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Long-term survival benefit from treatment at a specialty center after cardiac arrest

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Abstract

Introduction—The Institute of Medicine and American Heart Association have called for tiered accreditation standards and regionalization of post-cardiac arrest care, but there is little data to support that regionalization has a durable effect on patient outcomes. We tested the effect of treatment at a high-volume center on long-term outcome after sudden cardiac arrest (SCA).

Methods—We included patients hospitalized at one of 7 medical centers in Southwestern Pennsylvania after SCA from 2005 to 2013. Centers were one regional referral center with an organized systems for post-SCA care, two moderate volume tertiary care centers and 4 low-volume centers. We abstracted clinical characteristics and outcomes at hospital discharge, and for survivors to discharge we queried the National Death Index for long-term survival data. We used Cox regression to determine the unadjusted associations of baseline predictors and survival, and built an adjusted model controlling for baseline predictors.

Results—Overall, 987 patients survived to discharge. During 2196 person-years of follow-up, median survival was 5.3 years and there were 396 deaths. In unadjusted analysis, treating center, age, arrest location, Charlson Comorbidity Index, initial rhythm, cardiac catheterization, defibrillator placement, discharge disposition, and neurological status at discharge were associated with long-term outcome. In adjusted analysis, treatment at the high-volume cardiac arrest center was associated with improved survival compared to treatment at other centers (hazards ratio 1.49, 95% confidence interval 1.19 – 1.86).

Conclusion—Treatment at a high-volume cardiac arrest center with organized systems for post-arrest care is associated with a substantial long-term survival benefit after hospital discharge.

Keywords

Cardiac arrest; outcome; regionalization; survival

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Introduction

More than 500,000 Americans experience a sudden cardiac arrest (SCA) annually.[1] Despite advances in care, patient outcomes after SCA are poor, with only a 12% rate of favorable neurological recovery.[1] Among SCA patients who survive to hospital discharge, numerous factors are associated with long-term outcomes including baseline characteristics such as age, race, initial arrest rhythm, etiology and duration,[2–4] intermediate outcomes such as neurological status at hospital discharge,[5] and specific treatments such as use of targeted temperature management (TTM), coronary angiography and internal defibrillator implantation.[2, 6–8] Although individual interventions are associated with improved survival, the overall effect of treatment at a high-volume center with organized systems of care for SCA is less clear.

In July of 2015 the Institute of Medicine (IOM) released its report “Strategies to Improve Cardiac Arrest Survival: a time to act,” calling for tiered accreditation standards for post-arrest care centers.[9] Ten years earlier, amid debate in the resuscitation community about such standards,[10, 11] we established a Post-Cardiac Arrest Service (PCAS), implemented hospital-wide care protocols for SCA care, and developed a regional referral network for post-arrest care.[12] Regionalization of SCA care was encouraged by analogy to the experience with coronary interventions, major trauma, surgery, and stroke, where center volume and organized systems of care are associated with improved outcomes.[13–18] More directly, we observed that in-hospital mortality after SCA varies widely by region, and although center volume has not consistently been associated with short-term outcome after SCA, adherence to evidence-based quality metrics is associated improved survival to discharge at the hospital level.[19–22] In this study, we examine whether the effect of treatment at a high-volume cardiac arrest center influences long-term outcomes after SCA.

Methods

Setting

The entirety of this work was approved by the University of Pittsburgh Institutional Review Board to be conducted with a waiver of informed consent.

We included adult patients treated at 7 hospitals within an integrated health delivery system in Southwestern Pennsylvania, with a catchment area of 2.5 million people. Hospitals included one high-volume, regional referral center with an organized PCAS (Center 1), two moderate volume tertiary care centers (Centers 2 and 3) and 4 low-volume centers (Centers 4–7) (Supplemental Table 1).

The PCAS at Center 1 (Supplemental Appendix) is consulted by the Emergency Department on consecutive out-of-hospital arrest patients with return of spontaneous circulation (ROSC), accepts SCA transfers from outlying facilities, and is consulted by intensive care providers on the majority of in-hospital SCA patients that achieve ROSC. The PCAS coordinates care through the entire post-arrest course including initial resuscitation and diagnostic workup, intensive care and inpatient care, neurological prognostication in comatose patients, detailed neurocognitive testing in patients who have awakened, secondary prevention and

rehabilitation services. The PCAS also maintains an active quality assurance/improvement program that includes regular meetings, case review, feedback to emergency medical service providers and referring physicians, and 3- to 6- month telephone follow-up with discharged patients. Finally, the PCAS supports a research infrastructure with multiple ongoing clinical studies in this population. For patients transferred from one facility to another, we considered the final treating site to be the center for their index hospitalization.

Data Sources

We identified patients from our prospective registry of SCA patients and by querying the electronic medical record for the diagnosis of SCA (International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9CM code 427.5) at all 7 centers. For patients identified by ICD-9CM code, we confirmed the diagnosis of SCA with a structured chart review, which we have confirmed to be essential for accurate case ascertainment.[23] We included patients resuscitated from in-hospital or out-of-hospital SCA who survived to hospital discharge, and excluded those with SCA secondary to surgical etiology such as trauma, or neurological catastrophe. We extracted name, sex, date of birth, race, marital status, state of last known residence, and social security number, and used these data to query the National Death Index (NDI) 2013 NDI Final File to obtain long-term survival data. We linked NDI query results to our SCA cohort using the standard NDI probabilistic scoring approach, and considered a score of >30 to represent a true match.[24]

Potential modifying factors

For eligible patients, we performed a structured chart review to collect age, gender, race, arrest location (in-hospital vs out-of-hospital), transfer status, presenting rhythm (ventricular tachycardia/fibrillation (VT/VF), pulseless electrical activity (PEA), asystole or unknown), pre-arrest Charlson Comorbidity Index, post-arrest illness severity (Pittsburgh Cardiac Arrest Category, a validated 4-level illness severity index that stratifies patients by severity of brain injury and cardiopulmonary failure (Supplemental Appendix)),[25] performance of coronary angiography, automated defibrillator implantation (AICD), Pittsburgh Cerebral Performance Category (CPC) at hospital discharge and discharge disposition (home, acute rehabilitation, long-term acute care (LTAC), skilled nursing facility (SNF), or hospice). Race was self-identified by the subject or surrogate, then recoded by the investigator into one of the 10 categories recognized by the NDI. We included race as a covariate because previous studies have associated race with long-term outcome after SCA.

Statistical Analysis

We used descriptive statistics to summarize population characteristics, and report medians with interquartile ranges and numbers with corresponding percentages. We used Cox regression to determine the unadjusted associations of baseline predictors and survival, and built an adjusted model controlling for baseline predictors associated with survival at a level of $P < 0.1$. In unadjusted and adjusted models, there was no significant difference in the hazard of death across Centers 2–7 ($P = 0.36$ by Cox regression; $P = 0.48$ by log-rank test), so we report models where Center is treated as a binary variable. In adjusted models, we dichotomized initial rhythm, discharge CPC, and discharge disposition to avoid model over-fitting. We planned *a priori* to test for interactions between initial rhythm and cardiac

catheterization, and between Pittsburgh Cardiac Arrest Category and Center. As a sensitivity analysis, we repeated Cox regression including all hospitalized patients (both survivors to discharge and non-survivors). We inspected scaled Shoenfeld residuals and log-log plots to check model assumptions. All analyses were performed using Stata Version 13 (StataCorp, College Station, TX), and we considered a P value < 0.05 to be statistically significant for all analyses.

Results

Cohort characteristics and survival

Overall, we identified 3438 potentially eligible patients, of which 987 met inclusion and exclusion criteria (Figure 1). Baseline population characteristics at Center 1 were similar to those at other centers (Table 1, Supplemental Table 2). Overall, median age was 63 (interquartile range 51 – 75) years and 40% of the population was female. During 2196 person-years of follow-up, median survival time was 5.3 years and there were 396 deaths. The remaining 591 patients surviving to December 31, 2013 were censored after a median of 2.5 (interquartile range 1.3 – 4.3) years after SCA. Unadjusted median survival was 6.6 years for patients treated at Center 1 and ranged from 0.8 to 4.5 years for Centers 2 through 7 (Figure 2). The overall proportion of patients surviving to hospital discharge did not differ across centers (Supplemental Table 1, $P = 0.73$). However, post-discharge survival was significantly longer for patients treated at Center 1 ($P < 0.001$ for log-rank test), but did not differ across Centers 2 to 7 (log rank $P = 0.48$ after excluding Center 1). There was no change in long-term survival over time.

Unadjusted Cox regression

In unadjusted survival analysis, age, arrest location, Charlson Comorbidity Index, initial rhythm, cardiac catheterization, discharge disposition, AICD placement and CPC at discharge were significantly associated with long-term outcome (Table 2). Compared to patients treated at Centers 2 to 7, those treated at Center 1 had a 37% lower unadjusted hazard of death (95% confidence interval (CI) 21 – 49%, $P < 0.001$). Results were similar when we including both survivors to discharge and non-survivors (30% lower hazard of death at Center 1 (95%CI 26 – 34%, $P < 0.001$)) (Supplemental Figure 1).

Adjusted Cox regression

After adjusting for demographic, clinical and treatment variables, treatment at Center 1 was still associated with improved long-term survival compared to treatment at Centers 2 to 7, with the hazard of death 33% lower at Center 1 (95%CI 16 – 46%, $P < 0.001$) (Table 3). Results did not change when restricting the analysis to only non-transferred patients (data not shown). There was no significant interaction between cardiac catheterization and presenting rhythm or Pittsburgh Cardiac Arrest Category and Center.

Discussion

Our major finding is that treatment after SCA at a high-volume, regional referral center with an organized Post-Cardiac Arrest Service was independently associated with a substantial

long-term survival benefit compared to treatment at other centers. This finding is complementary to previous research that has associated short-term neurologically intact survival with regionalization of post-resuscitation care,[26–28] and further supports calls by the IOM, American Heart Association and others to develop regional systems of SCA care. [9, 29, 30]

Our data emphasize that case volume and hospital capabilities are only surrogates for delivery of post-cardiac arrest care, and that actual quality of performance should be the target of implementation strategies. Most centers in our analysis would meet IOM criteria for a Level 1 center able to provide around-the-clock neurological and cardiovascular intensive care. Furthermore, two centers with less favorable long-term outcomes compared to Center 1 are still high volume (>100 SCA cases annually), academic, tertiary care centers. This is consistent with prior research that does not consistently associate hospital volume with outcome.[21, 22] By contrast, we, and others, have reported that systematic implementation of a comprehensive bundle of post-arrest care is associated with improved outcomes, and have worked to foster a cross-disciplinary approach to patient care and quality improvement.[12, 31] The center effect we identified persisted despite adjustment for multiple measurable indicators of case mix and individual processes of care, further supporting the importance of comprehensive, coordinated post-resuscitation care for improving SCA outcomes. Given this, we suggest that development of an accreditation system for centers of excellence should include not only overall hospital capabilities and volume but also the requirement to develop organized systems for acute care, appropriate application of secondary prevention, continuous quality improvement, and engagement with rehabilitation and post-acute care providers.

Our findings confirm the long-term benefit associated with multiple components of post-arrest care including coronary angiography and internal defibrillator implantation, which remained significant predictors of outcome even after adjustment for arrest rhythm.[2, 6] Use of TTM has also been associated with long-term outcome benefits, but we did not test for an effect in this study because TTM was strongly collinear with treating center and PCAC (i.e. very few eligible patients failed to received TTM in this cohort). Finally, we confirm the influence of short-term neurological outcome after SCA on long-term survival. CPC and discharge disposition represent different aspects of post-arrest neurological recovery,[32] and both independently predicted outcome. Whether discharge disposition represents a modifiable care process in addition to a metric of injury severity remains an important question for future research.

Our work has several limitations. As an observational study with two data sources, it is possible that sampling bias explains some or all of the observed center effect. Patients at Center 1 were disproportionately identified from our prospective registry compared to patients at other Centers who were mostly identified via retrospective query of the electronic medical record. We note that measurable patient characteristics were well balanced across Centers (Table 1, Supplemental Table 2) and our estimate of center effect did not change in adjusted models. However, the possibility of important unmeasured confounders remains. Because key aspects of our electronic medical record were adopted at different years across sites, the duration of observation at some hospitals was substantially shorter at some sites

that others. We detected no effect of arrest year on survival and Cox regression should not be affected by differing durations of observation, but this may still be a potential source of artificial variability across centers.

Additionally, because our analysis tested the effect of the comprehensive bundle of care offered at Center 1 (Supplemental Appendix), we are unable to disentangle this intervention to report the effect of any particular element on long-term outcome. It may be that the observed benefits result from the entire system of care, or that a single or few elements are primarily responsible for the observed improvement in survival. For example, we note that CPC at hospital discharge did not differ substantially across centers, raising the possibility that the collaboration we have fostered with colleagues in rehabilitation medicine and the post-acute care they provide is largely responsible for the observed treatment effect. Given that both seemingly minor variations in the acute phase of critical illness,[33, 34] as well as post-acute rehabilitation,[35] have proven to result in a durable effect on neurocognitive outcomes, we hypothesize that no single intervention fully explains our findings. Nevertheless, future observational analyses and interventional trials are urgently needed to test the effect of specific elements of care on long-term patient-centered outcomes to inform an evidence-based approach to post-arrest care.

In conclusion, we present evidence of the effectiveness of regionalization of post-resuscitation care on long-term outcome after SCA. Further epidemiological studies in other care systems are needed to confirm our results. However, given evidence that regionalized care improves short-term SCA outcomes and prior success in number of other acute critical illnesses, we believe the time is right to move forward with implementation of regional systems for cardiac arrest care and referral of high-risk post-arrest patients to dedicated centers of excellence.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.
Cohort selection process

Figure 2.
Kaplan Meier survival estimates for sudden cardiac arrest victims surviving to hospital discharge, stratified according to treating center

Table 1

Cohort characteristics stratified by treating center

Characteristic	Overall (n = 987)	Center 1 (n = 680)	Centers 2–7 (n = 307)
Age, years	63 [51 – 75]	60 [60 – 71]	63 [54 – 75]
Female gender	397 (40)	279 (41)	118 (38)
Race			
White	766 (78)	536 (79)	230 (75)
Black/African American	132 (13)	75 (11)	57 (19)
Other/Not Specified	89 (9)	69 (10)	20 (7)
Out-of-hospital SCA	530 (54)	435 (51)	185 (60)
Interfacility transfer	363 (37)	313 (46)	50 (16)
Charlson Comorbidity Index	1 [0 – 3]	1 [0 – 3]	1 [0 – 3]
Initial Rhythm			
VT/VF	473 (48)	344 (51)	129 (42)
PEA	230 (23)	147 (22)	83 (27)
Asystole	128 (13)	86 (13)	42 (14)
Unknown	156 (16)	103 (15)	53 (17)
Pittsburgh Cardiac Arrest Category			
I	499 (51)	341 (50)	158 (51)
II	239 (24)	173 (25)	55 (22)
III	132 (13)	85 (13)	47 (15)
IV	80 (8)	54 (8)	26 (8)
Unknown	37 (4)	27 (4)	10 (3)
Cardiac catheterization	379 (38)	264 (39)	115 (37)
ICD implantation	76 (8)	46 (7)	30 (10)
Discharge CPC			
1	236 (24)	158 (23)	78 (25)
2	99 (10)	61 (9)	38 (12)
3	578 (59)	418 (61)	160 (52)
4	73 (7)	43 (6)	30 (10)
Discharge disposition			
Home	375 (38)	278 (41)	97 (32)
Acute rehabilitation	146 (15)	103 (15)	43 (14)
Long-term acute care	152 (15)	102 (15)	50 (16)
Skilled nursing facility	265 (27)	171 (25)	94 (31)
Hospice	48 (5)	26 (4)	22 (7)

Data are presented as median [interquartile range] or number (percentage).

Abbreviations: SCA – Sudden cardiac arrest; VT/VF – ventricular tachycardia/fibrillation; PEA – Pulseless electrical activity; ICD – Implantable cardioverter-defibrillator; CPC – Pittsburgh Cerebral Performance Category.

Table 2

Unadjusted associations of predictors with long-term hazard of death after SCA.

Characteristic	Hazards ratio (95% CI)	P value
Age, per year	1.04 (1.03 – 1.04)	<0.001
Female gender	1.03 (0.85 – 1.26)	0.74
Year of arrest	1.02 (0.97 – 1.07)	0.33
Race		0.20 across levels
White	Ref	–
Black/African American	1.02 (0.76 – 1.37)	0.89
Other/Not Specified	1.36 (0.98 – 1.87)	0.06
Out-of-hospital SCA	0.51 (0.41 – 0.62)	<0.001
Interfacility transfer	0.67 (0.54 – 0.83)	<0.001
Charlson Comorbidity Index	1.14 (1.10 – 1.18)	<0.001
Initial Rhythm		<0.001 across levels
VT/VF	Ref	–
PEA	2.09 (1.64 – 2.66)	<0.001
Asystole	1.89 (1.41 – 2.55)	<0.001
Unknown	1.63 (1.22 – 2.18)	0.001
Pittsburgh Cardiac Arrest Category		0.10 across levels
I	Ref	–
II	1.15 (0.90 – 1.47)	0.26
III	1.17 (0.87 – 1.58)	0.30
IV	1.55 (1.09 – 2.20)	0.02
Unknown	1.52 (0.96 – 2.41)	0.08
Cardiac catheterization	0.34 (0.27 – 0.43)	<0.001
ICD implantation	0.48 (0.30 – 0.77)	0.002
Discharge CPC		<0.001 across levels
1	Ref	–
2	1.64 (1.02 – 2.62)	0.04
3	2.62 (1.93 – 3.56)	<0.001
4	10.8 (7.37 – 15.8)	<0.001
Discharge disposition		<0.001 across levels
Home	Ref	–
Acute rehabilitation	1.43 (1.01 – 2.03)	0.04
Long-term acute care	3.81 (2.84 – 5.09)	<0.001
Skilled nursing facility	2.60 (1.97 – 3.41)	<0.001
Hospice	20.1 (13.8 – 29.4)	<0.001
Treating hospital		
Center 1	Ref	–
Center 2 to 7	1.58 (1.27 – 1.95)	<0.001

Abbreviations: SCA – Sudden cardiac arrest; VT/VF – ventricular tachycardia/fibrillation; PEA – Pulseless electrical activity; ICD – Implantable cardioverter-defibrillator; CPC – Pittsburgh Cerebral Performance Category.

Table 3

Final adjusted model for long-term hazard of death after SCA.

Characteristic	Adjusted hazards ratio (95% CI)	P value
Age, per year	1.03 (1.02 – 1.04)	<0.001
Out-of-hospital SCA	0.75 (0.61 – 0.94)	0.01
Interfacility transfer	1.06 (0.85 – 1.33)	0.62
Charlson Comorbidity Index	1.13 (1.08 – 1.18)	<0.001
Initial rhythm VT/VF	0.98 (0.78 – 1.23)	0.88
Cardiac catheterization	0.42 (0.32 – 0.54)	<0.001
ICD implantation	0.61 (0.38 – 0.98)	0.04
Discharge CPC 1–2 (vs 3–4)	0.61 (0.45 – 0.83)	0.002
Discharge to home or acute rehab (vs SNF, LTAC or hospice)	0.64 (0.49 – 0.83)	0.001
Treating hospital 2 to 7 (vs 1)	1.51 (1.20 – 1.90)	<0.001

Abbreviations: SCA – Sudden cardiac arrest; VT/VF – ventricular tachycardia/fibrillation; ICD – Implantable cardioverter-defibrillator; CPC – Pittsburgh Cerebral Performance Category; SNF – Skilled nursing facility; LTAC – Long-term acute care facility.