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Clinical paper

ECMO Cardio-Pulmonary Resuscitation (ECPR), trends in survival from an international multicentre cohort study over 12-years☆

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Abbreviations:
ECMO, Extra-Corporeal Membrane Oxygenation
CPR, Cardio Pulmonary Resuscitation
ECPR, Extra-Corporeal Membrane Oxygenation assisted Cardio Pulmonary Resuscitation
ELSO, Extracorporeal Life Support Organisation
VA, veno-arterial
VV, veno-venous
SAVE score, survival after VA-ECMO score

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ABSTRACT

Background: Use of Extracorporeal Membrane Oxygenation during cardiopulmonary resuscitation (ECPR) is increasingly being deployed as an adjunct to conventional CPR. It is unknown if this has been associated with improved outcomes.
Aims: To describe trends in survival and patient demographics for ECPR patients in the international Extracorporeal Life Support Organisation (ELSO) database over the past 12 years and identify factors associated with changes in survival.
Methods: Patients greater than 16 years of age who received ECPR between January 2003 and December 2014 were extracted from the ELSO registry and were divided into three 4-year cohorts (Cohort 1: 2003–2006, Cohort 2: 2007–2010, Cohort 3: 2011–2014). Univariable analysis was performed to compare demographics and outcomes of patients across the three cohorts. Univariable and multivariable analyses were then performed to identify factors independently associated with survival.
Results: 1796 patients treated with ECPR were extracted from the registry, aged 50 (±18.5) years. Annual ECPR episodes increased over 10-fold, from 35 to over 400 per year. Survival to hospital discharge was 29% overall (27% cohort 1, 28% cohort 2, 30% cohort 3 ($p = 0.71$)). Age, body weight and documented comorbidities increased over time. There was a reduction in complications associated with ECMO usage. After adjusting for confounders there was no change in the odds of survival over the time period examined.
Interpretation: Over the period 2003–2014, survival to hospital discharge was 29% for patients who require ECPR. Despite advances in provision of ECMO care and increasing co-morbidities of patients, there has been no change in risk-adjusted survival over time.

Introduction

Extracorporeal Membrane Oxygenation (ECMO) provides mechanical pulmonary and circulatory support for patients with cardiogenic shock refractory to conventional medical therapy.[1] When incorporated into Cardio Pulmonary Resuscitation (CPR) for patients who do not attain sustained return of spontaneous circulation with conventional resuscitation techniques, it is termed ECMO-CPR (ECPR). This technique utilises ECMO support during CPR to provide a perfusing circulation whilst reversible causes of the arrest can be treated.

In-hospital cardiac arrest treated with conventional CPR typically has a survival rate of 15–17% whilst out-of-hospital cardiac arrest survival is lower at 8–10%.[2,3] As prolonged hypoperfusion during conventional CPR leads to significantly worse outcomes, veno-arterial (VA) ECMO can rapidly restore perfusion and may therefore improve long-term survival.[4–6] However, survival rates

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with ECPR have been heterogeneous, with reported ranges of 15%–60%.[1,7]

In a retrospective, single-centre, propensity-matched analysis, Shin et al.[8] showed improved survival with favourable neurologic outcome for patients with in-hospital arrest treated with ECPR versus conventional CPR (hazard ratio (HR) 0.17, 95%CI 0.04–0.68). Other observational studies have found variable improvements in mortality with the use of ECPR.[9–11] A meta-analysis performed by Cardarelli et al.[12] in 135 patients from 1990 to 2007 showed a hospital survival rate to discharge with ECPR of 40%.

A small observational pilot study in Australia[13] using mechanical compression devices, ECPR and hypothermia for patients with refractory cardiac arrest demonstrated 5 of 11 patients with out-of-hospital cardiac arrest (45%) and 9 of 15 (60%) in-hospital cardiac arrest survival. Half of these survivors demonstrated a favourable neurological outcome. Haneya et al.[14] compared ECPR initiated in the Emergency Department for out-of-hospital cardiac arrest with ECPR initiated for in-hospital cardiac arrest, and found a survival rate of 42% for in-hospital arrest patients and 15% for patients with an out-of-hospital cardiac arrest.

The ability to understand the efficacy of ECPR is limited because most reports on ECPR are constrained by small sample sizes, narrow diagnosis groups and single institution reports, making generalisation difficult. Despite this, utilisation of ECPR appears to be increasing with a report from the ELSO registry describing four cases between 1992–1997 and 163 cases between 2004–2007.[15] Given the heterogeneity of data being published from single centres, an updated description is important to better understand survival outcomes among adult patients to recommend its use.

Prognostic scoring models may aid in risk adjusting outcomes for patients who require ECMO. Despite progress with scoring systems in veno-venous (VV) ECMO for respiratory support,[16,17] less has been published regarding VA-ECMO. Kim et al.[18] demonstrated that the Simplified Acute Physiology Score II could be used to predict survival in a case-mix that comprised multiple modalities of ECMO (VV, VA and ECPR). More recently, the SAVE score[19] has been developed and validated for use in patients who require VA-ECMO.

Our hypothesis was that reported use of ECPR has increased and that this has been associated with improved risk adjusted survival. Our aim was to describe the demographics and outcomes of patients undergoing ECPR, identify factors associated with survival and assess change in outcomes over time after adjusting for confounders. The primary outcome for this study was survival to discharge from hospital.

Methods

Ethics

Ethics approval for this study was obtained from The Alfred hospital research and ethics committee. (Ethics number: Alfred Health 39/16).

Study population and inclusion criteria

The ELSO registry collects data on ECMO used to support cardiorespiratory function in children and adults from institutions in 53 countries. Data are reported to the registry after approval by the local Institutional Review Boards. A data use agreement between ELSO and member centres allows ELSO to release limited de-identified datasets to the member centres for purposes of analysis for scientific publication, and waives the need for approval from individual reporting member centres. The registry defines ECPR as: "extracorporeal life support (ECLS) used as part of initial resuscitation from cardiac arrest. Patients who are haemodynamically unstable and placed on ECLS without cardiac arrest are not considered ECPR".[15]

We queried the ELSO registry for adult patients who received ECPR from 2003 to 2014. Only the first ECPR episode was included for analysis. Demographic data, pre-ECMO variables, ICD-09 diagnosis codes, procedure codes, physiology whilst supported on ECMO, ECMO complications, year of ECMO episode, as well as hospital outcome were extracted from the registry. No patient or hospital identifying information was extracted.

The pre-ECMO variables included arrest rhythm, time between admission and initiation of ECMO support, time from intubation to initiation of ECMO support, systolic and diastolic blood pressure within 6 h pre-cannulation, blood gases and ventilator settings. Individual ICD-09 diagnosis codes were consolidated (Supplementary Appendix 1) into diagnostic groups.

Statistical analysis

A data analysis plan was prospectively established and ratified by the investigators prior to analysis. Descriptive statistics were used to describe overall cases (n) and proportions (%). For normally distributed data, mean and standard deviation were reported. For non-parametric data, median and interquartile ranges were reported. Continuous variables were compared with Student's T, Q7 Wilcoxon signed-rank or Kruskal–Wallis tests, as appropriate. Categorical variables were compared using the χ^2 test for equal proportion. A two-sided p-value of ≤ 0.05 was taken to indicate statistical significance. Variables were subjected to a correlation matrix for analysis of co-linearity. Analyses were performed with STATA v12 (StataCorp. TX, USA).

ECPR episodes per year and annual survival to hospital discharge were calculated. Data were grouped into three 4-year cohorts; 2003–2006, 2007–2010 and 2011–2014. Univariable analysis was performed to compare demographics and outcomes across the three temporal cohorts and also to compare survivors with non-survivors. To assess the baseline severity of illness, SAVE scores[19] (Supplementary Appendix 2) were calculated for each patient. Given the absence of specific data to differentiate out-of-hospital from in-hospital cardiac arrests, a subgroup of patients who had ECMO started less than or equal to one hour after hospital admission was also identified.

Multivariable logistic regression models were constructed to identify factors independently associated with survival and to determine whether outcomes had changed over the three time periods after adjusting for confounders. Models were constructed sequentially, initially using the SAVE score as the main risk adjuster (model 1), then SAVE score components (model 2). Additional pre-ECMO diagnostic, demographic and physiology criteria, identified from the univariable analysis, were introduced (model 3) to fully adjust for patient severity of illness. Finally model 3 was extended to include ECMO complications (model 4). This final model was chosen to assess if any patient risk factors or changes in ECMO processes of care had affected survival rates over the three time periods.

Model discrimination and calibration were assessed using the area under the receiver operating characteristics curve and the Hosmer–Lemeshow C-statistic with associated p-value, respectively.

Results

Study population

1796 ECPR episodes (mean age 50 years (±18.5), 69% male) were extracted from the ELSO registry. Overall, 520 (29%) survived to hospital discharge. ECPR episodes reported to the ELSO registry

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