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Clinical paper

Relationship between age and outcomes of comatose cardiac arrest survivors in a setting without withdrawal of life support☆,☆☆

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ABSTRACT

Aim of the study: Previous studies on the relationship between age and outcomes after cardiac arrest were performed in settings where the majority of patients died after the withdrawal of life support (WLS). We examined the association between age and outcomes of comatose cardiac arrest survivors in a setting where WLS was not performed.
Methods: This single-centre retrospective observational study included adult comatose cardiac arrest survivors treated with targeted temperature management. In Korea, WLS is not permitted unless the patient is pronounced brain-dead. The primary outcome was poor neurologic outcome at hospital discharge, defined as Cerebral Performance Categories scores of 3–5. The secondary outcomes were in-hospital and six-month mortalities.
Results: A total of 534 patients were analysed. In multivariate analysis, age was not associated with in-hospital mortality (odds ratio [OR], 1.01; 95% confidence interval [CI], 0.99–1.02), but it was independently associated with neurologic outcome at hospital discharge (OR, 1.03; 95% CI, 1.02–1.05) and six-month mortality (OR, 1.05; 95% CI, 1.03–1.07). When age was categorised into 10-year intervals, age groups less than 61–70 years had significantly lower OR for poor neurologic outcome compared with the reference group (61–70 years), while the OR for poor neurologic outcome in age groups greater than 70 years did not differ from that in the reference group.
Conclusion: In a setting where WLS is not performed, we found that age was not associated with in-hospital mortality but was independently associated with neurologic outcome at hospital discharge and six-month mortality.

Introduction

The demographics of general populations are changing rapidly with increasing numbers of elderly individuals. Accordingly, an increasing number of elderly patients are being treated after cardiac arrest; currently, the majority of patients treated after cardiac arrest are elderly [1–4]. Elderly patients have diminished physiologic reserves and increased numbers of comorbid conditions, which may lead to worse outcomes in elderly patients compared to those of younger patients. A number of studies of patients in acute critical condition have reported old age to be associated with worse outcomes [5–8]. The attitude of the treating teams, as well as that of patient's family, toward post-resuscitation care is likely to be pessimistic in the case of elderly cardiac arrest survivors, which may result in an inappropriate limitation of evidence-based post-cardiac arrest interventions and care, including targeted tem-

Abbreviations: TTM, targeted temperature management; WLS, withdrawal of life support; ECMO, extracorporeal membrane oxygenation; OHCA, out of-hospital cardiac arrest; CPR, cardiopulmonary resuscitation; CPC, Cerebral Performance Categories; ROSC, restoration of spontaneous circulation; GCS, Glasgow Coma Scale; SOFA, sequential organ failure assessment; OR, odds ratio; HR, hazard ratio; CI, confidence interval.

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perature management (TTM). Thus, given the growing population of elderly cardiac arrest patients and the possibility that patient age itself can influence treatment decisions, an improved understanding of the independent effect of age on outcomes is increasingly important.

A number of studies of cardiac arrest patients have demonstrated an association between older age and worse outcomes after cardiac arrest [9–20]. However, information on the exact nature of the associations between age and outcomes in cardiac arrest survivors remains limited and should be reassessed. First, most studies on the relationship between age and outcomes after cardiac arrest were performed in settings in which the majority of cardiac arrest survivors died after withdrawal of life support (WLS) due to neurological injury [9–20]. Despite a thorough search, we could find only one study that was performed in a setting where WLS was not permitted, which included only a relatively small number of patients [21]. Several studies indicate that older patients are more likely to undergo WLS compared to younger patients [9,22,23]. Thus, in previous studies, the association between age and outcomes after cardiac arrest might have been affected by WLS. TTM has been shown to improve outcomes after resuscitation from cardiac arrest [24,25]. However, most of the studies did not report the proportion of patients treated with TTM or did not include in their analysis whether patients received TTM [3,11–14,16,17,20,26].

In Korea, WLS is not permitted unless the patient is pronounced brain-dead. Moreover, according to our institutional protocol, TTM is considered for all adult comatose non-traumatic cardiac arrest survivors irrespective of age. Thus, using data from comatose cardiac arrest survivors treated with TTM at our hospital, we sought to examine the association between age and outcomes of comatose cardiac arrest survivors in a setting where WLS is not performed. We hypothesised that older age would be associated not only with higher mortality but also with worse neurologic outcome.

Methods

Study design, population, and setting

This retrospective observational cohort study included adult comatose cardiac arrest survivors treated with TTM at Chonnam National University Hospital, a university-affiliated, 1005-bed hospital in Gwangju, Korea, from January 2008 to December 2015. The Institutional Review Board of Chonnam National University Hospital approved this study (CNUH-2016-104).

Both out-of-hospital and in-hospital cardiac arrest patients who were over 18 years of age and who underwent TTM were included. Patients were excluded if: (1) TTM was interrupted due to transfer to another facility, (2) they were treated with a different TTM protocol regarding target temperature (<32 °C) or duration (72 h), or (3) extracorporeal membrane oxygenation (ECMO) was applied during the post-cardiac arrest care. In Korea, all out-of-hospital cardiac arrest (OHCA) patients for which emergency medical systems are called receive cardiopulmonary resuscitation (CPR) at least until they are transferred to an emergency department unless there are signs of irreversible death. Thus, the decision to perform prehospital resuscitation is made irrespective of patient age. Our institution provides post-cardiac arrest care based on current resuscitation guidelines [27]. According to our protocol, TTM is considered for all adult non-traumatic cardiac arrest survivors who are unable to obey commands, irrespective of age. Patients were not eligible for TTM if they had intracranial haemorrhage, active bleeding, known malignancy in the end stages, or a poor pre-arrest neurologic status (Cerebral Performance Category [CPC] 3 or 4). All patients included in the analysis were treated with TTM with a target core body temperature of 32–34 °C maintained for 24 h following restoration of spontaneous circulation (ROSC).

Data collection

The following data were obtained from the electronic medical records: age, sex, comorbidities, first monitored rhythm, aetiology of cardiac arrest, location of cardiac arrest (out-of-hospital versus in-hospital), presence of a witness on collapse, bystander CPR, time to ROSC (defined as the time interval from recognition of cardiac arrest to ROSC), Glasgow Coma Scale (GCS) score on admission, levels of serum lactate and glucose immediately after ROSC, sequential organ failure assessment (SOFA) score within the first 24 h, time from ROSC to initiation of TTM (pre-induction time), time from initiation of TTM to achieving target temperature (induction duration), duration of rewarming, highest cumulative vasopressor index within 7 days after cardiac arrest [28], coronary angiography, implantable cardioverter defibrillator, vital status at hospital discharge (alive or dead), and neurologic outcome at hospital discharge. Comorbidities included coronary artery disease (angina pectoris, myocardial infarction), heart failure, hypertension, cerebrovascular accident (haemorrhagic stroke, ischaemic stroke), pulmonary disease (chronic obstructive pulmonary disease, restrictive lung disease, bronchiectasis, bronchial asthma), renal disease (chronic kidney disease), hepatic disease (liver cirrhosis), and diabetes. We categorised age into 10-year intervals. The primary outcome was poor neurologic outcome at hospital discharge, defined as CPC scores of 3–5 [29]. Secondary outcomes were in-hospital and six-month mortalities. Information on survival at 6 months after cardiac arrest was obtained using the National Health Insurance Service database, in which information regarding deaths was derived from Statistics Korea. By law, all deaths of South Koreans should be reported to Statistics Korea.

Statistical analysis

Categorical variables were presented as frequencies and percentages. Comparisons of categorical variables were performed using χ^2 or Fisher exact tests, as appropriate. Continuous variables were presented as median values with interquartile ranges because all continuous variables showed non-normal distributions. Mann–Whitney *U* tests were conducted for comparisons of continuous variables. Kruskal–Wallis tests were performed for comparisons of continuous variables among age groups. Multivariate logistic regression analysis was used to examine the association between age and outcomes after adjusting for potential confounders as determined by the univariate analyses. All variables with $p < 0.2$ in univariate analyses were included in the multivariate regression model. Backward selection was used to obtain the final model. Age was included in the model as a categorical variable, using the age group with the largest sample size (61–70 years) as the reference group. We also included age in the model as a continuous variable to obtain the adjusted odds ratios (OR) per year. Multivariate Cox proportional hazards regression analysis adjusted for potential confounders was used to estimate hazard ratios (HR) for six-month mortality. No adjustments were made for multiple comparisons. Data were analysed using PASW Statistics for Windows, version 18.0 (SPSS, Inc., Chicago, IL, USA). A two-sided significance level of 0.05 was used for statistical significance.

Results

Among 1093 adult cardiac arrest patients who achieved ROSC during the study period, 636 patients were treated with TTM (Fig. 1). Of these, seven were excluded because TTM was interrupted owing to transfer to another facility, 49 were excluded