International Journal of Cardiology xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

International Journal of Cardiology

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

Venoarterial extracorporeal membrane oxygenation after coronary artery bypass grafting: Results of a multicenter study☆

Fausto Biancari [a,*], Magnus Dalén [b], Andrea Perrotti [c], Antonio Fiore [d], Daniel Reichart [e], Sorosh Khodabandeh [b], Helmut Gulbins [e], Svante Zipfel [e], Mosab Al Shakaki [f], Henryk Welp [f], Antonella Vezzani [g], Tiziano Gherli [g], Jaakko Lommi [h], Tatu Juvonen [h], Peter Svenarud [b], Sidney Chocron [c], Jean Philippe Verhoye [i], Karl Bounader [i], Giuseppe Gatti [j], Marco Gabrielli [j], Matteo Saccocci [k], Eeva-Maija Kinnunen [a], Francesco Onorati [l], Giuseppe Santarpino [m], Khalid Alkhamees [n], Vito G. Ruggieri [i], Angelo M. Dell'Aquila [f]

[a] Department of Surgery, Oulu University Hospital, Oulu, Finland
[b] Department of Molecular Medicine and Surgery, Department of Cardiothoracic Surgery and Anesthesiology, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden
[c] Department of Thoracic and Cardio-Vascular Surgery, University Hospital Jean Minjoz, Besançon, France
[d] Department of Cardiothoracic Surgery, Henri Mondor University Hospital, AP-HP, Paris-Est University, Créteil, France
[e] Hamburg University Heart Center, Hamburg, Germany
[f] Department of Cardiothoracic Surgery, University Hospital Muenster, Muenster, Germany
[g] Division of Cardiac Surgery, University of Parma, Parma, Italy
[h] Cardiac Surgery, Heart and Lung Center, Helsinki University Central Hospital, Helsinki, Finland
[i] Division of Cardiothoracic and Vascular Surgery, Pontchaillou University Hospital, Rennes, France
[j] Division of Cardiac Surgery, Ospedali Riuniti, Trieste, Italy
[k] Department of Cardiac Surgery, Centro Cardiologico–Fondazione Monzino IRCCS, University of Milan, Milan, Italy
[l] Division of Cardiovascular Surgery, Verona University Hospital, Verona, Italy
[m] Cardiovascular Center, Paracelsus Medical University, Nuremberg, Germany
[n] Saud Al-Babtain Cardiac Center, Ministry of Health, Dammam, Saudi Arabia

ARTICLE INFO

Article history:
Received 7 December 2016
Received in revised form 16 February 2017
Accepted 24 March 2017
Available online xxxx

Keywords:
Coronary artery bypass
CABG
Post-cardiotomy
Heart failure
ECMO
ECLS
Extracorporeal membrane oxygenation
Extracorporeal life support

ABSTRACT

Background: The evidence of the benefits of using venoarterial extracorporeal membrane oxygenation (VA-ECMO) after coronary artery bypass grafting (CABG) is scarce.
Methods: We analyzed the outcomes of patients who received VA-ECMO therapy due to cardiac or respiratory failure after isolated CABG in 12 centers between 2005 and 2016. Patients treated preoperatively with ECMO were excluded from this study.
Results: VA-ECMO was employed in 148 patients after CABG for median of 5.0 days (mean, 6.4, SD 5.6 days). In-hospital mortality was 64.2%. Pooled in-hospital mortality was 65.9% without significant heterogeneity between the centers (I^2 8.6%). The proportion of VA-ECMO in each center did not affect in-hospital mortality ($p = 0.861$). No patients underwent heart transplantation and six patients received a left ventricular assist device. Logistic regression showed that creatinine clearance ($p = 0.004$, OR 0.98, 95% CI 0.97–0.99), pulmonary disease ($p = 0.018$, OR 4.42, 95% CI 1.29–15.15) and pre-VA-ECMO blood lactate ($p = 0.015$, OR 1.10, 95% CI 1.02–1.18) were independent baseline predictors of in-hospital mortality. One-, 2-, and 3-year survival was 31.0%, 27.9%, and 26.1%, respectively.
Conclusions: One third of patients with need for VA-ECMO after CABG survive to discharge. In view of the burden of resources associated with VA-ECMO treatment and the limited number of patients surviving to discharge, further studies are needed to identify patients who may benefit the most from this treatment.

1. Introduction

Acute heart failure after cardiac surgery is associated with high early mortality [1]. In these patients, venoarterial extracorporeal membrane oxygenation (VA-ECMO) is used as a rescue strategy without evidence of its benefits on the early and late outcome [2]. There is scarce data regarding postoperative VA-ECMO treatment after coronary artery bypass

☆ **Statement of authorship:** All the authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

* Corresponding author at: Department of Surgery, Oulu University Hospital, P.O. Box 21, 90029 Oulu, Finland.
E-mail address: fausto.biancari@oulu.fi (F. Biancari).

http://dx.doi.org/10.1016/j.ijcard.2017.03.120
0167-5273/

grafting (CABG). In this study, we investigated the outcomes of patients who underwent CABG and were postoperatively treated with VA-ECMO due to cardiac failure in 12 centers.

2. Methods

2.1. Patient population and data collection

Patients who received VA-ECMO due to cardiac or respiratory failure after isolated CABG at 12 centers from September 2005 to June 2016 were included in the present analysis. Preoperative and intraoperative characteristics were retrospectively collected in a dedicated datasheet. Follow-up information was collected by direct contact with the patients or their general practitioners, or by using medical records or national registry data. This study was approved by the Institutional Review Board (IRB) of the participating centers or a regional ethics committee, and it was not financially supported. Informed consent was collected in institutions where it was required by the internal IRB, otherwise it was waived.

Adult patients who required VA-ECMO treatment for acute cardiac or respiratory failure occurring within seven days after isolated CABG procedure were included in this analysis. Patients who were on VA-ECMO treatment before isolated CABG were excluded. Baseline characteristics were defined according to the EuroSCORE definition criteria [3]. Perioperative bleeding was stratified according to the E-CABG criteria [4]. The primary outcome of this study was in-hospital and mid-term mortality (1, 2, and 3 years).

3. Statistical analysis

Statistical analysis was performed using the SPSS v. 23.0 statistical software (IBM Corporation, 1 New Orchard Road Armonk, New York, USA) and the freely available software Meta-Analyst (http://www.cebm.brown.edu/openmeta/, accessed on October 20, 2016). No attempt to replace missing values was made. Continuous variables are reported as the median and mean with standard deviation (SD). Nominal variables are reported as counts and percentages. In view of the uneven proportion of treated patients in the participating centers, in-hospital mortality was pooled using a random-effects method and adjusted for the effect of proportion of VA-ECMO of each participating institution in meta-regression. Fisher exact test, Chi-square test, Mann-Whitney test and Kruskal-Wallis test were used for univariate analysis. C-statistics were performed to assess the predictive ability of continuous variables on the outcomes. Logistic regression was performed to identify predictors of in-hospital mortality by including in to the regression model all pre-VA-ECMO variables with $p < 0.2$ in univariate analysis. Survival was estimated by the Kaplan-Meier method. All tests were two-sided with the alpha level set at 0.05 for statistical significance.

4. Results

4.1. Baseline characteristics

One-hundred and forty-eight patients out of 24,527 patients (0.6%) required VA-ECMO after isolated CABG and their baseline characteristics are summarized in Table 1. Proportions of the patients were unevenly distributed between the centers (range, 0.2–1.4%). Only 24.3% of the patients were <60 years old, whereas 36.5% of the patients were ≥70 years old and 13.5% were ≥75 years old. The proportion of patients aged 70 years old varied significantly between institutions from 0% to 58.3% ($p = 0.005$). Four centers did not use this therapy in any patient aged 70 years or older. The highest proportion of patients aged 70 years or older was treated in the institution with the largest volume of patients (28 out of 48 patients). Elective procedure was performed in 12.8% of the patients (Table 2). The mean Syntax score was 32 (SD 13) and the EuroSCORE II was 19.2% (Table 1).

4.2. VA-ECMO data

VA-ECMO was inserted at the time of the surgery in 51.4% of the cases (Table 3). The mean delay to VA-ECMO was 17 (SD 30) hours. Left ventricular venting was inserted in 5 patients (3.4%), through the right superior pulmonary vein in three cases, through the left ventricle apex in one case and through the pulmonary artery in one case. Central cannulation was employed in 39.0% of the patients. VA-ECMO treatment lasted ≤3 days in 38.5% of the patients, 4–6 days in 19.6%, 7–10 days in 20.9% and >10 days in 20.9%. During a median of 5 days (mean, 6.4, SD 5.6 days) of treatment on VA-ECMO, the oxygenator was changed in 19.6% of the cases. Seventy-two patients (48.6%) were weaned from ECMO. Aortic cannulation was associated with a non-significant increased risk of reoperation for bleeding (49.2% vs. 37.1%, $p = 0.145$) and a larger amount of RBC transfusion (mean, 23.2, SD 21.0 vs. 13.3, SD 12.4 units, $p = 0.002$).

4.3. Postoperative mortality

In-hospital mortality was 64.2% (95 out of 148 patients) and ranged from 37.5% to 100% in different institutions ($p = 0.376$, Suppl. Fig. 1). Pooled proportion of mortality was 65.9% without significant heterogeneity between the centers (I^2 8.6%) (Suppl. Fig. 1). The proportion of VA-ECMO per institution was not associated with in-hospital mortality (meta-regression, $p = 0.861$).

In-hospital mortality was significantly lower in those patients with prolonged VA-ECMO treatment (≤3 days treatment: 89.5%, 4–6 days: 44.8%, 7–10 days: 58.1% and >10 days: 41.9%, respectively, $p < 0.0001$).

Advanced age did not affect in-hospital mortality. However, among patients aged 70 years or older, the lowest in-hospital mortality rate (57.1%) was observed in the center with the highest prevalence of septuagenarians (58.3%), but such a difference did not reach statistical significance ($p = 0.546$).

The mean left ventricular ejection fraction at discharge of 49 hospital survivors was 38.8% (SD 11.3%), and nine of them had a left ventricular ejection fraction ≥50%. Survival at 1, 2, and 3 years was 31.0%, 27.9% and 26.1%, respectively (Suppl. Fig. 2).

Pre-VA-ECMO lactate levels (area under the ROC curve 0.607, 95% CI 0.511–0.704) and peak lactate levels during VA-ECMO (area under the ROC curve 0.735, 95% CI 0.653–0.817) were predictive of in-hospital death in univariate analysis. Patients with pre-VA-ECMO blood lactate >2.0 mmol/L (69.0% vs. 48.0%, $p = 0.046$, crude OR 2.41, 95% CI 1.00–5.79) and peak lactate levels during VA-ECMO >6.0 mmol/L (83.6% vs. 44.9%, $p \leq 0.0001$, crude OR 6.23, 95% CI 2.86–13.59) had a significantly higher risk of in-hospital death.

Major neurological complications after the surgery (embolic stroke, hemorrhagic stroke and global cerebral ischemia) were also associated with a significantly increased in-hospital mortality (82.9% vs. 58.4%, $p = 0.008$, crude OR 3.442, 95% CI 1.324–8.947).

Logistic regression (Hosmer-Lemeshow's test: $p = 0.566$, area under the ROC curve: 0.73, 95% CI 0.64–0.82) showed that creatinine clearance ($p = 0.004$, OR 0.98, 95% CI 0.97–0.99), pulmonary disease ($p = 0.018$, OR 4.42, 95% CI 1.29–15.15) and pre-VA-ECMO blood lactate ($p = 0.015$, OR 1.10, 95% CI 1.02–1.18) were independent baseline predictors of in-hospital mortality.

4.4. Secondary outcomes

The median in-hospital stay was 14 days (mean, 23.1, SD 41.1 days) and the median stay in the intensive care unit was 10 days (mean, 15.2, SD 17.6 days). A major neurological event (ischemic stroke, hemorrhagic stroke and/or global cerebral ischemia) occurred after the surgery in 23.6% of the patients, adult respiratory distress syndrome in 14.9%, acute kidney injury requiring dialysis in 45.3%, repeat coronary revascularization in 8.8%, upper limb ischemia in 1.4% and lower limb ischemia in 10.8% of cases. Sternal wound infection was observed in 12.8% of the patients. Surgery for gastrointestinal complications was required in 10.8% of the patients (Table 4).

Perioperative bleeding was significant in a large number of patients as 81.8% of them required reoperation for excessive bleeding and/or transfusion of >4 units of red blood cells (E-CABG bleeding grades 2–3). Reoperation for excessive mediastinal bleeding was performed

Please cite this article as: F. Biancari, et al., Venoarterial extracorporeal membrane oxygenation after coronary artery bypass grafting: Results of a multicenter study, Int J Cardiol (2017), http://dx.doi.org/10.1016/j.ijcard.2017.03.120