Risk Factors for Developing Severe Acute Kidney Injury in Adult Patients With Refractory Postcardiotomy Cardiogenic Shock Receiving Venoarterial Extracorporeal Membrane Oxygenation

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Conflict of interest

The authors have not disclosed any potential conflict of interest regarding this study.

Running title

Acute kidney injury in VA-ECMO patients

Key words

Acute Kidney Injury; Extracorporeal Life Support; Cardiac Surgical Procedure;

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Abstract (326 words)

Objective: Post-cardiotomy cardiogenic shock (PCCS) occurs in 2-6% of patients undergoing cardiac surgery, and 1% of cardiac surgery patients will require mechanical circulatory support using Veno-Arterial Extracorporeal Membrane Oxygenation (VA-ECMO). Acute Kidney Injury (AKI) is a frequent complication in this population and negatively impacts the survival. We aimed to determine whether the timing of ECMO implantation influences the renal prognosis of these patients.

Design: Retrospective observational cohort study between January 2013 and December 2016.

Setting: An 18-bed surgical ICU in a university hospital.

Patients: 4796 consecutive adult patients that underwent cardiac surgery were included in the study and 347 (7.2%) were assisted with VA-ECMO for refractory PCCS. The patients that died during the first 48 hours after VA-ECMO implantation were excluded. The complete-case analysis included 257 patients.

Interventions: None.

Measurements: The primary outcome was the occurrence, within ten days following the VA-ECMO implantation, of a stage 3 AKI defined by the Kidney Disease: Improving Global Outcomes (KDIGO) group.

Main results: One hundred sixty-nine patients (65.7 %) presented with a KDIGO stage 3 AKI; 14 patients (5.4 %) died before the end of the follow-up period, without developing the primary outcome. 92% of patients with KDIGO 3 AKI received RRT, for a median duration of 7 [3, 16] days. Late implantation of VA-ECMO was independently associated with an increased risk of KDIGO stage 3 AKI (Odds Ratio 2.81 [95% CI 1.31, 6.07], $P = 0.008$). The other factors associated with KDIGO stage 3 AKI were pre-operative left ventricular ejection fraction, OR 1.03 [95% CI 1.01, 1.05], $P = 0.007$; intraoperative plasma transfusion OR 1.13 [95% CI 1.02, 1.26], $P = 0.022$, increased bilirubinemia level OR 1.013 [95% CI 1.001,

1.026], $P = 0.032$, and increased creatinine levels OR 1.012 [95% CI 1.006, 1.018], $P < 0.001$ on the day of implantation.

Conclusions: Significant kidney dysfunction is particularly frequent in patients with refractory PCCS assisted with VA-ECMO. Early implantation of ECMO may help prevent acute kidney injury.

Trial Registration: AKI ECMO Trial Registration: ClinicalTrials.gov Identifier NCT04082312

ABBREVIATIONS

ACT, Activated whole blood Clotting Time

AKI, Acute Kidney Injury

ASA, American Society of Anesthesiologists

BMI, Body Mass Index

CI, Confidence Intervals

COPD, Chronic Obstructive Pulmonary Disease

DO2, Dissolved O2

ECMO, ExtraCorporeal Membrane Oxygenation

ELSO, Extracorporeal Life Support Organization

KDIGO, Kidney Disease: Improving Global Outcomes

LVEF, Left Ventricular Ejection Fraction

OR, Odds Ratio

PCCS, Post-Cardiotomy Cardiogenic Shock

pCO2, CO2 Partial Pressure

pO2, O2 Partial Pressure

RRT, Renal Replacement Therapy

SAPS 2, simplified acute physiology score 2

SOFA, Sepsis-related Organ Failure Assessment

VA-ECMO, Veno-Arterial ExtraCorporeal Membrane Oxygenation

INTRODUCTION

Cardiogenic shock occurs in 2-6% of patients undergoing cardiac surgery (1). Approximately 1% of patients will require mechanical support using Veno-Arterial ExtraCorporeal Membrane Oxygenation (VA-ECMO) owing to refractory post-cardiotomy cardiogenic shock (PCCS) (2). Post-cardiotomy VA-ECMO is associated with a high morbidity that includes bleeding, ischemic events, and organ failure including acute kidney injury (AKI) (3). Indeed, AKI is one of the most frequent complications in patients supported by ECMO, with an incidence reaching up to 65% (4). Renal replacement therapy (RRT) is required in approximately 65% of patients (3), and is associated with increased mortality (5).

In the case of PCCS, two perioperative mechanisms may play a role in the development of AKI. First, low cardiac output associated with left ventricular failure leads to a decline in renal blood flow and glomerular filtration. Second, right ventricular failure may also impair glomerular filtration due to renal congestion. Both renal congestion and low cardiac output are treated by VA-ECMO which helps increase flow rate and arterial pressure while decreasing central venous pressure.

Through these protective mechanisms the timing of VA-ECMO implantation may influence the prognosis of patients with refractory PCCS. Our hypothesis was that early implantation of VA-ECMO may decrease the incidence of AKI in patients with PCCS. The aim of our study was to describe the incidence of acute kidney injury in adult patients with refractory PCCS supported by VA-ECMO and identify the risk factors for developing AKI.

METHODS

This study was approved by the ethics committee Ile de France 5 (reference B-7-15). Due to the retrospective design of the study, and in accordance with the decision of the ethics committee and French regulation and non-interventional studies, signed informed consent was waived. The study was conducted in accordance with the Declaration of Helsinki principles.

Design and setting

This observational single center retrospective study was conducted in the Surgical Intensive Care Unit of the Cardiology Institute of La Pitié-Salpêtrière University Hospital (Paris, France). All patients who underwent cardiac surgery admitted in our unit and assisted by VA-ECMO between January 2013 and December 2016 were screened. The exclusion criteria were i) chronic hemodialysis, ii) death occurring within the first 48 hours of VA-ECMO implantation and iii) multiple VA-ECMO episodes during the same hospitalization. Patients with VA-ECMO were identified through billing record in the electronic medical records system. All patient data was anonymized.

Main goals and Outcomes

Our primary objective was to describe the incidence of acute kidney injury in adult patients with refractory PCCS supported by VA-ECMO and identify the risk factors for developing AKI. The primary outcome was the occurrence of a stage 3 AKI defined by the Kidney Disease: Improving Global Outcomes (KDIGO) group (Supplemental Appendix) (6) within ten days of VA ECMO implantation. Stage 3 AKI was selected due to its potential for requiring RRT. During this ten days period (D1 to D10), AKI and death behave as competitive events (D1 represents the day following the implantation of ECMO). The primary outcome group was divided as follows (i) patients with stage 3 AKI within 10 days of VA

ECMO implantation (group 1); (ii) patients without stage 3 AKI 10 days after VA ECMO implantation (group 2, baseline category); (iii) patients that died between D2 and D10 of VA-ECMO support, without developing KDIGO stage 3 AKI (group 3). Death occurring before D2 of VA-ECMO implantation was an exclusion criterion.

Our second goal was to determine the short-term mortality risk factors in this population. The secondary outcome was defined as 30-day mortality after VA-ECMO implantation. Long-term outcomes including the 6-month mortality rate, and the 1-month and 6-month renal prognosis were also assessed.

Statistical analysis

Results are expressed as number of patients (%), median (interquartile range 25-75) or mean (± standard deviation). Shapiro-Wilk test was used to assess the normality assumption for continuous variables. The groups were compared using Kruskal-Wallis, Pearson Chi-square and Fisher tests. Univariable analyses and multivariable regression models were used to identify the risk factors for developing the primary and the secondary outcomes.

Risk factors analyzed included demographic factors (SAPS 2, SOFA, Pre-operative LVEF, chronic kidney failure, creatinine clearance, type of surgery), hemodynamic factors during intraoperative period (cardiopulmonary bypass time, transfusion, catecholamines), factors associated with VA-ECMO implantation (primary graft dysfunction, lactate, intraoperative or postoperative implantation, catecholamines), and biological factors at D1 of VA-ECMO support (creatinine, blood protein level, bilirubinemia, bicarbonates, lactate, urine output).

A multivariate logistic regression was used to model the occurrence of stage 3 AKI. This model was chosen to take into account the competing risk of death without developing a stage 3 AKI. The three levels consisted of patients with KDIGO stage 3 AKI (group 1), patients without KDIGO stage 3 AKI and alive at D10 (group 2 [baseline category]), and patients that

died before D10 without developing KDIGO stage 3 AKI (group 3). Candidate risk factors associated ($p < 0.05$) with this outcome in the univariable analysis were introduced into the multivariate model, and the final model was selected using backward stepwise selection method.

Risk factors for the 30-day mortality were demographic factors (age, BMI, SAPS 2, SOFA, LVEF, diabetes, dyslipidemia, hypertension, peripheral artery disease), intraoperative factors (transfusion), variables at VA-ECMO implantation (biventricular failure, primary graft dysfunction, lactate, inhaled nitric oxide, AKI at implantation, urine output), and type of surgery (heart transplantation, valve surgery, coronary bypass surgery, combined surgery).

Regarding the secondary outcome, the final logistic regression model was obtained using the same selection method as used for the analysis of the primary outcome.

Discrimination abilities was quantified using the Polytomous Discrimination Index (PD-Index) (7) for the final multinomial model of the occurrence of stage 3 AKI, and the Concordance Index (C-Index) (7) for the binary logistic model of 30-day mortality. Internal validation was performed with a bootstrap procedure using 500 repetitions (8), to quantify the optimism that may be expected when the multivariable model is applied to new, but similar, patients. Both apparent and optimism-corrected discrimination indexes were reported

Odds Ratio (OR) with their 95% confidence intervals (CI) was calculated. The complete-case method was used for the multivariable analyses. A sensitivity analysis using multiple imputations replaces missing values when appropriate was also performed (Supplemental Table 2). All tests were 2-sided and a *P*-value < 0.05 was considered for statistical significance. Statistical analyses were performed using R software (version 3.4.1, licenses GNU GPL, The R foundation for statistical computing, Vienna, Austria).

RESULTS

Study population

Between January 2013 and December 2016, 4796 patients underwent cardiac surgery with cardiopulmonary bypass. Among them, 347 (7.2%) experienced refractory PCCS and required VA-ECMO assistance (peripheral cannulation 94.8%) (Figure 1, flowchart).

257 patients were included in the final analysis. Demographic and outcome variables did not significantly differ between the patients included and excluded from the analysis. One hundred sixty-nine (65.7%) patients developed KDIGO stage 3 AKI within 10 days of VA-ECMO support. Demographic and clinical characteristics of the population are described in Table 1. The clinical management of VA-ECMO patients is described in the Supplementary Appendix.

VA-ECMO implantation

Table 2 shows data regarding perioperative management of the patients. The VA-ECMO was implanted intraoperatively in 159 patients (61.9%) and postoperatively in 98 patients (38.1%). A left ventricular venting was necessary in 105 patients (40.9%), most commonly an intra-aortic balloon pump per institutional protocol (No.=92, 35.8%). The causes of VA-ECMO implantation were left ventricular failure (No.=76, 29.6%), right ventricular failure (No.=45, 17.5%), biventricular failure (No.=88, 34.2%), primary graft failure (No.=30, 11.7%) or cardiac arrest (No.=15, 5.8%).

Risk factors for stage 3 AKI

During the follow-up period of ten days after VA-ECMO support, 169 patients (65.7 %) developed a KDIGO stage 3 AKI; 74 patients (28.8 %) did not develop a KDIGO stage 3 AKI and were still alive at D10; 14 patients (5.4 %) died before the end of the follow-up period, without developing the primary outcome. Renal replacement therapy was initiated in 156 patients (60.7%) from the overall cohort. 92% of patients with KDIGO stage 3 AKI received RRT for indications including ionic disorders (No.=79, 46.7%), anuria (No.=61, 36.1%) and fluid overload (No.=15, 8.9%). The median duration of RRT was 7 [IQR 3, 16] days.

Results from the univariate analysis assessing risk factors for developing KDIGO stage 3 AKI are presented in Table 2. SOFA, SAPS2, and urine output at Day 1 were excluded from the analysis due to a lack of data (>15% of data points missing). Figure 2 summarizes the results of the multivariate logistic regression. Factors independently associated with the development of KDIGO stage 3 AKI were bilirubinemia and creatinine levels on the day of ECMO implantation, the timing of ECMO implantation, pre-operative LVEF and intraoperative fresh frozen plasma transfusion. Complete multivariate results including group 3 patients is available in the Supplemental Table 1. The Polytomous Discrimination Index (PD-Index) for the final multivariate model of the occurrence of stage 3 AKI was 0.624. After internal validation, the optimism-corrected discrimination index was 0.294.

Risk factors for 30-day mortality

The 30 day mortality rate was 48.2% (124/257). The timing of VA-ECMO implantation did not reduce the mortality at D30 in the univariate analysis, with an intraoperative mortality rate of 44.7% (No.=71/159) vs. 54.1% (No.=53/98) for postoperative implantation OR 0.69 [0.40, 1.17] *P*=0.16. The 6 month mortality rate was 75.9% (n=154/203). Intraoperative implantation of VA-ECMO was associated with a lower mortality at 6 months, 69.8% (No. =88/126, 20.8% missing status) compared to 85.7% (n=66/77, 21.4% missing status) for

patients with postoperative implantation, OR=0.39 [0.17, 0.85], *P*=0.011. The factors associated with 30-day mortality after VA-ECMO implantation are presented in the Table 3. The Concordance Index (C-Index) for the binary logistic model of 30-day mortality was 0.721. After internal validation, the optimism-corrected discrimination index was 0.482.

Renal prognosis at one month (Supplemental Table 3) was good, with all but three patients recovered from their stage 3 AKI at 6 months.

DISCUSSION

To our knowledge, this study is the first to evaluate the risk factors for developing AKI in adult patients with refractory PCCS. In this population, intra-operative implantation of VA-ECMO appeared to be a protective factor for developing a stage 3 AKI.

The incidence of KDIGO stage 3 AKI in our cohort was 65.7%. This is higher than prior reported values from postoperative cardiac surgical patients without VA-ECMO assistance (9), but consistent with the results from Yan et al., who found an incidence of severe AKI of 48% at 48 hours after VA-ECMO implantation (10)**.** The use of renal replacement therapy was higher than previously described, with initiation of RRT in 60.7% of patients in the overall cohort (11). Typically, patients needing VA-ECMO support have a higher co-morbidity index and lower pre-operative LVEF. These patients are thus at higher risk for postoperative complications, including AKI. Additionally, the relatively high incidence of refractory PCCS in our cohort reflects the underlying health status of the population of an expert university hospital, with mean EuroSCORE II (12) predicting the intraoperative mortality of almost 20%.

The results of this study magnify the importance of the timing around implantation of VA-ECMO support. We found that intraoperative implantation of VA-ECMO had a protective effect on the development of KDIGO stage 3 AKI. Intraoperative implantation of VA-ECMO limits the duration of the low cardiac output associated with PCCS and thus helps prevent subsequent organ dysfunction. Hence, biological marker of organ dysfunction as hyperbilirubinemia was independent risk factor of KDIGO stage 3 AKI in our cohort.

Due to the design of our study, we were not able to assess the effect of developing an AKI 3 between D2-D10 on the 30 day mortality rate. The overlap between the exposition period to AKI and the mortality risk prevented modeling of the relationship between these two variables. Nonetheless this association has been extensively documented in past studies (13–

15). Given the high incidence of AKI, with 89% of patients developing at least KDIGO stage 1 AKI, preventative strategies may have a major impact on patient outcomes. The other 30-day mortality risk factors highlighted by our study are commonly described in both a post-cardiotomy population (16) and in VA-ECMO population [(15);(17)], including age, BMI, the presence of chronic arteriopathy and biventricular failure. The supplemental figure (Diagram Acyclic Graph) summarizes the results and the hypotheses stemming from this study and provides additional context with respect to cardiac surgery-associated AKI.

Our study has several limitations. First, because of its retrospective and single center design, unidentified confounding factors may have biased the multivariable analyses. Nonetheless, the risk factors we identified are consistent with the ones previously described, providing us with some external validity. Second, if missing data did not allow a full-set analysis, we used a sensitivity analysis using multiple imputations to replaces missing values. Third, the lack of long term follow-up, inherent to the retrospective design, prevented us from making conclusions regarding the effect of long-term mortality or renal outcome. Fourth, there was no detailed protocol regarding cardiopulmonary bypass weaning, decision for VA-ECMO implantation in case of refractory PCCS, or RRT initiation in the intensive care unit. However, our practices are relatively standardized, and it is unlikely that a patient with refractory PCCS during the perioperative period would not have been assisted by VA-ECMO.

CONCLUSIONS

In conclusion, this retrospective study is the first to emphasize the role of intraoperative VA-ECMO support in case of refractory PCCS, which could possibly decrease the incidence of KDIGO stage 3 AKI. AKI is the easier read-out of low cardiac output for intensivist, and other organ dysfunction might be avoided with early VA-ECMO support. Only a prospective study with randomization could definitely clarify the issue of timing in VA-ECMO support during PCCS.

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FIGURE LEGENDS

Figure 1. Flowchart

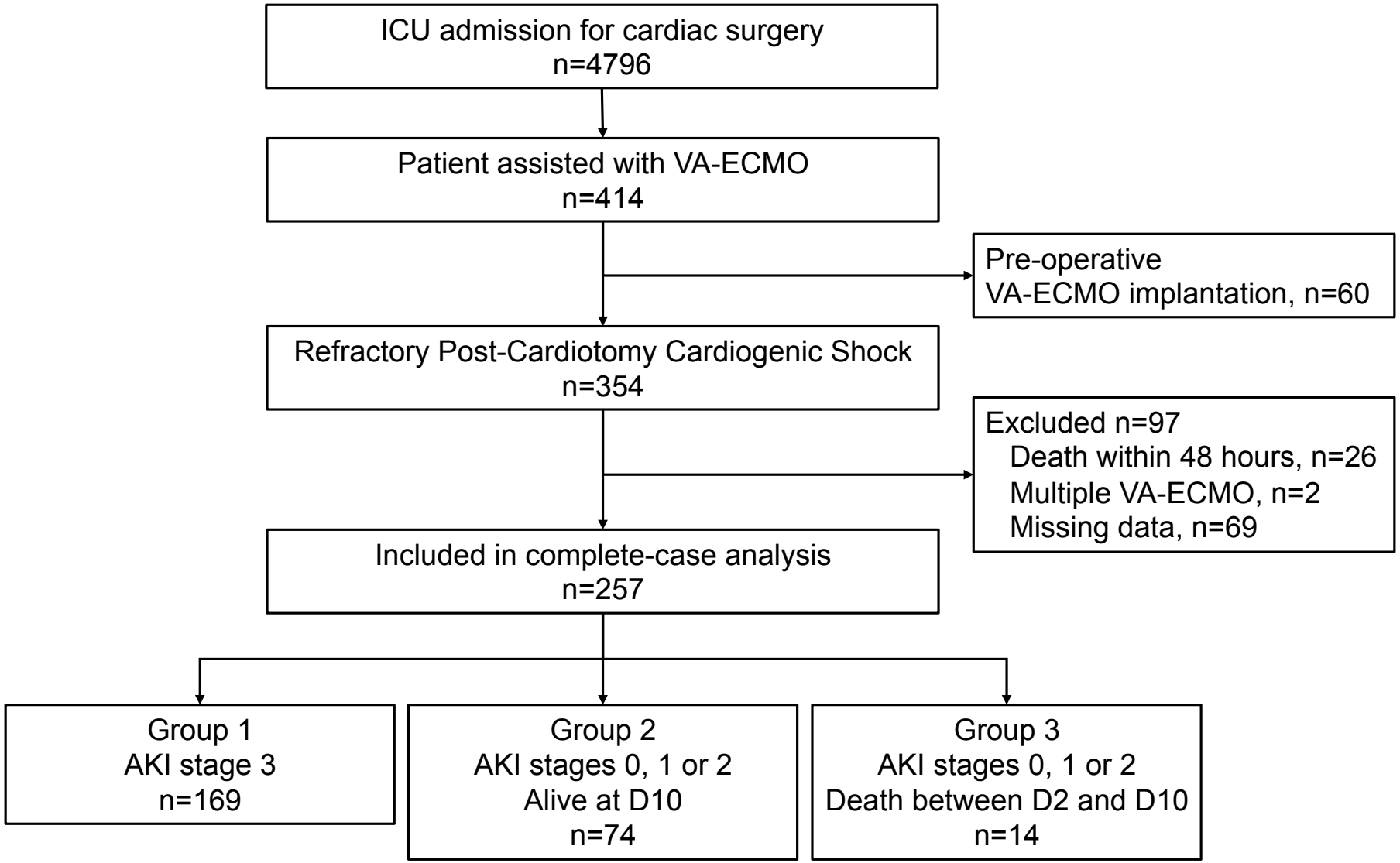
This flowchart shows the distribution of the patients among the three groups according to the primary outcome. AKI was defined by the KDIGO classification (6). D10 refers to the tenth day after VA-ECMO implantation. Death before D2 was an exclusion criterion

AKI, Acute Kidney Injury; ICU, Intensive Care Unit.

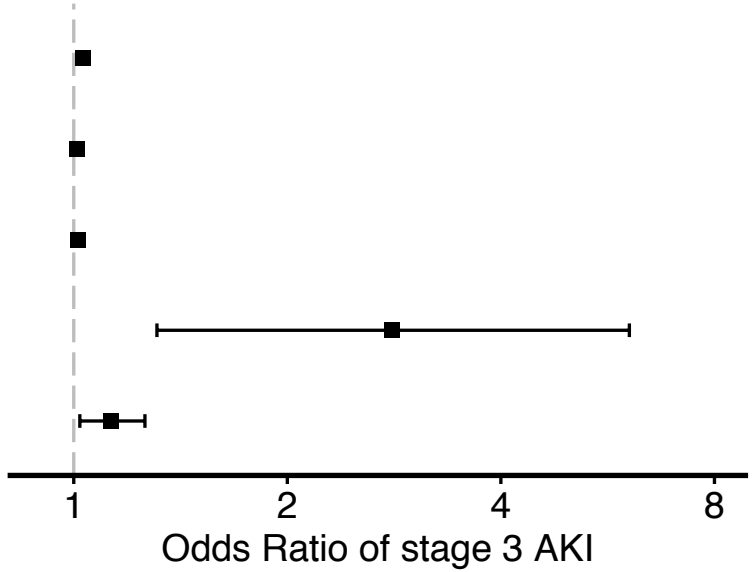
Figure 2. Adjusted odds ratios of KDIGO stage 3 Acute Kidney Injury.

Forrest plot of risk-adjusted odd ratios of stage 3 Acute Kidney Injury. Bilirubinemia and creatininemia refer to the worst values on the day of VA-ECMO implantation.

LVEF, Left Ventricular Ejection Fraction


ICU admission for cardiac surgery
n=4796
Patient assisted with VA-ECMO
n=414
Pre-operative
VA-ECMO implantation, n=60
Refractory Post-Cardiotomy Cardiogenic Shock
n=354
Excluded n=97
Death within 48 hours, n=26
Multiple VA-ECMO, n=2
Missing data, n=69
Included in complete-case analysis
n=257
Group 1
AKI stage 3
n=169
Group 2
AKI stages 0, 1 or 2
Alive at D10
n=74
Group 3
AKI stages 0, 1 or 2
Death between D2 and D10
n=14

	Odds Ratio [95% CI]	P–value
LVEF (per % increase)	1.03 [1.01, 1.05]	0.007
Creatininemia (per μmol/L increase)	1.012 [1.006, 1.018]	<0.001
Bilirubinemia (per μmol/L increase)	1.013 [1.001, 1.026]	0.032
Postoperative implantation of VA–ECMO	2.81 [1.31, 6.07]	0.008
Intraoperative fresh frozen plasma (per unit = 200mL)	1.13 [1.02, 1.26]	0.022



Supplemental Table 1: Multivariable analysis of risk factors for AKI in patients going under cardiac surgery supported by VA-ECMO

Factors	Outcome	Odds Ratio [95% CI]	p-value	Global p-value
Preoperative LVEF, per % increase	Group 1	1.029 [1.008, 1.050]	0.007	0.021
	Group 3	1.025 [0.984, 1.068]	0.241	
Post-operative vs per-operative VA-ECMO	Group 1	2.819 [1.308,6.073]	0.008	0.005
	Group 3	0.409 [0.044, 3.795]	0.431	
Bilirubinemia[a], per µmol/L increase	Group 1	1.013 [1.001, 1.026]	0.032	0.006
	Group 3	0.971 [0.928, 1.016]	0.209	
Creatininemia[b], per µmol/L increase	Group 1	1.012 [1.006, 1.018]	0.0001	0.0001
	Group 3	1.009 [0.998, 1.021]	0.099	
Per-operative fresh frozen plasma transfusion	Group 1	1.133 [1.18, 1.262]	0.022	0.019
	Group 3	1.229 [1.032, 1.464]	0.021	

Multinomial logistic regression modeling renal status within 10 days of VA-ECMO implantation for refractory pst-cardiotomy cardiogenic shock. Group 1 : patients that presented the primary outcome of KDIGO stage 3 AKI; Group 2 [baseline category] : patients that did not experience the primary outcome and that were still at risk of presenting the primary outcome at D10, e.g. were still alive at D10; Group 3 : patients that died between D2 and D10 of VA-ECMO support, without developing KDIGO stage 3 AKI.

[a] at the time of VA-ECMO implantation

[b] at day one after VA-ECMO implantation

LVEF, Left Ventricular Ejection Fraction; VA-ECMO, Veno-Arterial ExtraCorporeal Membrane Oxygenation

Table 2: Univariable analysis of potential risk factors for KDIGO stage 3 AKI

Factors	Patients with stage 3 AKI (No.=169)	Patients without stage 3 AKI		*P*-value
		alive at D10 (No.=74)	deceased before D10 (No.=14)	
Demographic characteristics and comorbidities				
SAPS 2	61.1 ± 18.3	53.7 ± 16.7	56.4 ± 19.2	0.043
SOFA	16.8 ± 3.2	11.7 ± 2.9	12.6 ± 3.9	<0.0001
Preoperative LVEF (%)	37.3 ± 16.9	30.6 ± 16.7	36.9 ± 16.6	0.011
Chronic kidney failure[a]	46 (27.2)	21 (28.4)	2 (14.2)	0.61
Creatinine clearance, ml/min	68 [46, 89]	73 [55, 97]		0.15
Type of surgery				0.0503
Heart transplant	29 (17.2)	28 (37.8)	2 (14.3)	
Valvular surgery	51 (30.2)	15 (20.3)	4 (28.6)	
Coronary bypass	36 (21.3)	11 (14.8)	2 (19.0)	
Combined surgery	17 (10.0)	4 (5.4)	1 (7.1)	
Others	36 (21.3)	16 (21.6)	5 (35.7)	
Intraoperative period				
Cardiopulmonary Bypass Time, min	123 [87, 181]	123 [89, 166]	123 [78, 158]	0.85
Red Blood Cell transfusion, number	2 [0, 5]	2 [0, 4]	3 [2, 6.5]	0.37
Platelet transfusion, number	1 [0, 1]	1 [0, 1]	1 [0.25, 1.75]	0.68
Plasma transfusion, number	3 [0, 6]	3.5 [0, 5]	6.5 [3, 8.75]	0.047
Cell salvage autologous transfusion, mL	450 [230, 682]	423 [240, 533]	717 [315, 840]	0.27
Epinephrine, yes/no	97 (57.4)	39 (52.7)	10 (71.4)	0.42
Epinephrine, µg/kg/min[b]	0.10 [0, 0.31]	0.07 [0, 0.22]	0.15 [0.02, 0.45]	0.17
Dobutamine, yes/no	50 (29.6)	31 (41.9)	5 (35.7)	0.17
Dobutamine, µg/kg/min[b]	0 [0, 5]	0 [0, 7]	0 [0, 9.5]	0.32
Norepinephrine, yes/no	87 (51.5)	33 (44.6)	7 (50)	0.61
Norpinephrine, µg/kg/min[b]	0.02 [0, 0.19]	0 [0, 0.19]	0.18 [0, 0.45]	0.36
VA-ECMO implantation				
Primary graft dysfunction	12 (7.1)	16 (21.6)	2 (14.3)	0.006
Lactate, mmol/L[b]	6.9 (3.8)	5.1 (3.2)	5.2 (2.7)	0.002
Intraoperative implantation	90 (53.2)	57 (77.0)	12 (85.7)	0.0004
Postoperative implantation	79 (46.7)	17 (22.9)	2 (14.3)	0.0004
Epinephrine, yes/no	123 (72.8)	42 (56.8)	10 (71.4)	0.049
Dobutamine, yes/no	36 (21.3)	27 (36.5)	4 (28.6)	0.046

Norepinephrine, yes/no	77 (45.6)	28 (37.4)	5 (35.7)	0.46
D1 VA-ECMO support				
Creatinine, µmol/L[b]	154.5 ± 77.5	113.3 ± 45.9	137.1 ± 42.4	0.0001
Protidemia, g/L[b]	47.2 ± 8.6	51.4 ± 9.2	50.9± 14.0	0.008
Bilirubinemia, µmol/L[b]	32.2 ± 21.3	42.6 ± 44.6	21.4 ± 29.0	0.01
Bicarbonates, mmol/L[b]	18.7 (4.5)	20.4 (3.9)	19.2 (4.7)	0.04
Lactate, mmol/L[b]	5.2 (3.7)	3.85 (2.5)	3.91 (2.5)	0.04
Urine output, ml	600 [135-1150]	1550 [1150-2250]	1325 [525-2300]	<0.0001

Results are count (%), mean ±SD or median [interquartile range 25, 75].

[a] Chronic kidney failure is defined by a Glomerular Filtration Rate < 60 ml/min

[b] Refers to the maximum dose or maximal value

AKI, Acute kidney injury; BMI, body mass index; COPD, chronic obstructive pulmonary disease; D10, Day ten of follow-up after VA-ECMO support; LVEF, left ventricular ejection fraction; SAPS 2, simplified acute physiology score 2; SOFA, Sepsis-related Organ Failure Assessment; VA-ECMO, Veno-Arterial ExtraCorporeal Membrane Oxygenation.

Table 3: Risk factors for D30 mortality

Factors	Deceased at D30 No.=124	Alive at D30 No.=133	Univariable analysis *P-value*	Multivariable analysis *Odds Ratio [95%CI]*	Multivariable analysis *P-value*
Demographic characteristics					
Age, years	66.8±11.8	60.3±13.5	<0.001	1.007 [1.002, 1.012]	0.003
BMI, kg/m^2	26.8±5.7	24.5±4.3	<0.001	1.015 [1.003, 1.026]	0.013
SAPS 2	63.7±18.4	48.4±16.3	<0.001	-	-
SOFA	16.5±3.7	13.6±3.5	<0.001	-	-
LVEF, %	40 [25, 50]	25 [20, 45]	<0.001	-	-
Diabetes	40 (32.3%)	28 (21.1%)	0.058		
Dyslipidemia	77 (62.1%)	60 (45.1%)	0.009	-	-
High blood pressure	81 (65.3%)	59 (44.4%)	0.001	-	-
Chronic arteriopathy	24 (19.4%)	9 (6.8%)	0.005	1.20 [1.01-1.44]	0.041
Intraoperative period					
Red Blood Cell transfusion, number	3 [0, 5]	2 [0, 4]	0.091	-	-
Cell salvage autologous transfusion, mL	475 [247, 725]	392 [228, 663]	0.082	-	-
VA-ECMO implantation					
Biventricular failure	53 (42.7%)	35 (26.3%)	0.008	1.15 [1.02-1.30]	0.028
Primary graft dysfunction	22 (16.5%)	8 (6.5%)	0.020	-	-
Lactate, mmol/L	6.1 [3.4, 9.2]	5.3 [3.0, 8.4]	0.069	-	-
Inhaled Nitric Oxid	10 (8.1%)	24 (18.0%)	0.030	-	-
AKI at implantation	76 (61.3%)	63 (47.4%)	0.035	-	-
Urine output	750 [200, 1390]	1125 [500, 1860]	0.008	-	-
Type of surgery			0.003	-	-
Heart transplantation	15 (12.1%)	44 (33.1%)	-	-	-
Valvular surgery	38 (30.6%)	32 (24.1%)	-	-	-
Coronary bypass	27 (21.8%)	22 (16.5%)	-	-	-
Combined surgery	13 (10.5%)	9 (6.8%)	-	-	-
Other surgery	31 (25.0%)	26 (19.5%)	-	-	-

Results are count (%), mean ±SD or median [interquartile range 25, 75]. Adjusted Odds Ratio of factors that did not achieve statistical significance in multivariable analysis are not presented.

Due to missing data, SOFA and SAPS2 were not included in the multivariable analysis.

AKI, Acute Kidney Injury; BMI, body mass index; COPD, chronic obstructive pulmonary disease; LVEF, left ventricular ejection fraction; SAPS 2, simplified acute physiology score 2; SOFA, Sepsis-related Organ Failure Assessment; VA-ECMO, Veno-Arterial ExtraCorporeal Membrane Oxygenation.