6-21-2021

Hospital length of stay, do not resuscitate orders, and survival for post-cardiac arrest patients in Michigan: A study for the CARES Surveillance Group

Robert A. Swor

Nai-Wei Chen

Jaemin Song

James H. Paxton

David A. Berger

See next page for additional authors

Authors

Robert A. Swor, Nai-Wei Chen, Jaemin Song, James H. Paxton, David A. Berger, Joseph B. Miller, Jim Pribble, and Joshua C. Reynolds

RESUSCITATION 165 (2021) 119 –126

Available online at www.sciencedirect.com

Resuscitation

journal homepage: www.elsevier.com/locate/resuscitation

Clinical paper

Hospital length of stay, do not resuscitate orders, and survival for post-cardiac arrest patients in Michigan: A study for the CARES Surveillance Group

Robert A. Swor[a,*], Nai-Wei Chen[b], Jaemin Song[a], James H. Paxton[c], David A. Berger[a], Joseph B. Miller[d], Jim Pribble[e], Joshua C. Reynolds[f]

[a] Department of Emergency Medicine, Oakland University William Beaumont School of Medicine, United States
[b] Division of Informatics and Biostatistics, Beaumont Research Institute Beaumont Health, United States
[c] Department of Emergency Medicine, Detroit Receiving Hospital & Sinai-Grace Hospital, Wayne State University School of Medicine, United States
[d] Department of Emergency Medicine, Henry Ford Health System, Wayne State University School of Medicine, United States
[e] Department of Emergency Medicine, Michigan Medicine University of Michigan, United States
[f] Department of Emergency Medicine, Michigan State University College of Human Medicine, United States

Abstract

Objective: Current guidelines recommend deferring prognostic decisions for at least 72 h following admission after Out of Hospital cardiac arrest (OHCA). Most non-survivors experience withdrawal of life sustaining therapy (WLST), and early WLST may adversely impact survival. We sought to characterize the hospital length of stay (LOS) and timing of Do Not Resuscitate (DNR) orders (as surrogates for WLST), to assess their relationship to survival following cardiac arrest.

Design: We performed a retrospective cohort study of probabilistically linked cardiac arrest registries (Cardiac Arrest Registry to Enhance Survival (CARES) and Michigan Inpatient Database (MIDB) from 2014 to 2017.

Patients: Adult (≥18 years) patients admitted following OHCA were included. We considered LOS ≤ 3 days (short LOS) and written DNR order with LOS ≤ 3 days (Early DNR) as indicators of early WLST. Our primary outcome was survival to hospital discharge. We utilized multilevel logistic regression clustered by hospital to examine associations of these variables, patient characteristics and survival to hospital discharge.

Measurement and Main Results: We included 3644 patients from 38 hospitals with >30 patients. Patients mean age was 62.4 years and were predominately male (59.3%). LOS ≤ 3 days (OR_{adj} = 0.11) and early DNR (OR_{adj} = 0.02) were inversely associated with survival to discharge. There was a non-significant inverse association between hospital rates of LOS ≤ 3 days and survival (p = 0.11), and Early DNR and survival (p = 0.83). In the multilevel model, using median odd ratios to assess variation in LOS ≤ 3 days and survival, patient characteristics contributed more to variability in surviival than between-hospital variation. However, between-hospital variation contributed more to variability than patient characteristics in the provision of early DNR orders.

Conclusions: We observed that LOS ≤ 3 days for post-arrest patients was negatively-associated with survival, with both patient characteristics and between-hospital variation associated with outcomes. However, between-hospital variation appears to be more highly-associated with provision of early DNR orders than patient characteristics. Further work is needed to assess variation in early DNR orders and their impact on patient survival.

Keywords: Cardiac arrest, Survival, Length of stay, End of life, Prognostication, WSLT

* Corresponding author at: Department of Emergency Medicine, William Beaumont Hospital, 3601 W. 13 Mile Rd, Royal Oak, MI 48073, United States.
E-mail addresses: raswor@beaumont.edu, raswor@aol.com (R.A. Swor).

https://doi.org/10.1016/j.resuscitation.2021.05.039
Received 2 March 2021; Received in revised form 17 May 2021; Accepted 28 May 2021
Available online xxx

Introduction

Improving clinical outcomes after out-of-hospital cardiac arrest (OHCA) requires a complex system of care, referred to commonly as the 'chain of survival'.[1,2] Substantial resources have been dedicated to improving factors identified in this model, including bystander recognition and intervention, public access defibrillation, prehospital and emergency care, and in-hospital care subsequent to return of spontaneous circualtion.[3–6] Critical care for OHCA patients continues to evolve, with discrete interest in neurocritical care for the post-arrest patient.[3,4] Evidence-based clinical decision making around neurologic prognostication and withdrawal from life sustaining therapies is crucial; awakening from coma with good functional recovery can occur more than 72 h after return of spontaneous circulation (ROSC) or 72 h after rewarming in patients treated with targeted temperature management (TTM).[5–7]

Coma following ROSC is common, even among those who ultimately experience good neurologic outcomes, and early neurological findings do not reliably predict a poor patient outcome.[8] Guidelines from the European Resuscitation Council (ERC) and American Heart Association (AHA) have summarized this literature, and confirm that there are no known clinical or laboratory features that sufficiently predict a poor prognosis within the first 72 h.[9,10] This early period of post-arrest coma is challenging for providers and families alike, who are faced with complex decisions regarding whether to continue or withdraw life-sustaining therapies (WLST). In North America, WLST for presumed poor neurologic prognosis is the single most common proximate cause of death among post-cardiac arrest patients.[11]

Limited literature characterizes post-arrest WLST, including the incidence of early WLST within 72 h and its potential impact on meaningful functional recovery. Two large registry-based observational studies indicate that early WSLT was common (33–43%) [5] and potentially could impact outcomes in 16–19% of patients exposed to early WSLT.[12] Both were conducted within academic tertiary care centers and regional systems of care. It remains to be determined if these estimates are observed in a more variegated cohort. Thus, we utilized a state-wide registry encompassing both academic and a number of community-based hospitals to tabulate post-arrest length of hospital stay (LOS) and short (≤3 days) LOS as a surrogate for early WLST. Our primary objective was to characterize hospital-level variability in the relationship between prevalence of LOS ≤ 3 days and subsequent survival to hospital. We also characterized the early use of do not resuscitate (DNR) orders (≤3 days) as an indicator of intent to WLST.

Methods

This study was approved by the William Beaumont Hospital Institutional Review Board and the CARES Data Sharing Committee.

Data sources

We performed a secondary analysis of two prospectively created registries in the state of Michigan: the Cardiac Arrest Registry to Enhance Survival (CARES) and the Michigan Inpatient Database (MIDB). CARES is a national OHCA registry that collects demographic, prehospital, emergency, and hospital-based data elements, including clinical outcomes through hospital discharge.[13] During the study period, CARES data was submitted from EMS agencies from a catchment area encompassing nearly 70% of the Michigan population (approximately 7 million persons).[14] The MIDB database, maintained by the Michigan Department of Community Health, records diagnostic, procedural, and outcome data for acute care admissions in the state of Michigan.[17]

Study cohort

We linked OHCA cases between CARES and MIDB using probabilistic linkage methodology at the patient level and have previously described this methodology.[15] We included all adult (≥18 years old) patients recorded in CARES with attempted prehospital resuscitation after non-traumatic OHCA from 2014 to 2017. We excluded 1) patients under 18 years of age; 2) traumatic cardiac arrest; 3) patients with pre-existing DNR orders at the time of cardiac arrest; 4) patients who did not survive to hospital admission; 5) patients who experienced immediate ROSC after only bystander CPR as identified in CARES; 6) patients transferred from the original receiving hospital, or transported out of state (precluding patient-level matching of EMS and inpatient records); and, 7) patients treated at hospitals with <30 cardiac arrest cases reported over the four-year study period.

Patient characteristics

Patient age, sex, arrest location type (e.g., private residence, health facility, public), arrest witness status (e.g., unwitnessed, bystander-witnessed, 911 responder-witnessed), and initial rhythm type (e.g., non-shockable, shockable) were obtained from the CARES. Hospital length of stay was obtained from MIDB.

Study outcomes and definitions

Our question of interest was whether patients had early WLST, defined as occurring within 3 days of arrest. The primary outcome was survival to hospital discharge as recorded in CARES. We used two surrogates for early WLST: hospital LOS of ≤3 days (LOS ≤ 3 days), or the provision of a DNR order associated with a LOS ≤ 3 days (Early DNR). Hospital LOS was abstracted from the MIDB database. As denoted by ERC and AHA guidelines on the timing of neurologic prognostication following cardiac arrest, we defined short hospital LOS as less than or equal to 3 days (LOS ≤ 3 days) between hospital arrival and time of death.[16] This determination was imperfect, as the MIDB database only determines date, but not time of discharge or death. Since hospital LOS is impacted by both physiologic events (e.g., death from cardiovascular collapse, brainstem herniation or multi-system organ failure) and clinical decisions to WLST, we performed a secondary analysis restricted to patients who had a documented do not resuscitate (DNR) order (as recorded in CARES), and a length of stay less than or equal to 3 days (Early DNR).

Statistical analyses

We have previously described the probabilistic matching and linkage of these two datasets.[15] Match scores were tabulated using a composite point score from points assigned to each of match variables including age, sex, date of arrest/hospital admission, and receiving hospital. We assigned weighted scores to each variable based on the

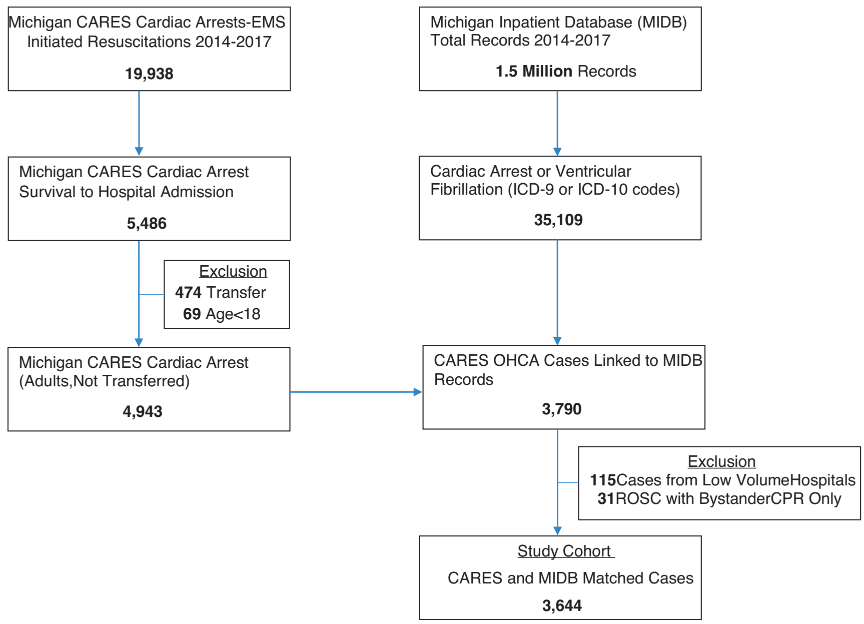

Fig. 1 – Case ascertainment of study patients.

perceived ability of each variable to provide an optimal match. We further determined the threshold from the distribution of match scores to identify the linkage of records from the same patient. The final study cohort included OHCA patients who were successfully linked to a MIDB record. The matching process was implemented using the SQL procedure in SAS.

Descriptive analyses summarized patient characteristics with *t*-test or Kruskal-Wallis test (continuous variables) and Chi-squared or

Table 1 – Characteristics of Study Patients by Status of Length of Stay and Status of Do-Not-Resuscitate.

Variables	All	Length of Stay			Do-Not-Resuscitate		
		≤3 days	>3 days	*p* value	≤3 days	>3 days	*p* value
n	3644	1813	1831		573	3071	
Patient Characteristics							
Age, years, mean ± SD	62.4 ± 16.1	63.7 ± 17.1	61.1 ± 14.9	<0.001	65.6 ± 17.5	61.8 ± 15.7	<0.001
Age, years, No. (%)							
18–39	336 (9.2)	186 (10.3)	150 (8.2)	<0.001	57 (10.0)	279 (9.1)	<0.001
40–64	1606 (44.1)	711 (39.2)	895 (48.9)		200 (34.9)	1406 (45.8)	
65–74	835 (22.9)	389 (21.5)	446 (24.4)		123 (21.5)	712 (23.2)	
≥75	867 (23.8)	527 (29.1)	340 (18.6)		193 (33.7)	674 (21.9)	
Sex, No. (%)							
Male	216 (59.3)	1025 (56.5)	1135 (62.0)	0.001	319 (55.7)	1841 (60.0)	0.06
Female	1484 (40.7)	788 (43.5)	696 (38.0)		254 (44.3)	1230 (40.0)	
Rhythm Type, No. (%)							
Non-shockable	2509 (68.8)	1431 (78.9)	1078 (58.9)	<0.001	482 (84.1)	2027 (66.0)	<0.001
Shockable	1135 (31.1)	382 (21.1)	753 (41.1)		91 (15.9)	1044 (34.0)	
Location, No. (%)							
Home/Residence	2465 (67.6)	1301 (71.8)	1164 (63.6)	<0.001	419 (73.1)	2046 (66.6)	<0.001
Public	625 (17.1)	219 (12.1)	406 (22.2)		44 (7.7)	581 (18.9)	
Nursing Home/Healthcare	554 (15.2)	293 (16.2)	261 (14.2)		110 (19.2)	444 (14.5)	
Arrest Witness Status, No. (%)							
Unwitnessed	1349 (37.0)	765 (42.2)	584 (31.9)	<0.001	268 (46.8)	1081 (35.2)	<0.001
Bystander	1673 (45.9)	750 (41.4)	923 (50.4)		236 (41.2)	1437 (46.8)	
911 Responder	622 (17.1)	298 (16.4)	324 (17.7)		69 (12.0)	553 (18.0)	
Outcome							
Survival in Hospital, No. (%)							
No	2566 (70.4)	1649 (90.9)	917 (50.1)	<0.001	568 (99.1)	1998 (65.1)	<0.001
Yes	1078 (29.6)	164 (9.0)	914 (49.9)		5 (0.9)	1073 (34.9)	

Note: SD = standard deviation.

Fisher's exact test (categorical variables). Our data had two-level structure with patients clustered within hospitals. Multilevel logistic regression models were used to examine the association between LOS $\leq$ 3 days and Early DNR, and survival to hospital discharge, adjusted for patient characteristics and clustering of patients within hospitals, respectively. We *a priori* selected patient age, sex, presenting cardiac rhythm, location of arrest, and witnessed collapse for inclusion as covariates since these are known variables associated with clinical outcomes after OHCA. Similar modeling approach was also used to examine the association between patient characteristics, LOS $\leq$ 3 days and Early DNR, adjusted for clustering of patients within hospitals. We estimated the median odds ratio (MOR) to indicate whether individual propensity of the binary outcome of interest was dependent on the hospitals. The MOR was defined as the median of values of odds ratios between the hospital at higher likelihood of the outcome and the hospital at lower likelihood of the outcome when randomly sampling two identical patients from different hospitals (ie, the median change in the odds of the outcome moving from one hospital to another hospital).[17,18] To better understand the magnitude of between-hospital variation on the likelihood of the outcome of interest, MOR and the reciprocal of the MOR was used to compare with the estimated odds ratios of patient characteristics in a multilevel logistic regression model.

To characterize variation in the prevalence of LOS $\leq$ 3 days and Early DNR across hospitals, we plotted the adjusted rates generated from the multilevel multivariable logistic models. Beta regression was used to examine the association between the adjusted rates of LOS $\leq$ 3 days or Early DNR and the adjusted proportions of patients surviving to hospital discharge across hospitals. All tests of statistical significance were two-sided with a significance level of 0.05. Analyses were performed using SAS version 9.4 (SAS Institute, Inc., Cary, NC).

Results

Of 3790 patients, we excluded 31 with ROSC after bystander CPR and 115 who were transported to hospitals treating fewer than 30 patients over the four-year study period. This yielded a final cohort of 3644 patients from 38 hospitals (Fig. 1). Patients mean (SD) age was 62.4 ± 16.1 years and were predominately male (59.3%). Approximately one-third (31.1%) had an initially shockable cardiac rhythm and the majority (67.6%) collapsed in a private

Table 2 – Results of Length of Stay and Do-Not-Resuscitate on Survival to Hospital Discharge from Multilevel, Multivariable Analysis.

			Survival to Hospital Discharge			
			As a Function of Length of Stay[a]		As a Function of Do-Not-Resuscitate[a]	
Variables	No. (%)	Observed Rate (%)	Odds Ratio (95% CI)	*p* value	Odds Ratio (95% CI)	*p* value
n	3644	49.7				
Length of Stay, days						
>3 days	1831 (50.2)	49.9	1 [Reference]			
≤3 days	1813 (49.7)	9.0	0.11 (0.09 to 0.13)	<0.001		
Do-Not-Resuscitate, days						
>3 days	3071 (84.3)	34.9			1 [Reference]	
≤3 days	573 (15.7)	0.9			0.02 (0.01 to 0.05)	< 0.001
Age, years						
18−39	336 (9.2)	27.7	1 [Reference]		1 [Reference]	
40−64	1606 (44.1)	35.4	0.89 (0.65 to 1.24)	0.49	0.97 (0.72 to 1.32)	0.85
65−74	835 (22.9)	28.3	0.63 (0.44 to 0.90)	0.01	0.72 (0.52 to 1.00)	0.05
≥75	867 (23.8)	20.9	0.60 (0.41 to 0.86)	0.006	0.59 (0.42 to 0.83)	0.003
Sex						
Male	2160 (59.3)	33.6	1 [Reference]		1 [Reference]	
Female	1484 (40.7)	23.7	0.84 (0.69 to 1.02)	0.08	0.85 (0.71 to 1.02)	0.07
Rhythm Type						
Non-shockable	2509 (68.8)	18.0	1 [Reference]		1 [Reference]	
Shockable	1135 (31.1)	55.2	4.60 (3.78 to 5.59)	<0.001	4.79 (3.98 to 5.75)	<0.001
Location						
Home/Residence	2465 (67.6)	26.0	1 [Reference]		1 [Reference]	
Public	625 (17.1)	48.6	1.68 (1.33 to 2.12)	<0.001	1.73 (1.40 to 2.15)	<0.001
Nursing Home/Healthcare	554 (15.2)	24.2	1.35 (1.03 to 1.76)	0.03	1.33 (1.03 to 1.72)	0.03
Arrest Witness Status						
Unwitnessed	1349 (37.0)	20.5	1 [Reference]		1 [Reference]	
Bystander	1673 (45.9)	34.2	1.40 (1.14 to 1.73)	0.002	1.50 (1.23 to 1.83)	<0.001
911 Responder	622 (17.1)	36.8	2.56 (1.97 to 3.32)	<0.001	2.31 (1.81 to 2.96)	<0.001
Measure of Variation or Clustering						
Hospital Level Variance		0.155		0.165		
Median Odds Ratio (MOR)		1.46		1.47		

[a] Adjusted effects of length of stay (LOS) and do-not-resuscitate (DNR) were estimated in multilevel logistic regression models, controlling for patient characteristics and the clustering of patients within hospitals.

residence. More than half of patients were witnessed by either bystanders or prehospital personnel. Approximately half (47.1%) received TTM and approximately one-third (29.6%) survived to hospital discharge. Half (49.7%) of patients had LOS $\leq$ 3 days and 15.7% had Early DNR. Patients with LOS $\leq$ 3 days and Early DNR tended to be older, female, present with a non-shockable initial cardiac rhythm, have an unwitnessed collapse, the arrest occurred in a private residence, and were less likely to survive to hospital discharge (Table 1).

We examined the association of LOS $\leq$ 3 days on survival to hospital discharge and quantified the general contextual effect by measures of between-hospital variation. In the multilevel logistic model, our results suggest that there is an inverse association between LOS $\leq$ 3 days and survival to hospital discharge (OR_{adj} = 0.11, 95% CI = 0.09–0.13). Patients with LOS $\leq$ 3 days were also more likely to have those characteristics traditionally associated with a poorer prognosis following OHCA, including older age, arrest in a private location, unwitnessed arrest, and non-shockable presenting cardiac rhythm (Table 2). In addition, the median odds ratio (MOR) across hospitals for survival to hospital discharge was 1.46, indicating that the median odds of survival to hospital discharge were 46% greater for a patient admitted to one hospital in any randomly-selected pair of hospitals. Multiple patient characteristics (age >65 years, initial shockable cardiac rhythm, collapse in public, and EMS-witnessed collapse) had a greater impact than median effect of clustering on the likelihood of hospital survival ($OR_{adj} > 1.46$ vs. $OR_{adj} < 0.68$). We found similar results examining the association of Early DNR (DNR $\leq$ 3 days on tables and graphics) and survival to hospital discharge in the multilevel logistic model (Table 2). There was an inverse association between Early DNR and survival to hospital discharge (OR_{adj} 0.02, 95% CI 0.01–0.05) and the MOR across hospitals was 1.47 for survival to hospital discharge.

We also characterized the variation of short LOS (LOS $\leq$ 3 days) and early DNR (DNR $\leq$ 3 days) by hospital, including the impact of patient characteristics. In our multilevel logistic model, the MOR across hospitals for LOS $\leq$ 3 days was 1.18, suggesting that multiple patient characteristics (age >40 years, shockable rhythm, publication or nursing home location, witnessed arrest) were of potentially larger relevance than between-hospital variation in the likelihood of short LOS ($OR_{adj} > 1.18$ or $OR_{adj} < 0.85$). Models of early DNR showed a different pattern. The MOR across hospitals for early DNR was as high as 3.16, suggesting that no measured patient characteristics were of greater relevance than between-hospital variation in the likelihood of early DNR ($OR_{adj} > 3.16$, or $OR_{adj} < 0.32$) (Table 3).

Fig. 2 presents the adjusted rates of short LOS (LOS $\leq$ 3 days) and early DNR across all 38 hospitals, adjusted for patient characteristics and the clustering of patients within hospitals. We observed large variation in the adjusted rate of early DNR by hospital (mean 13.9%, range 1.2–40.9%) but not for LOS $\leq$ 3 days by hospital (mean 49.5%, range 43.1–56.4%). For early DNR, 9/38 hospitals had adjusted rates significantly higher than the hospital average and 11/38 hospitals had significantly lower rates.

Table 3 – Results of Patient Characteristics on Short Length of Stay and Early Do-Not-Resuscitate from Multilevel, Multivariable Analysis.

Variables	No. (%)	Short Length of Stay[a,b] Observed Rate (%)	Odds Ratio (95% CI)	*p* value	Early Do-Not-Resuscitate[a,b] Observed Rate (%)	Odds Ratio (95% CI)	*p* value
n	3644	49.7	–	–	15.7	–	–
Age, years							
18–39	336 (9.2)	55.4	1 [Reference]		17.0	1 [Reference]	
40–64	1606 (44.1)	44.3	0.77 (0.60 to 0.99)	0.04	12.5	0.80 (0.56 to 1.14)	0.21
65–74	835 (22.9)	46.6	0.82 (0.62 to 1.07)	0.15	14.7	1.00 (0.68 to 1.47)	0.99
≥75	867 (23.8)	60.8	1.43 (1.09 to 1.89)	0.01	22.3	1.66 (1.14 to 2.41)	0.01
Sex							
Male	2160 (59.3)	47.4	1 [Reference]		14.8	1 [Reference]	
Female	1484 (40.7)	53.1	1.03 (0.89 to 1.19)	0.67	17.1	1.06 (0.86 to 1.31)	0.55
Rhythm Type							
Non-shockable	2509 (68.8)	57.0	1 [Reference]		19.2	1 [Reference]	
Shockable	1135 (31.1)	33.7	0.44 (0.37 to 0.52)	<0.001	8.0	0.42 (0.32 to 0.54)	<0.001
Location							
Home/Residence	2465 (67.6)	52.8	1 [Reference]		17.0	1 [Reference]	
Public	625 (17.1)	35.0	0.62 (0.51 to 0.75)	<0.001	7.0	0.44 (0.31 to 0.63)	<0.001
Nursing Home/Healthcare	554 (15.2)	52.9	0.86 (0.70 to 1.04)	0.12	19.9	0.92 (0.70 to 1.21)	0.55
Arrest Witness Status							
Unwitnessed	1349 (37.0)	56.7	1 [Reference]		19.9	1 [Reference]	
Bystander	1673 (45.9)	44.8	0.71 (0.61 to 0.83)	<0.001	14.1	0.76 (0.61 to 0.94)	0.01
911 Responder	622 (17.1)	47.9	0.70 (0.57 to 0.85)	0.001	11.1	0.49 (0.36 to 0.67)	<0.001
Measure of Variation or Clustering							
Hospital Level Variance			0.029			1.454	
Median Odds Ratio (MOR)			1.18			3.16	

[a] Short length of stay meant length of stay ≤3 days and early do-not-resuscitate meant do-not-resuscitate ≤3 days.
[b] Adjusted effects of patient characteristics were estimated in the multilevel logistic regression model, controlling for the clustering of patients within hospitals.

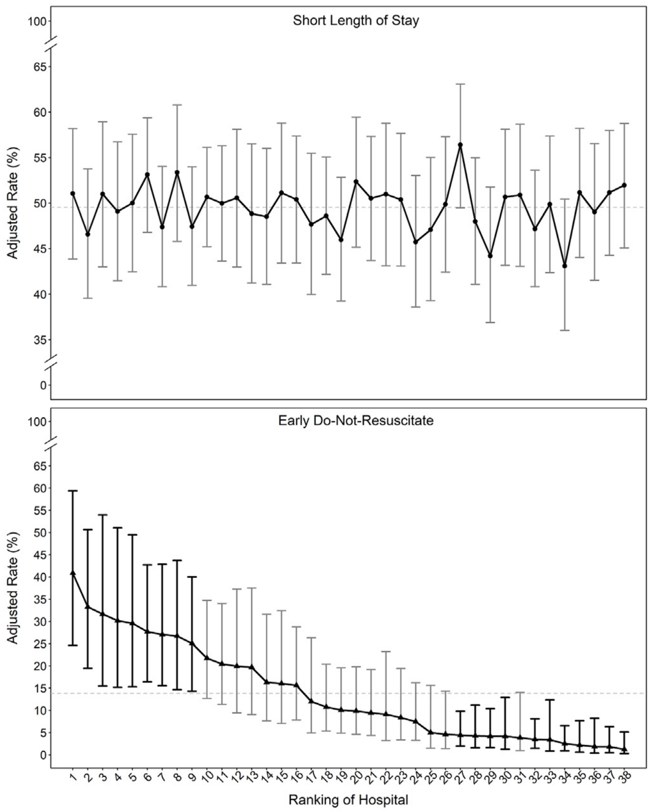

Fig. 2 – Variation among 38 hospitals in rates of short LOS and early DNR.
Footnote: These adjusted rates were estimated from multilevel logistic models, controlling for patient characteristics. Adjusted rates of early DNR were ranked from highest to lowest by hospital and adjusted rates of short LOS (LOS $\le$ 3 days) are depicted along with the ranking of hospitals of early DNR. Adjusted rates and the corresponding 95% confidence intervals for each hospital were plotted. Hospitals with adjusted rates significantly different from the overall mean adjusted rates (dashed line) were colored with dark confidence intervals.

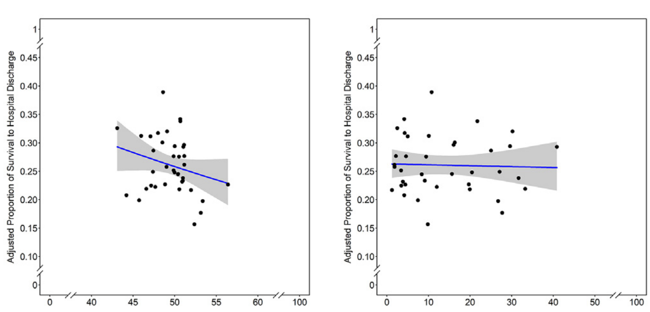

Fig. 3 – Rates of short LOS and early DNR versus proportions of survival to hospital discharge for each hospital.
Foot note: These adjusted rates on short LOS (LOS $\le$ 3 days) and early DNR, respectively, were estimated from multilevel logistic models, controlling for patient characteristics.

After adjusting for patient characteristics in Table 1, the adjusted proportion of survival to hospital discharge varied from 0.16 to 0.39 by hospital, estimated from the multilevel logistic model. Fig. 3 plots the adjusted rates of short LOS (LOS $\le$ 3 days) or early DNR (x-axis) versus the proportions of patients with survival to hospital discharge (y-axis) for each hospital. Beta regression suggested a small negative association between rates of LOS $\le$ 3 days and proportions of patients with survival to hospital discharge at the hospital level (regression coefficient = -0.03, $p = 0.11$). We did not identify any evidence of association between rates of early DNR and proportions of patients with survival to hospital discharge at the hospital level (regression coefficient = -0.001, $p = 0.83$).

Discussion

In North America, the most common cause of death after successful resuscitation from cardiac arrest is WLST. For this reason, it is important that clinicians and researchers have data regarding this process. In this cohort, the length of hospital stay after resuscitation from cardiac arrest was frequently short, with LOS $\le$ 3 days found in approximately half of our study population. Although LOS $\le$ 3 days was associated with decreased survival in this data set, almost 10% of those with LOS $\le$ 3 days survived to hospital discharge. We found that the rate of LOS $\le$ 3 days varied by hospital and was associated with differences in most patient characteristics measured in this analysis. Patient outcome was negatively associated with LOS $\le$ 3 days, there was significant variation in LOS $\le$ 3 days by hospital, but between-hospital variation was more likely associated with differences in patient characteristics.

During the study period, 15.7% of patients had an Early DNR order (a new DNR order written within 3 days of cardiac arrest); not surprisingly, outcomes were poor for these patients. We observed substantial variation by hospital in the rate of early DNR orders. However, between-hospital variation in Early DNR was more likely associated with the hospital, rather than patient characteristics.

These data are hypothesis-generating, with almost half of all patients admitted post-cardiac arrest staying in the hospital 3 days or less. While we initially observed that there was variation in the rate of LOS $\le$ 3 days by hospital, most of this variation appears to be due to differences in patient characteristics. Early DNR orders, however, vary substantially by hospital and that variation is not explained by patient characteristics considered in our analysis. The impact of this variation in practice on outcome is difficult to discern as an early DNR order was observed to be almost uniformly fatal in our study population. The adjusted variation in DNR provision by hospital is striking, however.

Sandroni et al. have suggested that early WLST for presumed neurologic death and futility may contribute to low post-arrest survival rates.[5,19] However, it is difficult to quantify the reasons that providers and families seek early WLST, due to the complexity of the decision-making involved. Hemodynamic collapse often occurs early after cardiac arrest, and is a more objective proximate cause of death.[20] However, a diagnosis of "futility" by clinicians could lead to withdrawal of care *directly* through the decisions of the provider, or *indirectly* through information given to families by physician or nursing care providers. Although a patient's wishes relating to DNR orders or advance directives are important, they are also underutilized.[21] Such written instructions often lack the level of detail needed to implement the patient's wishes.[21] Although existing literature suggests that practice variation in withdrawal of care may impact survival,[22] we believe that ours is the first study to link early DNR orders to outcomes for OHCA. Work by Fendler et al. exploring the "Get with the Guidelines® - Resuscitation" inpatient cardiac arrest registry has already quantified this issue for patients experiencing in-hospital cardiac arrest (IHCA).[24] However, IHCA patients may differ importantly from OHCA patients in this area. DNR status is often established at the time of hospital admission, and cardiac arrest for inpatient cardiac arrest is more likely a terminal event.[22] Early DNR identification may have an important role on impacting OHCA survival. We observed substantial variation in this variable between hospitals, which may reflect characteristics of the hospital, characteristics of the patient population served by the hospital, or both.[23,24] Hospitals near a large number of extended care facilities, or with a disproportionate elderly population, may treat more patients not desirous of aggressive post-resuscitative care. There may also be differences in the culture of practitioners or hospitals, especially in their inherent aggressiveness or sense of futility for post-cardiac arrest care, as previously described.[25] Early DNR may represent an active decision to *not* provide post-arrest care and could help to explain variation in OHCA outcomes between hospitals.

We also observed that patients treated with TTM had longer LOS than those who did not. This is in accordance with clinical guidelines, yet almost 40% of TTM patients had LOS $\leq$ 3 days. This finding suggests that these patients either succumb from cardiovascular causes or have life sustaining therapies withdrawn during TTM. Reasons for this should similarly be assessed.

Fundamentally these data support the need for further evaluation of the post arrest care process, including whether early withdrawal of care adversely impacts patient survival and how this process is implemented in the community. Prior literature exploring early WLST are parts of large multicenter trials or organized regions of cardiac arrest care, and were able to collect data to characterize this process as part of this process. Use of LOS $\leq$ 3 days and Early DNR may be more generally available as through registries such as CARES. This may allow for more widespread assessment of measures of WLST in emergency care systems.

Limitations

This study has several limitations, many of which are inherent to the use of secondary data from a large statewide database. Our data do not include comprehensive clinical information, such as hemodynamic data, that may be needed to generate a complete picture explaining the patient's proximate cause of death. Our data set also does not include patient comorbidities, socioeconomic factors, ethnicity or other cultural factors that may help to explain the variation in care provided by hospitals. Also, decisions regarding WLST are complex, involving caregiver attitudes, past medical history, patients' wishes, and decision-making by family and legally-authorized representatives. Beyond a documentation of new DNR orders, our data do not provide information that might impact these decisions. Early DNR orders were associated with an almost uniformly fatal outcome, which limits our ability to assess interpretation of variation in practice on patient survival. Finally, it is possible DNR status was decided prior to the cardiac arrest but only documented on hospital arrival. More granular data documenting this decision are needed to address this issue.

There are also limitations introduced by our methods for use of these data. In the first year of the study (2014), one-third of the state did not participate in CARES reporting. We also excluded 115 patients (3.1%) taken to hospitals that treated less than 30 OHCA cases during the study period. It is unknown how this may have affected our findings. We are also unable to assess the potential independent impact of non-comatose survivors who were resuscitated early, defibrillated and discharged intact after only a short length of stay.

Conclusion

Within Michigan, we observed that LOS $\leq$ 3 days in post-arrest patients is associated with lower survival to hospital discharge, varies by hospital, and is more likely explained by patient characteristics than by between-hospital variation. There was substantial variation in the provision of early DNR orders, which is not clearly explained by patient characteristics but in this study was not associated with hospital variation in survival. Further work is needed to understand the process whereby life-sustaining therapy is withdrawn, and the potential impact of the timing of this withdrawal on OHCA patient survival.

Funding

This work was supported in part by a grant from the Blue Cross Blue Shield Foundation of Michigan.

Conflict of interest statement

None of the authors report have any potential financial or ethical conflicts of interest to report regarding the contents of this work.

CRediT authorship contribution statement

Robert A. Swor: Conceptualization, Methodology, Writing - review & editing, Funding acquisition. **Nai-Wei Chen:** Methodology, Formal analysis. **Jaemin Song:** Conceptualization, Writing - original draft, Writing - review & editing. **James H. Paxton:** Writing - review & editing. **David A. Berger:** Funding acquisition, Writing - review & editing. **Joseph B. Miller:** Writing - review & editing. **Jim Pribble:** Writing - review & editing. **Joshua C. Reynolds:** Writing - review & editing.

REFERENCES

1. AHA. Out of Hospital Chain of Survival. CPR and First Aid Emergency Cardiovascular.
2. Cummins RO, Ornato JP, Thies WH, Pepe PE. Improving survival from sudden cardiac arrest: The "Chain of Survival" concept. *Circ AHA Statement*. Published online 1991.
3. Polderman KH. Emergency neurological life support: Resuscitation following cardiac arrest. *Neurocrit Care*. Published online 2017. https://doi.org/10.1007/s12028-017-0457-9.
4. Polderman KH. Emergency neurological life support: Resuscitation following cardiac arrest. *Neurocrit Care*. Published online 2015. https://doi.org/10.1007/s12028-015-0171-4.

5. Sandroni C, Geocadin RG. Neurological prognostication after cardiac arrest. *Curr Opin Crit Care*. Published online 2015. https://doi.org/10.1097/MCC.0000000000000202.
6. Gold B, Puertas L, Davis SP, et al. Awakening after cardiac arrest and post resuscitation hypothermia: Are we pulling the plug too early? *Resuscitation*. Published online 2014. https://doi.org/10.1016/j.resuscitation.2013.10.030.
7. Zanyk-Mclean K, Sawyer KN, Paternoster R, Shievitz R, Devlin W, Swor R. Time to awakening is often delayed in patients who receive targeted temperature management after cardiac arrest. *Ther Hypothermia Temp Manag*. Published online 2017. https://doi.org/10.1089/ther.2016.0030.
8. Cassina T, Clivio S, Putzu A, Villa M, Moccetti T, Fortuna D, Casso G. Neurological outcome and modifiable events after out-of-hospital cardiac arrest in patients managed in a tertiary cardiac centre: A ten years register. Med Intensiva 2020;44:409−19, doi:http://dx.doi.org/10.1016/j.medin.2019.05.006.
9. Callaway CW, Donnino MW, Fink EL, et al. Part 8: Post−cardiac arrest care. *Circulation*. Published online 2015. https://doi.org/10.1161/cir.0000000000000262.
10. Nolan JP, Soar J, Cariou A, et al. Post resuscitation care: Section 5 of the European Resuscitation Council Guidelines for Resuscitation 2015. *Notfall und Rettungsmedizin*. Published online 2015. https://doi.org/10.1007/s10049-015-0094-9.
11. Elmer J, Callaway CW. The brain after cardiac arrest. *Semin Neurol*. Published online 2017. https://doi.org/10.1055/s-0036-1597833.
12. May TL, Ruthazer R, Riker RR, et al. Early withdrawal of life support after resuscitation from cardiac arrest is common and may result in additional deaths. *Resuscitation*. Published online 2019. https://doi.org/10.1016/j.resuscitation.2019.02.031.
13. McNally B, Robb R, Mehta M, et al. Out-of-hospital cardiac arrest surveillance - cardiac arrest registry to enhance survival (CARES), United States, october 1, 2005-December 31, 2010. Morb Mortal Wkly Rep 2011;60:1−19.
14. Michigan Health and Hospital Association Data Services.
15. Tram J, Pressman A, Chen N-W, et al. Percutaneous mechanical circulatory support and survival in patients resuscitated from out of hospital cardiac arrest: A study from the CARES Surveillance Group. *Resuscitation*. Published online 2020. https://doi.org/10.1016/j.resuscitation.2020.10.046.
16. Panchal AR, Bartos JA, Cabañas JG, et al. Part 3: Adult basic and advanced life support: 2020 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation*. Published online 2020. https://doi.org/10.1161/CIR.0000000000000916.
17. Larsen K, Merlo J. Appropriate assessment of neighborhood effects on individual health: Integrating random and fixed effects in multilevel logistic regression. *Am J Epidemiol*. Published online 2005. https://doi.org/10.1093/aje/kwi017.
18. Larsen K, Petersen JH, Budtz-Jørgensen E, Endahl L. Interpreting parameters in the logistic regression model with random effects. *Biometrics*. Published online 2000. https://doi.org/10.1111/j.0006-341x.2000.00909.x.
19. Dragancea I, Cronberg T, Wise N, Al-Subaie N, Cranshaw J, Friberg H, Glover G, Pellis T, Rylance R, Walden A, Nielsen N. Protocol-driven neurological prognostication and withdrawal of life-sustaining therapy after cardiac arrest and targeted temperature management. Resuscitation 2017;117:50−7.
20. Elmer J, Torres C, Aufderheide TP, et al. Association of early withdrawal of life-sustaining therapy for perceived neurological prognosis with mortality after cardiac arrest. *Resuscitation*. Published online 2016. https://doi.org/10.1016/j.resuscitation.2016.01.016.
21. Richardson DK, Zive D, Daya M, Newgard CD. The impact of early do not resuscitate (DNR) orders on patient care and outcomes following resuscitation from out of hospital cardiac arrest. *Resuscitation*. Published online 2013. https://doi.org/10.1016/j.resuscitation.2012.08.327.
22. Fendler TJ, Spertus JA, Kennedy KF, Chan PS. Association between hospital rates of early do-not-resuscitate orders and favorable neurological survival among survivors of inhospital cardiac arrest. *Am Heart J*. Published online 2017. https://doi.org/10.1016/j.ahj.2017.05.017.
23. Carr BG, Goyal M, Band RA, et al. A national analysis of the relationship between hospital factors and post-cardiac arrest mortality. *Intensive Care Med*. Published online 2009. https://doi.org/10.1007/s00134-008-1335-x.
24. Okubo M, Schmicker RH, Wallace DJ, et al. Variation in survival after out-of-hospital cardiac arrest between emergency medical services agencies. *JAMA Cardiol*. Published online 2018. https://doi.org/10.1001/jamacardio.2018.3037.
25. Sayre MR, Swor R, Pepe PE, Overton J. Current issues in cardiopulmonary resuscitation. Prehospital Emergency Care 2003, doi:http://dx.doi.org/10.1080/10903120390937058.