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Clinical Paper

The relationship between age and outcome in out-of-hospital cardiac arrest patients☆

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ABSTRACT

Aim: To determine the association between age and outcome in a large multicenter cohort of out-of-hospital cardiac arrest patients.
Methods: Retrospective, observational, cohort study of out-of-hospital cardiac arrest from the CARES registry between 2006 and 2013. Age was categorized into 5-year intervals and the association between age group and outcomes (return of spontaneous circulation (ROSC), survival and good neurological outcome) was assessed in univariable and multivariable analysis. We performed a subgroup analysis in patients who had return of spontaneous circulation.
Results: A total of 101,968 people were included. The median age was 66 years (quartiles: 54, 78) and 39% were female. 31,236 (30.6%) of the included patients had sustained ROSC, 9761 (9.6%) survived to hospital discharge and 8058 (7.9%) survived with a good neurological outcome. The proportion of patients with ROSC was highest in those with age <20 years (34.1%) and lowest in those with age 95–99 years (23.5%). Patients with age <20 years had the highest proportion of survival (16.7%) and good neurological outcome (14.8%) whereas those with age 95–99 years had the lowest proportion of survival (1.7%) and good neurological outcome (1.2%). In the full cohort and in the patients with ROSC there appeared to be a progressive decline in survival and good neurological outcome after the age of approximately 45–64 years. Age alone was not a good predictor of outcome.
Conclusions: Advanced age is associated with outcomes in out-of-hospital cardiac arrest. We did not identify a specific age threshold beyond which the chance of a meaningful recovery was excluded.

1. Introduction

Out-of-hospital cardiac arrest (OHCA) afflicts more than 200,000 persons in North America each year and survival after OHCA treated by emergency medical services is approximately 10%.[1] Advanced age is associated with worse outcomes in many critical illnesses.[2–5] This has also been shown to be true in cardiac arrest, in studies performed both before[6–15] and after the era of targeted temperature management.[16–20] At the same time, there is wide variability in these studies as to the effect of age on outcomes, including studies showing no association.[21–23] No study has, to our knowledge, shown an age at which resuscitation attempts can be considered futile. In patients who achieve return of spontaneous circulation (ROSC) after cardiac arrest, efforts to predict outcomes using age, presenting rhythm, or physical exam findings such as fixed and dilated pupils, have been demonstrated to be unreliable particularly in the first 72 h after ROSC.[24]

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At our tertiary care center, we prospectively collected data on all patients who were successfully resuscitated from OHCA during a three-year period and found that advanced age was not significantly associated with either mortality or poor neurological outcome.[25] In that data set, patients in their 70 s, 80 s and 90 s who suffered a cardiac arrest but then achieved ROSC were not any more likely to do better or worse than younger patients. However, this finding was based on a relatively small sample of post-cardiac arrest patients. In order to test our hypothesis that age was not associated with worse outcomes in patients successfully resuscitated from OHCA (i.e., with ROSC), we performed a query of a much larger dataset, the CARES database. CARES, the Cardiac Arrest Registry to Enhance Survival, is a collaborative effort of the Centers for Disease Control and Prevention (CDC) and the Emory University Department of Emergency Medicine, which prospectively gathers data on out-of-hospital cardiac arrests via emergency medical services (EMS) reporting.

2. Methods

2.1. Design, setting and population

This was a retrospective, observational, cohort study of OHCA. The study was approved by the Institutional Review Board at Emory University. The CARES database was established in 2004 and currently consists of over 150,000 records, from 60 communities in 29 states and 11 state-based registries including: Alaska, Delaware, Hawaii, Illinois, North Carolina, Pennsylvania, Michigan, Minnesota, Oregon, Utah and Washington. Participating sites collect data from three sources that define the continuum of emergency cardiac care: 911 dispatch centers, EMS providers, and receiving hospitals. The CARES data registry contains information on OHCA of presumed cardiac etiology. For our study we excluded patients aged 16 or younger, patients where no resuscitation was attempted in the prehospital setting and patients where resuscitation efforts were terminated based on a do-not-resuscitate designation. We also excluded patients with missing data on the exposure (age), covariates or the outcomes. We included patients with a cardiac arrest between January 2006 and December 2013.

2.2. Measures

The primary outcome was survival to hospital discharge. Secondary outcomes included sustained return of spontaneous circulation (ROSC) defined as at least 20 min with a pulse, and neurologic outcome at hospital discharge as defined by the Cerebral Performance Category (CPC) score.[26] We considered a CPC of 1 or 2 a "good neurologic outcome" consistent with previous cardiac arrest investigations.[27–29]

2.3. Statistical analysis

We provide descriptive statistics for patient and arrest characteristics; counts and frequencies for categorical variables and medians with quartiles for non-normally distributed continuous variables. To allow for non-linear associations between age and the outcomes we categorized age into 5-year intervals. The age group with the largest sample size (age: 60–64 years) was a priori chosen as the reference group for all comparative analyses. Our primary outcome was survival and we first assessed the unadjusted relationship between age group and survival. A similar approach was used to compare ROSC and good neurological outcome between age groups.

We next performed multivariable logistic regression to assess the adjusted relationship between age group and mortality. Predetermined variables that were entered in the regression model included: year of arrest, sex, race (white, black, other and unknown), location of the arrest (home, nursing home and other), whether the arrest was witnessed, bystander cardiopulmonary resuscitation (CPR), and initial rhythm (shockable and nonshockable). Similar analyses were performed with ROSC and good neurological outcome as the outcome variables. We then performed similar analyses in a predefined subgroup of patients who had ROSC. To assess the discriminative capability of age (as a continuous variable) to correctly classify survival we created receiver operating characteristics (ROC) curves for survival in all patients and in those with ROSC. We calculated the area under the ROC curve (AUC) with 95% confidence intervals.

To further assess the relationship between age and survival we determined which polynomial terms of age best described the association between age and survival. We first fitted a univariable logistic regression model only including age as a continuous variable. We then added a quadratic term of age and used the likelihood-ratio test to evaluate whether this model provided a better fit as compared to the previous model. We also provide the Akaike information criteria (AIC) for all models. This was repeated adding cubic, quartic and quantic terms each time assessing the model fit as compared to the previous model. For those models that provided a statistical significant better fit then the previous model we calculated the predicted probabilities of survival for all ages included in the cohort (17–113 years) and plotted these to graphically illustrate the estimated association. To limit the influence of outliers we performed additional analyses excluding patients from age groups (as used previously) compromising <2% of the entire cohort leaving patients with an age between 35 and 94 years (95% of the cohort).

The results of the regression models are reported as odds ratios (OR) with 95% confidence intervals (95%CI). We used SAS version 9.4 (SAS Institute, Cary, NC, USA) for all analysis and consider a two-sided p-value <0.05 to be statistical significant. No adjustments were made for multiple comparisons.

3. Results

3.1. Patient population

A total of 101,968 people were included (Fig. 1). The median age was 66 years (quartiles: 54, 78) and 39% were female. The age distribution of the overall cohort is illustrated in the Supplemental Material. The majority of patients had a cardiac arrest at home (68%) and a nonshockable initial rhythm (77%). Additional patient and cardiac arrest characteristics are presented in Table 1. 31,236 (30.6%) of the included patients had sustained ROSC, 9761 (9.6%) survived to hospital discharge and 8058 (7.9%) survived with a good neurological outcome (Fig. 1).

3.2. Age and outcome in the complete cohort

The proportion of patients with ROSC, survival and good neurological outcome according to age group is presented in Fig. 2. The proportion of patients with ROSC was highest in those with an age <20 years (34.1%) and lowest in those with an age 95–99 years (23.5%). The relationship between age and ROSC appeared to be bimodal with the highest proportion of patient achieving ROSC in those age <25 years and in those between approximately 50 and 79 years old. Patients with an age <20 years had the highest proportion of survival (16.7%) and good neurological outcome (14.8%) whereas those aged 95–99 years had the lowest proportion of survival (1.7%) and good neurological outcome (1.2%), although the group with an age >100 years was limited by a relatively small sample size. The results of the multivariable analyses are presented in