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Review article

Comparing extracorporeal cardiopulmonary resuscitation with conventional cardiopulmonary resuscitation: A meta-analysis☆

Su Jin Kim[a], Hyun Jung Kim[b], Hee Young Lee[c], Hyeong Sik Ahn[b], Sung Woo Lee[a,*]

[a] Department of Emergency Medicine, College of Medicine, Korea University Hospital, Seoul, Republic of Korea
[b] Institute for Evidence-based Medicine, The Korean Branch of Australasian Cochrane Center, Department of Preventive Medicine, College of Medicine, Korea University, Seoul, Republic of Korea
[c] Center for Preventive Medicine and Public Health, Seoul National University Bundang Hospital, Gyeonggi-do, Republic of Korea

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ABSTRACT

Introduction: The objective was to determine whether extracorporeal cardiopulmonary resuscitation (ECPR), when compared with conventional cardiopulmonary resuscitation (CCPR), improves outcomes in adult patients, and to determine appropriate conditions that can predict good survival outcome in ECPR patients through a meta-analysis.
Methods: We searched the relevant literature of comparative studies between ECPR and CCPR in adults, from the MEDLINE, EMBASE, and Cochrane databases. The baseline information and outcome data (survival, good neurologic outcome at discharge, at 3–6 months, and at 1 year after arrest) were extracted. Beneficial effect of ECPR on outcome was analyzed according to time interval, location of arrest (out-of-hospital cardiac arrest (OHCA) and in-hospital cardiac arrest (IHCA)), and pre-defined population inclusion criteria (witnessed arrest, initial shockable rhythm, cardiac etiology of arrest and CPR duration) by using Review Manager 5.3. Cochran's Q test and I^2 were calculated.
Results: 10 of 1583 publications were included. Although survival to discharge did not show clear superiority in OHCA, ECPR showed statistically improved survival and good neurologic outcome as compared to CCPR, especially at 3–6 months after arrest. In the subgroup of patients with pre-defined inclusion criteria, the pooled meta-analysis found similar results in studies with pre-defined criteria.
Conclusion: Survival and good neurologic outcome tended to be superior in the ECPR group at 3–6 months after arrest. The effect of ECPR on survival to discharge in OHCA was not clearly shown. As ECPR showed better outcomes than CCPR in studies with pre-defined criteria, strict indications criteria should be considered when implementation of ECPR.

Introduction

Survival to hospital discharge rates are less than 10% and 20% respectively for out-of-hospital cardiac arrest (OHCA) and in-hospital cardiac arrest (IHCA), and good neurologic survival rates vary widely, from 50% to 85% of survivors according to regional variations.[1–4]

Extracorporeal cardiopulmonary resuscitation (ECPR), either during conventional cardiopulmonary resuscitation (CCPR) or when repetitive arrest events without return of spontaneous circulation (ROSC) for more than 20 min, is considered an alternative resuscitative method for patients who have a presumed reversible etiology of arrest (acute myocardial infarction, pulmonary embolism, etc.) who show no response despite advanced cardiac life support in emergency department, intensive care unit and catheterization room.[5–7] ECPR may preserve myocardial viability by enhancing coronary blood flow, thus increasing the chance of ROSC.[8]

As ECPR provides sufficient perfusion to vital organs until an effective cardiac output has been recovered, thus preventing organ failure, ECPR, compared to CCPR, may improve survival and neurological outcome long-term post-arrest. However, the advantages of ECPR as an alternative method to CCPR for increasing survival rate and attaining good cerebral performance category (CPC) score are still controversial, especially in OHCA, as well as in IHCA.

Moreover, outcomes of CCPR, despite standardized guidelines, show a multitude of discrepancies, with varying resuscitative

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* Corresponding author at: Department of Emergency Medicine, College of Medicine, Korea University, Inchon-ro 73, Seongbuk-gu, Seoul 02841, Republic of Korea.
E-mail address: kuedlee@korea.ac.kr (S.W. Lee).

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methods and strategies depending on regional variations and emergency response systems.[9] ECPR also has shown a wide range results due to its relatively limited indications and differing protocols. This is especially true in OHCA patients, which differ from IHCA cases in terms of characteristics of patients, common etiologies of arrest, pre-existing disease, low-flow time, bystander CPR quality.[10,11] Furthermore, the invasively high cost of ECPR and its applicability to only a limited patient population both play a considerable role in determining outcome. Although there are several studies regarding ECPR survival rates and neurological outcomes, evidence on conditions for predicting beneficial effects of ECPR compared to CCPR is lacking.[12–14]

Therefore, we performed an updated meta-analysis of observational studies, addressing whether ECPR, compared with CCPR, improves survival outcome and good neurological outcome (CPC 1, 2) in adult patients with cardiac arrest according to time interval after arrest (at discharge, 3–6 months, and 1 year). In addition, we analyzed outcomes of subgroups according to location of arrest (OHCA and IHCA). The primary objective was to determine whether ECPR results in better outcome than CCPR, regardless of time interval and location of arrest. Our secondary objective was to determine adequate predictors of better outcome in ECPR versus CCPR through subgroup analysis.

Methods

We used multiple comprehensive databases to find literature comparing outcomes of ECPR and CCPR. This study is based on the Cochrane Review Methods.[15]

Data source & literature searches

We searched MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials (CENTRAL) from August 1965 until February 2015 without restrictions on language or year of publication or type of publication. Further studies were additionally included from March 31 to July 31, 2015 during the review process. The following keywords and MeSH were searched through Medline: “heart arrest”, “extracorporeal membrane oxygenation”, and “resuscitation” (See Appendix 1 for the comprehensive list). Search strategies were adapted for other databases based on the MEDLINE strategy. After the initial electronic search, we hand-searched further relevant articles and bibliographies from identified studies. Articles identified were assessed individually for inclusion.

Study selection

Studies were assessed for inclusion independently by two reviewers (SJK and SWL) based on pre-defined selection criteria. Two reviewers independently assessed the titles and abstracts of included studies and then assessed the reports to ensure that they met our inclusion criteria. Any disagreement was discussed by the two reviewers. We excluded reports that did not completely fulfill our inclusion criteria.

Studies were included in our meta-analysis if they contained (1) adult (age ≥ 16 years) patients, (2) with either in-hospital or out-of-hospital cardiac arrest, (3) comparative study data between ECPR as the intervention group and CCPR as the control group, and (4) reported outcomes (survival and neurological outcome at discharge, 3–6 month, and 1 year after arrest). We excluded any studies that (1) contained only non-comparative outcomes of either ECPR or CCPR, (2) included cases with cardiogenic shock or post-cardiac surgery, (3) included pediatric patients (age < 16 years), (4) were comprised of a majority of arrest events caused by trauma, avalanche, hanging and/or drowning or (5) Do-Not-Attempt Resuscitation (DNAR) cases. Studies that were duplicates of the same patient cohort were not included.

Data extraction

The two reviewers independently extracted data from each study using a predefined data extraction form. Any disagreement was resolved by discussion.

The following variables were extracted from studies: (1) demographic, clinical, and treatment characteristics (e.g., inclusion criteria of studies, number of arrest patients in ECPR and CCPR groups, study location), (2) number of patients with reported outcomes (survival outcome at discharge, at 3–6 months, at over 1 year and good neurologic outcome at discharge, at 3–6 months, at over 1 year in comparative groups), (3) location of arrest, (4) study period, and (5) ECPR indications. When not otherwise specified, we considered 30-day survival as survival to hospital discharge. Good neurologic outcome was defined as a Glasgow–Pittsburgh Cerebral-Performance Category (CPC) score of 1 or 2 on the 5-category scale. If the above variables were not mentioned in the studies, we asked corresponding authors for the data via email.

Assessment of methodological quality

Two reviewers independently assessed the methodological qualities for each study using the Newcastle–Ottawa Scale for cohort studies. Any unresolved disagreements between reviewers were resolved through discussion or review from the third author (HYL). As tests for funnel plot asymmetry are generally only performed when at least 10 studies are included in the meta-analysis, publication bias was not assessable.

Statistical analysis

The main outcome was survival to hospital discharge and good neurologic outcome at discharge. The denominator for calculating rates of survival to hospital discharge was the number of adult patient with arrest. For dichotomous outcomes (survival rate, event rate of good neurologic outcome), data were pooled using Mantel–Haenszel method random-effects weighting, and the results were expressed as relative risks (RR) and 95% confidence intervals (CI). RR was used for survival events and good neurologic outcome, not for mortality. To estimate heterogeneity, we estimated the I^2 statistic, with values of 25%, 50%, and 75% considered low, moderate, and high, respectively. We conducted planned subgroup analyses according to (1) OHCA and IHCA, (2) selectively limited inclusions of the study population, such as cases of witnessed arrest, or cases with initial rhythm of ventricular fibrillation (VF)/ventricular tachycardia (VT), or presumed cardiac etiology or CPR duration >10–20 min. Sensitivity analysis was performed by the Newcastle–Ottawa scale, or through consideration of article quality through publication type. We used Review Manager version 5.3 for these analyses. Cochran's Q test and I^2 were calculated.

Results

Identification of studies

Searches of the databases yielded 1583 articles, excluding duplicates (Fig. 1). Of these, 1555 publications were excluded upon initial screening as it was clear from the title and abstract that they did not fulfill the selection criteria. For the remaining 28 articles, we obtained full manuscripts, and following scrutiny of these, we identified potentially relevant studies. Publications were further excluded if they were (1) duplicate data, (2) outcome