Resuscitation 110 (2017) 126–132

Contents lists available at ScienceDirect

Resuscitation

journal homepage: www.elsevier.com/locate/resuscitation

Clinical paper

Post-cardiac arrest shock treated with veno-arterial extracorporeal membrane oxygenation
An observational study and propensity-score analysis☆

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ARTICLE INFO

Article history:
Received 3 August 2016
Received in revised form 24 October 2016
Accepted 1 November 2016

Keywords:
Cardiac arrest
Extracorporeal life support
Shock

ABSTRACT

Purpose: Cardiogenic shock due to post-resuscitation myocardial dysfunction is a major cause of mortality among patients hospitalized after cardiac arrest (CA). Veno-arterial extracorporeal membrane oxygenation (VA-ECMO) has been proposed in the most severe cases but the level of evidence is very low. We assessed characteristics, outcome and prognostic factors of patients treated with VA-ECMO for post-CA shock.
Methods: Using a large regional registry, we focused on all CA admitted in ICU. Among those who developed a post-CA shock, prognostic was compared according to VA-ECMO use, using logistic regression and propensity score. Specific prognostic factors were identified among VA-ECMO patients.
Results: Among 2988 patients admitted after CA, 1489 developed a post-CA shock, and were included. They were mostly male (68%), with mean age 63 years (SD = 15). Fiflty-two patients (3.5%) were treated with VA-ECMO, mostly patients with ischemic cause of CA (67%). Among patients with post-CA shock, 312 (21%) were discharged alive (25% in VA-ECMO group, 21% in control group, P = 0.45). After adjustment for pre-hospital and in-hospital factors, survival did not differ among patients treated with VA-ECMO (OR for survival = 0.9, 95%CI 0.4–2.3, P = 0.84). After propensity-score matching, results were consistent. Among patients treated with VA-ECMO, initial arterial pH (OR = 1.7 per 0.1 increase, 95%CI 1.0–2.8, P = 0.04) and implantation of VA-ECMO over 24 h after ROSC (OR = 20.0, 95%CI 1.4–277.3, P = 0.03) were associated with survival.

Abbreviations: CA, cardiac arrest; CPC, cerebral performance category; CPR, cardio-pulmonary resuscitation; VA-ECMO, veno-arterial extra-corporeal membrane oxygenation; EMS, emergency medical service; ESM, electronic supplementary material; ICU, intensive-care-unit; IQR, interquartile-range; PCI, percutaneous coronary intervention; PRMD, post resuscitation myocardial dysfunction; ROSC, return of spontaneous circulation; SD, standard-deviation; TTM, targeted temperature management.

☆ A Spanish translated version of the abstract of this article appears as Appendix in the final online version at http://dx.doi.org/10.1016/j.resuscitation.2016.11.005.

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http://dx.doi.org/10.1016/j.resuscitation.2016.11.005

Conclusions: Post-CA shock is frequent and is associated with a high mortality rate. When used in selected patients, we observed that VA-ECMO could be an appropriate treatment.

Introduction

Survival rate after cardiac arrest (CA) remains disappointing, around 10%.[1,2] In-hospital mortality among patients with return of spontaneous circulation (ROSC) remains high, over 70%,[1,3,4] and is mainly attributable to neurological damages secondary to severe anoxic-ischemic brain injury and post-CA shock.[3,4] Post-CA shock is a mixed shock, including vasoplegia and myocardial dysfunction.[5,6] Post-resuscitation myocardial dysfunction (PRMD) corresponds to an early and severe diastolic and systolic dysfunction. Several authors reported the reversibility of post-CA myocardial dysfunction, described as a myocardial stunning.[5,7] This complication often requires inotropic support, usually dobutamine, combined with vasoactive drugs.[8] However, these treatments are often insufficient to control the circulatory failure.

Veno-arterial extracorporeal membrane oxygenation (VA-ECMO) has been proposed for refractory cardiogenic shock, especially when a reversible cause can be identified, such as acute myocarditis or intoxication.[9–11] Considering the reversibility of PRMD, this situation could analogously appear suitable for VA-ECMO. Even if relying on very poor evidence, recent guidelines suggest considering the use of a mechanical circulatory assistance device in this situation, to ensure adequate organ perfusion until a reliable neurological prognostication is performed.[8] Timing of implantation after ROSC could influence prognosis, and optimal timing of circulatory support in cardiogenic shock remains unknown.[12]

To date the interest of VA-ECMO in CA has been mostly assessed in the setting of refractory arrest (E-CPR),[13–17] but to the best of our knowledge, no data regarding VA-ECMO in the setting of post-CA shock are available. Since VA-ECMO is a time-consuming and expensive technique, careful evaluation of such a technique is crucial. In this situation, we hypothesized that VA-ECMO could be useful to overcome post-resuscitation myocardial dysfunction. We aimed to describe characteristics, outcome and prognostic factors of patients treated with VA-ECMO for post-CA shock in a large population-based registry of CA.

Materials and methods

Population and study setting

The Sudden Death Expertise Centre (SDEC) Registry has been previously described.[1,18] It consists in a population-based registry, concerning Paris (France) and its suburbs (residential population: 6.6 million). According to recent guidelines,[19] since May 2011, every case of out-of-hospital CA occurring in the area of interest, with age over 18 years, has been included in the SDEC registry. Exclusion criteria were obvious extra-cardiac cause of CA (trauma, drowning...) or refractory CA without ROSC. In this study, all patients admitted alive to the intensive care unit (ICU) after successfully resuscitated out-of-hospital CA occurring in greater Paris, between 15th May 2011 and 1st November 2015 were considered. All patients who developed a post-CA shock were included in the analysis. Post-CA shock was defined as the need for continuous norepinephrine or epinephrine infusion to maintain mean arterial pressure above 60 mmHg for more than 6 h following ROSC, despite adequate fluid loading, as assessed by the absence of preload-dependency indicators.[4]

Data collection

Data were collected prospectively according to Utstein templates for patient data collection.[20] General data included demographics characteristics and location of arrest. Concerning pre-hospital care, data recorded included presence of bystander, bystander cardio-pulmonary resuscitation (CPR), presence of shockable rhythm before advanced life support, dose of epinephrine during resuscitation, and survival until admission. For every hospitalized patient, the following in-hospital data were recorded: arterial pH and lactate on admission, therapeutic hypothermia, immediate coronary angiogram, VA-ECMO use, timing for implantation of VA-ECMO (early 24 h after ROSC, or later than 24 h from ROSC), outcome (death or discharge from hospital), and neurological status at discharge (according to CPC score,[21] considering a CPC score of 1 or 2 as a favorable outcome). For patients with VA-ECMO use, we reported LV systolic function assessed by transthoracic echocardiography using a qualitative evaluation previously published (normal LV function; moderately depressed; severely depressed).[22] In this qualitative evaluation, we defined normal LV function as LVEF over 50%, moderately depressed as LVEF between 30 and 50% and severely depressed LV function as LVEF below 30%.[23]

Regarding complications related to treatment, major bleeding was defined as: fatal bleeding, and/or symptomatic bleeding in a critical area or organ, and/or bleeding causing a fall in hemoglobin level of 20 g l^{-1} or more, or leading to transfusion of two or more units of whole blood or red cells.[24] Other complications related to VA-ECMO (including ischemia or thrombosis) were collected.

Two investigators reviewed each record for data completion and validity.

Statistical analysis

The methodology of this study is consistent with the STROBE checklist for observational studies.[25] Continuous data were expressed as mean+/−standard deviation (SD) or median (interquartile). Categorical data were expressed as frequencies and percentages. Comparisons of categorical variables used χ^2 test or exact Fisher test when appropriate. Student's t-test, Mann–Whitney or Kruskall–Wallis test were used for comparisons of continuous variables, when appropriate. We assessed normality using Shapiro–Wilk test, and this test showed a non-normal distribution for age, epinephrine, delays and lactate. We checked the linearity of quantitative variables using fractional polynomial regression. When linearity was absent, continuous variables were dichotomized according to median in overall population. Multivariate analysis was performed with logistic regression, with binary outcome (survival at hospital discharge), including variables associated with P value <0.15 in the univariate analysis. We performed sensitivity analysis using favorable neurological outcome (i.e., CPC 1 or 2 at discharge) as outcome.

Propensity score matching is a method used to balance observed covariates in the two treatment groups.[14,26,27] In this study, the propensity score was the conditional probability for getting