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Two-year survival and neurological outcome of in-hospital cardiac arrest patients rescued by extracorporeal cardiopulmonary resuscitation ☆

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ABSTRACT

Background: The clinical benefit of extracorporeal cardiopulmonary resuscitation (E-CPR) has been proved in short-term follow-up studies. However, the benefit of E-CPR beyond 1 year has been not known. We investigated 2-year outcome of patients who received E-CPR or conventional CPR (C-CPR).
Methods: We analyzed a total of 406 adult in-hospital cardiac arrest victims who underwent CPR for more than 10 min from 2003 to 2009. The two-year survival and neurological outcome of E-CPR ($n = 85$) and C-CPR ($n = 321$) were compared using propensity score-matched analysis.
Results: The 2-year survival with minimal neurological impairment was 4-fold higher in the E-CPR group than the C-CPR group (23.5% versus 5.9%, hazard ratio (HR) = 0.57, 95% confidence interval (CI) = 0.43–0.75, $p < 0.001$) by unadjusted analysis. After propensity-score matching, it was still 4-fold higher in the E-CPR group than the C-CPR group (20.0% versus 5.0%, HR = 0.53, 95% CI = 0.36–0.80, $p = 0.002$). In the E-CPR group, the independent predictors associated with minimal neurological impairment were age ≤65 years (HR = 0.46; 95% CI = 0.26–0.81; $p = 0.008$), CPR duration ≤35 min (HR = 0.37; 95% CI = 0.18–0.76; $p = 0.007$), and subsequent cardiovascular intervention including coronary intervention or cardiac surgery (HR = 0.36; 95% CI = 0.18–0.68; $p = 0.002$).
Conclusions: The initial survival benefit of E-CPR for cardiac arrest patients persisted at 2 years.

1. Introduction

Extracorporeal cardiopulmonary resuscitation (E-CPR) is a cardiopulmonary resuscitation (CPR) supported with a portable cardiopulmonary bypass system that enables circulation of oxygenated blood in the absence of adequate cardiac pumping. E-CPR has been increasingly used to treat patients with in-hospital arrest whose overall survival rate has still remained unsatisfactory [1,2].

Several observational studies have shown the feasibility of E-CPR [3–8] and improved short [9] to mid-term survival [10,11] in patients treated with E-CPR compared to conventional CPR (C-CPR). However, little is known whether the initial survival benefit of E-CPR over C-CPR could be maintained more than 1 year. Hence we investigated the 2-year clinical outcome of E-CPR and C-CPR. The results of E-CPR and C-CPR were compared further using propensity score-matched analysis. We also evaluated clinical characteristics associated with two-year survival.

2. Methods

2.1. Patients

We enrolled 1108 in-hospital cardiac arrest patients aged >20 years who had undergone CPR between January 2003 and June 2009 at Samsung Medical Center, a tertiary care university hospital in Seoul, Korea. We investigated the 2-year clinical outcome of this retrospective cohort, which short-term clinical outcome has been reported by us [9].The institutional review board approved the study protocol.

CPR duration was defined as the interval between initiation of CPR and the return of spontaneous circulation (ROSC) or death in C-CPR. CPR duration of E-CPR was defined as the interval between CPR and implantation of ECMO or death [3,7]. Patients who had the following contraindications of E-CPR were excluded ($n = 570$); age >80 years, previous severe neurologic damage, current intracranial hemorrhage, malignancy in the terminal stage, arrest of traumatic origin with uncontrolled bleeding, arrest of septic origin, irreversible multi-organ failure leading to cardiac arrest, and patients who signed "Do Not Resuscitate" orders. Patients with CPR duration of less than 10 min ($n = 121$) and unwitnessed arrest ($n = 11$) were also excluded for comparison of E-CPR and C-CPR. Finally a total of 406 patients were included in the analysis (Fig. 1).

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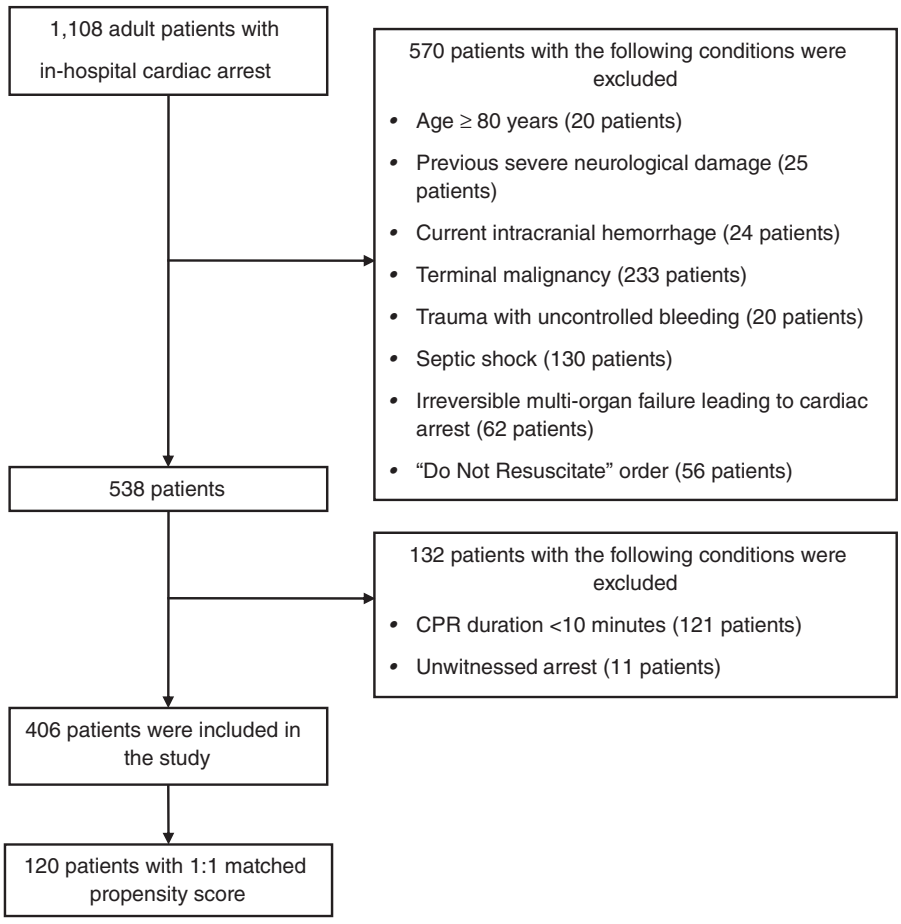

Fig. 1. Study flow.

2.2. E-CPR and C-CPR

E-CPR was defined as an intention-to-treat of hemodynamic support by extracorporeal membrane oxygenation (ECMO) during CPR before ROSC regardless of the success of ECMO implantation. E-CPR was done according to the discretion of the CPR team leader. A Capiox Emergency Bypass System (EBC™, Terumo, Tokyo, Japan), a portable ECMO device that can be primed at bedside within 3 min, was used. ECMO was considered mostly when there was prolonged arrest and no ROSC within 10–15 min after initiation of CPR, when ROSC could not be maintained due to recurrent arrest, or when the recovery without ECMO support was unlikely due to known severe left ventricular dysfunction or coronary artery disease despite relatively short CPR duration. ECMO was done by in-hospital staff interventional cardiologists or surgeons who were on standby and available round-the-clock.

Vascular cannulation was done percutaneously in a majority of case or surgically in challenging cases [9,12]. Vascular cannula sized 14 to 21 French and 21 to 28 French were used for arterial and venous access, respectively. A bypass catheter was inserted into the femoral artery to facilitate distal limb perfusion in the event of leg ischemia after arterial cannulation. Anticoagulation was accomplished by a bolus injection of unfractionated heparin, which was followed by a continuous intravenous infusion. The flow rate was set above 2.2 L/min/body surface area (m^2) initially, and was adjusted subsequently to maintain a mean arterial pressure above 65 mm Hg. The partial pressure of arterial oxygen in the right arm was maintained at greater than 100 mm Hg to ensure the sufficient oxygenation of the brain. Transfusion of red blood cell and fresh frozen plasma was performed to maintain intravascular volume.

ROSC was confirmed by palpation of peripheral arterial pulses in C-CPR. Return of spontaneous heart beat (ROSB) was confirmed by portable echocardiography in E-CPR.

2.3. Study endpoints

Clinical data including survival and the degree of neurological impairment were obtained from medical record reviews and telephone interviews conducted by trained research nurses. Two-year follow-up was checked in all survivors. Minimal neurological impairment was defined as the Modified Glasgow Outcome Score (MGOS) ≥ 4 [13]. The primary endpoint was a two-year survival with minimal neurologic impairment. Secondary endpoints were two-year survival and one-year survival with minimal neurological impairment. A long-term survivor was defined when a patient survived with minimal neurologic impairment for more than 2 years.

2.4. Propensity score matching

The propensity score matching analysis was performed to minimize the effect of selection bias and balance the covariates as described in our previous study [9]. Pre-CPR characteristics and CPR variables in Table 1 were included in the multiple logistic-regression models predicting the probability of receiving E-CPR. The burden of comorbidities estimated from the maximal value of the Sequential Organ Failure Assessment (SOFA) score and the Deyo–Charlson score 24 h prior to arrest was used to adjust the pre-arrest conditions [14–16]. Propensity score-matched 1:1 pairs were derived using a genetic matching algorithm without replacement [17,18]. Initial rhythms and study period were exactly matched, and CPR duration was additionally adjusted during the matching process using the propensity score and the Mahalanobis distance. The balance of covariates between the C-CPR and E-CPR group was tested after matching.

2.5. Statistical analysis

Continuous variables were expressed as the mean ± standard deviation or median with interquartile ranges. Continuous variables were compared using the Student's *t*-test or Wilcoxon rank sum test. Categorical variables were compared with a chi-square test or McNemar test. Cox regression analysis was used to estimate the hazard ratio (HR) modeling mortality or significant neurological deficit. Multivariate Cox regression analysis was used to evaluate independent factors related to survival with an adjustment for age, gender, CPR variables such as cause of arrest, initial rhythm, CPR duration, location of arrest, time period, the pre-arrest SOFA score, illness category, the Deyo–Charlson score, and subsequent intervention such as percutaneous coronary intervention, cardiac surgery, transplantation, or major surgery. Kaplan–Meier curves were plotted to show the survival trends, and a stratified log-rank test was used. The probability of 2-year survival with minimal neurologic impairment according to the CPR duration was calculated by logistic regression analysis. SAS version 9.1.3, R 2.10.1, and STATA 12.0 were used. A two-tailed p value <0.05 was considered significant.