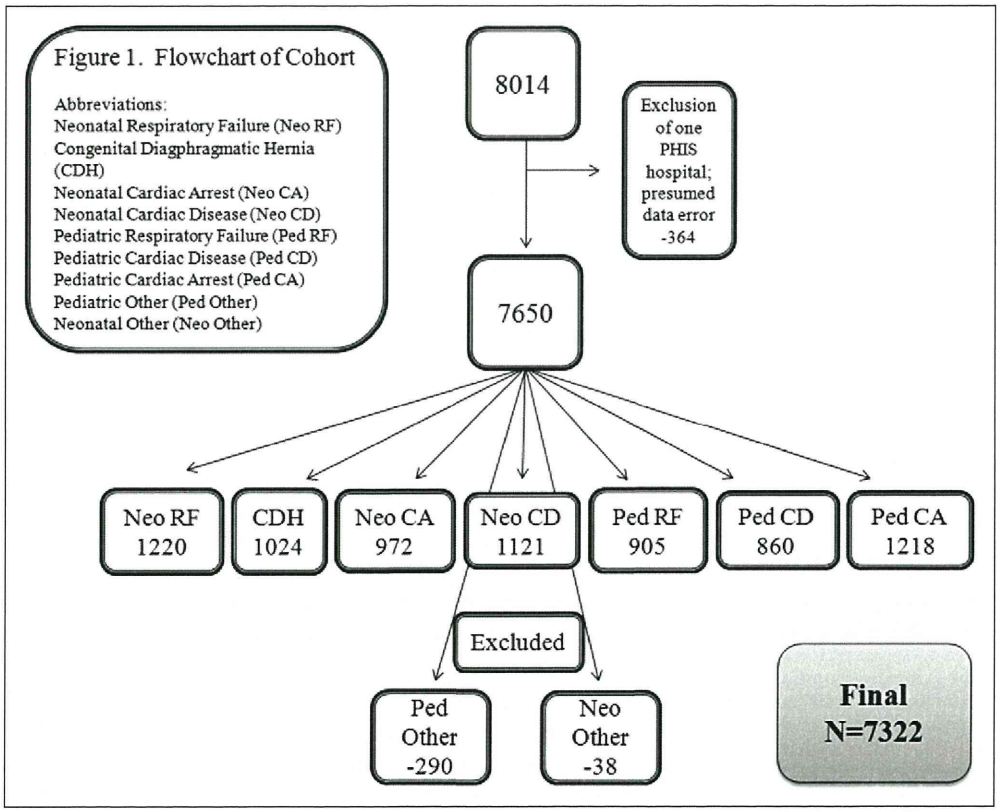

Figure 1. Flowchart of cohort inclusions, exclusions, and diagnostic categorization. PHIS = Pediatric Health Information System, Neo RF = neonatal respiratory failure, CDH = congenital diaphragmatic hernia, Neo CA = neonatal cardiac arrest, Neo CD = neonatal cardiac disease, Ped RF = pediatric respiratory failure, Ped CD = pediatric cardiac disease, Ped CA = pediatric cardiac arrest, Ped Other = pediatric other, Neo Other = neonatal other.

Study Variables

The primary outcome was in-hospital mortality and primary exposure was annual hospital ECMO volume. Covariates included demographics, year of admission, and ECMO indication. Risk Adjustment for Congenital Heart Surgery (RACHS-1) was used to adjust for complexity of cardiac surgical repair as mortality is increased for patients with single ventricle physiology after both cardiac surgery and E-CPR (18–20).

Hospital Variables

We created an average annual ECMO volume for each hospital over the study period using quarterly data and averaged to cases per year. Empirically, hospital volume was categorized as

low, medium, or high, that is, 0–19, 20–49, and greater than or equal to 50 average ECMO cases per year based on clinical assessment, respectively. Average annual ECMO volume was also evaluated continuously.

Subgroup Analysis

Two additional diagnostic categories, respiratory syncytial virus (RSV) bronchiolitis and stage 1 palliation in hypoplastic left heart syndrome (HLHS), were created due to their consistent coding to evaluate homogenous groups (Appendix 1, Supplemental Digital Content 1, http://links.lww.com/CCM/A754).

Statistical Analyses

Statistical analyses were performed using SPSS 18.0 (SPSS, Chicago, IL) and the R Language and Environment (21). Categorical data were compared using the chi-square test and continuous data using the Wilcoxon rank sum test; p value less than 0.05 was considered significant. Multivariable logistic regression was used to evaluate ECMO volume and hospital mortality. Center case-mix was adjusted for indication for ECMO which included age, ECMO support year, and RACHS-1 scores for classified congenital cardiothoracic procedures.

We also sought to evaluate a potential "cut point" for minimal annual ECMO volume associated with improved survival using a maximum likelihood approach. This approach is based on the assumptions that such a cut point exists and patients at centers falling on the same side of the cut point have the same chance of survival. A likelihood was calculated for each possible cut point and the optimal point was chosen as the value providing the highest likelihood. To assess the precision of the cut point estimate, a CI was calculated using a nonparametric bootstrap method (22).

RESULTS

Seven thousand three hundred twenty-two children meeting study criteria underwent ECMO support from 2004 to 2011. Children's hospitals within this cohort performed an average of 1 to 58 ECMO cases per year. Overall in-hospital mortality was 43%. Comparing patients who survived with those who died (**Table 1**), there were significant differences related to patient age, indication for ECMO, year of ECMO support, length of stay, and treating hospital ECMO volume. Fifteen hospitals were categorized as low-volume centers, 22 as medium-volume centers, and three as high-volume centers representing 16%, 69%, and 15% of the patient cohort, respectively.

Table 2 describes patient characteristics by ECMO volume category. Overall mortality was significantly higher at low-volume centers (47%) compared with medium- and high-volume centers (42% and 41%) ($p = 0.01$). However, the indication for ECMO also differed significantly by center volume categories, with more cardiac disease patients in the low ECMO volume group and more cardiac arrest cases treated at high-volume centers, whereas neonatal respiratory cases were more common at low- and medium-volume centers. ECMO indications by patient age groups (neonatal vs older children) are highlighted in Table 2.

After adjusting for these potential confounders, significantly higher mortality persisted at low-volume centers compared with medium- (odds ratio [OR], 0.86; 95% CI, 0.75–0.98) and high-volume centers (OR, 0.75; 95% CI, 0.63–0.89) (**Table 3**). Age was included within indication for ECMO as neonatal versus older patients. A second logistic regression model including average center volume as a continuous variable found that for each additional 10 patients per year, the odds of mortality decreased 5% (OR, 0.95; 95% CI, 0.92–0.98).

Subgroup Analysis

Because of concern regarding potential misclassification of ECMO indication, a subset of patients who had consistent ICD-9-CM procedure and diagnosis coding was evaluated. CDH (n = 1,016), HLHS with stage 1 palliation surgery (n = 522), and patients with RSV bronchiolitis (n = 217) were identified using the ICD-9-CM procedure and diagnosis codes described in Appendix 1 (Supplemental Digital Content 1, http://links.lww.com/CCM/A754). **Table 4** shows this subset and compares mortality by center volume. In-hospital mortality differed by indication and was 54% for CDH, 31% for RSV, and 62% for HLHS undergoing stage 1 palliation. A similar multivariable analysis of this subset adjusting for primary diagnosis as well as presence of a cardiac arrest and year of treatment found that patients treated at both medium and high ECMO volume centers had significantly lower odds of mortality (OR, 0.74; 95% CI, 0.56–0.98 and OR, 0.59; 95% CI, 0.42–0.83, respectively) compared with low-volume centers.

Finally, we evaluated center average annual ECMO volume and unadjusted mortality (**Fig. 2**). Evaluating death and the annual ECMO volume at each center, the maximum likelihood estimate of the optimal cutoff for volume was a minimum of 22 ECMO cases per year. An identical result was found when risk factors were included in logistic regression models. This was also the cutoff that produced the most significant difference between high- and low-volume centers ($p = 0.00001$). We found no evidence that the model assumptions were violated. The 95% bootstrap CI, from both univariate and multivariate models, was 22–28 average annual cases.

DISCUSSION

In this large retrospective multicenter database, we found that ECMO centers caring for fewer than 20 ECMO cases annually had significantly higher case-mix adjusted mortality than centers with larger ECMO volume. Centers had wide variation in application of ECMO by indication as well as length of stay. However, when defining indications in a manner similar to ELSO and using a subgroup analysis, we continued to find a survival benefit for infants and children treated at medium to large ECMO volume centers compared with those treated at smaller centers. There was no significant difference in mortality between the medium- and high-volume centers. ECMO requires complex coordination of multiple providers to deliver care. Logically such care would appear sensitive to case volume;

TABLE 1. Patient Demographics and Extracorporeal Membrane Oxygenation Center Volume Comparing Pediatric Survivors With Nonsurvivors

Variable	Survivors *n* = 4,191 *n* (%)	Nonsurvivors *n* = 3,131 *n* (%)	*p*
Age			< 0.001
0–7 d	2,342 (56)	1,760 (56)	
8–30 d	156 (4)	156 (5)	
31–365 d	721 (17)	494 (16)	
1–10 yr	663 (16)	432 (14)	
> 10 yr	309 (7)	289 (9)	0.83
Male	2,341 (56)	1,741 (56)	
Race			< 0.001
Black	814 (19)	453 (15)	
White	1,988 (47)	1,493 (43)	
Hispanic	656 (16)	479 (15)	
Asian	91 (2)	78 (3)	
Other	518 (12)	442 (14)	
Unknown	124 (3)	186 (6)	
Insurance			0.15
Public	2,122 (51)	1,579 (50)	
Private	1,417 (34)	1,120 (36)	
No insurance	87 (2)	63 (2)	
Other	411 (10)	259 (8)	
Unknown	154 (4)	110 (4)	
Length of stay (d)[a]	38 (21, 66)	19 (8, 19)	< 0.001
Indication for ECMO			< 0.001
Neonatal respiratory failure	986 (24)	236 (8)	
Congenital diaphragmatic hernia	475 (11)	549 (18)	
Neonatal cardiac arrest	417 (10)	555 (18)	
Neonatal cardiac disease	590 (14)	531 (17)	
Pediatric respiratory failure	511 (12)	394 (13)	
Pediatric cardiac arrest	636 (15)	582 (19)	
Pediatric cardiac disease	576 (14)	284 (9)	
Year of ECMO			0.02
2004–2007	1,858 (44)	1,473 (47)	
2008–2011	2,333 (56)	1,658 (53)	
Center volume (average ECMO cases/yr)			0.01
Low (0–19) (15 hospitals)	619 (15)	539 (17)	
Medium (20–49) (22 hospitals)	2,909 (69)	2,137 (68)	
High (≥ 50) (three hospitals)	663 (16)	455 (15)	

ECMO = extracorporeal membrane oxygenation.
[a]Data presented as median (interquartile ranges).

TABLE 2. Patient Characteristics by Center Extracorporeal Membrane Oxygenation Volume

Characteristic	Low $n = 1,158$	Medium $n = 5,046$	High $n = 1,118$	p
Overall mortality	539 (47)	2,137 (42)	455 (41)	0.01
Neonatal ECMO (< 31 d)	$n = 682$ (59)	$n = 3,050$ (60)	$n = 607$ (54)	
Indication for ECMO	n (%)	n (%)	n (%)	< 0.001
Respiratory failure	188 (28)	885 (29)	149 (25)	
Congenital diaphragmatic hernia	153 (22)	724 (24)	147 (24)	
Cardiac disease	202 (30)	792 (26)	127 (21)	
Cardiac arrest	139 (20)	649 (21)	184 (30)	
Neonatal mortality	320 (47)	1,292 (42)	259 (43)	0.09
ECMO year				0.001
2004–2007	370 (54)	1,459 (48)	268 (44)	
2008–2011	312 (46)	1,591 (52)	339 (56)	
Length of stay (d)[a]	32 (16, 62)	31 (17, 58)	31 (16, 60)	0.67
Pediatric ECMO	$n = 476$ (41)	$n = 1,996$ (40)	$n = 511$ (46)	
Indication for ECMO	n (%)	n (%)	n (%)	0.11
Respiratory failure	159 (33)	580 (29)	166 (33)	
Cardiac disease	120 (25)	603 (30)	137 (27)	
Cardiac arrest	197 (41)	813 (41)	208 (41)	
Pediatric mortality	219 (46)	845 (42)	196 (38)	0.05
ECMO year				0.08
2004–2007	211 (44)	797 (40)	226 (44)	
2008–2011	265 (56)	1,199 (60)	285 (56)	
Length of stay (d)[a]	23 (9, 47)	28 (11, 56)	26 (13, 47)	0.04

ECMO = extracorporeal membrane oxygenation.

however, this is the first large evaluation of case-mix-adjusted pediatric ECMO volume and mortality.

Numerous studies have suggested an inverse relationship between surgical volume and mortality (12, 23). Bucher et al (14) describe the positive impact of volume on in-hospital mortality in infants with CDH also using the PHIS database. Several reports found an association between small surgical volume and increased mortality (15, 24, 25). In addition, recent reports have found an increasingly complex relationship with decreased mortality overall and the greatest difference in survival shown in the most complex conditions (26, 27). ELSO does suggest that ECMO centers perform a minimum of six ECMO cases annually (28); however, this is based on expert opinion.

For our study, ECMO indications were based on diagnosis codes and age as PHIS does not have data regarding specific indication for ECMO. Centers differed both in annual case volume and case-mix. Survival with ECMO support differs by indication for cardiorespiratory failure with the lowest mortality among neonates with respiratory failure and substantially higher mortality for patients with cardiac failure after surgery for congenital heart disease, cardiac arrest, and E-CPR (29–35). The recent 2012 ELSO international report of infants with CDH treated from 2004 to 2011 had an average annual survival of 46% mirroring our results (36). Likewise, patients with pediatric respiratory failure requiring ECMO had the same average annual survival, 56%, echoing the in-hospital mortality of our cohort with similar diagnoses (29). Sherwin et al (32) found a 69% mortality after stage 1 palliation in patients with HLHS supported by ECMO, which is similar to our subgroup analysis mortality (62%) that included cardiac arrest patients who may be classified as E-CPR cases in ELSO (19). Our neonatal cardiac arrest survival was 43% and pediatric cardiac arrest survival was 52%, which are similar to recent survival reported with E-CPR (44–47%) (33–35).

The post hoc analysis for an annual volume threshold of 22 cases is substantially greater than the ELSO recommendation of six cases per year. The PHIS hospitals are predominately large freestanding U.S. Children's Hospitals and likely are not representative of all ECMO centers. Furthermore, information

TABLE 3. Center Volume and Mortality Risk Model

Factor	OR	95% CI
Center volume		
Low	1	Reference group
Medium	0.86	0.75–0.98
High	0.75	0.63–0.89
Indications for extracorporeal membrane oxygenation		
Neonatal respiratory failure	1	Reference group
Congenital diaphragmatic hernia	4.94	4.09–5.96
Neonatal cardiac disease	4.09	3.32–5.03
Neonatal cardiac arrest	6.21	4.97–7.76
Pediatric respiratory failure	3.28	2.70–3.99
Pediatric cardiac disease	2.54	2.04–3.16
Pediatric cardiac arrest	4.50	3.71–5.46
Years treated		
2004–2007	1	Reference group
2008–2010	0.86	0.78–0.95

OR = odds ratio.

regarding the ECMO program structure at each hospital is not available. Some institutions have a centralized unit and medical supervision for patients on ECMO, whereas others offer ECMO in several different locations and medical supervision ranges from a core group to inclusion of all critical care physicians. Unfortunately, evaluation of whether survival is affected by only hospital volume versus provider volume and/or specific ICU (i.e., neonatal vs pediatric vs cardiac) volume was not possible. The consistent association of higher mortality at small volume centers should be validated by additional study. However, our findings lend support to the regionalized approach used in the United Kingdom although there is potential risk in transporting these critically ill ECMO patients.

Our study is limited by the retrospective and observational nature of the data and that many ECMO specific data were not prospectively collected. When using ICD-9-CM codes, many patients have overlapping codes and we chose to devise rules for diagnostic indications that mirrored definitions used in the ELSO registry to enable comparison. Our method certainly misclassifies some cases; however, our data regarding survival by indication are generally similar to other reports. For instance, neonates sometimes had respiratory codes appropriate for older ages; therefore, assumptions were necessary regarding age. However, analysis of a subset of pediatric patients with CDH, RSV, and HLHS (more clearly defined diagnoses), despite a smaller number in the cohort, found

TABLE 4. Subgroup Analysis of Mortality and Center Volume

Variable	Congenital Diaphragmatic Hernia *n* = 1,016 *n* (%)	Respiratory Syncytial Virus *n* = 217 *n* (%)	Hypoplastic Left Heart Syndrome Stage 1 Palliation *n* = 522 *n* (%)	*p*
Age[a] (d)	0 (0, 1)	30 (1,654)	0 (0, 1)	< 0.001
Male	596 (59)	136 (63)	305 (58)	0.52
Year of extracorporeal membrane oxygenation				0.01
2004–2007	500 (49)	81 (37)	245 (47)	
2008–2011	516 (51)	136 (63)	277 (53)	
Cardiac arrest	86 (9)	71 (31)	303 (58)	< 0.001
Mortality	544 (54)	90 (42)	321 (62)	< 0.001
In-hospital mortality by center volume	*p* = 0.26	*p* = 0.002	*p* = 0.53	
Low	*n* = 152	*n* = 34	*n* = 67	
Number of deaths, *n* (%)	87 (57)	23 (68)	45 (67)	
Medium	*n* = 718	*n* = 132	*n* = 366	
Number of deaths, *n* (%)	387 (54)	48 (39)	224 (61)	
High	*n* = 146	*n* = 60	*n* = 89	
Number of deaths, *n* (%)	70 (48)	19 (32)	52 (58)	

[a]Data presented as median (interquartile ranges).