Long-Term Outcomes of Out-of-Hospital Cardiac Arrest Care at Regionalized Centers

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Study objective: It is unknown whether regionalization of postarrest care by interfacility transfer to cardiac arrest receiving centers reduces mortality. We seek to evaluate whether treatment at a cardiac arrest receiving center, whether by direct transport or early interfacility transfer, is independently associated with long-term outcome.

Methods: We performed a retrospective cohort study including adults resuscitated from out-of-hospital cardiac arrest in southwestern Pennsylvania and neighboring Ohio, West Virginia, and Maryland, which includes approximately 5.7 million residents in urban, suburban, and rural counties. Patients were treated by 1 of 78 ground emergency medical services agencies or 2 air medical transport agencies between January 1, 2010, and November 30, 2014. Our primary exposures of interest were interfacility transfer to a cardiac arrest receiving center within 24 hours of arrest or any treatment at a cardiac arrest receiving center regardless of transfer status. Our primary outcome was vital status, assessed through December 31, 2014, with National Death Index records. We used unadjusted and adjusted survival analyses to test the independent association of cardiac arrest receiving center care, whether through direct or interfacility transport, on mortality.

Results: Overall, 5,217 cases were observed for 3,629 person-years, with 3,865 total deaths. Most patients (82%) were treated at 42 non–cardiac arrest receiving centers with median annual volume of 17 cases (interquartile range 1 to 53 cases per center annually), whereas 18% were cared for at cardiac arrest receiving centers receiving at least 1 interfacility transfer per month. In adjusted models, treatment at a cardiac arrest receiving center was independently associated with reduced hazard of death compared with treatment at a non–cardiac arrest receiving center (adjusted hazard ratio 0.84; 95% confidence interval 0.74 to 0.94). These effects were unchanged when analysis was restricted to patients brought from the scene to the treating hospital. No other hospital characteristic, including total out-of-hospital cardiac arrest patient volume and cardiac catheterization capabilities, independently predicted outcome.

Conclusion: Both early interfacility transfer to a cardiac arrest receiving center and direct transport to a cardiac arrest receiving center from the scene are independently associated with reduced mortality. [Ann Emerg Med. 2019;73:29-39.]

Please see page 30 for the Editor's Capsule Summary of this article.

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SEE EDITORIAL, P. 40.

INTRODUCTION

Sudden cardiac arrest is the most common cause of death in high-income countries.[1] Most patients who are transported to the hospital after achieving return of spontaneous circulation do not survive to discharge, although outcome varies both regionally and between hospitals.[2-5] Because of this variability in outcomes and the complexity of sudden cardiac arrest care, both the National Academy of Medicine[6] and the American Heart Association[7] suggest development of regional systems of care. Although hospital-level characteristics such as case volume or advanced procedural capabilities are inconsistently associated with inhospital mortality,[4,8-12] small studies suggest long-term benefit from care at specialty centers that provide a comprehensive bundle of sudden cardiac arrest care.[13,14] Similarly, allowing emergency medical services (EMS) to bypass nearby hospitals in favor of transport directly to specialized centers has been associated with improved outcomes in several regions.[15,16]

Multiple strategies have been used to ensure appropriate triage and access to specialized care. Trauma systems designate tiers of hospitals according to available resources and case volume, and EMS or initial receiving hospitals direct transport of patients to these centers according to severity of injury.[17,18]

Editor's Capsule Summary

What is already known on this topic

It is unknown whether regionalization of post–out-of-hospital cardiac arrest care can improve outcomes.

What question this study addressed

Is interfacility transfer to specialized cardiac arrest receiving centers associated with reduced mortality?

What this study adds to our knowledge

In a database analysis of 5,217 out-of-hospital cardiac arrest from all causes, treatment at a cardiac arrest receiving center was independently associated with reduced hazard of death (adjusted hazard ratio 0.84; 95% confidence interval 0.74 to 0.94) compared with treatment at a non–cardiac arrest receiving center.

How this is relevant to clinical practice

This will not change practice but should prompt further study to determine whether regionalization of out-of-hospital post–cardiac arrest care can reduce mortality.

Current treatment of acute stroke similarly uses many primary stroke centers that provide rapid access to time-sensitive early interventions, followed by transfer of specific patients to comprehensive stroke centers for complex ongoing specialty care.[19] Traditionally, patients with sudden cardiac arrest are delivered to the nearest facility after return of spontaneous circulation. Aside from single-center reports, it is unknown whether subsequent transfer to a receiving center for continued acute and postacute care affects outcomes of patients with sudden cardiac arrest.

We examined initial treatment and long-term survival after sudden cardiac arrest in a geographic region with multiple health systems to test the hypotheses that treatment at a center receiving a high volume of interfacility sudden cardiac arrest referrals, whether through direct transport from the scene by EMS providers or early interfacility transfer within 24 hours of arrest, is independently associated with reduced long-term mortality.

MATERIALS AND METHODS

Setting

Southwestern Pennsylvania and neighboring Ohio, West Virginia, and Maryland include approximately 5.7 million residents in urban, suburban, and rural counties spanning 43,300 square miles. The 78 ambulance services included in this study perform greater than 95% of EMS transports in the region. Ground transports are performed with a combination of basic and advanced life support (ALS) ambulances staffed with emergency medical technicians and paramedics, who operate within a single regional system and use statewide treatment protocols. Cardiac arrest responses in the region are dispatched as a single-tier ALS response staffed at the paramedic level and may be assisted by first responders at the emergency medical responder level. EMS medical directors from 4 major health networks provide individual medical oversight of these agencies: UPMC, Allegheny Health Network, St. Clair Hospital, and Excela Health. Two air medical transport agencies are responsible for interfacility transports of critically ill patients among 46 short-term acute care hospitals in the catchment area for these health networks (Figure 1).

We assembled a multi-institution collaboration to generate a regional cohort of EMS-transported patients resuscitated from out-of-hospital sudden cardiac arrest. The University of Pittsburgh served as the coordinating center. All aspects of the present study were approved with a waiver of informed consent by the institutional review boards of the University of Pittsburgh, Allegheny Health Network, St. Clair Hospital, and Excela Health.

Data Collection and Processing

Coinvestigators at each site queried the medical records of the EMS agencies under their medical command from January 1, 2010, to November 30, 2014, for cases of out-of-hospital sudden cardiac arrest. During the study period,

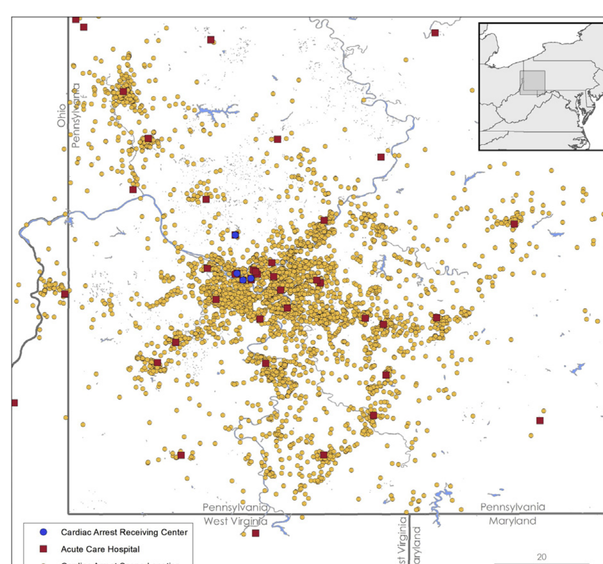

Figure 1. Cardiac arrest scene locations and included acute care hospitals in southwestern Pennsylvania and surrounding Ohio, West Virginia, and Maryland.

each of these agencies used a common National EMS Information Systems–compliant Web-based out-of-hospital electronic health record (emsCharts, Warrendale, PA) (see Appendix E1, available online at http://www.annemergmed.com, for details). During the study period, the system was National EMS Information Systems version 2.2 compliant. emsCharts has custom reporting software that allows identification of cases and reporting of data based on multiple fields in the record. Once the electronic query is built, the contents of specified fields are pulled and aggregated automatically, without the need for manual chart abstraction (see Appendix E1, available online at http://www.annemergmed.com, for details). We queried emsCharts to identify likely cases of sudden cardiac arrest with transport to a hospital during the study period, which we considered to be any patients with a medical category of "cardiac arrest" or documentation of any of the following in the EMS record: chest compressions, defibrillation, or automated defibrillator use. Each site abstracted identifiable data from emsCharts, including patient name, address, social security number, age, race, and sex, which we used to query the National Death Index for patients' vital status through December 31, 2014. The National Death Index is a comprehensive database of vital statistics obtained from state death records that has been used extensively to determine vital status.[13,20-23] We linked National Death Index results to patient records by using probabilistic linkage (Appendix E1, available online at http://www.annemergmed.com)[13] and then deidentified and aggregated each site's data for analysis.

We included patients treated and transported by EMS after resuscitation from sudden cardiac arrest from January 1, 2010, to November 30, 2014. We excluded patients younger than 16 years, those for whom resuscitation was not attempted because of obvious signs of death in the field, those transported with ongoing cardiopulmonary resuscitation (CPR) and without return of spontaneous circulation at transfer of care to the initial receiving hospital, those transported to or from hospitals outside our study's catchment area, and those with no receiving hospital listed (ie, termination of resuscitation in the field). We implemented these exclusions through the initial emsCharts query and then again during data cleaning and aggregation. We included patients regardless of arrest cause (traumatic versus "medical") for several reasons. First, out-of-hospital data are not sufficient to define arrest cause in many cases (eg, a low-velocity motor vehicle crash may occur as a result of a medical cardiac arrest, whereas syncope and ground-level fall may lead to arrest from cervical spine fracture that is not recognized until advanced imaging is performed. Second, the historical dichotomization of medical versus traumatic arrests does not parallel observed pathophysiologic differences across distinct arrest cause. Medical causes such as subarachnoid hemorrhage, heroin overdose, and acute myocardial infarction may in fact differ more from one another than exsanguination from gastrointestinal hemorrhage or spontaneous pneumothorax does from traumatic-cause arrests. As a post hoc analysis, we repeated all statistical procedures, excluding arrests presumed to be trauma, to confirm the stability of our findings.

Outcome Measures

Our primary exposures of interest were interfacility transfer within 24 hours of presentation to the initial receiving hospital, and final treatment at a facility receiving a high volume of interfacility sudden cardiac arrest transfers regardless of route of presentation (transfer by EMS directly from the scene or interfacility transfer). We linked EMS records for scene to initial hospital transports and for interfacility transports by using probabilistic linkage on first and last name, date of birth, social security number, and hospital (ie, the initial receiving hospital for a scene chart matched the referring hospital for interfacility chart). We linked charts matching with a probability greater than or equal to 0.75, which corresponded to near-perfect matching on at least 4 of 5 criteria. We then manually inspected matches with probabilities greater than or equal to 0.5 to link these charts according to full available data.

We additionally abstracted clinical covariates of interest, including age, sex, race, and medical history. EMS providers classified race from a drop-down list of options. For medical history classification, we used text-based search strategies of free-text medical history documentation to categorize the presence or absence of automatic implantable cardioverter-defibrillator or pacemaker in situ, atrial fibrillation, coronary artery disease or past myocardial infarction, congestive heart failure, previous cardiac arrest, cardiac conduction disease, structural heart disease, venous thromboembolism, vascular disease, alcohol abuse, tobacco abuse, other recreational drug abuse, anemia, any malignancy, hypertension, hyperlipidemia, diabetes, cirrhosis, neurologic disease or dementia, psychiatric disease, renal disease or dialysis dependence, pulmonary or respiratory tract disease, gastrointestinal disease, other medical history not classified as one of the above, unknown medical history, or no medical history. We treated each of these as a binary predictor. Arrest-specific covariates included arrest cause, which we dichotomized as traumatic or medical; witnessed collapse; provision of bystander CPR; shockable arrest rhythm at any time during resuscitation; number of epinephrine doses administered during CPR; EMS dispatch to CPR interval; interval from CPR to return of spontaneous circulation; and transport time from scene to first receiving hospital.

We considered the treating hospital to be the last hospital at which the patient received care (ie, receiving hospital from the scene for nontransferred patients and receiving hospital from interfacility transport for transferred patients). We inspected overall sudden cardiac arrest case volume per center for natural break points in the data and categorized hospitals as low-volume centers if they treated fewer than 100 out-of-hospital cardiac arrest patients during the 4-year study period, moderate-volume centers if they treated 100 to 399 patients, and high-volume centers if they treated at least 400 patients. Next, we evaluated only the number of patients received by each center through interfacility transfer and categorized hospitals as cardiac arrest receiving centers if they received at least one patient through interfacility transfer every quarter during the study period. As a sensitivity analysis, we varied this cutoff as described below and compared our results. This designation was developed according to observed referral patterns in the present cohort and was not known to EMS agencies at patient care.

We defined additional hospital-level characteristics with 2010 Centers for Medicare & Medicaid Services Hospital Cost Report Information System, a publicly available hospital-level database with detailed information on structural data on all US hospitals. These included teaching status (using the resident-to-bed ratio, classifying hospitals as nonteaching if they had no resident trainees, small teaching hospitals if the ratio was more than zero and less than 0.2, and large teaching hospitals if the ratio was 0.2 or greater), total number of licensed beds, and total number of licensed ICU beds, which we tested as continuous predictors and categorized by quartile. Using 2010 Centers for Medicare & Medicaid Services MedPar data, we classified hospitals according to their annual cardiac catheterization procedure volume ($\geq$160 versus $<$160 cases/year) and annual volume of mechanically ventilated patients ($\geq$400 versus $<$400 adjusted mechanical ventilation cases annually). We used *International Classification of Diseases, Ninth Revision, Clinical Modification* procedure codes to identify cases of cardiac catheterization (37.22, 37.23, 88.53, 88.54, 88.55, 00.66, 36.04, 36.06, and 36.07) and mechanical ventilation (96.70, 96.71, and 96.72).

Our primary outcome of interest was vital status through December 31, 2014, which we identified through National Death Index search results.

Primary Data Analysis

We used descriptive statistics to summarize overall population characteristics. We used survival analysis to estimate the effects of interfacility transfer to or initial treatment at a cardiac arrest receiving center on hazard of death after up to 5 years of observation. Our a priori analysis plan was to use hierarchic Cox proportional hazards models to control for patient- and hospital-level characteristics in unadjusted and adjusted regression. However, the relationship between transfer and outcome was complex and time varying. Therefore, we used piecewise exponential survival regression, splitting the data into blocks 0 to 1, 1 to 3, 3 to 7, and greater than 7 days postarrest. We selected these epochs according to biological plausibility and previous research.[24-26] Briefly, we believed that during days 0 to 1 and 1 to 3, patients would be at high risk for rearrest or early withdrawal of life-sustaining treatment for perceived poor neurologic prognosis,[24,25] that days 3 to 7 were the period during which delayed neurologic prognostication is recommended by consensus guidelines,[26,27] and that beyond day 7 was the postacute period during which a majority of subjects would have revealed their neurologic trajectory but still be at risk for medical sequelae of out-of-hospital cardiac arrest, critical illness, and preexisting comorbidities.[13,24,25]

We first estimated univariable patient- and hospital-level associations of predictors with mortality (adjusted only for epoch), using clustered sandwich estimators to account for correlation between patients within the same hospital. For variables missing not at random, we included a predictor level of “missing” in our analysis. We assessed pairwise correlations of independent predictors to ensure there was no severe multicollinearity. Then, we used a backwards stepwise approach as further exploration of our cohort, sequentially eliminating predictors with an adjusted association with outcome at a threshold of $P>.10$ to build a final adjusted regression model. In this final model, we explored and included significant interaction terms between predictors and epoch. Next, we calculated coefficients for the effect of each treating hospital on outcome both with and without adjustment for patient-level characteristics. To describe between-hospital variation in outcome, we computed all pairwise comparisons of these coefficients to calculate exact unadjusted and adjusted median hazards ratios.[28]

We performed a number of sensitivity and secondary analyses to confirm the robustness of our main results. First, we compared various piecewise splits of our time variable, up to the extreme case splitting at every death to obtain perfectly constant hazard functions. Second, to minimize the potential of referral bias in patients undergoing interfacility transfer, we tested the independent effect of cardiac arrest receiving center status on outcome, restricting analysis to the cohort of nontransferred patients. Third, we varied our case-volume cutoffs defining overall sudden

Table 1. Baseline population characteristics, stratified by treatment at a cardiac arrest receiving center or non–cardiac arrest receiving center.

Characteristic	Treated at CARC (n=920)	Treated at Non-CARC (n=4,297)
Transferred for care	350 (38)	40 (1)
Age (SD), y	61 (18)	66 (18)
Female sex	363 (39)	1,683 (39)
Race		
White	456 (50)	3,287 (77)
Black	75 (8)	351 (8)
Other	8 (1)	37 (1)
Unknown	381 (41)	622 (14)
Nontraumatic arrest	819 (89)	4,183 (97)
Shockable rhythm	526 (57)	1,962 (46)
Witnessed status		
Unwitnessed	339 (37)	1,086 (25)
Witnessed	511 (56)	1,982 (46)
Missing	70 (9)	1,229 (29)
Bystander CPR		
None	33 (4)	117 (3)
Layperson	231 (25)	963 (22)
Professional	246 (27)	993 (23)
Unknown	410 (45)	2,224 (52)
Dispatch-to-CPR interval, min		
<10	68 (7)	189 (4)
10–19	100 (11)	247 (6)
≥20	136 (15)	366 (9)
Missing	616 (70)	3,495 (81)
Epinephrine doses, mg		
1–2	241 (26)	794 (18)
3–4	238 (26)	1,329 (31)
5–6	112 (13)	847 (20)
>6	46 (5)	380 (9)
None documented	273 (30)	947 (22)
Time from scene to receiving hospital, min		
<10	335 (47)	2,268 (53)
≥10	369 (51)	1,811 (42)
Missing	16 (2)	190 (4)
Documented medical history		
AICD/PPM	50 (5)	269 (6)
Atrial fibrillation	73 (8)	315 (7)
CAD/MI	168 (18)	909 (21)
Congestive heart failure	226 (13)	557 (13)
Cardiac arrest	11 (1)	47 (1)
Cardiac conduction disease	19 (2)	58 (1)
Structural heart disease	20 (2)	94 (2)
Venous thromboembolism	78 (2)	24 (3)
Vascular disease	26 (3)	168 (4)
Alcohol abuse	26 (3)	91 (2)
Tobacco abuse	11 (1)	44 (1)
Other drug abuse	46 (5)	167 (4)
Anemia	30 (3)	174 (4)
Malignancy	86 (9)	473 (11)
Diabetes	199 (22)	999 (23)
Hypertension	306 (33)	1,550 (36)
Hyperlipidemia	96 (10)	397 (9)
Cirrhosis	27 (3)	69 (2)
Neurologic disease	131 (14)	837 (19)
Psychiatric disease	105 (11)	524 (12)
Renal disease/dialysis	98 (11)	402 (9)
Pulmonary/respiratory disease	191 (21)	911 (21)
Gastrointestinal disease	93 (11)	413 (10)
Other medical history	280 (30)	1,519 (35)
Unknown medical history	126 (14)	433 (10)
None	120 (13)	481 (11)

CARC, Cardiac arrest receiving center; *AICD/PPM,* automatic implantable cardioverter/defibrillator or permanent pacemaker; *CAD/MI*, coronary artery disease or myocardial infarction.
Categorical data are presented as raw No. (%), and continuous data are presented as mean (SD).

cardiac arrest case volume and cardiac arrest receiving center status, defining cardiac arrest receiving centers variably as receiving between 4 and 48 total transfers during the study period. Fourth, we tested for the possibility of systematically biased EMS-level transport of patients with sudden cardiac arrest from the scene to the initial treating hospital according to cardiac arrest receiving center status. To do this, we constructed a propensity score predicting transport to the closest hospital versus EMS bypass of the closest hospital. This score accounted for patient-level characteristics (transfer status, age, sex, race, medical versus traumatic arrest cause, shockable rhythm, witnessed status, bystander CPR, dispatch-to-CPR interval, epinephrine doses administered, and the 26 binary medical history variables listed in Table 1), transport time, and distance to, density of, and cardiac arrest receiving center status of the hospitals surrounding the arrest scene. We included transfer status in this model to account for potential survival bias, whereby transferred patients might be expected to be healthier (because they survived transfer), and referral bias, whereby transferred patients might be expected to be sicker (because they were deemed to exceed the capabilities of the referring hospital). We used this model instead of simply adjusting for bypass of the closest hospital in our initial regression model because our region's cardiac arrest receiving centers are located in areas with a high density of surrounding hospitals. This results in a greater opportunity for patients who are transported to cardiac arrest receiving centers to have bypassed the nearest facility by chance because of overall hospital density, without necessarily implying systematically biased selection of initial hospital by cardiac arrest receiving center status. We then built a propensity score–adjusted piecewise exponential survival model to test the independent effect of cardiac arrest receiving center status and transfer status on outcome. Fifth, we performed a series of post hoc analyses to confirm that our findings were robust. We removed traumatic arrests from the cohort and repeated the adjusted analyses described above. Next, to account for potential secular trends, we tested for an association of calendar quarter or year with outcome. We assessed the fit of survival models by examining plots of deviance and Cox-Snell residuals. We used Stata (version 14.2; StataCorp, College Station, TX) for all statistical analyses and ArcGIS (version 10.4; ESRI, Redlands, CA) for all geospatial analyses.

RESULTS

Our initial query identified 7,887 cases of EMS-transported out-of-hospital cardiac arrest during the study period. Of these, we excluded 2,670 (Figure 2), leaving 5,217 cases and 3,629 person-years of observation. There were 3,865 deaths (74% of subjects), with the remaining subjects surviving until December 31, 2014. Overall, median survival time was 1 day (interquartile range [IQR] 1 to 1,309 days), and 2,659 patients (51%) died on this day. Day 1 mortality differed significantly by cardiac arrest receiving center status (240/920 [26%]) for cardiac arrest receiving centers versus 2,419/4,297 [56%] for non–cardiac arrest receiving centers; difference -30% (95% CI -33% to -27%). Conditional on surviving through day 1, overall median survival was 1,593 days (IQR noncalculable). Overall, 390 patients (7.5%) were transferred to a cardiac arrest receiving center within 24 hours of arrest. No patient underwent multiple interfacility transfers. Mean age was 65 years (SD 18 years) and 2,046 (39%) were women (Table 1). Of all patients, 4,297 (82%) were treated at 42 non–cardiac arrest receiving centers with median annual volume of 17 cases per center annually (IQR 1 to 53 cases), 485 (9%) were treated at 3 lower-volume cardiac arrest receiving centers with average annual volume 41 cases per center (SD 30), and 435 (8%) were treated at a single high-volume cardiac arrest receiving center with an average of 109 cases per year.

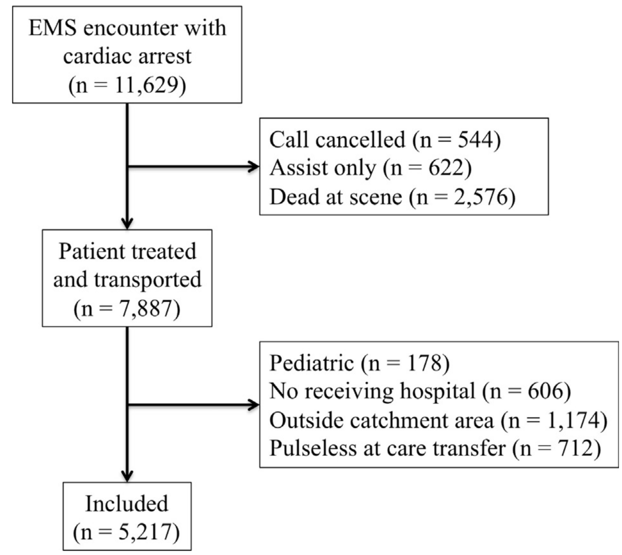

Figure 2. Overall patient cohort and exclusions.

In unadjusted analysis of patient-level characteristics, transfer to a cardiac arrest receiving center was associated with a reduction in the hazard of death (unadjusted hazard ratio [HR] 0.72; 95% CI 0.63 to 0.81), as were multiple patient-level factors (Table E1, available online at http://www.annemergmed.com). Treatment at a cardiac arrest receiving center was associated with a 27% reduction in the hazard of death compared with treatment at a non–cardiac arrest receiving center (Table 2). When we compared the 3 lower-volume cardiac arrest receiving centers with the single higher-volume cardiac arrest receiving center, there was no difference in survival (P=.49 for the unadjusted HR). Treatment at a center with a high volume of mechanical ventilation was associated with lower hazard of death (unadjusted HR 0.77; 95% CI 0.62 to 0.96) (Table 2). Overall, out-of-hospital cardiac arrest case volume, hospital size, and teaching status were not associated with outcome. The unadjusted median hazards ratio for hospital effect was 1.52 (IQR 1.23 to 1.97).

In adjusted models, treatment at a cardiac arrest receiving center was independently associated with a reduced hazard of death compared with treatment at a non–cardiac arrest receiving center (adjusted HR 0.84; 95% CI 0.74 to 0.94) (Table 3). These effects were unchanged when analysis was restricted only to nontransferred patients brought from the scene to the treating hospital (Table 3). When we compared the 3 lower-volume cardiac arrest receiving centers with the single higher-volume cardiac arrest receiving center, there was no difference in survival (P=.72 for the adjusted HR). Transfer status was independently associated with lower hazard of death (adjusted HR 0.31; 95% CI 0.20 to 0.48).

Table 2. Hospital characteristics and unadjusted associations with patient-level outcome.

Hospital-Level Characteristic	Treating Hospitals (n=46)	Unadjusted HR (95% CI)
CARC status (vs non-CARC)	4 (9)	0.73 (0.59–0.91)
OHCA case volume (cases/y)		
Low (<25)	28 (61)	1 [Reference]
Moderate (25–99)	15 (34)	1.02 (0.83–1.25)
High (≥100)	3 (7)	0.89 (0.68–1.17)
Total licensed beds*		
Small (<157)	22 (50)	1 [Reference]
Moderate (157–409)	18 (41)	1.03 (0.85–1.26)
Large (≥410)	4 (9)	0.80 (0.61–1.04)
Total intensive care beds*		
Small (<14)	14 (38)	1 [Reference]
Moderate (14–28)	15 (41)	1.03 (0.85–1.25)
Large (≥29)	8 (22)	0.81 (0.64–1.03)
Academic status*		
Nonteaching hospital	27 (64)	1 [Reference]
Small teaching hospital	6 (14)	1.03 (0.78–1.35)
Large teaching hospital	9 (21)	0.88 (0.68–1.15)
High-volume mechanical ventilation center*	6 (14)	0.77 (0.62–0.96)
High-volume cardiac catheterization center*	19 (43)	0.97 (0.80–1.18)

OHCA, Out-of-hospital cardiac arrest.
*Total number reported for several variables is less than 46 because Centers for Medicare & Medicaid Services data were not available for all hospitals.

There was a significant interaction between transfer status and time, with the effect of transfer driven by reduced mortality in the day 0 to 1 epoch. In contrast, transferred patients had increased hazard of death in each subsequent epoch (Table 3). Other than cardiac arrest receiving center status, no other hospital-level predictors independently predicted outcome. After adjustment for patient-level characteristics, the median hazards ratio for hospital effect was 1.27 (IQR 1.12 to 1.49).

Results did not change in sensitivity analyses comparing various epoch splits. Sensitivity analyses exploring various break points in our definition of overall sudden cardiac arrest case volume and cardiac arrest receiving center categorization yielded similar estimates (data not shown). In our propensity score–adjusted analysis accounting for the possibility of ground EMS-level referral bias, our results also did not change. There was no meaningful change in our results when traumatic arrests were excluded, and no association with calendar quarter of treatment with outcome.

LIMITATIONS

Our study has several important limitations. Because of the observational design of our work, we report the association between cardiac arrest receiving center and survival but cannot assert causality. However, we believe that our work represents the highest possible level of evidence short of a randomized trial, and is supportive of conducting future interventional research in this area. Because clinical data were available only from the out-of-hospital record, some information, including postarrest neurologic assessment, was not available. This is one potential source of bias, although the direction of this effect is difficult to determine. It may be that the sickest patients are most likely to be transferred to specialized care from primary or secondary hospitals, biasing our results toward the null, or that these patients experience rapid limitation of care at these outlying facilities, increasing the estimated effect size. Also, in accordance with our a priori analysis plan, we did not adjust for multiple hypothesis testing. The *P* values for our main effect size are sufficiently small that they would remain statistically significant despite a conservative adjustment (eg, Bonferroni correction), but the *P* values presented in Table 3 do not account for the number of hypotheses tested.

We were unable to obtain data from several EMS agencies in the region that receive medical direction from outside the 4 regional health systems. The agencies we included represent the majority of services, including all of the area's large services, and are responsible for greater than 95% of EMS responses. Nonincluded services follow the same statewide protocols and represent a minority of transports, making it unlikely that their exclusion introduced systematic bias to our results. It may also be that some patients included in the analysis transiently regained pulses before hospital arrival without sustained return of spontaneous circulation. This may have artificially increased estimates of early postarrest mortality, although 26% of patients in our study survived at least 30 days, consistent with previous outcome estimates in similar multicenter cohorts, suggesting that this was not a major source of bias.[8]

The generalizability of our findings to other geographic regions is also uncertain. Record linkage to vital statistics, or even hospital outcome data, requires access to identifiable patient information, making it difficult to develop a national cohort. Regional data likely represent the highest level of available evidence short of an interventional trial. The overall distribution of demographic and arrest-specific characteristics in our cohort, as well as their association with patient outcomes, is like those described in

Table 3. Multivariable survival models for both overall and limited to nontransferred patients transported directly from the out-of-hospital cardiac arrest scene to the treating hospital.

Characteristic	Overall Cohort (n=5,217), Adjusted HR (95% CI)	Nontransfers Only (n=4,827), Adjusted HR (95% CI)
Transferred to CARC	0.31 (0.20–0.48)	–*
Final treating hospital CARC	0.84 (0.74–0.94)	0.84 (0.75–0.94)
Epoch, days		
0–1	1 [Reference]	1 [Reference]
1–3	0.28 (0.24–0.32)	0.28 (0.24–0.32)
3–7	0.10 (0.08–0.13)	0.10 (0.08–0.13)
≥7	0.001 (0.001–0.001)	0.001 (0.001–0.001)
Epoch-transfer interaction		
Transfer×day 0–1	1 [Reference]	–
Transfer×days 1–3	4.42 (3.38–5.79)	–
Transfer×days 3–7	9.13 (6.48–12.86)	–
Transfer×days ≥7	3.52 (1.73–7.18)	–
Age	1.01 (1.00–1.01)	1.01 (1.00–1.01)
Female sex	0.91 (0.88–0.95)	0.90 (0.87–0.94)
Nontraumatic arrest	0.68 (0.61–0.77)	0.67 (0.59–0.77)
Witnessed arrest		
Unwitnessed	1 [Reference]	1 [Reference]
Witnessed	0.84 (0.77–0.91)	0.84 (0.77–0.91)
Missing	0.70 (0.60–0.82)	0.71 (0.60–0.83)
Dispatch-to-CPR interval, min		
<10	1 [Reference]	1 [Reference]
10–19	1.10 (0.89–1.34)	1.08 (0.88–1.30)
≥20	1.27 (1.06–1.51)	1.23 (1.05–1.45)
Missing	1.50 (1.29–1.74)	1.47 (1.28–1.70)
Epinephrine doses, mg		
None documented	1 [Reference]	1 [Reference]
1–2	2.21 (1.93–2.54)	2.29 (1.99–2.63)
3–4	2.64 (2.28–3.08)	2.68 (2.28–3.14)
5–6	2.90 (2.47–3.41)	2.93 (2.47–3.47)
>6	2.95 (2.48–3.50)	2.91 (2.45–3.45)
Time from scene to receiving hospital, min		
<10	1 [Reference]	1 [Reference]
≥10	0.90 (0.84–0.96)	0.90 (0.84–0.96)
Missing	0.83 (0.69–1.00)	0.82 (0.69–0.97)
Documented medical history		
Congestive heart failure	1.07 (1.00–1.14)	1.06 (0.99–1.14)
Venous thromboembolism	1.19 (1.08–1.31)	1.19 (1.11–1.28)
Malignancy	1.07 (0.99–1.15)	1.07 (0.99–1.15)
Hypertension	1.08 (1.03–1.13)	1.09 (1.04–1.14)
Neurologic disease	1.06 (1.00–1.12)	1.05 (0.99–1.10)
Renal disease/dialysis	1.14 (1.07–1.21)	1.12 (1.05–1.19)
Pulmonary/respiratory disease	1.09 (1.04–1.14)	1.08 (1.03–1.13)
Other medical history	1.12 (1.06–1.19)	1.12 (1.06–1.19)
Unknown	0.92 (0.85–1.00)	0.92 (0.85–0.99)

*Dashes indicate

other large out-of-hospital cardiac arrest cohorts.[29,30] Similarly, our region is not an outlier in terms of hospitals, beds or intensive care beds per capita (Figure E1, available online at http://www.annemergmed.com). However, whether our region's 4 cardiac arrest receiving centers perform similarly to cardiac arrest receiving centers in other regions is unknown. That being said, the cardiac arrest receiving centers in our study are hubs of the region's major competitive health networks, improving the generalizability of our results. Finally, although we report associations with long-term survival after out-of-hospital cardiac arrest, quality of life and degree of functional recovery for these survivors is unknown. Survivors of critical illness in general,[31-33] and anoxic brain injury specifically,[34,35] may experience significant functional, cognitive, and psychological limitations. In the United States, the National Death Index aggregates data from death certificates, which can be used to determine individuals' vital status. Although some international studies have used governmental databases to estimate long-term functional status,[36] no such data source exists in America, making this sort of linkage impossible. Therefore, any future prospective trial of postarrest care regionalization must evaluate not only for vital status but also patient-centered outcomes, including measures of quality of life and functional recovery.

DISCUSSION

The findings that early interfacility transfer to a cardiac arrest receiving center or direct transport to a cardiac arrest receiving center from the scene is independently associated with improved long-term survival support calls to create regionalized systems for postarrest care.[6,7] These results are consistent with improved short-term outcomes observed when EMS bypass of non–cardiac arrest receiving centers was instituted in some regions.[15,16] A regional system of many primary hospitals with a smaller number of cardiac arrest receiving centers parallels modern care for trauma and acute stroke, and may be advantageous in many regions where direct transport to cardiac arrest receiving centers by EMS is infeasible because of geographic or other constraints. Although survival bias and referral bias may contribute to the protective effect of interfacility transfer, a cardiac arrest receiving center treatment effect persisted when analysis was restricted only to nontransferred patients, supporting the existence of a true outcome difference between centers. Given the prevalence of out-of-hospital sudden cardiac arrest, the potential for improved outcomes through optimization of regionalized care is considerable.

Overall, the median hazards ratio for hospital effect revealed moderate unexplained variability in outcome. Treatment at one randomly selected hospital compared with treatment at another randomly selected hospital resulted in a 27% difference in the long-term hazard for mortality, even after accounting for measurable sources of variation. Despite this, no hospital-level characteristic except for cardiac arrest receiving center status was an independent predictor of outcome. Although some previous studies have associated hospital characteristics with short-term survival after sudden cardiac arrest, only the availability of cardiovascular interventions has been consistently associated with better outcomes.[4,8-12] Our work does not address what features of cardiac arrest receiving center care explain the increase in survival. Moreover, some arrest causes may require subspecialty care beyond general cardiac arrest receiving center capabilities. We do not, for example, propose that patients with arrests caused by major trauma be transported to a cardiac arrest receiving center that is not a Level I trauma center. Other populations may benefit from extracorporeal membrane oxygenation, toxicologic specialty care, or other critical care interventions.

The temporal pattern of mortality suggests several potential mechanisms. Cardiac arrest receiving center care is associated with a substantial mortality reduction in the first day after out-of-hospital cardiac arrest. Large multicenter analyses demonstrate that most postarrest deaths in the first day are due to withdrawal of life-sustaining therapy for perceived poor neurologic prognosis.[25] Because neurologic prognostication is imprecise early after cardiac arrest, early interfacility transfer may prevent premature assumption of poor outcome and mortality. Delayed neurologic prognostication may also explain the increase in late mortality associated with cardiac arrest receiving center care. A smaller but considerable proportion of early deaths are also due to multisystem organ failure or rearrest.[25] Cardiac arrest receiving centers may provide robust systems of general critical care or coronary revascularization, thereby also reducing early mortality. Aggressive early care including targeted temperature, ventilator, and hemodynamic management may also reduce the risk of secondary neurologic injury, further reducing mortality.[37]

It is likely that organized systems of care rather than any single hospital-level characteristics result in optimal postarrest care. This concept was recently formalized by the National Academy of Medicine,[6] which envisioned tiers of hospitals stratified by ability to care for acute coronary syndrome, hemodynamic instability, recurrent arrhythmias, and postanoxic coma. Clinically, these characteristics may also define patients likely to benefit from transfer to a cardiac arrest receiving center. The awake patient without anoxic brain injury, for example, will likely derive little benefit from a center capable of providing neurocritical care, whereas the hemodynamically stable patient with a respiratory cause of sudden cardiac arrest does not require advanced cardiac care capabilities. In our study, granular hospital-level data were not available for many included centers, although all cardiac arrest receiving centers regardless of volume met the National Academy of Medicine's description of a Level I center. Sufficient postarrest patient-level characteristics were not available to explore the differential benefit of transfer or cardiac arrest receiving center care in specific patient subpopulations. Data sets including this detailed patient-level information might reveal subgroups of patients most likely to benefit from transfer to a cardiac arrest receiving center.

In conclusion, linking regional data derived from 78 EMS services, 46 hospitals, and 4 health networks in a defined geographic region to vital statistics demonstrated a reduction in long-term mortality associated with both transfer to a cardiac arrest receiving center and initial cardiac arrest receiving center care among nontransferred patients. Further studies may explore whether the observed associations with reduced mortality lead to improved long-term functional outcomes and replicate our findings in other geographic regions.

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IMAGES IN EMERGENCY MEDICINE

(continued from p. 18)

DIAGNOSIS:

Gastric outlet obstruction caused by intragastric balloon. The CT revealed an air- and fluid-filled intragastric balloon in the proximal midstomach, measuring 12 cm and occluding much of the gastric lumen, with minimal passage of oral contrast into the small bowel (Figures 1 to 3). An upper endoscopy was performed. The balloon was punctured multiple times with a Carr-Locke needle and biopsy forceps (Figure 4). This caused deflation of the balloon and allowed its endoscopic extraction. The patient tolerated oral intake postprocedure, with resolution of her symptoms.

Gastric outlet obstruction after intragastric balloon placement occurs primarily because of spontaneous deflation and distal migration of the balloon. However, balloon overinflation may also cause obstructive gastrointestinal symptoms, as in our patient. These complications may occur in the first few days after placement. It is a diagnostic challenge because patients can have nonpathologic nausea and vomiting during the first week after balloon insertion.[1] Urgent CT of the abdomen on presentation is essential for early diagnosis. If left untreated, the obstruction may result in gastric wall ischemia, necrosis, and perforation, requiring emergency surgery. Early endoscopic balloon deflation by puncture and extraction is recommended to prevent further complications.[2,3]

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