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Clinical paper

Long-term survival following in-hospital cardiac arrest: A matched cohort study☆

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ABSTRACT

Background: Each year, 200,000 patients undergo an in-hospital cardiac arrest (IHCA), with approximately 15–20% surviving to discharge. Little is known, however, about the long-term prognosis of these patients after discharge. Previous efforts to describe out-of-hospital survival of IHCA patients have been limited by small sample sizes and narrow patient populations

Methods: A single institution matched cohort study was undertaken to describe mortality following IHCA. Patients surviving to discharge following an IHCA between 2008 and 2010 were matched on age, sex, race and hospital admission criteria with non-IHCA hospital controls and follow-up between 9 and 45 months. Kaplan–Meier curves and Cox PH models assessed differences in survival.

Results: Of the 1262 IHCAs, 20% survived to hospital discharge. Of those discharged, survival at 1 year post-discharge was 59% for IHCA patients and 82% for controls ($p < 0.0001$). Hazard ratios (IHCA vs. controls) for mortality were greatest within the 90 days following discharge (HR = 2.90, $p < 0.0001$) and decreased linearly thereafter, with those surviving to one year post-discharge having an HR for mortality below 1.0. Survival after discharge varied amongst IHCA survivors. When grouped by discharge destination, out of hospital survival varied; in fact, IHCA patients discharged home without services demonstrated no survival difference compared to their non-IHCA controls (HR 1.10, $p = 0.72$). IHCA patients discharged to long-term hospital care or hospice, however, had a significantly higher mortality compared to matched controls (HR 3.91 and 20.3, respectively; $p < 0.0001$).

Conclusion: Among IHCA patients who survive to hospital discharge, the highest risk of death is within the first 90 days after discharge. Additionally, IHCA survivors overall have increased long-term mortality vs. controls. Survival rates were varied widely with different discharge destinations, and those discharged to home, skilled nursing facilities or to rehabilitation services had survival rates no different than controls. Thus, increased mortality was primarily driven by patients discharged to long-term care or hospice.

Introduction

Each year in the United States, an estimated 200,000 patients experience an in-hospital cardiac arrest (IHCA).[1] For these patients, prognosis is poor, with probability of surviving to discharge estimated at only 15–20%.[2] This rate reflects steady improvements with time–among the 374 hospitals participating in the "Get With The Guidelines-Resuscitation" registry, survival to discharge increased from 13.7% in 2000 to 20.7% in 2009.[3] Because in-hospital mortality is a crucial metric along which hospitals are evaluated, several studies have examined survival-to-discharge following IHCA.[1,2,3] Little is known, however, about the long-term

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prognosis of IHCA patients who survive to discharge. Previous efforts to describe out-of-hospital survival in this patient population have been limited by small sample sizes[4] and narrow patient populations.[5] Survival to discharge has been reported to range between 21.9–34% for IHCA patients in the United States,[6–8] however, very little is known about these patients' survival following hospital discharge. Here, we aim to estimate long-term survival of IHCA patients following hospital discharge, and determine whether variation in this outcome can be explained by indicators evaluable prior to hospital discharge.

Methods

Patient population, exposure criteria, and death determination

The Emory University Institution Review Board, also acting as the ethical review board, approved this research (IRB #00050806; Atlanta, GA). The Emory Office of Quality and Risk (EOQR) collects and reviews data on all IHCAs that occur at either Emory University Hospital (579 hospital beds) or Emory University Hospital Midtown (511 hospital beds), which are both tertiary care facilities located in Atlanta, Georgia. The EOQR manually enters each IHCA into an electronic databank based on a physical form that is filled out during the code. All IHCAs are captured including those that occur during diagnostic procedures, inside the operating room, or in monitored units. The EOQR provided clinical and demographic data were obtained for all patients that had an IHCA while admitted from 2008 to 2010. To construct a non-IHCA control group for matching, we collected clinical and demographic data for all patients who presented to the same two hospitals between June 1, 2007 and May 31, 2011 and did not experience an IHCA. Death status and date, if applicable, were retrieved from the United States Social Security Death Index (SSDI) for all patients on November 14, 2011.

Statistical analysis

Matching methodology

For each IHCA patient surviving to discharge, we matched up to three non-IHCA hospital controls on demographics and admission characteristics. Matching demographics included race (White, Black, Hispanic or other), gender (male, female), and age (±2 years). Hospital admission criteria for matching were admission source, level of admission urgency, and admitting specialty, including all major subspecialties (Table 1 and Table S1). IHCA patients for whom no matches could be identified were excluded from analysis. Matching was performed first, without viewing outcomes,[9] and was performed within the "Coarsened Exact Matching" package of the R statistical and programming environment.[10] Coarseness bins were set to zero to obtain an exact match for all matching criteria except age, for which the bins were set to match within 2 years while minimizing the distance between cases and controls.[11]

Statistical methodology

The primary outcome was time to death. Crude outcomes estimates for overall survival (OS) at 1 and 3 years in the IHCA and control non-IHCA patient cohorts were obtained and using Kaplan–Meier curves. Differences were assessed using the Log-rank test with confidence bands (95%) computed based on the Greenwood variance[12] and lower limits modified based on Peto,[13] to better reflect uncertainty proportional to the degree of censoring.

Cox proportional hazards regression models[14] were used to assess survival differences over time between IHCA and non-IHCA control patients. Models included IHCA status as the only predictor and the matched design was accounted for using a frailty term including a unique identifier for each matched cluster.[15] Proportional hazards assumptions were assessed for all models by regressing the scaled Schoenfeld residuals against the log-time.[16] No violations were noted. The hazard ratio (HR) and 95% confidence intervals for mortality for IHCA patients versus non-IHCA matched controls were calculated from the maximum-likelihood estimates for IHCA in the proportional hazards regression model. Sub-analyses to calculate HR's during discrete observation windows following discharge were conditional on survival until at least the first day of the observation window.

In secondary analyses, survival comparisons between IHCA patients and their controls were stratified by discharge disposition and categorized into one of four distinct strata: (1) home without health services; (2) home with health services, skilled nursing, rehabilitation, intermediate care facility or short-term hospital stay; (3) long-term hospital care and; (4) hospice care. We performed two separate sets of secondary analyses. First, we stratified data by discharge status of the IHCA patients, while retaining each of the respective matched controls–allowing for discordance in discharge disposition between IHCA patients and their controls. Thus, the hazard ratios for these analyses reflect survival of IHCA patients given a specific discharge disposition benchmarked against the "average" non-IHCA matched hospital control and HR's largely reflect early pre-discharge effects of IHCA (which dictate discharge disposition) on long-term survival.

Secondly, we stratified by discharge location but included only IHCA patients and their matched controls concordant on discharge disposition, thus effectively including discharge disposition as a post-hoc matching criteria. By removing discharge-discordant clusters, short-term effects of IHCA sufficient to alter discharge disposition are removed and the hazard ratios described for each discharge stratum best reflect only the long-term effects of IHCA. Survival differences and calculation of hazards ratios in these secondary analyses were performed using similar Kaplan–Meier curves and Cox proportional hazards frailty models as those described for the primary outcomes.

Results

Between January 1, 2008 and December 31, 2010, among 145,054 hospital admissions, 1,262 individual patients experienced an IHCA, with 253 (20.0%) surviving to hospital discharge (Fig. 1), a rate similar to previous estimates of survival-to-discharge following IHCA.[5] Of the 253 survivors, 238 (94%) were successfully matched to at least one non-IHCA hospital control with 196 (82%), 28 (12%), and 14 (6%) matched to 3, 2, and one controls, respectively. The 15 IHCA patients for whom a match could not be identified were excluded from analysis. Among the 238 survivors, 51% were male, 52% were black, and the mean age was 61 (±14.3; Table 1). There were no differences in the IHCA patients versus controls for any of the matching criteria (Table 1). IHCA patients surviving to discharge spent, on average, significantly more time in the hospital than their non-IHCA counterparts (mean 26.1 days versus 7.6 days, respectively; $p < 0.001$) with, on average, 7 days spent as in-patients in the IHCA group prior to cardiac arrest.

Overall survival at one year following discharge for IHCA patients was 59% (95% confidence interval: 53–66%), versus 82% (79–85%) for controls ($p < 0.0001$; Fig. 2a). Similarly, overall survival at three years for IHCA patients was 52% (42–60%), versus 69% (64–73%) for controls ($p < 0.0001$; Fig. 2a).

Overall mortality in IHCA patients was increased versus their matched controls, with a hazard ratio (HR) associated with IHCA of 2.35 (1.79–3.08; $p < 0.0001$; Fig. 2b). The HR of mortality in IHCA patients versus controls was greatest shortly following discharge, and this increase was confined to the first year following discharge (Fig. 2b). Over the first 90 days following discharge, the HR for mortality for the IHCA group versus controls was 2.90 (1.96–4.25;