



Review article

Extracorporeal resuscitation for refractory out-of-hospital cardiac arrest in adults: A systematic review of international practices and outcomes[☆]



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ABSTRACT

Aim: Extracorporeal resuscitation during cardiopulmonary resuscitation (ECPR) deploys rapid cardiopulmonary bypass to sustain oxygenated circulation until the return of spontaneous circulation (ROSC). The purpose of this systematic review is to address the defining elements and outcomes (quality survival and organ donation) of currently active protocols for ECPR in refractory out-of-hospital cardiac arrest (OHCA) of cardiac origin in adult patients. The results may inform policy and practices for ECPR and help clarify the corresponding intersection with deceased organ donation.

Methods: We searched Medline, Embase, Cochrane and seven other electronic databases from 2005 to 2015, with no language restrictions. Internal validity and the quality of the studies reporting outcomes and guidelines were assessed. The review was included in the international prospective register of systematic reviews (Prospero, CRD42014015259).

Results: One guideline and 20 outcome studies were analyzed. Half of the studies were prospective observational studies assessed to be of *fair to good* methodological quality. The remainder were retrospective cohorts, case series, and case studies. Ages ranged from 16 to 75 years and initial *shockable* cardiac rhythms, witnessed events, and a reversible primary cause of cardiac arrest were considered favorable prognostic factors. CPR duration and time to hospital cannulation varied considerably. Coronary revascularization, hemodynamic interventions and targeted temperature management neuroprotection were variable. A total of 833 patients receiving this ECPR approach had an overall reported survival rate of

Abbreviations: ECPR, extracorporeal resuscitation; ROSC, return of spontaneous circulation; OHCA, out-of-hospital cardiac arrest; CPC, cerebral performance category; GOS, Glasgow Outcome Scale; LOE, level of evidence; ILCOR, International Liaison Committee on Resuscitation; RCTs, randomized controlled trials; TTM, targeted temperature management; IABP, intra-aortic balloon pump; DBD, donation after brain death; cDCD, controlled donation after circulatory determination of death; ELSO, extracorporeal life support organization.

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22%, including 13% with good neurological recovery. Additionally, 88 potential and 17 actual deceased organ donors were identified among the non-survivor population in 8 out of 20 included studies. Study heterogeneity precluded a meta-analysis preventing any meaningful comparison between protocols, interventions and outcomes.

Conclusions: ECPR is feasible for refractory OHCA of cardiac origin in adult patients. It may enable neurologically good survival in selected patients, who practically have no other alternative in order to save their lives with quality of life, and contribute to organ donation in those who die. Large, prospective studies are required to clarify patient selection, modifiable outcome variables, risk-benefit and cost-effectiveness.

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Introduction

Sudden cardiac arrest is the main cause of death worldwide in previously healthy people. The global incidence of OHCA in adults is 62 cases per 100,000 persons per year, from which 75 to 85% have a cardiac origin.¹ Despite recent improvements in enhancing successful resuscitation in the prehospital setting, overall outcomes remain poor in most venues.¹ The overall reported survival to hospital discharge is 6% in North America,¹ 9% in Europe, 11% in Australia and 2% in Japan.²

Extracorporeal resuscitation deploys a modified form of cardiopulmonary bypass, maintaining circulation until an effective cardiac output can be restored. This technique enhances coronary blood flow and preserves the heart's viability, increasing the chance of ROSC. The supply of oxygenated blood flow to the body and brain prevents organ dysfunction and increases the likelihood of survival with a good neurological recovery.³ It is referred to as ECPR for patients in cardiac arrest when conventional resuscitation attempts fail, and it provides oxygenated circulation to extend the time window to diagnose and treat the underlying primary cause of the arrest. In recent years, ECPR has been proposed as an effective therapy not only for in-hospital cardiac arrest, but also for OHCA.^{4,5} However, the results have been mixed due to heterogeneity in study populations, interventions and patient follow-up. In OHCA events, adult patients are known to be younger, previously healthy and the cause of cardiac arrest is more likely of cardiac origin. Therefore, these sudden death episodes are potentially more reversible than in patients who suffer an in-hospital cardiac arrest associated with many comorbidities. Given ROSC is not achieved in the majority of refractory OHCA^{1,2} the ECPR strategy may be a final option for these selected patients "too healthy to die".⁶

The purpose of this systematic review is to address the defining elements and outcomes (quality survival and organ donation) of currently active protocols for ECPR in refractory OHCA of cardiac origin in adult patients. Further understanding of survival outcomes versus risks of anoxic brain injury and death may inform policy and practices for ECPR and the corresponding intersection with deceased organ donation and transplantation.

Methods

Design of the study and search strategy

A systematic review of the literature was conducted according to health care reviews from the University of York's Center for Reviews and Dissemination.⁷

Medline (OvidSP), Embase (OvidSP), Cochrane (Wiley) and seven other electronic databases were searched by an expert librarian (EG) from January 1st, 2005 to May 25, 2015 with no language restrictions. Articles identified included variations of the terms ECPR or extracorporeal circulation, found as textwords in the Title/Abstract or MeSH. These were combined with variations of resuscitation, out of hospital, in hospital, cardiac and

organ donation terms found in the Title/Abstract or MeSH. We also searched Google Scholar, clinicaltrials.gov, as well as reference lists of included studies, abstracts, unpublished reports, personal libraries (IO-D), professional organization reports and government agency statements on ECPR. Two reviewers (IO-D & LH) extracted main variables. Internal validity and the quality of the studies reporting outcomes and guidelines were assessed. The review was included in the international prospective register of systematic reviews (Prospero, CRD42014015259) (see Additional file 1 for search strategy details).

We used a modified PICOTS format. **Population:** adults with refractory OHCA of cardiac origin, who were considered candidates for ECPR; **Intervention:** ongoing resuscitation during transport, followed by ECPR and other adjunctive therapies until and/or early after ROSC; **Control:** although most of the selected studies are single-arm studies, conventional resuscitation was compared to the ECPR strategy in applicable studies; **Outcomes:** description of practices based on ECPR protocols applied to the population, survival with quality of life according to a cerebral performance category (CPC) score 1–2 or Glasgow Outcome Scale (GOS) score 4–5 at discharge, and potential organ donation; **Time:** from January 2005 to May 2015; **Setting:** organizations that produced recommendations or conducted studies consistent with our eligibility criteria.

Eligibility criteria

Studies reporting results from ECPR in adult patients with refractory OHCA of cardiac origin and recommendations for ECPR endorsed by any professional society or health care authority were included. We excluded editorials, reviews, abstracts, letters or personal opinions. Human studies that included patients with cardiac arrest of non-cardiac origin (e.g. trauma, massive bleeding, hypothermia, poisoning, near drowning, etc.) and animal studies were also excluded. Two trained reviewers (IO-D & LH) selected the studies and screened citations, retrieved the full texts and independently reviewed them to assess study eligibility. Disagreements were resolved by consensus or after input of two other expert reviewers (SDS & FB). We used EndNote manager software (End-Note X7.1 version, by Thomson Reuters) to manage the collection of publications. Fig. 1 presents the flow chart study selection process (PRISMA).

Data extraction and quality assessment

Two reviewers (IO-D and LH) extracted data after creating an Excel (Excel version 2013, by Microsoft Office) data collection tool that was piloted in a sample from included studies. The spreadsheet tabulated the following variables: authors, country, setting, year of protocol, methodology, eligibility criteria, number of cases, interventions, timelines, results (survival with quality of life and potential/actual deceased donors) and conclusions.

The internal validity of the studies was assessed (See Table 1) independently by four reviewers (IO-D, LH, SDS & FB) and guideline

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