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Predictors of favorable and poor prognosis in unwitnessed out-of-hospital cardiac arrest with a non-shockable initial rhythm

Tatsuma Fukuda *, Takehiro Matsubara, Kent Doi, Naoko Fukuda-Ohashi, Naoki Yahagi

Department of Emergency and Critical Care Medicine, Graduate School of Medicine, The University of Tokyo, 7-3-1, Hongo, Bunkyo-ku, Tokyo, 113-8655, Japan

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ABSTRACT

Background: Unwitnessed OHCA patients with non-shockable initial rhythms account for nearly half of all OHCA patients, and their prognosis is extremely poor. To date, no studies have focused on these patients. This study aimed to investigating the predictors of favorable and poor prognosis in these patients.
Methods: We conducted a nationwide, population-based, observational study of data from the All Japan Utstein Registry, which included 121,081 adult OHCA patients subjected to resuscitation attempts from January 1, 2010 to December 31, 2010. The primary endpoint was favorable neurological outcome one month after OHCA.
Results: Of the eligible 120,721 patients, 68,024 (56.3%) were unwitnessed OHCA patients with non-shockable initial rhythms. A younger age (18–64 years: as a reference; 65–84 years: OR 0.68, 95% CI 0.54–0.87, $p = 0.0019$; ≥85 years: OR 0.46, 95% CI 0.33–0.63, $p < 0.0001$), conversion to shockable rhythm (OR 2.14, 95% CI 1.43–3.13, $p = 0.0003$), and pre-hospital ROSC (OR 94.85, 95% CI 75.71–119.35, $p < 0.0001$) were independently associated with a favorable neurological outcome. Favorable neurological outcome rate was 28.8% in unwitnessed OHCA patients with non-shockable initial rhythms with all three favorable predictors, and 0.18% in patients without any of the three predictors (OR 230.34, 95% CI 127.37–402.96, $P < 0.0001$).
Conclusions: It may be worthwhile to provide maximum lifesaving medical resources for patients with all of the favorable predictors (<65 years, conversion to shockable rhythm, and pre-hospital ROSC); however, continued resuscitation efforts for patients without these predictors should likely be restrained.

1. Introduction

Out-of-hospital cardiac arrest (OHCA), a condition with one of the poorest prognoses, is experienced by 125,000, 275,000, and 375,000 individuals annually in Japan, Europe, and the USA, respectively [1–4]. Although the rate of survival after OHCA has increased along with advances in care throughout the "chain of survival," it remains low [5,6].

The prognosis is especially poor in cases of unwitnessed OHCA with non-shockable initial rhythms [2,7,8]. In fact, a lack of witnesses and a non-shockable rhythm are the main criteria in the pre-hospital termination of resuscitation (TOR) rule [9–14]. Unwitnessed OHCA patients with non-shockable initial rhythms account for nearly half of all OHCA patients, and their prognosis is extremely poor [1,2,7,8]; therefore, these patients are considered suitable candidates for TOR. On the other hand, it is extremely important to identify the factors that contribute to a favorable prognosis in such cases because there are a limited number of patients who will be discharged with a favorable outcome in these many cases. To date, no studies have focused on a large sample of unwitnessed OHCA patients with non-shockable initial rhythms.

This study aimed to investigating the predictors of both favorable and poor prognosis in unwitnessed OHCA patients with non-shockable initial rhythms.

2. Methods

2.1. Study design and participants

We conducted a population-based cohort study of data from the All-Japan Utstein Registry of the Fire and Disaster Management Agency (FDMA), a prospective, nationwide, population-based registry system of all OHCA patients maintained via Utstein-style data collection [15].

All adults aged ≥18 years who suffered from OHCA and for whom resuscitation was attempted by emergency medical service (EMS) personnel with subsequent transport to emergency hospitals from January 1 to December 31, 2010 were enrolled in this study. Patients whose data and information regarding the onset time, call receipt time, hospital arrival time, airway management status, or the public access automated external defibrillator (AED) usage status were missing or unknown were excluded from the analysis.

Abbreviations: OHCA, out-of-hospital cardiac arrest; TOR, termination of resuscitation; FDMA, Fire and Disaster Management Agency; EMS, emergency medical service; AED, automated external defibrillator; CPR, cardiopulmonary resuscitation; AHA, American Heart Association; ILCOR, International Liaison Committee on Resuscitation; ROSC, return of spontaneous circulation; CPC, Glasgow–Pittsburgh cerebral performance category; ANOVA, analysis of variance; OR, odds ratio; CI, confidence interval; SD, standard deviation; ADL, activity of daily living.

* Corresponding author. Tel.: +81 3 3815 5411; fax: +81 3 3814 6446.
E-mail address: tatsumafukuda-jpn@umin.ac.jp (T. Fukuda).

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This study was conducted in accordance with the amended Declaration of Helsinki. The FDMA and the Institutional Review Board of The University of Tokyo approved this study with a waiver of informed consent because of the anonymous nature of the data.

2.2. Study setting

Japan comprises an area of approximately 378,000 km^2 with 47 prefectures, and the population of Japan in 2010 was approximately 128 million, with approximately 107 million people aged ≥18 years [16].

The EMS system in Japan has been described previously [2,17–19]. In 2010, EMSs were provided by municipal governments via 802 fire stations with dispatch centers [20]. An ambulance team usually comprises three EMS personnel, including at least one professionally trained emergency lifesaving technician. Some emergency lifesaving technicians are authorized to secure infusion lines, administer epinephrine, perform endotracheal intubation and defibrillation, and lead cardiopulmonary resuscitation (CPR). CPR is performed in conformity with the Japanese CPR guidelines, which are based on the guidelines stipulated by the American Heart Association (AHA) and the International Liaison Committee on Resuscitation (ILCOR) [21–23]. EMS personnel are not allowed to terminate resuscitation out of hospital except in specific situations such as decapitation, rigor mortis, livor mortis, or decomposition; advance directives, living wills, or do-not-attempt-resuscitation orders are not generally accepted in Japan [21,24]. Therefore, nearly all OHCA patients treated by EMS personnel are transported to an emergency hospital [25].

2.3. Data collection and quality control

The data were collected prospectively using Utstein-style templates and included information regarding the sex, age, bystander witness status, bystander CPR status, etiology of arrest, initial cardiac rhythm, public-access AED usage, defibrillation by EMS, presence of an emergency lifesaving technician or physician in the ambulance, administration of epinephrine, and type of airway management. The definitions of terms related to OHCA care such as cardiac arrest, bystander CPR, or etiology of arrest conformed to those in the ILCOR statement [15].

A series of EMS times, including the call receipt, vehicle arrival at the scene, contact with the patient, initiation of CPR, departure from the scene, and hospital arrival, were also recorded according to the clock used by each EMS system.

The outcome data included the return of spontaneous circulation (ROSC) prior to hospital arrival, 1-month survival, and neurological status at one month after OHCA. The 1-month follow-up data were collected by the EMS personnel in charge of each patient with OHCA. The EMS queried the medical control director at the hospital and received a written response, including reconfirmation of the etiology of the arrest. If the patient was not at the hospital, the EMS personnel conducted a follow-up investigation.

The data forms were completed by the EMS personnel in charge of the patients, and the data were integrated into the Utstein registry system on the FDMA database server. FDMA logically evaluated the data using the computer system and returned the data forms to the respective fire stations for reconfirmation unless the data were complete.

2.4. Study endpoints

The primary endpoint was a favorable neurological outcome at 1 month after OHCA, defined a priori as a Glasgow–Pittsburgh cerebral performance score category (CPC) of 1 or 2 (good performance or moderate disability, respectively). A CPC of 3, 4, or 5 (severe disability, vegetative state, or death, respectively) was regarded as an unfavorable neurological outcome [15]. The secondary endpoint was the 1-month survival.

2.5. Statistical analysis

The total sample size in this nationwide, population-based study was determined according to the number of patients registered in the All-Japan Utstein Registry database in 2010.

Continuous and categorical variables were assessed using an analysis of variance (ANOVA) and χ^2 test, respectively. A multivariate logistic regression analysis was performed to examine the contribution of each predictor to one-month survival and a favorable neurological outcome. Odds ratios (OR) and their 95% confidence intervals (CI) were calculated after adjusting for potential confounding factors such as sex, age (18–64, 65–84, ≥85 years), bystander CPR status, etiology of arrest, conversion to shockable rhythm, epinephrine administration, advanced airway management, time from call to hospital arrival (<15, 15–29, ≥30 min), and pre-hospital ROSC. Despite having a non-shockable initial rhythm, patients for whom more than one defibrillation was performed prior to arrival at the hospital were regarded as patients with conversion to shockable rhythm.

We divided the patients into the following four groups based on the multivariate logistic regression analysis results: (Group A) patients who were <65 years of age, converted to shockable rhythm, and had pre-hospital ROSC; (Group B) patients who did not qualify for Group A but had pre-hospital ROSC; (Group C) patients who were below the age of 65 or converted to shockable rhythm but did not qualify for Group A or B; and (Group D) patients who did not qualify for Group A, B, or C.

We compared the outcomes between the four groups. The ORs and 95% CIs for favorable outcomes were calculated for each group versus group D, which served as the reference group.

All statistical analyses were performed using JMP Pro 10.0.2 software (SAS institute Inc., Cary, NC, USA). All tests were two-tailed, and P values of < 0.05 were considered statistically significant.

3. Results

A total of 123,095 OHCA patients were documented during the study period. Of the 121,081 adult OHCA patients subjected to resuscitation attempts, the following were excluded: 6 with an unknown time of onset, call receipt, or hospital arrival; 317 with an unknown airway management status; and 37 with an unknown public access AED usage status (Fig. 1). Of the remaining 120,721 patients, 68,024 (56.3%; 95% CI, 56.1–56.6%) were unwitnessed OHCA patients with non-shockable initial rhythms, 44,218 (36.6%; 95% CI, 36.4–36.9%) were witnessed OHCA patients with non-shockable initial rhythms, 2266 (1.9%; 95% CI, 1.8–2.0%) were unwitnessed OHCA with shockable initial rhythms, and 6213 (5.1%; 95% CI, 5.0–5.3%) were witnessed OHCA patients with shockable initial rhythms.

Table 1 lists the baseline demographic characteristics and outcomes for the adult OHCA patients in each group according to the witness status and initial cardiac rhythm. The overall mean age was 74.1 years, and the proportion of male patients was 57.5%. Compared to the patients with shockable initial rhythms, patients with non-shockable initial rhythms were older, and the proportions of male and cardiac etiology were lower. Regarding pre-hospital care, there was a tendency to administer epinephrine primarily to patients with shockable initial rhythms, whereas advanced airway management was implemented primarily in unwitnessed patients. The prognoses were more favorable for patients with shockable initial rhythms and for witnessed patients, and the 1-month survival and favorable neurological outcome rates were approximately 15-fold and 35-fold higher, respectively, in patients with witnessed OHCA and shockable initial rhythms relative to those with unwitnessed OHCA and non-shockable initial rhythms.

Table 2 lists the results of a multivariate logistic regression analysis for favorable outcomes in unwitnessed OHCA with a non-shockable initial rhythm. A younger age, conversion to shockable rhythm, and pre-hospital ROSC were independently associated with an improved outcome. In contrast, pre-hospital epinephrine administration and advanced airway management implementation were associated with a poor outcome. Cardiac etiology was associated with a poor 1-month survival and, conversely, a favorable neurological outcome.

Table 3 lists the outcomes in each of the four groups according to the factors of age, conversion to shockable rhythm, and pre-hospital ROSC. Pre-hospital ROSC achievement (Groups A and B) correlated closely with a favorable prognosis. Even without pre-hospital ROSC, the prognosis was significantly favorable if patients were either <65 years of age or converted to a shockable rhythm (Group C) when compared with patients aged >65 years who did not convert to a shockable rhythm (Group D). In patients who were <65 years of age, converted to a shockable rhythm, and achieved pre-hospital ROSC (Group A), the 1-month survival rate was 40.9% and the favorable neurological outcome rate was 28.8%; compared with patients lacking all of these predictors (Group D), the OR for 1-month survival was 75.70 (95% CI, 45.41–124.16; $P < 0.0001$) and the OR for a favorable neurological outcome was 230.34 (95% CI, 127.37–402.96; $P < 0.0001$).

4. Discussion

In this large, nationwide, population-based cohort study of patients with OHCA, we identified the factors that affected both favorable and poor prognoses in unwitnessed OHCA patients with non-shockable initial rhythms.

The prognosis of patients with all favorable predictors (Group A), specifically an age <65 years, conversion to a shockable rhythm, and achievement of pre-hospital ROSC, was extremely favorable, whereas