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Short communication

# Cardiac arrest does not affect survival in post-operative cardiovascular surgery patients undergoing extracorporeal membrane oxygenation☆

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ABSTRACT

*Background:* Veno-arterial extracorporeal membrane oxygenation (ECMO) is rapidly evolving as bailout option in patients with refractory cardiogenic shock after cardiovascular surgery (CV). Cardiac arrest represents a common and severe complication in the immediate post-operative phase. We therefore evaluated the impact of cardiac arrest at time of ECMO implantation on short- and long-term mortality in patients following CV surgery.

*Methods and Results:* We included 385 patients undergoing veno-arterial extracorporeal membrane oxygenation therapy following CV surgery at a university-affiliated tertiary-care center into our single-center registry. Thirty patients underwent cardiopulmonary resuscitation (CPR) followed by immediate initiation of ECMO support. During a median follow-up time of 44 months (IQR 21–76 months), 68% of patients ($n = 262$) died. We did not detect a significant impact of CPR during ECMO initiation on 30-day mortality (HR 1.04, 95%CI 0.89–1.83, $P = 0.86$) as well as for long-term mortality (HR 1.01, 95%CI 0.63–1.61, $P = 0.97$). Results were virtually unchanged for 30-day (HR 0.88, 95%CI 0.44–1.73, $P = 0.70$) and long-term mortality (HR 0.93, 95%CI 0.54–1.60, $P = 0.79$) after adjustment for age, sex, left ventricular ejection fraction, SAPS2 score, type of CV surgery, and year of study inclusion in order to unveil a potential negative confounding.

*Conclusion:* Cardiac arrest did not affect short-tem and long-term mortality in a large cohort of patients with therapy refractory cardiogenic shock undergoing ECMO support following CV surgery. Our results suggest that the decision to initiate ECMO support in this specific patient population should not be influenced by the occurrence of cardiac arrest.



## Introduction

Veno-arterial extracorporeal membrane oxygenation (ECMO) is rapidly evolving as bailout option in patients with refractory cardiogenic shock or severe respiratory deficiency after cardiovascular (CV) surgery.[1] Patients requiring veno-arterial ECMO support following CV surgery represent a highly vulnerable patient population with a poor prognosis despite highest possible medical support. Initiation of ECMO support in patients with severe therapy refractory cardiogenic shock is frequently accompanied and complicated by cardiac arrest. With an incidence of up to 8%, cardiac arrest represents a common and severe complication in the immediate post-operative phase following major CV surgery[2] and is associated with poor survival.[3] However, as early ECMO support leads to a rapid restoration of circulation and maintains adequate end-organ perfusion,[4–6] this might alleviate the adverse prognostic impact of cardiac arrest in patients with severe cardiogenic shock following CV surgery.

A more detailed understanding regarding the prognostic impact of cardiac arrest prior to ECMO implantation may either help to strengthen the role of ECMO support in this specific post-surgical

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setting or to avoid an unrestrained use of ECMO that is associated with a disproportionately increase of hospital costs and resources consumption. We therefore evaluated the impact of cardiac arrest at time of ECMO implantation on short- and long-term mortality in patients following CV surgery.

## Methods

### *Study population*

We enrolled adult patients undergoing veno-arterial ECMO support after CV surgery at the Vienna General Hospital, a university-affiliated tertiary care center into our registry. The study protocol was approved by the Ethics Committee of the Medical University of Vienna and complies with the Declaration of Helsinki. A detailed methodology and the study protocol have been published previously.[7]

### *ECMO device and management*

ECMO therapy was implemented in patients with clinical signs of cardiogenic shock, such as systolic arterial hypotension (<80 mmHg), signs of end-organ failure despite optimized supportive therapy (i.v. fluids, inotropes, intraaortic balloon pump) and hemodynamic instability (cardiac index <1.8 L $kg^{-2}$ body surface area and pulmonary wedge pressure ≤20 mmHg). The ECMO circuit consisted of a centrifugal pump console (Bio-Console560; Medtronic, USA or CardioHelp system; Maquet, Germany) and a membrane oxygenator (Affinity-NTTM; Medtronic, USA or HLS module advanced; Maquet, Germany) as previously published.[7] The entire ECMO system was serviced daily by the on-shift intensive care physician or an experienced perfusionist. Mechanical ventilation was reduced to peak airway pressures below 25 $cmH_2O$ and low respiratory tidal volumes (6–8 ml $kg^{-1}$). $FiO_2$ was set to maintain an arterial $pO_2$ between 80 and 100 mmHg.

### *Clinical definitions and study endpoints*

Cardiopulmonary resuscitation was performed in the respective patients either in the operating room or at the intensive care unit followed by immediate initiation of ECMO support. Blood samples were collected pre-operatively at time of admission and analyzed according to local laboratory standard procedure. The simplified acute physiology score (SAPS)-2 score and the European System of Cardiac Operative Risk Evaluation (EuroSCORE) were calculated as previously described.[8] The primary study endpoint was all-cause 30-day mortality and overall long-term mortality during the entire observation period was defined as secondary study endpoint. Mortality data was obtained by screening the national register of death.

### *Statistical methods*

Discrete data were presented as count and percentage values and analyzed using Chi-square test. Continuous data were presented as median and inter-quartile range (IQR) and compared using Mann–Whitney statistics. Cox proportional hazard regression analysis was applied to evaluate the effect of cardiopulmonary resuscitation (CPR) on mortality. With 19 events in the CPR group and 243 events in the other group, the power to detect a hazard ratio of 1.5 is approximately 40%, the power to detect a hazard ratio of 2 is approximately 83% when using a log-rank test at a two-sided level of significance of 5%. To account for potential negative confounding effects we adjusted for age, sex, left ventricular ejection fraction, SAPS2 score, type of CV surgery, and year of study inclusion. Year of study inclusion was used as continuous variable in the model. Kaplan–Meier analysis was used to depict the effect of CPR on survival and compared using log-rank test. SPSS 23 (IBM Corp, NY, USA) was used for all analyses.

## Results

### *Baseline characteristics*

Between September 2003 and June 2014 at total of 10,547 patients underwent CV surgery at the Medical University of Vienna. Veno-arterial ECMO therapy following cardiovascular surgery was needed in 385 patients, who were subsequently enrolled into our registry. The median age was 65 years (IQR: 55–72) and seventy percent of patients ($n = 271$) were male. The patients had a median SAPS2 score of 46 points (IQR: 31–60) and a median EuroSCORE of 10 points (IQR: 8–13). Detailed baseline characteristics and characteristics of patients with and without CPR are presented in Table 1. ECMO cannulation was performed femoral-femoral in 52% of patients, subclavian-femoral in 38% of patients, and central-femoral in 10% of patients. Other indications for ECMO support were weaning failure from cardiopulmonary bypass (56%), immediate postoperative cardiogenic shock in the operating room (23%), immediate post-transplant cardiac graft failure in the operating room (4%), immediate postoperative respiratory failure in the operating room (3%), postoperative bleeding/tamponade with cardiogenic shock (4%), and miscellaneous conditions (5%). ECMO therapy was initiated in 110 patients after valve surgery, in 48 after coronary artery bypass graft (CABG) surgery, in 84 after combined CABG-valve surgery, in 68 patients after cardiac transplantation, in 31 patients after ventricular assisting device implantation, in 24 after aortic reconstruction and in 20 after other CV surgeries. Thirty patients (8%) underwent CPR followed by immediate initiation of ECMO support. Forty percent of patients were resuscitated within the operating room. The initial rhythm was ventricular fibrillation/tachycardia in 50% of patients. In 11 patients (37%) CPR was performed with opened chest. Detailed characteristics of CPR are displayed in Table 2.

### *Cardiopulmonary resuscitation and outcome*

During a median follow-up time of 44 months (IQR 21–76 months, minimum 4 months, maximum 127 months), 19 patients in the CPR group and 243 patients in the control group died. We did not detect a significant impact of CPR during ECMO initiation on 30-day mortality (HR 1.04, 95%CI 0.89–1.83, $P = 0.86$) as well as for long-term mortality (HR 1.01, 95%CI 0.63–1.61, $P = 0.97$). Results were virtually unchanged for 30-day (HR 0.88, 95%CI 0.44–1.73, $P = 0.70$) and long-term mortality (HR 0.93, 95%CI 0.54–1.60, $P = 0.79$) after adjustment for age, sex, left ventricular ejection fraction, SAPS2 score, type of CV surgery, and year of study inclusion. These results are further illustrated by Kaplan–Meier analysis for 30-day mortality (Fig. 1A; log-rank $P = 0.86$) and 2-year mortality (Fig. 1B; log-rank $P = 0.80$). Among the characteristics of cardiopulmonary resuscitation pH ($P = 0.008$) and base excess ($P = 0.05$) demonstrated a significant association with 30-day mortality in the univariable Cox-regression analysis.

## Discussion

Our results suggest that cardiac arrest at time of ECMO implantation has no adverse impact on survival in patients with severe therapy refractory cardiogenic shock following CV surgery. Short-term as well as long-term survival of patients requiring ECMO support did not significantly differ in patients with and without cardiac arrest prior to ECMO implantation. This finding is particularly compelling as cardiac arrest is generally associated with