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Original Article

Central extracorporeal membrane oxygenation as a bridge to recovery in patients with myocardial stunning after coronary artery bypass grafting

Mohamed Abdel Fouly

Department of Cardiothoracic Surgery, Cairo University, Giza, Egypt

Abstract

Background: The role of central extracorporeal membrane oxygenation (ECMO) post coronary artery bypass grafting (CABG) in older patients is debatable. The objectives of our study were to investigate the role of central veno-arterial (V-A) ECMO as a bridge to recovery in patients with myocardial stunning after CABG and its effect on mortality in this group of patients.

Methods: Seventy-five patients had central ECMO as a bridge to recovery after CABG because of myocardial stunning; 45 of them (60%) had survived (group 1), and mortality occurred in 30 patients (40%) (group 2). Preoperative risk factors such as hypertension, stroke, and renal failure were comparable between groups. In non-survivors, left main disease was more common (19 (63.3%) vs. 13 (28.9%); p= 0.003) and SYNTAX score was higher (Median 33 (25th- 75th percentiles); 33 (29- 35) vs. 26 (25- 32); p< 0.001).

Results: Cross-clamp time was shorter in group 1 (58 minutes; (52-62) vs 115.5 minutes; (84- 161) in group 2; p< 0.001). Cardiopulmonary bypass time was shorter in group 1 compared to group 2 (83; (70-90) vs. 155.5; (60 -120) minutes; p< 0.001). ECMO duration was longer in group 2 (6 days; (6-7) vs. 3 days; (3-4); p<0.001). Stroke occurred in 10 patients (33.33%) in group 2 vs. 1 patient (2.22%) in groups 1; p< 0.001. Longer cross-clamp (OR: 1.61, 95% CI: 1.11- 2.31, p= 0.011) and bypass time (OR: 1.76; 95% CI: 1.57- 1.99; p= 0.048) predicted postoperative mortality.

Conclusion: Central ven-arterial extramembrane oxygenation can be used as a bridge to recovery in patients with stunned myocardium post coronary bypass grafting, especially in centers where heart transplantation and ventricular assist devices are not available.

KEYWORDS

Central extracorporeal membrane oxygenation; Coronary artery bypass grafting; Mechanical circulatory

Article History

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Introduction

Central extracorporeal membrane oxygenation (ECMO) provides physiological flow to the body in an antegrade patten; in addition, it offloads the left ventricle and avoids the complications of peripheral ECMO, including leg ischemia [1]. Stunned myocardium is a viable myocardium salvaged by coronary reperfusion with prolonged postischemic dysfunction after reperfusion, and this must be differentiated from hibernating myocardium, which improves after reperfusion [2].

The role of ECMO as a bridge to recovery in patients with stunned myocardium after coronary artery bypass grafting (CABG) is the subject of ongoing research. High-risk patients present to CABG increasingly, and the risk of mortality is high,

Corresponding author: Mohamed Abdel Fouly mhafez1982.gf@gmail.com

especially in patients with left ventricular dysfunction and left main disease. The impact of ECMO on those patients is controversial, and factors affecting mortality vary widely. Therefore, we investigated the role of central veno-arterial (V-A) ECMO as a bridge to recovery in post-CABG myocardial stunning and its effect on mortality in this group of patients.

Patients and Methods:

Study design and patients:

This is a retrospective cohort study that was conducted from January 2010 till January 2020. During this period, 75 patients had central V-A ECMO as a bridge to recovery post-CABG myocardial stunning; 60% of them (n=45) had survived and successfully weaned from ECMO (group 1), and 40% of them (n=30) died (group 2). The data of those 75 patients were collected, and patients were assigned to either group according to the outcome.

The data collected included preoperative variables: age, sex, left main disease, SYNTAX score, and comorbidities, such as hypertension, preoperative stroke, and renal failure. Operative data included ischemic and bypass times, and the number of coronary bypass grafts. Postoperative data included complications from central ECMO as disseminated intravascular coagulation (DIC), acute kindy injury (AKI), intracerebral hemorrhage as well as the duration of ECMO.

Data collection was approved by the Institutional Review Board, and patients' consent was waived.

We included patients who had elective three or four vessels CABG, including left main disease with depressed myocardial function (ejection fraction (EF) < 40%) and patients aged more than 50 years. Postoperatively, central ECMO was inserted after the failure of weaning from cardiopulmonary bypass (CPB) with maximum inotropes and intra-aortic balloon pump (IABP) insertion. V-A ECMO was inserted centrally, and the sternum was left open.

We excluded young aged patients less than 50 years old because, in those patients, ECMO would be a bridge for either LVAD or heart transplant. Patients who had an emergency CABG or a concomitant procedure as aortic valve surgery or patients with ischemic mitral regurge and off-pump CABG were excluded. We excluded patients with right ventricular (RV) failure post-CABG because they were candidates for biventricular assisted devices (BIVAD).

Surgical procedures:

Central ECMO was performed through direct surgical cannulation of the right atrium and aorta, which were already done during the primary procedure. Left ventricular (LV) decompression was performed with placing a vent via the right superior pulmonary vein (direct LV apical vent was the second option) [3]. The size of the cannulae depends on the body surface area, the calculated flow of the ECMO. Lactate levels were followed up to monitor tissue perfusion during ECMO perfusion. The cannulae were secured in their position to prevent cannulae displacement. Fixation of the cannulae was done to the skin at different levels, and the patients were heavily sedated with a muscle relaxant to avoid body movement with the possibility of decannulation [4].

Table 1: Preoperative patients' characteristics. Continuous variables are presented as median (25th and 75th percentiles) and categorical variables as number and percent

	Survivors (Group 1; n=45)	Non-survivors (Group 2; n=30)	p-value
Age (Years)	67 (63- 69)	66 (64- 70)	0.97
Male	30 (66.67%)	20 (66.67%)	>0.99
Left main disease	13 (28.89%)	19 (63.33%)	0.003
SYNTAX score	26 (25- 32)	33 (29- 35)	<0.001
Hypertension	33 (73.33%)	21 (70%)	0.797
Stroke	4 (8.89%)	1 (3.33%)	0.642
Renal failure	2 (4.44%)	3 (10%)	0.383

At the end of the procedure, the chest was left open with an occlusive dressing or using a dacron patch, which facilitated reopening, especially if there were general ooze around the cannulae from anticoagulation. LV output was preserved by following the pulsatile wave of the native heart on the arterial monitor as ECMO flow was non-pulsatile. Follow up echocardiography was used to follow the LV ejection fraction as well as monitoring the recovery of myocardial function and guide us through the process of weaning.Continuous intravenous heparin was installed hourly with close monitoring of activated clotting time (ACT) and activated partial thromboplastin time (aPTT), which must be regularly done to avoid excessive bleeding from over anticoagulation or ECMO membrane clotting from inadequate anticoagulation [4].

Statistical Analysis

Continuous variables were presented as the 50th (median), 25th and 75th percentiles and were compared using the Wilcoxon rank-sum test. Nominal variables were presented as number and percent and were compared using the Chi-square or Fisher exact test when the expected frequency is less than 5.

Univariable logistic regression analysis was used to identify the factors affecting mortality. Variables with p-value <0.25 in the univariable analysis were included in a multivariable logistic regression analysis. The goodness of fit was tested with the Hosmer-Lemeshow test, and the p-value of the model was 0.99, indicating the suitability of the model. All analyses were performed using Stata 16 (Stata Corp- College Station- Texas- USA).

Results

Preoperative patients' characteristics:

Seventy-five patients had central ECMO as a bridge to recovery in post-CABG myocardial stunning; 45 of them survived and mortality occurred in 30 patients (40%). Preoperative variables were compared between both groups. No statistical significance was detected between both groups regarding preoperative risk factors as diabetes, hypertension, stroke, and renal failure. (Table 1) In non-survivors, left main disease was more common (19 (63.3%) vs. 13 (28.9%); p= 0.003) and SYNTAX score was higher (Median 33 (25th- 75th percentiles); 33 (29- 35) vs. 26 (25- 32); p< 0.001).

Operative data:

Cross-clamp and CPB times were statistically different between both groups where cross-clamp time in survivors' group was 58 minutes (25th-75th percentiles: 52-62) compared to that in the non-survivor group (median 115.5 minutes; 84-161). CPB time in survivors was 83 minutes (70-90) compared to 155.5 minutes (60 -120) in the non-survivors (Table 2).

Postoperative outcomes:

Longer duration of ECMO was recorded in non-survivors (median 6; 6-7 days) compared to 3 days in survivors (3-4). Causes of death were DIC (n= 14; 46.67%), stroke (n= 10; 33.33%) and renal failure (n= 10; 33.33%) (Table 3). Predictors of mortality are shown in Table 4.

Discussion

Postcardiotomy cardiogenic shock (PCCS) occurring after CABG is associated with high mortality [6, 7], and V-A ECMO has been utilized as a salvage mechanical circulatory support in those patients [8, 9]. The decisions of using such an invasive technique or its weaning remain controversial.

Table 2: Operative characteristics of the patients. Continuous variables are presented as median (25th and 75th percentiles) and categorical variables as number and percent

	Survivors (Group 1; n= 45)	Non-survivors (Group 2; n=30)	p-value
Cross-clamp time (minutes)	58 (52- 62)	115.5 (60 -120)	<0.001
CPB time (minutes)	83 (70 – 90)	155.5 (84- 161)	<0.001
Number of grafts	4 (3- 4)	4 (3- 4)	0.056

CPB: cardiopulmonary bypass

Table 3: Postoperative outcomes. Continuous variables are presented as median (25th and 75th percentiles) and categorical variables as number and percent

	Survivors (Group 1; n= 45)	Non-survivors (Group 2; n=30)	p-value
Renal failure	11 (24.44%)	10 (33.33%)	0.401
DIC	0	14 (46.67%)	<0.001
Stroke	1 (2.22%)	10 (33.33%)	<0.001
Duration of ECMO (Days)	3 (3- 4)	6 (6- 7)	<0.001

DIC: disseminated intravascular coagulation; ECMO: extracorporeal circulation

V-A ECMO in patients with refractory PCCS is used as a "bridge to recovery" or as a bridge to destination therapy with LVAD or orthotopic heart transplantation [10 – 12].Nevertheless, central ECMO itself carries a significant risk of morbidity, especially if prolonged [13]. In this study, we investigated the causes of post-CABG myocardial stunning and the relation between ischemic time and total bypass time to myocardial stunning beside the role of central ECMO as a bridge for recovery. Left main disease and high SYNTAX score, together with prolonged ischemic and bypass times, were associated with increased mortality.

In our study, we found that one of the most important predictors of myocardial stunning was ischemic and bypass times, and this was reported in the literature where Doenst and colleagues found that ischemic times greater than 30 min was associated with a steadily increasing mortality [14]. Furthermore, Al-Sarraf and coworkers found that high-risk patients (EuroScore ≥ 6) with ischemic times >90 minutes and those with ischemic times < 60 min and ≤ 90 minutes were respectively 4.7 and 3.1 times more prone to death than those with ischemic times ≤ 60 min [15]. It was noted that a large number of cases in the non-survivor group were with left main coronary artery stenosis this was explained with inadequate myocardial protection of these patients during aortic cross-clamping with the classic antegrade cardioplegia that will be unable to go through the left coronary artery system due to proximal obstruction in the left main trunk and this raises the importance of combining both techniques of antegrade and retrograde cardioplegia in dealing with those patients, and this was reported by Onorati and coworkers that the combined route of intermittent blood cardioplegia allows better results in left main stem disease [16] and it was similar to a retrospective study conducted by Bar and colleagues on patients undergoing CABG surgery with valve repair or replacement with long ischemic time and receiving antegrade followed by retrograde cardioplegia demonstrating that mortality was lower in these patients [17].

Table 4: Logistic regression analysis for factors affecting mortality

	Univariable analysis		Multivariable analysis	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age	0.99 (0.88- 1.12)	0.893	-	-
Gender	1 (0.37- 2.66)	0.99	-	-
Left main disease	4.25 (1.59- 11.37)	0.004	4.45 (0.1- 197.42)	0.44
SYNTAX score	1.29 (1.14- 1.47)	0.001	0.32 (0.88- 1.98)	0.18
Hypertension	0.85 (0.31- 2.36)	0.753	-	-
Renal failure	2.39 (0.37- 15.23)	0.357	-	-
Stoke	0.35 (0.037- 3.33)	0.363	-	-
Ischemic time	1.086 (1.04- 1.139)	0.001	1.61 (1.11- 2.31)	0.011
CPB	1.06 (1.029- 1.08)	0.001	1.76 (1.57- 1.998)	0.048
Number of grafts	2.63 (0.97- 7.14)	0.058	0.051 (0.0005- 5.57)	0.214

CI: confidence interval; CPB: cardiopulmonary bypass; OR: odds ratio

Strong relation was realized between mortality and SYNTAX score because increased Syntax score denotes the degree of vessel stenosis and degree of calcification with more time consumed by the surgeon in distal grafting of the coronaries and consequently longer ischemic as well as bypass times. Central ECMO as a bridge for recovery in our center effectively reduced the mortality of post-CABG stunned myocardium to 40%, especially it was the only modality available in our center ten years back before the new era of LVAD and heart transplant, and this was confirmed in the literature by Gregoire and colleagues where sixty-five patients (47%) of his study had survived till discharged from ICU after central ECMO insertion [18].

In our center, criteria of weaning depend on a lot of parameters : (1) Hemodynamic assessments in the form of mean blood pressure >60 mmHg , cardiac index >2.4 L/min/m2 with, pulmonary capillary wedge pressure <18 mm Hg and central venous pressure <18 mmHg.(2) Echocardiographic parameters of LV function, such as LVEF, aortic velocity-time integral, and lateral mitral annulus peak systolic velocity together with the doppler parameters reflecting LV filling pressures (i.e., mitral velocities).

When dealing with ideal duration for V-A ECMO, there was a great controversy in literature about exact duration, but in our study, it was clear that early weaning of ECMO has an essential role in reducing the mortality, in the survivors group duration was 3 days compared to 6 days in non-survivors and this produced significant statistical effect on mortality and this goes hand in hand with what was mentioned by Myles and colleagues where survival was highest when weaning was done on the fourth day of ECMO and it decreased when going into the second week [19]. Additionally, the predictive value of ECMO duration has been recently discussed by Smith and coworkers in their Extracorporeal Life Support Organization (ELSO) registry analysis of almost 2700 patients submitted to VA-ECMO where the study showed that best survival was observed with VA-ECMO weaning at the fourth day of support [19]. Finally, the most common causes of death from the increased duration of ECMO were DIC, renal failure, and intracerebral hemorrhage from anticoagulation or part of hematological failure from SIRS.

Study limitations

The major limitations are the retrospective design and the small sample size as it's an expensive technique that requires trained personals including nurses, cardiac surgeons, intensivist as well as perfusionist with close monitoring and observation of this patient group for best outcome beside it needs more sophisticated techniques as LVAD or heart transplant for better outcome as central ECMO may be used as a bridge for other destination therapy not only bridge for recovery.

Conclusion

Central veno-arterial extracorporeal membrane oxygenation can be used as a bridge to recovery in patients with stunned myocardium post coronary bypass grafting, especially in centers where heart transplantation and ventricular assist devices are not available.

Conflict of interest: Authors declare no conflict of interest.

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