



Clinical paper

Long-term neurological outcomes in patients after out-of-hospital cardiac arrest[☆]



Youn-Jung Kim, Shin Ahn, Chang Hwan Sohn, Dong-Woo Seo, Yoon-Seon Lee, Jae Ho Lee, Bum Jin Oh, Kyoung Soo Lim, Won Young Kim*

Department of Emergency Medicine, University of Ulsan College of Medicine, Asan Medical Center, Seoul, South Korea

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ABSTRACT

Aim: The main treatment goal in survivors of out-of-hospital cardiac arrest (OHCA) is a favorable neurologic outcome. Little is known, however, about long-term trends of neurologic status in OHCA survivors. This study was designed to assess the rates of long-term neurologic recovery and survival according to neurologic status at one month.

Methods: This retrospective observational study assessed all adult OHCA survivors (≥ 18 years) admitted to a tertiary hospital in an urban area who achieved return of spontaneous circulation (ROSC) between July 2005 and August 2013. Neurologic outcomes were measured by Cerebral Performance Category (CPC) score and patients were categorized according to CPC score at 1 month. Their neurologic status was re-evaluated 6, 12, and 24 months after cardiac arrest.

Results: Of 778 OHCA cases, 282 patients (36.2%) were admitted to our hospital, and 279 were included in this study. At one month, 84 (30.1%) survivors were assessed with the CPC with 42.8% ($n = 36$) having good neurologic outcome and 57.1% ($n = 48$) poor neurologic outcome. Only two patients with poor neurologic outcome (4.1%) showed improved neurologic status from CPC 3 to CPC 2, during the first 6 months and none showed neurologic improvement after 6 months. The estimated 3-year survival was much higher for CPC 1 (96.4%) than for CPC 4 (24.2%) survivors.

Conclusions: Neurologic recovery of OHCA survivors with poor neurologic outcomes at one month was rare and did not occur more than 6 months after cardiac arrest.

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Introduction

Out-of-hospital cardiac arrest (OHCA) remains a major public health burden, with a global average incidence among adults of 55 OHCA per 100,000 person-years and an average survival rate of 7%.¹ One important goal of treatment is to enhance the survival to discharge rate after OHCA.^{2,3} A second critical goal in OHCA survivors is to enhance neurologic outcomes after OHCA.^{2,3} Despite medical advances and post-resuscitation care in cardiac arrest (CA) survivors, hypoxic brain damage remains a major cause of mortality and poor neurologic outcomes.^{4–6}

Cerebral Performance Category (CPC) is a five category scale widely used to measure functional neurologic status in CA survivors.^{7,8} CPC measured at hospital discharge in resuscitated CA

patients has been associated with long-term survival outcomes.^{9–11} Less is known, however, about long-term changes in neurologic status over time in OHCA survivors. In South Korea, it is legally prohibited to withdraw life-supporting treatment from resuscitated patients; ultimately, resuscitated patients with poor neurologic outcomes are hospitalized to receive conservative care until they die. The costs and medical resource use required to care for these patients with poor neurologic outcomes have made it important to understand long-term changes in neurologic status of OHCA survivors.¹² This study therefore assessed the trends over time in neurologic status and long-term survival rate of OHCA survivors based on their CPC scores at 1 month. We hypothesized that the neurological improvement would rarely occur in OHCA survivors with bad CPC despite prolonged life-supporting treatment.

Material and methods

Study design and population

This retrospective cohort study included all persons aged ≥ 18 years who experienced non-traumatic OHCA and were resuscitated

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* Corresponding author at: Department of Emergency Medicine, University of Ulsan College of Medicine, Asan Medical Center, 88, Olympic-ro 43-gil, Songpa-gu, Seoul 05505, South Korea.

E-mail address: wonpia73@naver.com (W.Y. Kim).

successfully in the emergency department (ED) of a university-affiliated teaching hospital in Seoul, Korea, with approximately 100,000 visits per year, between July 1, 2005 and August 31, 2013. In South Korea, emergency medical service (EMS) providers are encouraged to pick up patients and bring them immediately to the ED while administering cardiopulmonary resuscitation (CPR) during ambulance transport. EMS providers are not permitted to declare death in the field after one cycle of CPR, except if patients show obvious signs incompatible with life. Patients in this study who experienced OHCA were administered CPR and post-resuscitation care, including coronary intervention and targeted temperature management (TTM), in accordance with the then current Advanced Cardiac Life Support guidelines of 2005 or 2010.^{2,13} Beginning in 2009, TTM for CA survivors consisted of the use of a cooling device with self-adhesive, hydrogel-coated pads (Artic Sun; Medivance, Louisville, KY, USA).

Patients were excluded from this study if they had a do-not-resuscitate order, they expired in the ED before admission to the intensive care unit, or they were lost to follow-up.

CPC scores at 1, 6, 12, and 24 months were determined by reviewing the electronic medical records of these patients and by follow-up telephone interviews with the patient or a family member as a primary caregiver. One board-certified, clinically active emergency physician who was blinded of our hypothesis during data collection determined the CPC scores. All eligible patients were followed up until August 31, 2015. This study was approved by the Institutional Review Board of Asan Medical Center, which waived the requirement for informed consent due to the retrospective nature of this study.

Data

Detailed CPR data were obtained from the prospective CPR registry of our hospital ([Online resource 1](#)). For each patient, an emergency room physician handwrote a CPR report using the Utstein style,⁷ and the data were verified and entered into the web-based registry by the principal investigator. Data recorded from the registry included demographic characteristics, cause of CA, initial rhythm at the scene, bystander administration of CPR, post-neurologic outcomes (CPC results), and survival duration. The date of patient's death was obtained from the National Health Insurance Service in South Korea. Neurologic status was classified according to the CPC,^{7,14,15} a scale that included five categories. CPC 1 was defined as conscious and alert with good cerebral performance; CPC 2 as conscious and alert with moderate cerebral performance; CPC 3 as conscious with severe cerebral disability; CPC 4 as comatose or in a persistent vegetative state; and CPC 5 as brain dead or dead by traditional criteria. The patients were divided into two groups based on their CPC scores at one month: a good neurologic outcome group (CPC 1 and 2) and a poor neurologic outcome group (CPC 3–5).^{14,15} Survival time was calculated as time from date of resuscitation to date of death or August 31, 2015.

Statistical analysis

Continuous variables are expressed as mean \pm standard deviation (SD) when normally distributed and median with interquartile range (IQR) when non-normally distributed. Categorical data are presented as absolute numbers and percent. Differences between means were analyzed by one-way analysis of variance (ANOVA) or the Kruskal–Wallis test. Differences between categorical variables were analyzed by the Chi-square test or Fisher's exact test, as appropriate. Survival in the four CPC categories was assessed by nonparametric Kaplan–Meier survival analysis and compared by log-rank tests. Two-tailed *P*-values less than 0.05 were considered

statistically significant. All statistical analyses were performed with SPSS version 18.0 (IBM, Armonk, NY).

Results

Between July 1, 2005, and August 31, 2013, 778 adult, non-traumatic CA patients arrived in our ED, of who 282 (36.2%) survived to hospital admission. Of these patients, three were lost to follow-up and excluded; thus the study finally included 279 patients, of median age 62 years ([Fig. 1](#)). The demographic and clinical findings of our study patients are summarized in [Table 1](#). Despite more than half of CAs being witnessed by others, only 100 (35.8%) received bystander CPR and only 41 (14.7%) had an initial shockable rhythm. Of 279 patients who survived to hospital admission, 45 patients received TTM. The initial rhythm at the scene and the etiology of arrest differed significantly among the groups of patients with good neurologic outcomes, poor neurologic outcomes, and non-survivors at 1 month ($p < 0.001$). Shockable rhythm at the scene was documented in 47.2% of patients with good neurologic outcome, and only in 22.9% of patients with bad neurologic outcome and 6.7% of non-survivors ($p < 0.001$). Presumed cardiogenic arrest was the most common etiology of arrest in patients with good neurologic outcome (83.3%) and those with bad neurologic outcome (54.2%), while in non-survivors, respiratory arrest (29.7%) and other medical causes (31.8%) were the major etiologies ($p < 0.001$).

Between enrollment and the 1 month follow-up, 195 patients (69.9%) died; of the 84 surviving patients, 28 (33.3%) were classified as CPC 1, eight (9.5%) as CPC 2, 15 (17.9%) as CPC 3, and 33 (39.3%) as CPC 4 at 1 month ([Fig. 1](#)). Of these 84 patients, 19 (22.6%), including three with CPC 3 and 16 with CPC 4 died before the 6-month follow-up visit, and of the 65 survivors, 62.5% ($n = 5$) in CPC 2, 16.7% ($n = 2$) in CPC 3 and no patients (0%) in the CPC 4 showed improved outcome. After 6 months there were no more improvements of outcome.

There were 43 deaths during 4090 person-months of follow-up. The median follow-up for the study patients was 42.5 months (interquartile range, 9.3–85.3 months). The estimated 3-year survival rate was significantly higher in patients with CPC 1 than CPC 4 (96.4% vs. 24.2%, $p < 0.001$, log-rank test) ([Fig. 2](#)).

Discussion

This retrospective cohort study using prospective registry data investigated the long-term trends over time in neurologic status among OHCA survivors according to their CPC scores at 1 month. Several patients classified as CPC 2 at 1 month showed improvements at 6 months, whereas only two (4.1%) of 48 survivors with poor neurologic status at 1 month (CPC 3) showed improvements in neurologic status, to CPC 2, within the first 6 months. Moreover, after 6 months, none of the study patients showed neurologic improvement or worsening, except for death. The two patients with improved neurologic outcomes included a woman aged 49 years and a man aged 58 years. Both presented with ventricular fibrillation as an initial rhythm and had no comorbid disease, and each received less than 4 min of prehospital CPR. In the ED, the female patient received 11 min of CPR and the male patient received 43 min of CPR before ROSC. Within 24 months, 79.2% (34/48) of the survivors with poor neurologic outcomes at 1 month had died, compared with none of the survivors with good neurologic outcomes at 1 month.

Many previous studies have analyzed functional and neurologic status in CA survivors after hospital discharge.^{5,6,16–19} Despite the differences in methodology, most studies have suggested that survivors with good neurologic outcome at hospital discharge have a high long-term survival rate with an acceptable quality of

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