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Appropriate timing of veno-arterial extracorporeal membrane oxygenation initiation after cardiac surgery

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Abstract

Background Veno-arterial extracorporeal membrane oxygenation (VA-ECMO) can be initiated during cardiac surgery or later in ICU according to the hemodynamic profile and organ perfusion. Our aim was to study the appropriate timing of post-cardiotomy ECMO (PC-ECMO) initiation. We retrospectively analyzed 152 adult patients supported with PC-ECMO in our cardiac center between 2016 and 2022. The patients were divided into two groups: the intra-operative ECMO and the postoperative ECMO groups. The primary outcome was all-and-on-ECMO hospital mortality. The secondary outcomes included ECMO duration, new need for dialysis, cerebrovascular stroke, and length of ICU stay.

Results Our cohort analysis revealed that 81(53.3%) patients were intra-operatively supported with VA-ECMO while 71(46.7%) patients were postoperatively supported in ICU. The postoperative ECMO group had significantly lesser SAVE score ($p = 0.001$), higher SAVE risk classes ($p < 0.001$), and higher SOFA score ($p = 0.008$) compared to the intra-operative ECMO group. The postoperative ECMO group had significantly more frequent hospital mortality ($p = 0.003$), on-ECMO mortality ($p = 0.006$), cerebrovascular stroke ($p = 0.034$), acute renal failure requiring dialysis ($p < 0.001$), and lesser lactate clearance at 12 h ($p = 0.016$) and at 24 h ($p = 0.023$) compared to the intra-operative group. There were statistically insignificant differences between the two groups regarding post-ECMO hospital mortality, cerebral bleeding, limb ischemia, ECMO, and ICU duration. Postponed postoperative ECMO insertion was associated with an increased risk of death (HR 1.628, 95%CI 1.102–2.403, p =0.014) with cox-proportional hazard regression. Logistic multivariable regression showed that atrial fibrillation (OR 6.2, 95% CI 2.71–61.84, $p = 0.002$), initial SOFA score (OR 1.46, 95% CI 1.041–3.83, $p = 0.001$), and postoperative ECMO insertion (OR 1.93, 95% CI 1.04–8.73, $p = 0.031$) were the predictors of hospital mortality.

Conclusions Postponed ECMO insertion in critically sick patients was associated with increased mortality after cardiac surgery. Early intra-operative initiation of PC-ECMO may have the potential to improve outcomes after cardiac surgeries.

Keywords SAVE score, SOFA score, Lactate clearance, Extracorporeal membrane oxygenation, Mortality

Background

The use of veno-arterial extracorporeal membrane oxygenation (VA-ECMO) with cardiac surgery is common but its application depends on the cardiac surgeons and each center's policy and experience [1, 2]. Being an invasive procedure, resource-consuming, and associated with many morbidities, the decision to initiate

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post-cardiotomy VA-ECMO (PC-ECMO) is challenging to the surgeons to avoid unnecessary early mechanical support hoping that the clinical condition will improve by maximizing medical therapy [2–5]. To minimize the worse outcomes, ECMO should be initiated before the irreversible impaired tissue perfusion and multi-organ injury [6]. The complexity of patients undergoing cardiac surgery due to pre-operative risk profile, systematic effects of cardiopulmonary circulation, and operative complications makes the time to initiate VA-ECMO challenging. The decision to early start ECMO or wait longer with maximizing medical therapy is challenging with each patient developing post-cardiotomy shock. The objective of this study was to review all patients who underwent PC-ECMO in our center and whether the timing of ECMO (intra-operatively vs. postoperatively) affected the outcomes.

Methods

Study design and population

This was a retrospective single-center cohort study that enrolled all adult patients who were supported with VA-ECMO after cardiac surgery. The study was conducted in King Faisal Specialist Hospital and Research Center (KFSHRC) and was approved by the Institutional Review Board and given the reference number (2191042). All patients studied were ≥ 18 years old and received cardiac surgeries in KFSHRC and managed in the cardiac surgical intensive care unit between 2016 and 2022. We excluded all patients who had ECMO for non-surgical reasons and those who were referred on-ECMO from other centers.

ECMO initiation and scores

ECMO insertion was done by the cardiac surgeons in all patients either in the operation room or later in the ICU with refractory cardiogenic shock. We used the Survival after Veno-arterial ECMO (SAVE) and Sequential Organ Failure Assessment (SOFA) scores to evaluate our patients. The SAVE score was created in 2015 specifically to assess the patients before VA-ECMO initiation with a score range (– 35 to 17) and 5 risk classes [7]. The SAVE score consists of many variables (age and body weight of the patients, presence of renal, liver, and neurological dysfunctions, etiology of cardiogenic shock, peak inspiratory pressure, duration of invasive ventilation before ECMO, pre-ECMO arterial diastolic and pulse pressures, and occurrence of cardiac arrest). The SOFA score is a general score for critically ill patients and was tested in many patient groups including patients on VA-ECMO [8, 9]. The SOFA score consists of 6 variables (mean arterial blood pressure, serum bilirubin, platelet count, serum creatinine, PaO2/FiO2, Glasgow Coma Scale) and each one varies from – 4 to 4. It can be repeated every 48 h to assess organ function improvement or deterioration. We calculated SOFA score at 3 points; before ECMO initiation and then on the third and fifth days. The change of SOFA was calculated as the differences between the 3rd or 5th day and the initial score.

The studied variables and outcomes

The primary outcome was all-and-on-ECMO hospital mortality. The secondary outcomes included ECMO duration, a new need for dialysis, cerebrovascular stroke, and length of ICU stay. The pre-operative variables collected included age, diabetes mellitus, renal impairment, coronary and cerebrovascular diseases, underlying heart disease, and previous cardiotomy. The underlying heart diseases included ischemic cardiomyopathy due to coronary artery disease, adult congenital heart disease, rheumatic heart disease, and idiopathic dilated, restrictive, or hypertrophic cardiomyopathy. The operative variables included the type of surgery, cardiopulmonary bypass (CPB) time, aortic cross-clamping time, intra-aortic balloon pump (IABP) use. Most of the patients studied had isolated valves or combined valve and CABG surgeries. The laboratory variables included pre-operative hemoglobin, platelet count, serum creatinine, bilirubin, and liver enzymes. Blood lactate was measured at 4 points: at ECMO initiation (L0), 12 h (L12) and 24 (L24) h later and the peak value. Lactate clearance was calculated at 2 points: 12 and 24 h after ECMO initiation [10]:

$$\mathrm{LC}-\mathrm{T12}=(\mathrm{L12}-\mathrm{L0})\div \mathrm{L0}\times 100$$

$$\mathrm{LC}-\mathrm{T24}=(\mathrm{L24}-\mathrm{L0})\div \mathrm{L0}\times 100$$

Statistical analysis

Data were summarized as frequency (with percentage) for categorical data and median (with interquartile range Q1–Q3) in quantitative data due to skewed data distribution. The Mann-Whitney test was used for comparing quantitative variables. Chi-square ($\chi 2$) test was used for comparing categorical data. Two-sided p values < 0.05 were considered significant. The Kaplan-Meier method was used to get the survival curves of the intra-operative and postoperative ECMO groups. The log-rank test was used for comparison between the survival curves. Cox-proportional hazard analysis and logistic multivariable regression were done for hospital mortality. The statistical package for the Social Sciences (SPSS) version 28 was used for statistical analysis (IBM Corp., Armonk, NY, USA).

Results

The pre-ECMO patients characteristics

After reviewing 195 VA-ECMO-supported adult patients, 152 adult post-cardiotomy patients supported with VA-ECMO were enrolled after the exclusion of

non-cardiotomy patients. The intra-operative ECMO group included 81(53.3%) while the postoperative (ICU) ECMO group included 71(46.7%) patients. There were no significant differences between both groups regarding pre-operative demographic, clinical, operative or ECMO cannulation variables. The postoperative ECMO group had significantly lesser median SAVE score ($p = 0.001$), higher SAVE risk classes ($p < 0.001$), and higher median SOFA score ($p = 0.008$) compared to the intra-operative ECMO group (Table 1).

Table 1 Clinical characteristics of the study patients

Variables		All patients ($n = 152$)	Intra-operative ECMO group ($n = 81$,53.3%)	Postoperative ECMO group ($n = 71$,46.7%)	*P* value
Age(years)		47(31,56)	46.3(31.2,56)	47(31.4,56.3)	0.88
BMI (kg/m^2)		26.2(22.3,32.1)	26.6(22.3,32.7)	26.1(22.3,32)	0.97
Gender (*n*, %)	male	88(57.9)	52(64.2)	36(50.7)	0.093
	female	64(42.1)	29(35.8)	35(49.3)	
Diabetes mellitus (*n*, %)		50(32.9)	24(29.6)	26(36.6)	0.36
Systemic hypertension (*n*, %)		52(34.2)	25(30.9)	27(38)	0.353
Chronic kidney disease (*n*, %)		31(20.4)	18(22.2)	13(18.3)	0.55
ESRD on dialysis (*n*, %)		7(4.6)	3(3.7)	4(5.6)	0.71
Atrial fibrillation (*n*, %)		49(32.2)	22(27.2)	27(38)	0.15
Previous cerebral stroke (*n*, %)		11(7.2)	8(9.9)	3(4.2)	0.18
Previous cardiotomy (*n*, %)		78(51.3)	40(49.4)	38(53.5)	0.61
Heart disease (*n*, %)	RHD	57(37.5)	35(43.2)	22(31)	0.17
	Ischemic cardiomyopathy	27(17.8)	11(13.6)	16(22.5)	
	Idiopathic cardiomyopathy	31(20.4)	16(19.8)	15(21.1)	
	ACHD	17(11.2)	6(7.4)	11(15.5)	
	Others	20(13.2)	13(16)	7(9.9)	
ECPR (*n*, %)		3(2)	1(1.2)	2(2.8)	0.59
Type of surgery (*n*, %)	Valve surgery	71(46.7)	39(48.1)	32(45.1)	0.81
	CABG	8(5.3)	2(2.5)	6(8.5)	
	CABG+valve surgery	18(11.8)	10(12.3)	8(11.3)	
	Aortic surgery	9(5.9)	5(6.2)	4(5.6)	
	Heart transplantation	24(15.8)	13(16)	11(15.5)	
	Lung transplantation	15(9.9)	9(11.1)	6(8.5)	
	Pulmonary endarterectomy	1(0.7)	1(1.2)	0	
	LVAD insertion	6(3.9)	2(2.5)	4(5.6)	
Cardiopulmonary bypass (min)		218(167,317)	250(168,328)	196.5(165,287)	0.053
Aortic cross clamping (min)		145(105,174)	146.5(105.5,194)	134(105,168)	0.29
IABP use (*n*, %)		27(17.8)	15(18.5)	12(16.9)	0.79
SAVE score		− 1(− 5,3)	1(− 4,4)	− 3(− 6, 2)	0.001
SAVE risk class (*n*, %)	I	16(10.5)	16(19.8)	0	< 0.001
	II	48(31.6)	26(32.1)	22(31)	
	III	44(28.9)	21(25.9)	23(32.4)	
	IV	38(25)	17(21)	21(29.6)	
	V	6(3.9)	1(1.2)	5(7)	
Initial SOFA score		12(10,14.5)	11(9,14)	13(10,15)	0.008
Cannulation approach (*n*, %)	Central	87(57.2)	47(58)	40(56.3)	0.9
	Peripheral	55(36.2)	28(34.6)	27(38)	
	Central then peripheral	6(3.9)	4(4.9)	2(2.8)	
	Peripheral then central	4(2.6)	2(2.5)	2(2.8)	

Data were presented as count with percentage or median with the 25th and 75th interquartiles

BMI body mass index, *RHD* rheumatic heart disease, *ESRD* end-stage renal disease, *IABP* intra-aortic balloon pump, *SOFA score* Sequential Organ Failure Assessment, *ECPR* extracorporeal cardiopulmonary resuscitation, *SAVE* survival after veno-arterial ECMO, *ACHD* adult congenital heart disease

Laboratory data of the patients studied

The postoperative ECMO group had significantly higher blood lactate levels at ECMO initiation($p = 0.04$), 12 h later (p=0.032), and 24 h later($p = 0.041$) with lesser lactate clearance at 12 h ($p = 0.016$) and 24 h ($p = 0.023$) after ECMO support compared to the intra-operative ECMO group. The postoperative ECMO group had significantly lesser median hemoglobin level ($p < 0.001$), platelet count ($p = 0.01$), and GFR ($p = 0.004$) compared to the intra-operative ECMO group (Table 2).

Outcomes of the patients studied

The postoperative ECMO group had significantly higher hospital mortality ($p = 0.003$), on-ECMO mortality ($p = 0.006$), cerebrovascular stroke ($p = 0.034$), and acute renal failure requiring dialysis ($p < 0.001$) compared to the intra-operative group. There were statistically insignificant differences between the two groups regarding post-ECMO hospital mortality, cerebral bleeding, limb ischemia, ECMO duration, and ICU stay (Table 3, Fig. 1).

Cox-proportional hazard analysis showed that postponed postoperative ECMO insertion was associated with an increased risk of death (HR 1.628, 95% CI 1.102–2.403, p =0.014). Univariable analysis of mortality and logistic multivariable regression showed that atrial fibrillation (OR 6.2, 95% CI 2.71–61.84, $p = 0.002$), initial SOFA score (OR 1.46, 95%CI 1.041–3.83, $p = 0.001$), and postoperative insertion (OR 1.93, 95% CI 1.04–8.73, $p = 0.031$) were the predictors of hospital mortality (Tables 4 and 5).

The logistic regression model had a goodness-of-fit by Hosmer-Lemeshow test (Pearson chi^2 = 26.81, p value = 1) and the mean variance inflation factor (VIF) was 1.13. The univariate analysis showed significant differences between the study survivors and non-survivors regarding CKD, previous cardiotomy SAVE score, and cardiopulmonary bypass time. However, these variables were not independent predictors of mortality in the logistic multivariable regression. Lactate clearance was not included in the logistic model due to multicollinearity with postoperative ECMO variable as evidenced by high VIF. Kaplan-Meier curves showed a decreased survival with postoperative ECMO initiation compared to intra-operative ECMO with log-rank $p = 0.012$ (Fig. 2).

Discussion

The main finding of this observational study was that early intra-operative initiation of PC-ECMO was associated with decreased hospital mortality after cardiac surgeries. The postoperative ECMO group had significantly higher hospital mortality ($p = 0.003$), on-ECMO mortality ($p = 0.006$), acute cerebrovascular stroke ($p = 0.034$), and acute renal failure requiring dialysis ($p < 0.001$) compared to the intra-operative group.

PC-ECMO is required for refractory post-cardiotomy cardiogenic shock (PCS) that occurs in about 0.3–3.6% of total cardiotomies according to the different reports due to variations in study populations, surgery types and complications, cardiac centers experiences, and policies [2, 3, 6]. Our cohort analysis

Table 2 Laboratory variables of the patients studied

Variables	All patients	Intra-operative ECMO group	Postoperative ECMO group	*P* value
Hemoglobin(gm/L)	98.5(86.5,110.5)	106(93,118)	91(80,102)	< 0.001
Platelet count (10^{*9}/L)	86(50.5,159.5)	101(61,178)	69(43,144)	0.011
Base excess(mmol/L)	– 6.8(– 10.4, – 4.6)	– 6.4(– 10.2, – 4.6)	– 7.6(– 11.2, – 5.3)	0.12
Blood HCO3 (mmol/L)	18.6(15.7,20.45)	18.8(16.7,20.6)	18.4(14.5,20.4)	0.27
ALT (units/L)	37.85(22.25,139.6)	37.1(23,96.1)	42.8(21.2,198.9)	0.58
AST (units/L)	119.05(54.65,270.4)	119(54.7,247.8)	119.1(54.6,315.7)	0.54
Serum creatinine (µmol/L)	105(67,147)	99(66,132)	119(75,155)	0.119
GFR (mL/min/1.73 m^2)	54.5(42,60)	60(44,60)	49(39,60)	0.004
Serum bilirubin (µmol/L)	32(17.45,67.85)	28.8(15.8,42.9)	56.5(21.6,132.9)	< 0.001
INR	1.7(1.4,2.3)	1.7(1.4,2.2)	1.8(1.5,2.4)	0.12
Initial blood lactate (mmol/L)	8.45(5.7,12.15)	7(5.6,11.2)	9.5(6.2,13.5)	0.04
Lactate at 12 h (mmol/L)	8.8(4.9,15.4)	5.9(4.4,14.2)	8.7(5.3,17)	0.032
Lactate at 24 h (mmol/L)	4.6(2.4,11.95)	3.2(2.2,10)	4.5(2.7,13.5)	0.041
Peak lactate (mmol/L)	16.5(11.9,25)	14.7(10.8,25)	16.8(13.8,25)	0.11
Lactate clearance % (LC-T12)	8.39% (– 28.46,35)	26.29% (– 18.04,35.42)	4.35% (– 34.71,33.83)	0.016
Lactate clearance % (LC-T24)	42.17% (– 18.99,65.54)	44.64% (– 19.64,64.56)	28.24% (– 18.34,68.97)	0.023

Data were presented as median with the 25th and 75th interquartiles

ALT alanine transaminase, *AST* aspartate transferase, *INR* international normalized ratio, *GFR* glomerular filtration rate, *LC* lactate clearance

Table 3 Clinical outcomes of the patients studied

Variables	All patients (*n* = 152)	Intra-operative ECMO group (*n* = 81,53.3%)	Postoperative ECMO group (*n* = 71,46.7%)	*P* value
Hospital mortality (*n*, %)	104(68.4)	47(58)	57(80.3)	0.003
On-ECMO mortality (*n*, %)	74(48.7)	31(38.3)	43(60.6)	0.006
ECMO weaning (*n*, %)	78(51.32)	50(61.73)	28(39.44)	0.002
Post-decannulation mortality (*n*, %)	30(19.7)	16(19.8)	14(19.7)	0.99
New need for CRRT	72(47.4)	26(32.1)	46(64.8)	< 0.001
Limb ischemia (*n*, %)	17(11.2)	6(7.4)	11(15.5)	0.12
Bowel ischemia (*n*, %)	6(3.9)	2(2.5)	4(5.6)	0.42
Bowel surgery (*n*, %)	1(0.7)	0	1(1.4)	0.47
Cerebrovascular stroke (*n*, %)	28(18.4)	9(11.1)	19(26.8)	0.013
Ischemic stroke (*n*, %)	18(11.8)	6(7.4)	12(16.9)	0.034
Cerebral bleeding (*n*, %)	9(5.9)	3(3.7)	6(8.5)	0.31
ECMO days	6(3,10.5)	6(3,11)	6(3,10)	0.94
ICU days	17(7,32)	14(7,31)	19(7,38)	0.38
SOFA-D3	14(10,17)	12(9,15)	16(13,18)	< 0.001
SOFA-D5	15(9,18)	12(8,16)	17(13,19)	< 0.001
SOFA(D3-1)	2.5(2,3)	2(2,3)	3(2,3)	0.15
SOFA(D5-3)	1(– 1,2)	– 1(– 1,1)	1(0,2)	0.002
SOFA(D5-1)	3(– 1,5)	1(– 2,4)	4(1,5)	0.001
Post-ECMO durable LVAD (*n*, %)	2(1.3)	2(2.5)	0	0.49
Post-ECMO heart transplantation (*n*, %)	4(2.6)	3(3.7)	1(1.4)	0.62

Data were presented as count with frequency or median with the 25th and 75th interquartiles

ECMO extracorporeal membrane oxygenation, *LVAD* left ventricular assist device, *CRRT* continuous renal replacement therapy, *SOFA score* Sequential Organ Failure Assessment

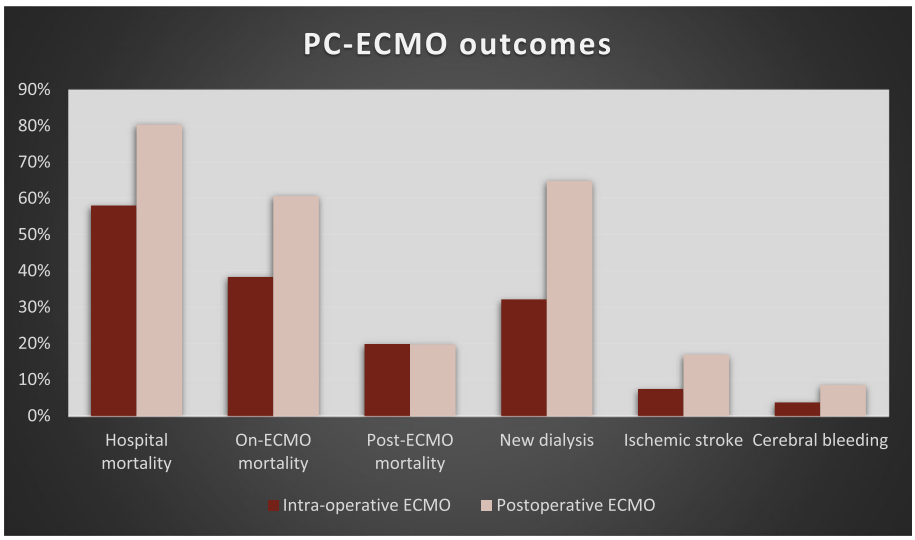

Fig. 1 The outcomes of PC-ECMO in intra-operative and postoperative groups

revealed that the total hospital mortality was 68.4% and of them 74 (48.7%) patients died on ECMO. Our results were similar to the reports from large multicenter studies of PC-ECMO [11–13]. Mariani et al. studied 2003 patients with PC-ECMO from 34 centers and reported 60% mortality [11]. Biancari et al. studied 781 patients with PE-ECMO from 19 centers and reported a total mortality of 64.4% and subgroup

Table 4 Univariate analysis according to hospital mortality

Variables		Non-survivors (*n* = 104, 68.4%)	Survivors (*n* = 48, 31.6%)	*P* value
Age (years)		48(32, 57)	43(31, 56)	0.18
Gender, male (*n*, %)		59(56.7)	29(60.42%)	0.4
Body mass index (kg/m^2)		27.2(22.75, 33.1)	24.9(22.3, 29.9)	0.19
Chronic kidney disease (*n*, %)		28(26.9)	3(6.3)	0.004
ESRD on dialysis (*n*, %)		6(5.77)	1(2.08)	0.43
Previous cardiotomy (*n*, %)		60(57.7)	18(37.5)	0.014
Atrial fibrillation (*n*, %)		43(41.35)	6(12.5)	< 0.001
Heart disease (*n*, %)	RHD	42(40.4)	15(31.3)	0.057
	Ischemic cardiomyopathy	19(18.3)	8(16.7)	
	Idiopathic cardiomyopathy	21(20.2)	10(20.8)	
	ACHD	12(11.54)	5(10.4)	
	other	8(7.69)	12(25)	
Type of surgery (*n*, %)	Valve surgery	52(50)	19(39.6)	0.005
	CABG	5(4.81)	3(6.25)	
	Combined CABG+valve surgery	14(13.5)	4(8.3)	
	Aortic surgery	8(7.69)	1(2.1)	
	Heart transplantation	16(15.4)	8(16.7)	
	Pulmonary endarterectomy	1(0.9)	0	
	Lung transplantation	4(3.8)	11(22.9)	
	LVAD insertion	6(5.8)	0	
Cardiopulmonary bypass (min)		237(169–319)	192(149–250)	0.016
Aortic cross-clamping (min)		160(108–179)	124(93–163)	0.04
IABP (*n*, %)		19(18.3)	8(16.7)	0.8
Cannulation approach (*n*, %)	Central	62(59.6)	25(52.1)	0.36
	Peripheral	33(31.7)	22(45.8)	
ECMO timing (*n*, %)	Intra-operative	46(44.2)	34(70.8)	< 0.001
	Postoperative	58(55.77)	14(29.2)	
SAVE score		− 3(− 6, 0.5)	3(1, 5)	< 0.001
Initial SOFA score		13.5(12, 16)	9(8, 11)	< 0.001
SOFA after 48 h		16(14, 18)	9(8, 11)	< 0.001
Initial blood lactate (mmol/L)		9.75(6.55, 13.4)	5.8(4.8, 8.3)	< 0.001
Lactate at12 h (mmol/L)		11.25(7.3, 18.9)	4.1(2.8, 6.4)	< 0.001
LC% at 12 h		− 24.15(− 59.22, 15.3)	39.29(7.25, 52.17)	< 0.001
Lactate at 24 h (mmol/L)		6.55(4.05, 20)	1.9(1.4, 3.1)	< 0.001
LC% at 24 h		20.71(− 72.64, 53.15)	66.04(53.1, 77.78)	< 0.001

Data were presented as count with percentage or median with the 25th and 75th interquartiles

ESRD end-stage renal disease, RHD: rheumatic heart disease, *IABP* intra-aortic balloon pump, *SOFA score* Sequential Organ Failure Assessment, *SAVE* survival after veno-arterial ECMO, *ACHD* adult congenital heart disease

analysis showed a mortality of 76.1% in patients aged > 70 years [12]. Biancari et al. [13] studied 1269 patients with PC-ECMO and reported hospital mortality of 70.7% (vs. 63.7%) in the central and peripheral cannulation groups respectively. There were no significant differences in the cannulation approaches in our cohort analysis. Most mortality reports described the variables associated with mortality but there is little data about the importance of timing of PC-ECMO.

In our cohort, we found that postoperative ECMO insertion was associated with a 22% higher hospital mortality compared to the intra-operative ECMO insertion and the patients of both groups did not have significant differences regarding the pre-operative clinical variables or the surgical details. Moreover, postoperative ECMO was associated with an increased hazard ratio in the Cox-proportional regression and was an independent predictor of mortality in the logistic multivariable regression.

Table 5 Logistic multivariable regression for predicting mortality

Variables	OR	95% CI	*P* value
Initial SOFA	1.46	1.041–3.83	0.001
Postoperative insertion	1.93	1.04–8.73	0.031
Chronic kidney disease	1.21	1.021–6.214	0.061
SAVE score	0.84	0.642–1.068	0.072
Prior cardiotomy	0.63	0.264–3.463	0.82
Atrial fibrillation	6.2	2.71–61.84	0.002
CPB time	1.042	0.82–1.82	0.64

SAVE survival after veno-arterial ECMO, *CPB* cardiopulmonary bypass, *SOFA* Sequential Organ Failure Assessment score

Mariani et al. reported that the post-operative ECMO group had a 7% higher mortality despite having lesser pre-operative and intra-operative risk profiles [11].

We found that the pre-ECMO laboratory variables were statistically worse in the postoperative ECMO group including anemia, thrombocytopenia, and lactic acidosis. Ideally, ECMO should be considered before anaerobic metabolism (indicated with hyperlactatemia) and multi-organ injury [6]. Hyperlactatemia was linked to different worse outcomes during VA-ECMO support with different cut-off values for differentiating hospital mortality [14, 15]. The postoperative ECMO insertion was associated with significant hyperlactatemia at ECMO initiation and delayed clearance at the 12th and 24th hours. Lactate clearance was a strong independent predictor of hospital mortality in patients with cardiogenic shock [10].

Mariani et al. [11] reported that 22.8% of patients with postoperative ECMO had cardiac arrest compared to 11.2% in the intra-operative ECMO group which may be due to long waiting to take a decision for ECMO initiation. In our relatively small cohort, we did not have a large number of cardiac arrests and ECPR. Hemodynamic deterioration despite maximizing medical therapy requires an early consideration of mechanical circulatory support before developing cardiac arrest [16, 17].

Regarding the cerebral and renal outcomes, the postoperative ECMO group had significantly higher frequencies of acute cerebrovascular strokes, acute kidney injury, and new need for dialysis compared to the intra-operative ECMO group. Mariani et al. [11] reported a significant increase in multi-organ failure in the postoperative ECMO group. We used the SOFA and SAVE scores for the risk assessment of the patients studied. The postoperative ECMO group had a higher initial SOFA score and an increased trend over the next few days indicating the clinical severity and occurrence of multiorgan affection compared to the intra-operative ECMO group. The increased trend of SOFA score in the postoperative group together with the delayed lactate clearance indicates the delayed ECMO support and occurrence of multi-organ injury. Increased SOFA trend was linked to mortality in patients with VA-ECMO [4, 9]. Initial SOFA score was an independent predictor of hospital mortality with PC-ECMO in our cohort analysis. Atrial fibrillation was an independent predictor of mortality with PC-ECMO in our cohort. This finding is consistent with Saxena et al.

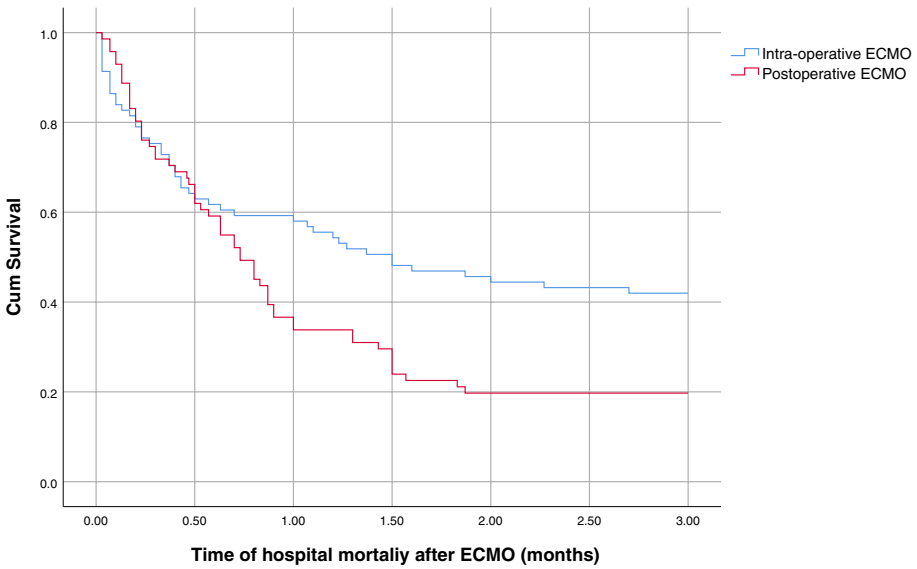

Fig. 2 Kaplan-Meier curves of the intra-operative and postoperative ECMO groups (log-rank $p = 0.012$)

[18] who reported the association between pre-operative atrial fibrillation and hospital mortality with PC-ECMO [18]. Mariani et al. [19] recently analyzed 2058 patients with PC-ECMO from 34 centers and reported that atrial fibrillation was an independent predictor of mortality during follow-up.

The postoperative ECMO group had a significantly lower median SAVE score with increased frequencies of the higher-risk classes. The SAVE score was initiated for predicting survival with VA-ECMO with a good discrimination but its validity for PC-ECMO is still controversial [7]. Despite the non-survivors having significantly lower SAVE scores compared to the survivors in our study, it was an insignificant predictor in the logistic multivariable regression.

The surgeons usually initiate the intra-operative ECMO for patients with high pre-operative risk and with failed weaning off cardiopulmonary bypass. The patients with pre-operative low-risk profiles and borderline hemodynamics, the surgeons usually postpone ECMO insertion hoping that the patients will improve with medical therapy and avoid the risks of ECMO. However, this may result in deterioration of hemodynamics, multi-organ injury, and increased risks of cardiac arrest, morbidities, and hospital mortality.

Conclusions

Postponed ECMO insertion in critically sick patients was associated with increased mortality after cardiac surgery. Early intra-operative initiation of PC-ECMO may have the potential to improve outcomes after cardiac surgeries.

Limitations

The study is a single-center experience with a retrospective observational analysis. We could not get detailed data about the hemodynamic profile and vasopressors during and postoperatively to calculate the vasopressor score. However, we calculated the SAVE and SOFA scores to assess the clinical severity of the patients studied. We could not get the criteria of ECMO weaning especially the aortic velocity time integral (VTI) and lateral mitral annulus peak systolic velocity (TDSa).

Abbreviations

BMI	Body mass index
CABG	Coronary artery bypass graft
CI	Confidence interval
CKD	Chronic kidney disease
CRRT	Continuous renal replacement therapy
ECMO	Extracorporeal membrane oxygenation
ECPR	Extracorporeal cardiopulmonary resuscitation
GFR	Glomerular filtration rate
OR	Odds ratio
IABP	Intra-aortic balloon pump
SAVE	Survival after veno-arterial ECMO
SOFA	Sequential organ failure assessment
LC	Lactate clearance
LVAD	Left ventricular assist device

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Authors' contributions

ML participated in study design, data collection, statistical analysis, and manuscript writing. EH, PM, MGL, and MJM participated in data collection and interpretation. All authors read and approved the final manuscript.

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Availability of data and materials

The data of the study is available with the corresponding author.

Declarations

Ethics approval and consent to participate

The study was approved by the ethical committee of King Faisal Heart Center, was given a reference number (2191042) and waived from specific consent as there is no personally identifiable data or photos.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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