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Clinical paper

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 and 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]; $P < 0.01$) 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]; $P < 0.01$). 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]; $P < 0.001$).

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

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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 st andardized "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 (Fig. 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), 3–7 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, 3–7 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 h 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.

Fig. 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]: 1–8 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 and 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 Fig. 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 3–7 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%