



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



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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.

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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

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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 $\geq 50\%$. 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

Table 1
Baseline characteristics.

Baseline variables	Overall series	Hospital survivors 53 patients	In-hospital deaths 95 patients	p-Value
Age (years)	65.4 (9.4)	64.4 (9.8)	65.9 (9.2)	0.357
<60	36 (24.3)	13 (24.5)	23 (24.2)	0.879
60–69	58 (39.2)	22 (41.5)	36 (37.9)	
>69	54 (36.5)	18 (34.0)	36 (37.9)	
Females	32 (21.6)	9 (17.0)	23 (24.2)	0.306
Hemoglobin (g/L)	126 (2.6)	13.1 (2.5)	12.3 (2.1)	0.030
Platelets (10 ⁹ /L)	220 (93)	215 (82)	223 (98)	0.726
eCCr (mL/min)	72 (34)	83 (34)	66 (32)	0.001
Dialysis	6 (4.2)	1 (1.9)	5 (5.4)	0.311
Pulmonary disease	25 (16.9)	5 (9.4)	20 (21.1)	0.070
Diabetes	59 (39.9)	21 (39.6)	38 (40.0)	0.964
Stroke	11 (7.4)	3 (5.7)	8 (8.4)	0.539
Extracardiac arteriopathy	67 (45.3)	26 (49.1)	41 (43.2)	0.489
Atrial fibrillation	18 (12.2)	7 (13.2)	11 (11.6)	0.771
Previous PCI	44 (29.7)	17 (32.1)	27 (28.4)	0.641
Previous cardiac surgery	5 (3.4)	0	5 (5.3)	0.160
Left ventricular ejection fraction				0.642
31–50%	51 (34.7)	19 (35.8)	32 (34.0)	
21–30%	30 (20.4)	11 (20.8)	19 (20.2)	
<21%	30 (20.4)	8 (15.1)	22 (23.4)	
Diagnosis				0.746
Stable angina	40 (27.0)	16 (30.2)	24 (25.3)	
Unstable angina	16 (10.8)	6 (11.3)	10 (10.5)	
NSTEMI	26 (17.6)	7 (13.2)	19 (20.0)	
STEMI	66 (44.6)	24 (45.3)	42 (44.2)	
Complication after PCI	15 (10.1)	3 (5.7)	12 (12.6)	0.258
Critical preoperative status	83 (56.1)	32 (60.4)	51 (53.7)	0.491
Preop. tracheal intubation	19 (12.8)	4 (7.5)	15 (15.8)	0.202
Preoperative IABP	22 (14.9)	9 (17.0)	13 (13.7)	0.634
Ventricular arrhythmias	31 (24.0)	8 (17.0)	23 (28.0)	0.158
Out-of-hospital cardiac arrest	10 (6.8)	3 (5.7)	7 (7.4)	1.000
Ventricular septal defect	5 (3.4)	1 (1.9)	4 (4.2)	0.655
Unconsciousness	16 (10.8)	5 (9.4)	11 (11.6)	0.687
Coronary artery status				
Left main stenosis	77 (52.0)	30 (56.6)	47 (49.5)	0.493
Left main stenosis equivalent	18 (12.2)	8 (15.1)	10 (10.5)	0.440
Occlusion of LAD and Cx	9 (6.1)	4 (7.5)	5 (5.3)	0.722
No. diseased vessels	2.7 (0.6)	2.8 (0.5)	2.7 (0.6)	0.419
Syntax score	32.0 (13.1)	33.2 (13.7)	31.3 (12.9)	0.479
EuroSCORE II (%)	19.2 (17.7)	18.4 (19.3)	19.5 (16.9)	0.392

Continuous variables are reported as mean and standard deviation (in parentheses). Categorical variables are reported as absolute number and percentages (in parentheses). Clinical variables are reported according to the EuroSCORE II definition criteria [3]. eCCr: estimated creatinine clearance rate; PCI: percutaneous coronary intervention; NSTEMI: non ST-elevation myocardial infarction; STEMI: ST-elevation myocardial infarction; IABP: intra-aortic balloon pump; LAD: left anterior descending artery; Cx: circumflex artery.

in 51.9% of patients. Patients received a median of 11 units of red blood cells (mean, 17, SD 17 units), 4 units of fresh frozen plasma (mean, 14, SD 21 units) and 3 units of platelets (mean, 28, SD 72 units). The median postoperative nadir hematocrit was 23.0% (mean 21.0, SD 11.2%) and the median nadir hemoglobin was 74 g/L (mean, 76, SD 14 g/L).

No heart transplantation was performed in this series. Six patients received a left ventricular assist device and two of them (33.3%) died during the in-hospital stay. One patient died 26 days after surgery. The remaining three patients receiving a left ventricular assist device were alive at 35, 323 and 993 days, respectively, after the primary surgery.

Table 2
Operative data.

Operative variables	Overall series	Hospital survivors 53 patients	In-hospital deaths 95 patients	p-Value
Urgency status				0.749
Elective	19 (12.8)	5 (9.4)	14 (14.7)	
Urgent	34 (23.0)	14 (26.4)	20 (21.1)	
Emergency	80 (54.1)	29 (54.7)	51 (53.7)	
Salvage	15 (10.1)	5 (9.4)	10 (10.5)	
Revascularization technique				0.518
On-pump with arrest	131 (88.5)	46 (86.8)	85 (89.5)	
Off-pump	7 (4.7)	2 (3.8)	5 (5.3)	
Heart beating on perfusion	9 (7.5)	4 (7.5)	5 (5.9)	
Conversion to on-pump with arrest	1 (0.7)	1 (1.9)	0	
At least one mammary artery graft	120 (81.1)	42 (79.2)	78 (82.1)	0.670
Bilateral mammary a. grafts	49 (33.1)	14 (26.4)	35 (36.8)	0.196
Radial artery graft	3 (2.0)	0	3 (3.2)	0.553
Number of distal anastomoses	3.0 (1.1)	3.1 (1.1)	2.9 (1.2)	0.219
Cross-clamping time (min)	68 (32)	66 (23)	69 (37)	0.951
Cardiopulmonary bypass time (min)	146 (76)	137 (68)	151 (80)	0.350

Continuous variables are reported as mean and standard deviation (in parentheses). Categorical variables are reported as absolute number and percentages (in parentheses). Urgency status is reported according to the EuroSCORE II definition criteria [3].

Table 3
ECMO and postoperative bleeding data.

	Overall series	Hospital survivors 53 patients	In-hospital deaths 95 patients	
<i>ECMO data</i>				
Primary indication to ECMO				0.266
Low cardiac output	124 (83.8)	46 (86.8)	28 (82.1)	
Cardiac arrest	21 (14.2)	5 (9.4)	16 (16.8)	
Hypoxia	3 (2.0)	2 (3.8)	1 (1.1)	
Delay to ECMO (hours)	17 (30)	20 (37)	15 (26)	0.570
ECMO inserted at surgery	76 (51.4)	25 (47.2)	51 (53.7)	0.447
<i>Arterial cannulation sites</i>				
Aorta	59 (39.9)	20 (37.7)	39 (41.1)	0.693
Femoral artery	82 (55.4)	30 (56.6)	52 (54.7)	0.827
Distal perfusion	66 (44.6)	25 (47.2)	41 (43.2)	0.638
Axillary artery	19 (12.8)	7 (13.2)	12 (12.6)	0.920
Switch to peripheral cannulation	5 (3.4)	3 (5.7)	2 (21.1)	0.329
Left ventricular venting	5 (3.4)	3 (5.7)	2 (2.1)	0.350
Change of oxygenator	29 (19.6)	12 (22.6)	17 (17.9)	0.485
<i>ECMO duration (days)</i>				
<3 days	6.4 (5.6)	9.1 (6.1)	4.9 (4.8)	<0.0001
3–5 days	57 (38.5)	6 (11.3)	51 (53.1)	<0.0001
6–10 days	29 (19.6)	16 (30.2)	13 (13.7)	
>10 days	31 (20.9)	13 (24.5)	18 (18.9)	
>10 days	31 (20.9)	18 (34.0)	13 (13.7)	
Pre-ECMO SvO ₂ (%)	71 (24)	75 (24)	68 (24)	0.097
Pre-ECMO lactate (mmol/L)	7.4 (5.5)	6.0 (4.6)	8.1 (5.8)	0.036
Peak-ECMO lactate (mmol/L)	8.1 (6.3)	4.9 (3.5)	9.9 (6.7)	0.036
Postop. IABP	47 (32.0)	13 (29.5)	34 (33.0)	0.680
Postop. IABP with ECMO	38 (25.9)	11 (25.0)	27 (26.2)	0.878
<i>Postoperative bleeding data</i>				
Nadir hematocrit (%)	21.0 (11.2)	20.4 (8.8)	21.3 (12.4)	0.566
Nadir hemoglobin (g/L)	75.8 (13.6)	77.2 (12.7)	75.0 (14.1)	0.384
Transfused RBC units	17 (17)	15 (13)	19 (19)	0.800
Transfused FFP units	14 (21)	10 (14)	17 (24)	0.424
Transfused platelet units	28 (72)	15 (46)	34 (83)	0.902
Reoperation for bleeding	62 (41.9)	23 (43.4)	39 (41.1)	0.782
<i>E-CABG bleeding grades</i>				
0	5 (3.4)	1 (1.9)	4 (4.3)	0.656
1	20 (13.7)	6 (11.5)	14 (14.9)	
2	46 (31.5)	15 (28.8)	31 (33.0)	
3	75 (51.4)	30 (57.7)	45 (47.9)	

Continuous variables are reported as mean and standard deviation (in parentheses). Categorical variables are reported as absolute number and percentages (in parentheses). ECMO: extracorporeal membrane oxygenation; CPB: cardiopulmonary bypass; SvO₂: mixed oxygen vein saturation; RBC: red blood cell; FFP: fresh frozen plasma; IABP: intra-aortic balloon pump.

5. Discussion

The results of this multicenter retrospective study confirmed the efficacy of VA-ECMO as a salvage treatment in one third of patients experiencing acute cardiac or respiratory failure after CABG [1,5–8].

This study allowed an analysis of different scenarios underlying the conditions requiring VA-ECMO early after CABG. In fact, we observed that several of these procedures were performed on elective basis or for stable angina. This observation suggests that not infrequently acute heart and respiratory failure may occur after CABG also in low-risk patients [9].

In this series, only 10% of the patients underwent coronary angiography and 8% underwent a repeat coronary revascularization procedure. These findings suggest that technical failure or incomplete coronary revascularization was suspected in a small number of patients. These issues, though of infrequent occurrence, are of clinical importance because if left unrecognized, they may jeopardize any attempt of salvaging the critically ischemic myocardium. Indeed, in view of the stable preoperative conditions of many of these patients, the use of multiple arterial grafts and the diffuse nature of coronary artery disease as stratified by the Syntax score, clinicians should have suspected graft failure, incomplete coronary revascularization or complications of the native coronary arteries in a larger number of patients. Indeed, a strategy of early re-coronarography and repeat revascularization has been demonstrated effective in preventing severe myocardial ischemia and improving outcome in patients with signs of postoperative myocardial infarction after CABG [10,11].

This study showed that salvage of patients after CABG was attempted also in elderly patients (37% of patients were aged 70 years or older) with similar results compared to younger patients. Therefore, the present data suggest that VA-ECMO could be used with success also in the elderly. It is worth noting that the outcome in the elderly might have been affected by differences in ECMO expertise and patient selection. In fact, the proportion of patients aged 70 years or older varied significantly between institutions and the largest proportion of these elderly patients was treated in the institution with the largest volume (28 out of 48 patients) and reported the lowest in-hospital mortality (57.1%). Therefore, it is likely that such an excellent outcome among elderly could not be replicated in centers without adequate ECMO expertise. In fact, previous studies showed that increased age is associated with a significantly higher early mortality after postcardiotomy VA-ECMO, but there is a lack of specific data in patients who underwent isolated CABG [1,7,8,12]. Indeed, most of series reported on the use of postcardiotomy VA-ECMO only in relatively young patients [8,13].

The uneven proportion of patients treated with VA-ECMO suggests that its use could be effectively implemented also in smaller centers if patient selection is strict. In fact, some centers are prone to provide ECMO treatment in selected patients based on their young age and absence of severe comorbidities. However, the policy of offering VA-ECMO treatment to patients with increased age and critical preoperative conditions revealed to provide satisfactory early and mid-term results.

Pre-ECMO and peak levels of blood lactate on VA-ECMO were observed being of prognostic importance, but it remains unclear whether

Table 4
Outcomes.

Outcomes	No. (%) / mean (SD)
In-hospital death	95 (64.2)
In-hospital stay (days)	23.1 (41.1)
Intensive care unit stay (days)	15.2 (17.6)
Major neurological event	35 (23.6)
Ischemic stroke	22 (14.9)
Hemorrhagic stroke	11 (7.4)
Global cerebral ischemia	14 (9.5)
Tracheostomy	34 (25.6)
Pneumonia	51 (34.7)
Adult respiratory distress syndrome	22 (14.9)
Sepsis	36 (24.3)
Renal replacement therapy	67 (45.3)
Ventricular septal rupture	1 (0.7)
Ventricular wall rupture	1 (0.7)
Coronary angiography	15 (10.2)
Additional cardiac procedures	
Percutaneous coronary intervention	7 (4.7)
Redo coronary bypass	5 (3.4)
Mitral valve procedure	3 (2.1)
Aortic valve replacement	1 (0.7)
Ventricular septal defect repair	1 (0.7)
Heart transplantation	0
Left ventricle assist device	6 (4.1)
Upper limb ischemia	2 (1.4)
Lower limb ischemia	16 (10.8)
Lower limb revascularization	4 (2.7)
Major lower limb amputation	1 (0.7)
Sternal wound infection	19 (12.8)
Superficial	13 (8.8)
Deep	6 (4.1)
Mediastinitis	0
Pancreatitis	3 (2.0)
Liver injury	81 (54.7)
Gastrointest. complications requiring surgery	16 (10.8)
Multiorgan failure	54 (36.5)

SD: standard deviation.

it could be a target of interventions in these critically ill patients [1]. So far, it remains the most clinically relevant biomarker in the assessment in VA-ECMO patients [8]. It is worth noting, that particularly pre-VA-ECMO blood lactate may be of prognostic importance as demonstrated by logistic regression. In presence of preoperative renal failure and pulmonary disease, the prognosis of patients with increased blood lactate may be dismal and this may contraindicate postcardiotomy VA-ECMO. However, these findings should be view considering the small size of this series and should be confirmed by future studies.

Perioperative bleeding is recognized as a significant problem in postcardiotomy VA-ECMO patients. In this series, 42% of the patients required reoperation for bleeding and a mean of 17 units of transfused red blood cells was transfused in these patients. These figures confirm the severity of this complication and are likely to be responsible for other secondary end-organ complications. Although the retrospective nature of this study prevented an evaluation of the degree of heparinization on VA-ECMO, most of these patients were treated under almost normal activated clotting times. This could explain why the oxygenators were changed in 20% of these patients. Despite this, severe bleeding is often profuse during the early hours after surgery. This has led some centers to prefer central cannulation because of the frequent need for reoperation for surgical hemostasis and removal of clots from the pericardium [1].

Isolated reports [14] as well as the results of this series indicate that prolonged treatment on VA-ECMO may be beneficial in selected patients. However, analysis of the prognostic impact of the duration of ECMO therapy may be biased by its early discontinuation in patients with significant comorbidities and signs of irreversible metabolic derangements and/or severe end-organ injury as well as in those who experienced early recovery of cardiopulmonary function. Still, these findings suggest that a careful evaluation of the potential benefits of

prolonged VA-ECMO support should be seriously considered before discontinuing invasive treatment of patients who are not fully recovered and without signs contraindicating its prolonged use.

In this series, IABP and left ventricular venting were sporadically used during VA-ECMO. The use of IABP is considered to improve coronary perfusion and decrease left ventricular overload [15,16]. Clinical studies confirmed this beneficial effect on the coronary flow [17], even if a study by Schroeter et al. [18] suggested that IABP may improve coronary flow only during antegrade ECMO. Despite these evidences, a recent large clinical study demonstrated a detrimental effect of IABP during postcardiotomy VA-ECMO [19]. Although the combined use of IABP and VA-ECMO may be theoretically beneficial, there is a need for further experimental and clinical studies to demonstrate its safety and efficacy. Similarly, the benefit of using a left ventricular venting in this setting is still unproven.

In this study, no patient underwent heart transplantation, whereas ventricular assist device was inserted in only six patients. Indeed, most of studies on postcardiotomy VA-ECMO did not report on any patient undergoing heart transplantation or ventricular assist device as an ultimate salvage strategy. However, some studies demonstrate that a few of these patients may survive after heart transplantation or ventricular assist device [20,21]. The severity of end-organ injury of patients on ECMO as well as the difficulties in proper allocation of organs and resources may explain the limited use of these treatments in postcardiotomy VA-ECMO patients. Future studies should assess the early and late outcome of patients undergoing heart transplantation or ventricular assist device implantation to evaluate whether these treatments are justified in the acute setting after cardiac surgery.

Analysis of the costs of VA-ECMO treatment after CABG was not performed because we had evidence of significant differences in terms of costs of this therapy in the participating centers. However, in view of the proved benefits of this treatment in one third of patients and the small proportion of patients needing it, VA-ECMO may be a cost-effective salvage strategy. Still, there is a need of standardized criteria for adequate resource allocation towards patients who may most benefit of post-cardiotomy VA-ECMO support.

There are some limitations related to this study that need to be acknowledged. First, the retrospective nature is a major limitation of this analysis. However, data on large number of baseline, perioperative and ECMO-related parameters were retrieved from these patients and allowed a reliable assessment of the baseline risk and outcomes of these patients. Second, this study collected data from twelve centers of cardiac surgery with possibly significant differences in the revascularization strategy and perioperative treatment. Furthermore, differences in the availability of, criteria for, and experience in mechanical circulatory support in cardiac surgery patients might exist between the centers. However, pooled analysis suggested that in-hospital mortality was not heterogeneously distributed between the centers. Third, the small size of this series prevented an adequate analysis of interinstitutional differences in terms of outcome. We attempted to reduce the bias possibly related to volume and expertise in ECMO therapy by pooling the data using a meta-analytic approach, which took in to account the volume of patients treated in each center. However, the pooled proportion of in-hospital mortality was similar to the crude proportion (65.9% vs. 64.2%) without a statistically significant heterogeneity (I^2 8.6%). Meta-regression further confirmed that the proportion of VA-ECMO in each center did not affect the in-hospital mortality. Fourth, we do not have data on the function of the right ventricle, which prevented analysis of the prognostic importance of failing right ventricle either associated or not with left ventricular failure.

In conclusion, this study confirmed that VA-ECMO allows discharge from the hospital in one third of patients with severe acute heart or respiratory failure after CABG. In view of the burden of resources associated with VA-ECMO treatment, prospective multicenter studies are advocated to better assess the early and long-term outcome of these patients and to evaluate the value of IABP, left ventricular venting and

postoperative angiography and repeat revascularization in this setting. Furthermore, future studies should establish standard criteria for adequate resource allocation towards patients who may most benefit of this treatment.

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Conflicts of interest

The authors state that they do not have any conflicts of interest related with this study.

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