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Clinical paper

The association between diabetes status and survival following an out-of-hospital cardiac arrest: A retrospective cohort study☆

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ABSTRACT

Background: Sudden cardiac arrest (SCA), confirmed absence of cardiac mechanical activity, is the leading cause of heart-related death in the US. Almost 85% of SCA occur out-of-hospital (OHCA), with very poor rates of return of spontaneous circulation (ROSC) and survival to hospital discharge. We sought to determine if diabetes status was associated with survival or ROSC following an OHCA.
Methods: We completed a retrospective cohort study using data from the Toronto Regional RescuNet Epistry dataset, based upon data definitions defined by the Resuscitation Outcomes Consortium (ROC) Epistry-Cardiac Arrest and the Strategies for Post Arrest Resuscitation Care (SPARC) network datasets. Adults ≥18 years of age who experienced an OHCA, had data on diabetes status, and were treated by Emergency Medical Services (EMS) between 2012–2014 were included in the analysis (n = 10,097). We used bivariate analyses to examine relationships between diabetes status, Utstein elements and outcomes, and logistic regression to determine predictors of survival.
Results: Diabetes prevalence was 27.8% (95% CI: 27.0–28.7). A larger proportion of those with diabetes had a non-shockable initial rhythm (28.8% vs. 25.1%; $p < 0.01$) and did not survive to hospital discharge (92.1% vs. 89.2%, $p < 0.001$). Diabetes status is associated with a decrease in survival, independent from a number of Utstein elements (adjusted OR = 0.76; 95% CI: 0.64–0.91, $p = 0.003$).
Conclusions: This is the first Canadian study to examine the association between diabetes status and OHCA outcomes. Our findings suggest that diabetes status prior to arrest is associated with decreased survival. The growing prevalence of diabetes globally suggests a future burden related to OHCAs.

Introduction

Q2 Sudden cardiac arrest (SCA), confirmed absence of cardiac mechanical activity, is a significant public health issue and the leading cause of heart-related death in the United States (US).[1] Approximately 85% of SCA occur out-of-hospital, leading to 326,200 deaths each year in the US[1] and one death every 13 min in Canada.[2] Of those out-of-hospital cardiac arrests (OHCAs) treated by Emergency Medical Services (EMS), only 10.6% survive to hospital discharge and 8.3% have favorable neurological outcomes.[1] Several core Utstein elements have consistently predicted survival among EMS-treated arrests, including age, gender, witnessed arrest, arrest location, bystander cardiopulmonary resuscitation (CPR), first monitored rhythm, and EMS response times.[3,4] These variables have been shown to predict approximately 72% of the variation in survival[3,4] however, a portion of the variation remains unaccounted for, suggesting that there are unknown patient variables associated with survival after an OHCA. Identification of these variables would be an opportunity to reduce the public health burden of OHCA.[4] Q3

The most common preventable comorbidities associated with SCA include coronary artery disease, myocardial infarction, and heart failure.[5] Diabetes is a risk factor for all these comorbidities and has been shown to be associated with a 2–4 fold increase in the risk of SCA.[6–8] Cardiac autonomic neuropathy, a common and serious complication of type 1 (T1) and type 2 (T2) diabetes,[9–11] results from damage to autonomic fibers that innervate the heart and blood

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vessels and increases the risk of SCA.[12] Cardiac autonomic neuropathy has been linked to resting tachycardia, prolonged QT interval, increased silent myocardial ischemia and infarction, and increased mortality.[13,14] Results from the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial confirm that cardiac autonomic neuropathy is associated with a 1.55–2.95 times risk of all-cause and cardiovascular disease (CVD) mortality independent of multiple CVD risk factors.[15] Others report that men with T2 diabetes have a 2.26-fold increase in SCA risk compared to men without diabetes, even after adjusting for age, body mass index (BMI), systolic blood pressure (SBP), smoking, cholesterol, known coronary artery disease (CAD), and family history of CAD.[16]

Globally, 8.3% of individuals aged 20–79 years of age[17] and 25.9% of individuals over 65 years of age in the US have diabetes.[18] In 2015, 9.3% of Canadians had diabetes, and this is projected to increase by 44% in the next decade.[19] Diabetes is one of the largest public health emergencies of the 21st century. The World Health Organization (WHO) suggests diabetes is the third highest risk factor for premature mortality in the world[20]; it is estimated that slightly more men than women have diabetes, and one in two individuals remain undiagnosed due to misinterpretation or lack of symptoms early in the course of disease.[21] Diabetes complications are common, and while there are no internationally agreed upon standards for diagnosing or measuring diabetes complications, it is estimated that up to 50% of individuals have complications at the time of diagnosis.[22]

Diabetes and its complications are a major cause of early mortality, and existing health statistics underestimate the number of these deaths.[23] Better understanding the burden of diabetes and its complications would help direct public health actions, and improve care for all people with diabetes.[24] The primary objective of this study was to determine the association between diabetes status (T1 and T2) and survival to hospital discharge from OHCA. The secondary objectives were to determine the association between diabetes status, and any ROSC and neurological outcome, at hospital discharge.

Methods

Study design and population

We completed a retrospective cohort study using data from the Toronto Regional RescuNet Epistry dataset and definitions developed by the Resuscitation Outcomes Consortium (ROC) Epistry-Cardiac Arrest and the Strategies for Post Arrest Resuscitation Care (SPARC) network datasets.[25,26] This dataset is a population-based registry of consecutive OHCA attended by 911-initiated EMS first responders in southern Ontario, serving a population of over 6.6 million residents in Durham, Halton, Muskoka, Peel, Simcoe, Toronto and York.[27] Data are collected from pre-hospital call reports from seven land EMS agencies, fire departments, and one air ambulance service, and from in-hospital records from 44 destination hospitals and entered into a secure database. The Research Ethics Board at each participating hospital has given ethics approval for all retrospective studies using the Toronto RescuNet Epistry-Cardiac Arrest database. Adults ≥18 years of age who experienced an OHCA, had data on diabetes status, and were treated by EMS between 2012–2014 were included in the analysis (n = 10,097).

Measures

Exposure

Diabetes status was ascertained using a variable based on the in-hospital record (yes, no, not noted). If this information was missing or status was not noted, data on diabetes status was obtained from the pre-hospital call report.

Covariates

The Utstein elements are the most widely used set of variables closely associated with OHCA outcomes.[3] The following Utstein elements were obtained and used in our analysis: age (years), gender, witness status (EMS/bystander witnessed, unwitnessed), location (public, private/residential, other),[28] first response CPR (bystander, EMS, none) bystander application of automatic external defibrillator (AED), first monitored rhythm (ventricular fibrillation and ventricular tachycardia [shockable], or pulseless electrical activity and asystole [non-shockable]), EMS response time (call to 911 to arrival on scene time interval), and etiology of arrest. Etiology was defined as either obvious cause (e.g., drug overdose, asphyxiation, drowning) or presumed cardiac cause when there was no identifiable obvious cause of arrest.

Outcomes

Survival to hospital discharge (yes/no) was our primary outcome. Secondary outcomes included any ROSC during the resuscitation attempt (yes/no) and neurological outcome at hospital discharge based on the modified Rankin Scale (mRS) of 0–2 (favourable) or 3–5 (unfavourable).[29]

The amount of missing data for most variables was negligible, ranging from 0% to about 2%, with the exception of EMS response time, which had 10.2% missing data (Table 1). The missing data occurred in cases where the first EMS responders were not from RescuNET participating services. Missing data was less than 1% for this variable in all cases where RescuNET participating EMS responders arrived first.

Statistical analysis

Univariate statistics, including frequency counts, percentages and means, were used to describe the prevalence of diabetes and other characteristics of the study population. Bivariate associations between diabetes status and each of the Utstein data elements and outcomes were assessed using χ^2 tests and t-tests, as appropriate. Multivariable logistic regression was used to investigate the relationship between diabetes status and each of the outcomes (separately) while adjusting for the Utstein data elements. Preliminary steps included performing model diagnostics, such as assessing multicollinearity using the variance inflation factor (VIF) and testing for non-linearities between the predictors and outcome. There was no evidence of multicollinearity, but we did determine the need for a non-linear specification of age, which was represented using age and age^2 in the modeling. Next, we tested for plausible interactions between diabetes status and age, gender, whether arrest was witnessed and location of arrest, but none were found. To build a final model, we employed a hierarchical approach, starting with modeling diabetes status alone, then cumulatively adding clusters of variables. The Utstein elements were added in three clusters: demographics (age, gender), circumstances of arrest (witnessed, location, first-response CPR, etiology), followed by first monitored rhythm. We excluded response times from the final model due to the large amount of missing data. Nested models were compared using the likelihood ratio test (LRT). Clusters were left in the model if they significantly contributed to model fit based on the LRT. Only 4.2% of cases were missing data for one or more of the covariates and could not be included in the modeling. Data analysis was undertaken using SPSS version 23. A two sided p-value of $p < 0.05$ was used to establish statistical significance.