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Impact of Timing of Cardiac Arrest During Hospitalization on Survival Outcomes and Subsequent Length of Stay

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Abstract

Background—In-hospital cardiac arrest (IHCA) is common and often fatal. However, the association between timing of cardiac arrest and likelihood of survival to discharge, neurological status, and subsequent hospital length of stay (LOS) is unknown.

Methods—Within the Get-With-The-Guidelines Resuscitation registry, we identified 175,904 patients between 2000 and 2014 with an IHCA. Time from admission to IHCA was categorized as <3, 3-7, or >7 days from admission. Multivariable hierarchical logistic regression models examined the association between timing of IHCA and survival to discharge, and, among survivors, favorable neurological survival (cerebral performance category score of 1) and LOS after IHCA.

Results—Overall, 83,811 (47.6%) of IHCAs occurred <3 days from admission, whereas 47,713 (27.1%) and 44,380 (25.5%) occurred between 3-7 and >7 days from admission, respectively. Cardiac arrests occurring later during the hospitalization were associated with lower survival ([reference: <3 days]; for 3-7 days: adjusted OR 0.93 [0.90-0.96]; for >7 days: adjusted OR 0.89 [0.86-0.92]; $P<.01$) and favorable neurological survival ([reference: <3 days]; for 3-7 days: adjusted OR 0.83 [0.77-0.89], for >7 days: adjusted OR 0.55 [0.51-0.59]; $P<.01$). Among survivors, later timing of IHCA was associated with longer subsequent LOS ([reference: <3 days]; for 3-7 days: 2.7 additional days [2.2-3.2]; for >7 days: 6.8 additional days [6.3-7.3]; $P<.001$).

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Conclusion—Most IHCA occur after 3 hospitalization days. Patients with IHCA after 3 hospital days had lower rates of survival to discharge, and, among survivors, lower rates of favorable neurological survival and longer duration of hospitalization from the time of cardiac arrest.

Introduction

In-hospital cardiac arrest (IHCA) is common in the U.S., with an estimated 200,000 cases annually.¹ Unlike other medical conditions such as stroke and myocardial infarction, in which patients present with related disease symptoms on admission, IHCA occurs after a patient's hospitalization and often as a manifestation of severe illness. To date, the timing of IHCA during a hospitalization has not been described. Moreover, the association between when IHCA occurs during a hospitalization and survival is unknown. It is possible that occurrence of IHCA during the initial days of a hospitalization reflects acute rapid-deteriorating disease and may be associated with lower survival. Alternatively, it is possible that IHCA occurring late during a hospitalization (e.g., >1 week) reflects severe chronic disease and patient frailty that may also be associated with lower survival. Additionally, among those surviving to hospital discharge, a better understanding of the timing of IHCA on the likelihood of favorable neurological survival and subsequent length of stay (LOS) would provide insights on the timing of IHCA on morbidity and resource use. Understanding these relationships may help informed discussions about patient prognosis between clinicians and families.

Accordingly, within American Heart Association's Get With The Guidelines (GWTG)-Resuscitation, a large national registry of IHCA, we examined when IHCA occurs during a hospitalization and evaluated the association between the timing of IHCA and overall survival. Moreover, among those surviving to discharge, we assessed its association with favorable neurological status and subsequent hospital LOS.

Methods

Study Database

GWTG-Resuscitation is a large, prospective, national quality-improvement registry of in-hospital cardiac arrests. It is sponsored by American Heart Association, which oversees the registry's data collection, analysis, reporting and research studies. Its design has been described in detail previously.² In brief, cardiac arrest in the registry is defined as the absence of a palpable central pulse, apnea. Consecutive patients with a cardiac arrest, without Do-Not-Resuscitate orders, and who received cardiopulmonary resuscitation (CPR) are identified and enrolled by specially trained personnel using an online, interactive case report form. Hospital participation is voluntary with data collected using standardized "Utstein-style" definitions for all patient variables and outcomes to facilitate uniform reporting across hospitals.^{3,4} Data accuracy is ensured by rigorous certification of hospital staff along with usage of standardized software with data checks. An error rate in data abstraction of 2.4% has previously been reported.²

Study Population

For this study, we identified 225,909 patients 18 years of age or older with an index in-hospital cardiac arrest between 2000 and 2014 in GWTG-Resuscitation (Figure 1). We excluded 41,125 patients with IHCA occurring in arrest locations related to procedural areas (e.g., cardiac catheterization lab, operating rooms), as these patients have distinctly different etiologies and outcomes after IHCA. We also excluded patients with missing or implausible timing of arrest (n=1715), and time from admission to arrest of greater than 30 days (n=7165). Our final cohort comprised of 175,904 patients from 693 hospitals with an IHCA.

Study Outcome and Independent Variable

The primary study outcome was survival to hospital discharge. Among those surviving to discharge, we assessed favorable neurological survival (defined as a Cerebral Performance Category score of 1) and LOS from the time of IHCA as secondary end points.

Our independent variable was the timing of IHCA during the hospitalization, which was defined *a priori* as the number of calendar days from initial admission to IHCA and categorized as <3 days (early), 3 to 7 days, and >7 days (late) from admission.

Statistical Analysis

For descriptive purposes, we compared baseline patient and cardiac arrest characteristics by timing of cardiac arrest (<3 days, 3 to 7 days, and >7 days from admission) using chi-square tests for categorical variables and the Mann-Whitney Wilcoxon nonparametric test for continuous variables.

Multivariable hierarchical regression models were used to assess the relationship between timing of cardiac arrest and survival to discharge. We employed 2-level hierarchical models to adjust for clustering of patients within hospitals, with individual hospitals modeled as random effects and other patient and hospital characteristics modeled as fixed effects within each hospital.⁵ In addition to timing of cardiac arrest, the following 18 variables from a previously validated model for risk-standardizing survival after in-hospital cardiac arrest were included for model adjustment:⁶ age (<50, 50-59, 60-69, 70-79, 80 years), sex, initial cardiac arrest rhythm (asystole, pulseless electrical activity [PEA], ventricular fibrillation, pulseless ventricular tachycardia [VT]), location of arrest (intensive care, telemetry, and non-monitored units), comorbid conditions and medical conditions present within 24 hours of cardiac arrest (prior heart failure, myocardial infarction during index admission, renal insufficiency, hepatic insufficiency, hypotension, septicemia, acute stroke, diabetes mellitus, metabolic or electrolyte abnormality, metastatic or hematologic malignancy, and major trauma), and the following interventions in place at the time of cardiac arrest (continuous intravenous vasopressor, mechanical ventilation, and hemodialysis). If timing of cardiac arrest was associated with survival to discharge, we then evaluated its association with survival separately for “non-shockable” (asystole and PEA) and “shockable” (ventricular fibrillation and pulseless VT) cardiac arrest rhythms.

Among those who survived to hospital discharge, we constructed a separate multivariable hierarchical logistic regression model to assess whether the timing of cardiac arrest was

associated with favorable neurological survival. Additionally, the association between timing of cardiac arrest and hospital LOS from the time of cardiac arrest was evaluated with multivariable hierarchical linear regression models. These models adjusted for timing of cardiac arrest, as well as the same covariates for the aforementioned model for survival to discharge. For both of these analyses among survivors, results were evaluated for the overall cohort and then separately for non-shockable and shockable cardiac arrest rhythms.

All study analyses were performed with SAS 9.2 (SAS Institute, Cary, NC) and R version 2.10.0.⁷ Hierarchical models were fitted with the use of the GLIMMIX macro in SAS and evaluated at a 2-sided significance level of 0.05. Drs. Qazi and Chan had full access to the data and take responsibility for its integrity. All authors have read and agree to the manuscript as written. The institutional review board of the Mid America Heart Institute approved the study protocol.

Results

Our study population comprised 175,904 patients with an IHCA at 693 hospitals. The mean age of the study population was 65.7 ± 15.8 years, of which 57.9% were male, and over 25% were of non-white race (Table 1). More than 4 in 5 patients had a non-shockable cardiac arrest rhythm of asystole or PEA, and approximately two-thirds of patients developed an IHCA in an intensive care unit. At least 30% of patients had diabetes mellitus, renal insufficiency, or hypotension or were receiving treatment with a continuous intravenous vasopressor infusion or mechanical ventilation at the time of cardiac arrest.

Figure 2 displays the distribution of timing of IHCA in the cohort. The mean time from admission to IHCA was 5.3 ± 6.3 days, and median time was 3 days (interquartile range [IQR]: 1 to 8 days). Overall, nearly half (83,811 [47.6%]) of IHCAs occurred <3 days from admission, whereas 47,713 (27.1%) and 44,380 (25.5%) occurred between 3-7 days and >7 days from admission, respectively.

Survival to Discharge

The overall rate of survival to discharge was 17.6%, and the rate of survival by day of IHCA is illustrated in Figure 3. Patients with an IHCA occurring <3 days from admission had a survival rate of 18.3% (15,381/83,811), as compared with 17.8% (8485/47,713) for IHCAs occurring 3 to 7 days after hospitalization and 16.1% (7142/44,380) for IHCAs occurring >7 days from admission (Table 2). After adjustment for patient and cardiac arrest factors, IHCAs occurring later during the hospitalization were associated with modestly lower survival (reference [<3 days]; for 3-7 days: adjusted OR 0.93 [95% CI: 0.90-0.96]; $P<0.001$ for >7 days: adjusted OR 0.89 [95% CI: 0.86-0.92]; $P<0.001$). However, this association pertained only to patients with a shockable IHCA (P for interaction between shockable and non-shockable rhythms of <0.001) (Table 2).

Neurological Outcome

Among 24,800 patients who survived to hospital discharge with data on discharge neurological status available, 13,791 (55.6%) had favorable neurological survival. Unadjusted rates of favorable neurological survival differed based on timing of IHCA, with

rates of 60.1%, 55.6%, and 45.7% among those with an IHCA <3 days, 3-7 days, and >7 days from admission, respectively (Table 3). After multivariable adjustment, rates of favorable neurological survival were lower among patients with an IHCA occurring later during the hospitalization (reference [<3 days]; for 3-7 days: adjusted OR 0.83 [95% CI: 0.77-0.89], for >7 days: adjusted OR 0.55 [95% CI: 0.51-0.59]; both $P<0.001$). This association was consistent among patients with shockable and non-shockable cardiac arrest rhythms (Table 4).

Length of Stay

Among those surviving to hospital discharge, the mean LOS from IHCA to hospital discharge was 16.5 ± 18.9 days, and the median time was 12 days (IQR: 6-20). Patients with an initial rhythm of asystole or PEA had mean and median LOS from time of IHCA of 18.4 ± 21.2 days and 13.0 days (IQR: 7.0-23.0), respectively. In contrast, patients with an initial rhythm of ventricular fibrillation or pulseless VT had shorter mean and median LOS from time of IHCA of 13.5 ± 14.3 days and 10.0 days (IQR: 6.0-17.0), respectively. After adjusting for patient and cardiac arrest factors, later timing of IHCA was associated with longer hospital LOS after IHCA (reference [<3 days]; for 3-7 days: 2.7 additional days [95% CI: 2.2-3.2], for >7 days: 6.8 additional days [95% CI: 6.3-7.3]; both $P<0.001$), and this relationship was similar for both shockable and non-shockable cardiac arrests (Table 5).

Discussion

In a large national registry, we described the epidemiology of the timing of IHCA from hospital admission and its association with survival to discharge, neurological outcomes and subsequent hospital LOS. We found that nearly half of patients have their IHCA within the first 3 days of hospital admission, while approximately one-quarter each have their IHCA between 3 to 7 days and after 7 days of their hospitalization. Patients with IHCAs occurring later during a hospitalization had a modestly lower odds of surviving to hospital discharge. In contrast, there was a sizable dose-response difference in rates of favorable neurological survival and subsequent LOS among patients with IHCAs occurring after 3 days from hospital admission. Collectively, our findings provide initial insights on the importance of the timing of IHCA on both survival and LOS outcomes.

Although several studies have identified predictors of survival after IHCA⁸⁻¹⁵, none has previously evaluated the association between timing of IHCA and subsequent prognosis and resource use. In routine practice, clinicians may perceive that an IHCA occurring late during a hospitalization may represent the culmination of severe illness and patient frailty and may express futility in resuscitation care. Although we found that patients with IHCA occurring late (>1 week) during a hospitalization had 11% lower relative odds of surviving to hospital discharge, this translated to only ~2% lower absolute rate of survival to discharge. These findings challenge potentially fatalistic assumptions of resuscitation futility in patients with prolonged hospitalizations.

However, we did find that neurological outcomes were worse in patients who survived to hospital discharge if their IHCA occurred after 3 days into a hospitalization. Thus, even though the difference in absolute rates of survival to discharge for IHCAs occurring later

during a hospitalization were small, an IHCA occurring later during a hospitalization was associated with worse health status—an outcome of great importance to cardiac arrest survivors. Moreover, we found marked differences in hospital LOS and, thus, resource use among those with IHCA occurring after 3 days after hospital admission. The longer hospital stay in these patients likely reflects increased frailty and deconditioning, as well as illness severity and susceptibility to hospital-acquired infections. We were not able to quantify differences in actual resource use by timing of IHCA, as we did not have access to outpatient visit data, post-discharge rehabilitation and skilled nursing care costs, or actual inpatient expenditures. Nonetheless, our study is, to date, the first study to examine the timing of IHCA on survival and neurological outcomes, as well as subsequent LOS.

Our study did have some limitations. First, we were able to adjust for multiple confounders but residual confounders may exist which may affect our study results. Secondly, GTWG-Resuscitation is a voluntary registry with representation from about 15% of large U.S hospitals. Thus, the registry may not be representative of all U.S hospitals. Third, discharge CPC data was missing in ~15% of survivors; therefore, this secondary outcome should be interpreted with some caution. Fourth, although we were able to assess subsequent LOS after IHCA, we did not have information on costs incurred after IHCA to quantify the actual difference in actual resource use by timing of IHCA. Nonetheless, LOS is likely to be a reasonable proxy of resource use.

In conclusion, we found that more than half of IHCA occur after the first 3 days of admission, and one-quarter after a week of being hospitalized. Patients with IHCA after 3 hospital days had lower rates of survival to discharge, and, among survivors, lower rates of favorable neurological survival and longer duration of hospitalization from the time of cardiac arrest.

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Figure 1.
Definition of the study cohort.

Figure 2.
Distribution of Timing of IHCA by Day of Hospitalization.

Figure 3.
Proportion of patients surviving to discharge by day of IHCA.

TABLE 1

Patient and cardiac arrest characteristics of the study cohort

	Total n = 175,904	Days from Admission to IHCA			P
		<3 Days n = 83,811	3 to 7 Days n = 47,713	>7 Days n = 44,380	
Age (years)					< 0.001
Mean $\pm$ SD	65.7 $\pm$ 15.8	65.0 $\pm$ 16.4	67.3 $\pm$ 15.2	65.5 $\pm$ 15.0	
Gender					< 0.001
Male	57.9%	56.7%	58.4%	59.6%	
Race/Ethnicity					
White	68%	69.3%	69.0%	64.3%	
Black	22.3%	20.6%	22.0%	25.9%	< 0.001
Other	9.7%	10.1%	8.9%	9.7%	
Initial rhythm					
Asystole	58,388 (33.2%)	26,424 (31.5%)	16,133 (33.8%)	15,831 (35.7%)	
PEA	83,989 (47.7%)	40,521 (48.3%)	22,435 (47.0%)	21,033 (47.4%)	< 0.001
Pulseless VT	13,943 (7.9%)	6867 (8.2%)	3840 (8.0%)	3236 (7.3%)	
VF	19,584 (11.1%)	9999 (11.9%)	5305 (11.1%)	4280 (9.6%)	
Event Location					
Intensive care unit	115,163 (65.4%)	59,094 (70.5%)	27,895 (58.5%)	28,174 (63.5%)	
Telemetry unit	33,651 (19.1%)	13,686 (16.3%)	10,075 (21.1%)	8493 (19.1%)	< 0.001
Non-monitored unit	29,525 (16.8%)	12,069 (14.4%)	9743 (20.4%)	7713 (17.4%)	
Comorbid conditions					
CHF during admission	39,182 (22.3%)	16,896 (20.2%)	11,501 (24.2%)	10,785 (24.4%)	< 0.001
MI during admission	29,764 (17.0%)	15,414 (18.4%)	7908 (16.6%)	6442 (14.6%)	< 0.001
Renal Insufficiency	65,628 (37.4%)	28,303 (33.9%)	18,029 (37.9%)	19,296 (43.6%)	< 0.001
Hepatic Insufficiency	14,764 (8.4%)	6880 (8.2%)	3833 (8.1%)	4051 (9.2%)	< 0.001
Hypotension	52,911 (30.2%)	27,474 (32.9%)	12,740 (26.8%)	12,697 (28.7%)	< 0.001
Septicemia	32,444 (18.5%)	14,364 (17.2%)	7680 (16.1%)	10,400 (23.5%)	< 0.001
Acute Stroke	6841 (3.9%)	2690 (3.2%)	1939 (4.1%)	2212 (5.0%)	< 0.001
Diabetes Mellitus	56,541 (32.2%)	24,310 (29.1%)	16,128 (33.9%)	16,103 (36.4%)	< 0.001

	Days from Admission to IHCA				P
	Total n = 175,904	<3 Days n = 83,811	3 to 7 Days n = 47,713	>7 Days n = 44,380	
Metabolic / Electrolyte Abnormality	35,052 (20.0%)	17,956 (21.5%)	8618 (18.1%)	8478 (19.2%)	< 0.001
Metastatic Malignancy	21,622 (12.3%)	9059 (10.8%)	6312 (13.3%)	6251 (14.1%)	< 0.001
Major Trauma	6509 (3.7%)	3474 (4.2%)	1465 (3.1%)	1570 (3.5%)	< 0.001
Time to CPR, minutes (inter-quartile range)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.546
Weekend or Night	94471 (53.7%)	44116 (52.6%)	26400 (55.3%)	23955 (54.0%)	< 0.001
Interventions in place at time of IHCA					
IV vasopressor	58,894 (33.5%)	31,000 (37.0%)	14,063 (29.5%)	13,831 (31.2%)	< 0.001
Mechanical Ventilation	69,603 (39.6%)	35,298 (42.1%)	16,262 (34.1%)	18,043 (40.7%)	< 0.001
Hemodialysis	6692 (3.8%)	2067 (2.5%)	1946 (4.1%)	2679 (6.0%)	< 0.001

Abbreviations: CHF, congestive heart failure; CPR, cardiopulmonary resuscitation; IHCA, in-hospital cardiac arrest; IV, intravenous; MI, myocardial infarction; SD, standard deviation; VF, ventricular fibrillation; VT, ventricular tachycardia

TABLE 2
Association between timing of IHCA and survival to discharge

Timing of IHCA	Survival to Discharge	Adjusted OR (95% CI)	P value
<i>Overall Cohort</i>			
<3 days	18.3%	(reference)	
3-7 days	17.8%	0.93 (0.90, 0.96)	<0.001
> 7 days	16.1%	0.89 (0.86, 0.92)	<0.001
<i>VF and Pulseless VT</i>			
<3 days	39.7%	(reference)	
3-7 days	36.5%	0.83 (0.79, 0.89)	<0.001
> 7 days	29.6%	0.66 (0.62, 0.70)	<0.001
<i>Asystole and PEA</i>			
<3 days	13.0%	(reference)	
3-7 days	13.3%	0.98 (.94, 1.02)	0.28
> 7 days	13.4%	1.02 (.98, 1.06)	0.37

Abbreviations: CI, confidence interval; IHCA, in-hospital cardiac arrest; OR, odds ratio; PEA, pulseless electrical activity; VF, ventricular fibrillation; VT, ventricular tachycardia

Table 3**Rates of favorable neurological survival**

Favorable neurological survival was defined as a cerebral performance category score of 1 (little to no neurological disability) among those surviving to hospital discharge.

	Total	Time from Admission to IHCA			P value
	n = 24800	<3 Days n = 12347	3-7 Days n = 6827	>7 Days n = 5626	
CPC at Discharge					< 0.001
CPC 1:	13791 (55.6%)	7423 (60.1%)	3799 (55.6%)	2569 (45.7%)	
CPC 2	6642 (26.8%)	3114 (25.2%)	1846 (27.0%)	1682 (29.9%)	
CPC 3:	3330 (13.4%)	1324 (10.7%)	931 (13.6%)	1075 (19.1%)	
CPC 4:	1026 (4.1%)	480 (3.9%)	249 (3.6%)	297 (5.3%)	
CPC 5:	11 (0.0%)	6 (0.0%)	2 (0.0%)	3 (0.1%)	

Abbreviation: IHCA, in-hospital cardiac arrest

Table 4
Association Between Timing of IHCA and Favorable Neurological Survival

Among patients who survived to hospital discharge, IHCAs occurring after 3 days from admission were associated with a lower likelihood for favorable neurological survival (defined as a cerebral performance category score of 1).

Timing of IHCA	Favorable Neurological Survival (CPC=1)	Adjusted OR (95% CI)	P value
<i>Overall Cohort</i>			
<3 days	60.1%	(reference)	<0.001
3-7 days	55.6%	0.83 (0.77, 0.89)	<0.001
> 7 days	45.7%	0.55 (0.51, 0.59)	<0.001
<i>VF and Pulseless VT</i>			
<3 days	66.3%	(reference)	
3-7 days	64.8%	0.91 (0.82, 1.01)	0.08
> 7 days	56.3%	0.60 (0.53, 0.68)	<0.001
<i>Asystole and PEA</i>			
<3 days	55.2%	(reference)	
3-7 days	49.6%	0.78 (0.72, 0.85)	<0.001
> 7 days	40.7%	0.52 (0.48, 0.57)	<0.001

Abbreviations: CI, confidence interval; IHCA, in-hospital cardiac arrest; OR, odds ratio; PEA, pulseless electrical activity; VF, ventricular fibrillation; VT, ventricular tachycardia

Table 5
Association between Timing of IHCA and Additional LOS

Among patients who survived to hospital discharge, IHCAs occurring after 3 days from admission were associated with longer LOS from the time of IHCA.

Timing of IHCA	Additional LOS After IHCA days (95% CI)	P value
<i>Overall Cohort</i>		
<3 days	(reference)	(reference)
3-7 days	2.7 (2.2, 3.2)	<0.001
> 7 days	6.8 (6.3, 7.3)	<0.001
<i>VF and Pulseless VT</i>		
<3 days	(reference)	(reference)
3-7 days	3.1 (2.4, 3.9)	<0.001
> 7 days	6.7 (5.8, 7.6)	<0.001
<i>Asystole and PEA</i>		
<3 days	(reference)	(reference)
3-7 days	2.5 (1.8, 3.1)	<0.001
> 7 days	6.8 (6.1, 7.4)	<0.001

Abbreviations: CI, confidence interval; IHCA, in-hospital cardiac arrest; PEA, pulseless electrical activity; VF, ventricular fibrillation; VT, ventricular tachycardia