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Clinical paper

The time dependent association of adrenaline administration and survival from out-of-hospital cardiac arrest☆

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ABSTRACT

Background: Recommended for decades, the therapeutic value of adrenaline (epinephrine) in the resuscitation of patients with out-of-hospital cardiac arrest (OHCA) is controversial.
Purpose: To investigate the possible time-dependent outcomes associated with adrenaline administration by Emergency Medical Services personnel (EMS).
Methods: A retrospective analysis of prospectively collected data from a near statewide cardiac resuscitation database between 1 January 2005 and 30 November 2013. Multivariable logistic regression was used to analyze the effect of the time interval between EMS dispatch and the initial dose of adrenaline on survival. The primary endpoints were survival to hospital discharge and favourable neurologic outcome.
Results: Data from 3469 patients with witnessed OHCA were analyzed. Their mean age was 66.3 years and 69% were male. An initially shockable rhythm was present in 41.8% of patients. Based on a multivariable logistic regression model with initial adrenaline administration time interval (AATI) from EMS dispatch as the covariate, survival was greatest when adrenaline was administered very early but decreased rapidly with increasing (AATI); odds ratio 0.94 (95% Confidence Interval (CI) 0.92–0.97). The AATI had no significant effect on good neurological outcome (OR = 0.96, 95% CI = 0.90–1.02).
Conclusions: In patients with OHCA, survival to hospital discharge was greater in those treated early with adrenaline by EMS especially in the subset of patients with a shockable rhythm. However survival rapidly decreased with increasing adrenaline administration time intervals (AATI).

Introduction

Out-of-hospital cardiac arrest (OHCA) continues to be a major public health problem in industrialized nations, accounting for the majority of deaths in adult males.[1,2] In patients with OHCA, the importance of early recognition, prompt initiation of chest compressions, early activation and arrival of emergency medical services (EMS) personnel, and optimal post-resuscitation in-hospital care are all well documented.

Although recommended for nearly a century, over the past decade, adrenaline's (epinephrine's) value, when administered by EMS in the management of patients with OHCA, has been questioned. In animal studies, adrenaline's effectiveness in ventricular fibrillation arrest is time-dependent. We therefore hypothesized that adrenaline's impact on survival and neurological status, when given to patients with OHCA arrest, would decrease with increasing time intervals between EMS dispatch and the time at which the initial dose of adrenaline was administrated, the adrenaline administration time interval (AATI).

Methods

The purpose of this study was to assess the time-sensitive effect of adrenaline when administered by EMS to patients with

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witnessed OHCA. We evaluated survival and neurological status of such patients in Arizona who received adrenaline by EMS and whose data were entered into the Save Hearts in Arizona Registry and Education (SHARE) database.[3,4]

Population and emergency medical services

In 2010, Arizona had 6.4 million residents (http://quickfacts.census.gov/qfd/states/04000.html), with 62-licensed acute care hospitals. The Arizona Department of Health Services establishes EMS protocols, but the scope of practice, provider certification, EMS crew configuration, vehicle deployment, dispatch and response intervals, all vary somewhat across the state.[5] In 2010, there were 19,428 licensed out-of-hospital providers statewide; Basic EMT [12,901], EMT-intermediate [99] and paramedics [6488]).[5] One hundred and twenty EMS agencies, responding to approximately 80% of the state's population, participated in the state-sponsored SHARE Program.[5] This program provided the data collection and infrastructure for this study and has been previously described in detail.[3–7] The vast majority of Arizona has an all ALS response, which means that while first responders (e.g., law enforcement) may begin CPR on scene as trained responders, the medical responders performing resuscitation are paramedics. In Arizona, paramedics not only can, but also are encouraged to administer adrenaline for OHCA. A paramedic was involved in the resuscitation effort in the vast majority of the patients. While some providers utilized automated time stamp technologies in their monitor–defibrillations to record drug delivery on their monitor/defibrillators, others recorded the times manually or from memory post-event. Emergency Medical Service data was obtained from the EMS patient care reports and the outcomes were obtained either directly from the hospitals or from the State Office of Vital Records.[3,5]

Data collected from participating EMS systems and hospitals are manually entered into an Access 2007 (Microsoft, Redmond, WA) database by an experienced team of trained data coordinators who link and abstract the information.[5]

Data analysis

Data from 1 January 2005 to 30 November 2013 in the SHARE database were analyzed. There were 17,208 cases available for analysis. Following the exclusion of paediatric patients (age less than 18 years), adults with "Do Not Resuscitate" documentation, EMS-witnessed arrests, non-cardiac arrests, those not given adrenaline, and missing data for response variables, a total of 8629 adult OHCA of presumed cardiac aetiology who received adrenaline by EMS were available for detailed analysis. Of these 3469 had a witnessed OHCA and is the subset of patients herein analyzed (Fig. 1). The zero time for the adrenaline administration time interval (AATI) was taken as the time of EMS dispatch as this was the most reliable time available. Variables included patient age, sex, bystander CPR, the type of bystander CPR, the time interval from dispatch to EMS arrival at scene, time between dispatch and the initial adrenaline administration time interval (AATI), initial EMS electrocardiographic rhythm, presence and number of defibrillation shock(s), hospital survival and Cerebral Performance Category (CPC) score at hospital discharge (Tables 1 and 2).

The AATI, time interval from EMS dispatch to the time that adrenaline, was first administered, was calculated in patients in whom both time intervals were available. Survival of patients to hospital discharge are reported, using both the latest Utstein style that recommends reporting on all primary cardiac arrest and the original Utstein style that recommended reporting arrests due to shockable rhythms.[8,9] In addition we report in this analysis, the percent of survival of patients with favourable neurological outcome

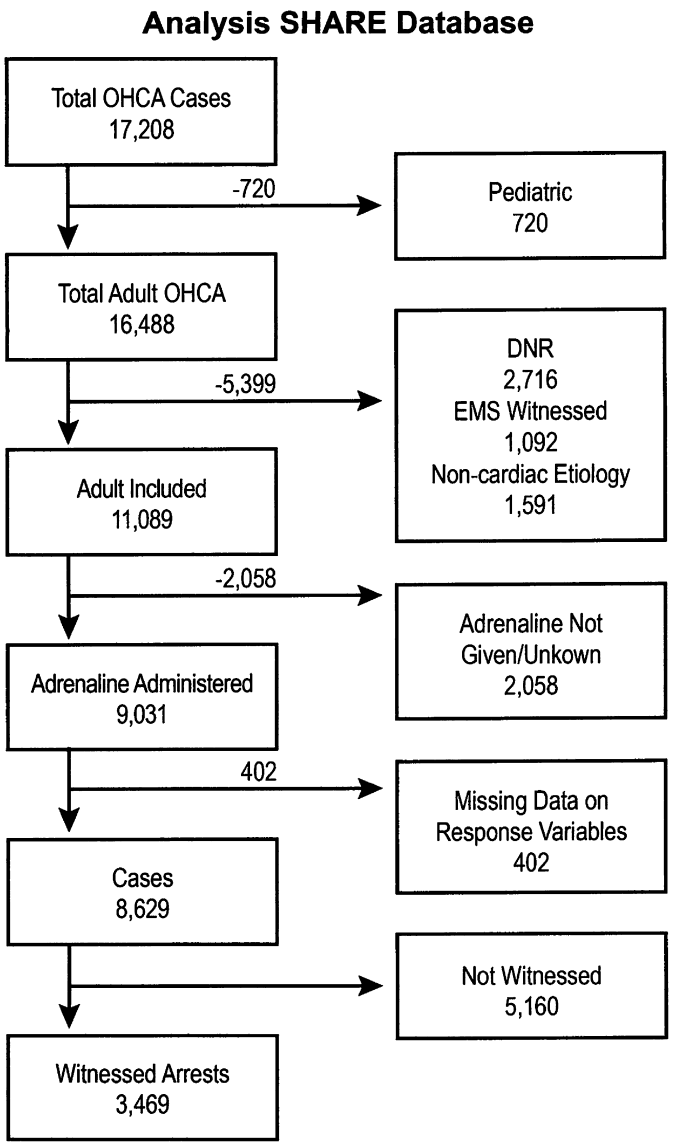

Fig. 1. A diagram of case analysis in the Save Hearts in Arizona Registry and Educational (SHARE) database of patients with out-of-hospital cardiac arrest (OHCA) used to select adult patients with witnessed cardiac arrest who received adrenaline by Emergency Medical Services personnel (EMS).

[CPC 1 or 2] at the time of discharge, using the Glasgow-Pittsburg CPC scale which has five categories: (1) *Good cerebral performance*; (2) *Moderate cerebral disability;* (3) *Severe cerebral disability*; (4) *Coma or vegetative state*; and (5) *Death*.[10]

Statistics

The primary outcomes for this study were survival to hospital discharge and survival with favourable neurological outcomes among patients with witnesed OHCA. Descriptive statistics were used to describe the study population and are reported frequency as percent (%) or as means with standard deviations (SD). Logistic regression was used to assess the association between the time of adrenaline administration and outcomes and to study the difference between the adrenaline administration time-dependent survival curves of those with an initially shockable or non-shockable rhythm. We adjusted for potential clustering effects of EMS agencies since patients treated by the same agency are