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Inter-hospital variability in post-cardiac arrest mortality☆

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ABSTRACT

Aim: A growing body of evidence suggests that variability in post-cardiac arrest care contributes to differential outcomes of patients with initial return of spontaneous circulation after cardiac arrest. We examined hospital-level variation in mortality of patients admitted to United States intensive care units (ICUs) with a diagnosis of cardiac arrest.
Methods: Patients with a primary ICU admission diagnosis of cardiac arrest were identified in the 2002–2005 Acute Physiology and Chronic Health Evaluation (APACHE) IV dataset, a multicenter clinical registry of ICU patients.
Results: We identified 4674 patients from 39 hospitals. The median number of annual patients was 33 per hospital (range: 12–116). Mean APACHE score was 94 (±38), and overall mortality was 56.8%. Age, severity of illness (acute physiology score), and admission Glasgow Coma Scale were all associated with increased mortality ($p < 0.001$). There was no survival difference for patients admitted from the emergency department vs. the inpatient floor. Among institutions, unadjusted in-hospital mortality ranged from 41% to 81%. After adjusting for age and severity of illness, institutional mortality ranged from 46% to 68%. Patients treated at higher volume centers were significantly less likely to die in the hospital.
Conclusions: We demonstrate hospital-level variation in severity adjusted mortality among patients admitted to the ICU after cardiac arrest. We identify a volume–outcome relationship showing lower mortality among patients admitted to ICUs that treat a high volume of post-cardiac arrest patients. Prospective studies should identify hospital-level and patient care factors that contribute to post-cardiac arrest survival.

Introduction

Overall survival after cardiac arrest is poor,[1,2] and has remained largely unchanged over time.[3,4] Furthermore, despite international efforts to develop and disseminate cardiac arrest treatment guidelines, significant outcome variability persists among individual emergency medical service (EMS) systems and hospital. Reported rates of survival to hospital discharge range from 1% to 31% after out-of-hospital cardiac arrest[2,5] and 0% to 42% after in-hospital cardiac arrest.[6] Although numerous pre-arrest,[3,7,8] and intra-arrest[9–15] factors contribute to this variability, much less is known about the relative contribution of post-cardiac arrest care.

Post-cardiac arrest care is now recognized as a critical link in the chain of survival.[16,17] Therapeutic hypothermia and formalized post-cardiac arrest treatment protocols decrease morbidity and mortality.[18–21] However, substantial inter-hospital variability in mortality of patients that achieve initial return of spontaneous circulation (ROSC) has been reported.[8,22] Mortality differences have been associated with hospital-based factors as well as patient care factors.[23,24] Although likely to be a universal phenomenon, all of these data are from sites outside the United States (US).

The goal of this study was to examine within the US health care system the variability in mortality of patients that achieve initial ROSC after cardiac arrest. Documenting inter-hospital variability of

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post-cardiac arrest mortality is the first step in understanding the role of post-cardiac arrest care in the overall chain of survival. Ultimately, identifying the sources of variability is essential to optimize post-cardiac arrest care. This study utilized a large clinical intensive care unit (ICU) database to determine site-dependent variability in adjusted in-hospital mortality and the association between mortality and hospital case volume.

Methods

Study design and patients

We conducted a retrospective cohort study using the Acute Physiology and Chronic Health Evaluation (APACHE) IV database (Cerner Corporation, Kansas City, MO). APACHE is an ICU clinical information system used by participating hospitals within the US for benchmarking and quality improvement.[25] Patient demographics, admission source, primary admission diagnosis, and detailed laboratory and physiologic variables are collected in the first 24 h of ICU admission. Trained clinical coordinators supervised data collection at each site. Data quality is ensured with extensive on-site training, automated software that prevents implausible values, and data audits that occur regularly at both the local and central level. Hospitals participating in APACHE are diverse in size, ownership, academic status and region of the country. APACHE contains data from all types of ICUs within participating hospitals, including medical, surgical, mixed medical–surgical, coronary care units, and other specialty ICUs. The APACHE IV dataset has been utilized in several recent ICU outcomes studies.[25–27]

All patients admitted to an APACHE hospital ICU with the diagnosis of cardiac arrest from 2002 to 2005 were eligible for this analysis. ICU admission diagnosis is determined by the admitting team in conjunction with the local APACHE data coordinator, and represents the single diagnosis most responsible for the ICU admission. We excluded patients less than 18 years of age, ICU readmissions, and patients transferred into the ICU from outside hospitals. Not all hospitals participated in APACHE for the entire study period. To ensure that hospitals with short lengths of participation did not overly influence the analysis, we also excluded hospitals with less than 12 cardiac arrest patients per year or less than 20 cardiac arrest patients total.

Variables and risk adjustment

The primary outcome variable was in-hospital mortality. Clinical variables for risk adjustment included age, Glasgow Coma Scale (GCS), whether or not the patient was mechanically ventilated, and acute physiology score (APS), a composite severity of illness measure strongly associated with in-hospital mortality.[28] The APS is recorded upon admission to the ICU and includes physiologic variables such as temperature, mean arterial pressure, heart rate, respiratory rate, oxygen delivery, pO_2, arterial pH, serum sodium, serum potassium, serum creatinine, hematocrit, and white blood cell count. Hospital-level variables included region of the country, teaching status and annual case volume. Region was categorized by state into northeast, south, midwest and west. Teaching status was defined by membership in the American Association of Medical College's Council of Teaching Hospitals (COTH) and was categorized into academic (residents in the ICU plus COTH member), community with housestaff (residents in the ICU without COTH membership), and community (no residents in the ICU). Hospital case volume was defined as the number of cardiac arrest patients admitted to the ICU per year; hospital case volume was categorized into natural cut-points based on the observed distribution.

Table 1
Hospital characteristics.

Characteristic	*n* = 39
Teaching status	
Academic	10 (26)
Community with housestaff	13 (33)
Community	26 (41)
Number of hospital beds	384 [280–650]
Region	
Northeast	3 (8)
Southeast	17 (44)
Midwest	8 (21)
West	11 (28)
Annual ICU admissions for cardiac arrest	
Median [IQR]	33 [19–48]
Range	12–116
Hospital volume (cases/year)	
<20	12 (31)
20–34	11 (28)
35–50	8 (21)
>50	8 (21)

ICU = intensive care unit; values are expressed as a frequency (%), median [interquartile range], or range.

Analysis

Patient and hospital characteristics are presented as frequency (percent), mean ± standard deviation, or median [range or interquartile range], as appropriate. Multivariate logistic regression was used to determine factors independently associated with in-hospital mortality and compare outcomes across hospitals as described above. Generalized estimating equations with robust Huber–White confidence intervals were used to account for clustering by center.[29] For all models, covariates and functional forms were determined *a priori* based on each variable's hypothesized relationship to the primary outcome (in-hospital mortality). To determine factors associated with mortality, all covariates were retained in the final model. To compare outcomes between hospitals, only patient-level covariates were included. Calibration and discrimination of this model were examined using the Hosmer–Lemeshow test and the *C* statistic, respectively. Hospital-specific risk-adjusted mortality was obtained from the regression results using conditional standardization based on mean and modal values of the model covariates.[30] All analyses were performed with Stata 9.2 (College Station, TX), and a two-tailed *p*-value of <0.05 was considered significant. This research used a de-identified dataset and was considered exempt from human subjects review by the University of Pennsylvania Institutional Review Board.

Results

Study population

The initial dataset contained 5386 post-arrest patients in 57 hospitals. We excluded 215 patients in 18 very low volume hospitals, resulting in 39 hospitals in the final sample (Table 1). Just over half of the hospitals were academic hospitals (26%) or community hospitals with housestaff (33%). Most hospitals were located in the southeast (44%), west (28%), or midwest (21%). The median number of hospital beds at each facility was 384 (IQR 280–650), and the median number of cardiac arrest admissions per hospital was 33 (range: 12–116).

Of 5171 remaining patients, 4674 patients met inclusion criteria. The average patient was aged 66 years, and just under half (46.5%) were female. The average GCS on admission was 7 (3–15),

Table 2
Patient characteristics.

Variable	Value ($n = 4674$)
Age	66 ± 15
Female (%)	46.5
APACHE III score	94 ± 38
Acute physiology score	81.2 ± 37.0
GCS on admission	7 [3–15]
Race (%)	
White	64.0
Black	16.8
Hispanic	5.0
Asian	2.0
Other	12.4
Admission source (%)	
Emergency department	44.7
Hospital floor	44.7
Direct admission	7.0
Other	3.6
ICU type (%)	
Mixed	50
Cardiac	18.3
Medical	17.5
Surgical	8.3
Other	1.7
Requiring mechanical ventilation (%)	89.3
Hospital discharge location (%)	
Home	23.2
Other hospital	5.7
Skilled nursing facility	14.0
Dead	57.1

APACHE = acute physiology and chronic health evaluation; GCS = Glasgow Coma Scale; variables presented as percents, mean ± standard deviation, or frequency (%).

and the average APACHE score was 94 (±38). Equal percentages of patients (44.7%) were admitted from the ED and from the hospital floor. Most patients (89.3%) required mechanical ventilation. Overall in-hospital mortality was 56.8%. 23.2% of the population were discharged home, and 14% were discharged to a skilled nursing facility. Additional demographic data are detailed in Table 2.

Unadjusted analyses

Unadjusted mortality varied widely between hospitals (Figure 1a). In-hospital mortality was similar for patients admitted from the ED and from the hospital floor (56.8% vs. 56.2%, $p = 0.26$). Median length of stay for all patients was 2.8 days. Patients who died during the admission had a median length of ICU stay of less than 2 days (1.6). ICU length of stay was significantly longer for survivors than nonsurvivors (3.8 days vs. 1.6 days; Table 3).

Table 3
Unadjusted patient outcomes.

Variable	Value ($n = 4670$)
In-hospital mortality (%)	
All patients	56.8
Admitted from ED	56.2
Admitted from other location	57.2
ICU length of stay (days)	
All patients	2.8 [1.2–5.7]
Survivors	3.8 [2.1–7.5]
Non-survivors	1.6 [0.7–3.7]

ICU = intensive care unit; ED = emergency department; variables presented median [interquartile range] or percents.

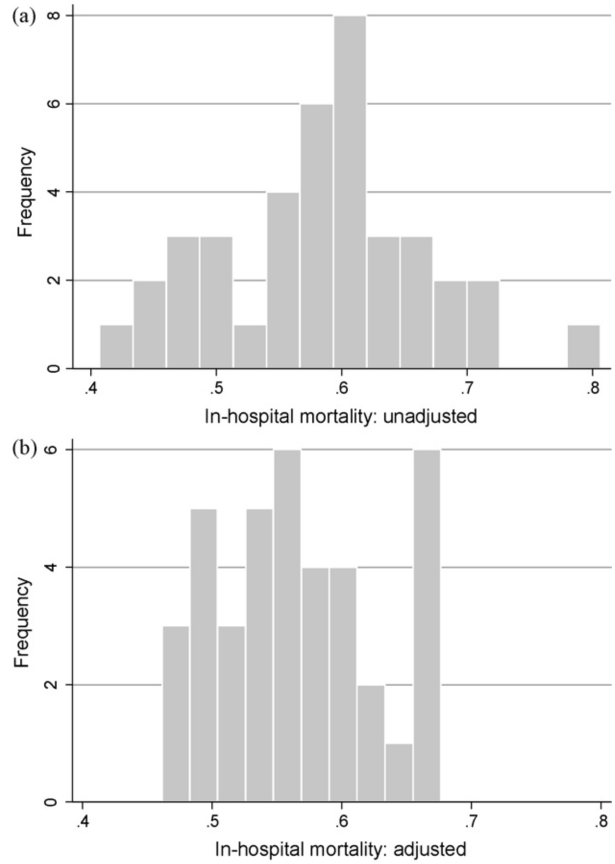

Figure 1. Frequency of in-hospital mortality among APACHE Hospitals: (a) unadjusted rates; (b) rates adjusted for age, severity of illness and ventilation status.

Adjusted analyses

The final predictive model showed good discrimination (C statistic = 0.81) and calibration (p value for goodness of fit test = 0.52). Using the standardized adjusted mortality, inter-hospital variation in mortality decreased somewhat but was still significant, ranging from 46% to 68% (Figure 1b). Patient-level factors associated with in-hospital mortality included age (OR for every 10 year increase 1.16, 95% CI 1.11–1.22), acute physiology score (OR for every 10 point

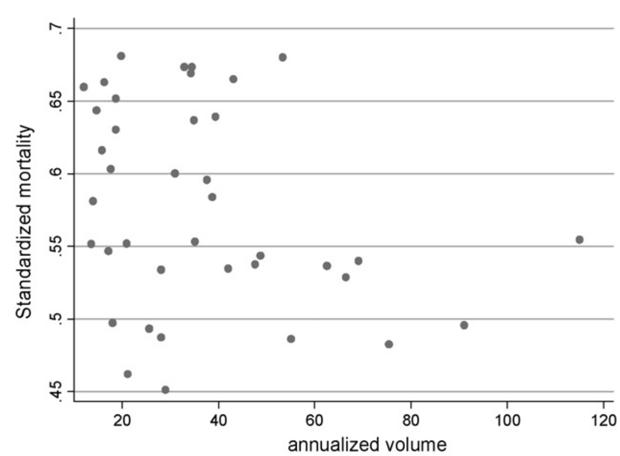

Figure 2. In-hospital mortality rate (mortality rates standardized by age, acute physiology score, Glasgow Coma Scale on admission and ventilation status) vs. annualized post-arrest volume: scatter plot of APACHE ICUs.

Table 4
Results of the logistic regression model for in-hospital mortality for patients admitted to the ICU after cardiac arrest.

Variable	OR	95% CIs	*p* value
Age (per 10 units)	1.16	1.11–1.22	<0.001
Acute physiology score (per 10 units)	1.33	1.29–1.37	<0.001
GCS on ICU admission (per 1 point)	0.94	0.92–0.96	<0.001
Mechanical ventilation on ICU admission			
Non-ventilated	1.00	–	–
Ventilated	1.85	1.34–2.54	<0.001
Admission source			
Non-ED	1.00	–	–
ED	1.04	0.90–1.21	0.56
Region			
South	1.00		
Northeast	1.24	0.70–2.19	0.45
Midwest	0.76	0.57–1.02	0.07
West	0.81	0.56–1.18	0.27
Hospital teaching status			
Academic	1.00	–	–
Community/teaching	0.84	0.61–1.15	0.28
Community	0.92	0.64–1.31	0.63
Hospital volume (cases/year)			
<20	1.00	–	–
20–34	0.78	0.55–1.11	0.16
35–50	0.71	0.45–1.11	0.13
>50	0.62	0.45–0.86	0.01

GCS = Glasgow Coma Scale; ICU = intensive care unit; ED = emergency department; OR = odds ratio; CI = confidence interval. Odds ratios are adjusted for all listed variables; confidence intervals and *p* values adjusted for clustering by center using generalized estimating equations.

increase 1.33, 95% CI 1.29–1.37), and GCS on ICU admission (OR for every point increase 0.94, 95% CI 0.92–0.96) (Table 4). The need for mechanical ventilation on admission was also associated with mortality (1.85, 95% CI 1.33–2.54).

Standardized mortality as a function of hospital volume is demonstrated graphically in Figure 2. Increasing annual ICU case volume was associated with lower hospital mortality, largely driven by poor outcomes at some small hospitals. Relative to hospitals that treated fewer than 20 cardiac arrest patients per year, a non-significant trend towards decreasing mortality was observed for hospitals that treated 20–34 (OR 0.78, 95% CI 0.55–1.11), and 35–50 (OR 0.71, 95% CI 0.45–1.11) patients per year. Hospitals that treated more than 50 cardiac arrest patients per year had a significantly lower mortality than hospitals that treated fewer than 20 patients per year (OR 0.62, 95% CI 0.45–0.86). No association was observed between in-hospital mortality and type of hospital (academic vs. community with housestaff vs. community).

Discussion

We demonstrate inter-hospital variability in severity adjusted post-cardiac arrest mortality in patients admitted to the ICU after successful resuscitation from cardiac arrest. In addition, we observed an inverse relationship between the volume of cardiac arrest patients treated in the ICU and in-hospital mortality. These findings are consistent with previous work that has demonstrated wide variability in post-cardiac arrest mortality outside the US,[22–24] and the relationship between experience (volume) and outcomes in other critically ill patient populations.[27,31–33]

Increasingly, attention has focused on the importance of post-cardiac arrest care on patient outcomes. Specific critical care interventions, most notably induced hypothermia, have been demonstrated to decrease mortality and morbidity,[18–21] and are recommended in current treatment guidelines.[34] However, implementation remains poor.[35,36] Additional post-arrest therapies that have been associated with improved outcome include early percutaneous coronary intervention,[20,37] fever prevention,[38] and glycemic control.[39] Furthermore, premature withdrawal of care has been implicated as a source of variable outcomes.[16] This study is the first to demonstrate inter-ICU variability in severity adjusted post-cardiac arrest mortality within the US health care system.

The variability in post-cardiac arrest mortality observed in our study of US hospitals between 2002 and 2005 is similar to what has been reported in a number of studies outside the US over the past three decades. Enghdalle et al. reported in-hospital mortality of 56% vs. 67% ($p < 0.001$) for patients admitted to two different Swedish hospitals within the same EMS system between 1980 and 1996.[23] Langdhalle et al. reported in-hospital mortality ranged from 44% to 66% for patients admitted to four Norwegian hospitals after out-of-hospital cardiac arrest between 1995 and 1999.[8] It is interesting to note that the hospital with the lowest in-hospital mortality rate in this study had twice the patient volume of the other three hospitals. Most recently, Herlitz et al. reported that 1-month mortality after hospital admission following out-of-hospital cardiac arrest ranged from 58% to 86% among 21 Swedish hospitals.[22]

Our analysis has several limitations. We use a large proprietary database that provides detailed clinical information. This dataset allows us to perform high-quality severity adjustment, but the included hospitals uniformly have demonstrated a commitment to quality assurance by participating in the APACHE clinical information system. If anything, this might serve to reduce inter-hospital variation in outcome, making it more likely that the observed variation is real. While this may influence the overall survival in our cohort, there is no reason to believe that bias of the included ICUs would differ by volume of patients with cardiac arrest. An additional selection bias may exist in that we had no details about the individual resuscitation or the organization of code teams within hospitals.

A number of pre-arrest and intra-arrest variables known to be associated with outcome were not controlled for due to limitations of the data. Systematic difference in these variables could have contributed to outcome variability. However, we believe that we were able to adequately adjust for case-mix using age, GCS, acute physiology score, and mechanical ventilation, all of which were found to be independent predictors of mortality. In addition, we had no access to procedures performed in the post-cardiac arrest period. Therefore, we were unable to control for or investigate specific therapies associated with improved outcomes including therapeutic hypothermia or cardiac catheterization. While these interventions could potentially explain some of the variability between hospitals demonstrated in our analysis, the goal of our analysis was to describe the variability that exists in outcomes and to demonstrate the relationship between volume and outcome. The causal pathway for post-arrest mortality is complex and the contribution of individual interventions to decrease mortality will need to be rigorously tested to explain the variability that we describe. Future work should be directed at examining processes of care that might explain the observed variation, such as therapeutic hypothermia and other advances in critical care for these patients.

Our outcomes are limited to in-hospital mortality, length of hospital stay, and hospital disposition. We could not differentiate the effect of do not resuscitate orders on in-hospital mortality. It is unknown if post-arrest management practices with respect to withdrawing care differ by hospital type, ICU type, or region of the country, and this is fertile ground for future research. Local and regional discharge practices could also contribute to variability in rates of in-hospital death. That is, post-arrest patients who die in the hospital would have been identified in our analysis, but patients who are transferred to inpatient or home hospice would not have been identified. This variability may be accounted for by insurance, family resources, or other factors. Data were not available regarding long term outcomes and we cannot comment on the long-term morbidity and mortality associated with cardiac arrest.

Conclusions

In-hospital mortality varies significantly among patients admitted to US intensive care units after initial resuscitation from cardiac arrest, and one potential source of outcome variability is patient volume. These results suggest the need for additional research to delineate best-practices and to optimize post-cardiac arrest care. If variability in patient care is found to be causal, then development, dissemination and implementation of comprehensive post-cardiac arrest care guidelines should be considered. Furthermore, the volume–outcome relationship supports development and prospective evaluation of regional post-arrest care centers.[40]

Conflict of interest

BGC & JK have no pertinent disclosures. RMM serves on the BLS Subcommittee of the American Heart Association Emergency Cardiac Care Committee as a fellow. AAK is an employee of Cerner Corporation and owns shares of Cerner stock. RWN serves on the ACLS Subcommittee of the American Heart Association Emergency Cardiac Care Committee.

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