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Warning symptoms preceding out-of-hospital cardiac arrest: Do patient delays matter?☆

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ABSTRACT

Background: Although increasing patient delays between symptom onset and activation of emergency medical services (EMS) can lead to poorer outcomes following acute myocardial infarction, its effect in out-of-hospital cardiac arrest (OHCA) populations is unclear.
Methods: Between 1st January 2003 and 31st December 2011, we included adult patients with anginal warning symptoms and subsequent EMS witnessed OHCA of presumed cardiac aetiology from the Victorian Ambulance Cardiac Arrest Registry. Multivariable logistic regression was used to assess the impact of patient delay time (i.e. symptom onset to EMS call time) on survival to hospital discharge.
Results: A total of 1056 EMS witnessed OHCA were screened, of which 515 (48.8%) reported chest pain or anginal equivalent symptoms. The median patient delay time was 25 min (interquartile range [IQR] 9–89 min), and did not differ across survivors and non-survivors. However, patients in lowest quartile of patient delay (≤8 min) also experienced significantly higher rates of non-shockable arrest rhythms and circulatory compromise. A total of 16 baseline and clinical characteristics were tested in a multivariable model of survival to hospital discharge, of which, only six were retained in the final model, including: age, dyspnoea, vomiting, shockable arrest rhythm, systolic blood pressure, and patient delay time. Every 30 min increase in patient delay time was independently associated with a 2.3% (95% CI: 0.4%, 4.1%; p = 0.02) reduction in the odds of survival to hospital discharge. Among patients with ST-segment deviation on the pre-arrest ECG, every 30 min increase in patient delay time was associated with a 3.4% reduction in the odds of survival (OR 0.966, 95% CI: 0.937, 0.996; p = 0.03).
Conclusion: Increasing delays in activating EMS before the onset OHCA may be associated with reduced survival. Future research could explore whether increasing public awareness of the warning symptoms leads to earlier medical contact for OHCA.

Introduction

Out-of-hospital cardiac arrest (OHCA) is the most common pathophysiological mechanism of death following acute myocardial infarction (AMI) [1]. Patients ignoring or inappropriately responding to prodromal symptoms present a significant challenge for the early treatment of AMI and the prevention of OHCA [2,3]. To date, much of the evidence that has been gathered about the impact of patient delays on clinical outcomes after AMI has involved populations who survive long enough to receive in-hospital treatment [4]. As a result, relatively little is known about the impact of patient delays on survival in OHCA populations [5,6].

Obtaining accurate pre-arrest information from OHCA populations is, however, inherently difficult and often limited to family or bystander accounts [6]. In comparison, emergency medical service (EMS)-witnessed OHCA offer a unique opportunity to collect pre-arrest data which are often lacking in the majority of OHCA events. Several reports involving EMS witnessed OHCA populations have shown that chest pain and anginal warning symptoms are present

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in as many as half of all patients prior to collapse [7,8]. Whether the duration of these warning symptoms hold further prognostic value is unclear.

In this study, we sought to assess the association between delays from symptom-onset to activation of emergency medical services (EMS) and survival to hospital discharge in patients with EMS witnessed OHCA.

Methods

Study design

This was a retrospective observational study of adult (aged ≥16 years) EMS witnessed OHCA of presumed cardiac aetiology between 1st January 2003 and 31st December 2011. We excluded patients who arrested on arrival at hospital and cases with a 'do not resuscitate' directive. As the symptom onset time was infrequently recorded in patients without pain symptoms, we also excluded patients if they did not report chest pain or anginal equivalent symptoms. Ethics approval for this project was granted by the Monash University Human Research Ethics Committee.

Setting

The study setting was Melbourne, Australia, which has a population of 4.1 million people distributed across 9900 square kilometres. The EMS comprises a two-tiered response involving approximately 1500 advanced life support paramedics and 300 intensive care paramedics.

Data sources

The study design, methodology, and definitions used in this report have been described in detail elsewhere [7]. OHCA data were extracted from the Victorian Ambulance Cardiac Arrest Registry (VACAR), a population-based registry of OHCA events attended by EMS in Victoria, Australia [9]. In-field patient care records are captured electronically, the data from which are synchronised wirelessly to a central clinical database. The VACAR identifies potential cardiac arrest events using a database search and manual review of patient care records. Eligible cases are entered into the registry according to international recommendations and definitions [10]. Cardiac arrest aetiology is identified from in-field patient care records, and is presumed to be of cardiac cause in the absence of a known precipitator (e.g. trauma, overdose, drowning etc.). Event survival denotes evidence of sustained return of spontaneous circulation (ROSC) on the treatment record on arrival at the emergency department. Survival to hospital discharge was defined as discharge from acute hospital care. Survival to hospital discharge is verified from hospital medical records in transported cases, and cross-validated against official government death records.

In addition to the Utstein-style descriptors captured by the VACAR, baseline and pre-arrest clinical variables including prodromal symptoms and clinical observations (e.g. systolic blood pressure, respiratory rate, heart rate, and Glasgow coma score), were manually extracted from treatment records by two investigators (ZN and JB) using a standardised electronic case report form. The accuracy of data capture was verified through a random audit of 15% of all manually extracted data. Patient delay time was defined as the time in minutes between symptom onset and call to EMS. Anginal equivalent symptoms were defined as non-traumatic arm, shoulder, neck or jaw pain, with or without chest pain.

Data analysis

The primary outcome measure was survival to hospital discharge. In the included sample, 4 (0.8%) cases had missing survival outcome and 23 (4.5%) cases had missing patient delay time. Categorisation of pre-arrest clinical observations was performed using locally weighted scatterplot smoothing (LOWESS), as described in detail elsewhere [7]. Unadjusted comparisons of baseline and clinical observations were performed for non-survivors and survivors to hospital discharge using the χ^2 test and Wilcoxon rank-sum test, as appropriate. Similarly, we compared baseline and clinical observations of patients across quartiles of patient delay time using the $\chi 2$ test and Kruskal Wallis rank test.

To assess the impact of patient delay time on survival to hospital discharge we constructed a multivariable logistic regression model consisting of patient delay time, in addition to baseline and clinical characteristics. A total of 16 candidate variables which reached significance during unadjusted comparisons ($p < 0.05$) were entered into a stepwise logistic regression model, and variables were backward eliminated at a threshold of $p > 0.10$. We assessed model discrimination performance using the area under the receiver operating characteristic curve (AUC). Effect sizes were reported as odds ratios (OR) and 95% confidence intervals (CI). The effect size for patient delay time was reported as increments of 30 min.

In a subgroup analysis, we re-analysed the parsimonious models separately in patients with and without ST-segment deviation on the pre-arrest electrocardiogram (ECG). As 9.8% (n = 50) of patients had one or more missing variables in our models, we supplemented the primary analysis with a sensitivity analysis consisting of multiple imputation to handle missing data. Twenty imputed datasets were generated, and the final model provided point estimates and confidence intervals which account for the variance within, and between, imputed datasets.

For all analyses, a two-sided significance level of less than 0.05 was considered statistically significant. Statistical analyses were undertaken using Stata Statistical Software 14 (StataCorp, 2015, College Station, TX).

Results

We identified 1379 adult EMS witnessed OHCA of presumed cardiac aetiology, of which 323 were excluded due to missing treatment records (n = 132), do not resuscitate directives (n = 129), or arrests after arrival at hospital (n = 62). The remaining 1056 cases underwent manual screening, of which 515 (48.8%) cases reported a prodromal symptom of chest pain or anginal equivalent (e.g. arm/shoulder pain).

Unadjusted comparisons

Tables 1 and 2 present the baseline and clinical characteristics of included patients, respectively, stratified by survival outcome. When compared to non-survivors, survivors were younger, more often male, and were more likely to experience shockable arrest rhythms ($p < 0.001$ for all comparisons). Non-survivors reported significantly higher rates of dyspnoea, abdominal pain, and vomiting, and more often experienced derangements in vital signs and circulatory compromise.

Patient delay time

The median patient delay time was 25 min (IQR 9–89), and was similar across non-survivors and survivors to hospital discharge (Table 1; 24 vs. 29 min, $p = 0.84$). Also, the median patient delay time did not differ across genders, pre-existing conditions, location of arrest, or arrest rhythm (data not shown). Table 3 compares