Association of arterial blood pH at cannulation with 1-year survival among VA-ECMO recipients: the three seven rule

Nabil Dib[1], Yaniss Belaroussi[1], Alexandre Mansour[1], Nabila El Gueddari[1], Amedeo Anselmi[1], Karl Bounader[1], Marie Aymami[1], Jean-Philippe Verhoye[1], Vincent AUFFRET[1], Nicolas Nesseler[1], and Erwan Flecher[1]

[1]Hopital Pontchaillou

August 24, 2022

Abstract

Objective We aimed to describe the clinical outcomes of patients receiving veno-arterial extracorporeal membrane oxygenation therapy considering clinical context and pH at cannulation. **Methods** We reviewed all patients having received veno-arterial extracorporeal membrane oxygenation therapy at a tertiary referral center during the 2005-2020 period with 1-year complete follow up. Our cohort was divided in three groups according to the pH level at cannulation: pH<7 (group 1), pH 7-7.2 (group 2) and pH>7.2 (group 3). Survival was analyzed using Kaplan–Meier method. Association between pH group and survival was estimated using a Cox model. **Results** Among the 951 patients in our database, 572 were included in 3 different groups according to their pH at implantation: 60 patients in group 1, 115 in group 2 and 397 in group 3. Main indications of mechanical support were refractory cardiogenic shock (36%), post cardiotomy (28%), early graft failure (12%), refractory cardiac arrest (11%). One-year survival rate was 13% in group 1, 36% in group 2, 43% in group 3 respectively (p<0.001). Death mainly occurred within the first month. The strong correlation between pH and lactates led to propose a simple "three seven rule": pH<7 and lactate >7 was associated with <7% survival. **Conclusion** Extracorporeal veno-arterial membrane oxygenation should be considered with caution in patients with pH<7. Lactates and pH level might be important parameters to elaborate a new score to predict survival in this population. The simplicity of the "three seven rule" can be very relevant when facing emergency situations.

Association of arterial blood pH at cannulation with 1-year survival among VA-ECMO recipients: the three seven rule

Nabil Dib MD, MSc[a]; Yaniss Belaroussi MD, MSc[a] ; Alexandre Mansour MD, PhD[b] ; Nabila El Gueddari MD[a] ; Amedeo Anselmi MD, PhD[a]; Karl Bounader MD, MSc[a] ; Marie Aymami MD, MSc[a] ; Jean-Philippe Verhoye MD, PhD[a] ; Vincent Auffret MD, PhD[c] ; Nicolas Nesseler MD, PhD[b] ; Erwan Flécher MD, PhD[a].

[a] Department of Cardiothoracic and Vascular Surgery, Rennes University Hospital, Rennes, France

[b] Division of Cardiac Anesthesia, Pontchaillou University Hospital, Rennes, France

[c] Division of Cardiology, Pontchaillou University Hospital, Rennes, France

Corresponding author:

Dr. Nabil Dib, Hôpital Pontchaillou, Service de chirurgie thoracique et cardiovasculaire, rue Henri Le Guilloux, 35033 Rennes Cedex 9, France.

Tel. +33684934158; email: nabil.dib@anemf.org

Funding statement : no

Conflict of interest: none to declare

Data Availability Statement : Data are available for the journal's editor

This study was approved by the ethics committee of Rennes University Hospital (IRB n° 22.70).

Words count: 4451

Central message : For a very acid patients (pH<7) a simple easy reminder "three seven rule" might be useful waiting for a better and more appropriate survival score in this severe population

Perspective statement: Considering the increasing use of ECMO worlwide and the constant worsening of the patients, an adapted tool to predict survival is essential to avoid futile implantations. The present data may contribute to this making decision process, in accordance with real life situations.

Abstract

Objective

We aimed to describe the clinical outcomes of patients receiving veno-arterial extracorporeal membrane oxygenation therapy considering clinical context and pH at cannulation.

Methods

We reviewed all patients having received veno-arterial extracorporeal membrane oxygenation therapy at a tertiary referral center during the 2005-2020 period with 1-year complete follow up. Our cohort was divided in three groups according to the pH level at cannulation: pH<7 (group 1), pH 7-7.2 (group 2) and pH>7.2 (group 3). Survival was analyzed using Kaplan–Meier method. Association between pH group and survival was estimated using a Cox model.

Results

Among the 951 patients in our database, 572 were included in 3 different groups according to their pH at implantation: 60 patients in group 1, 115 in group 2 and 397 in group 3. Main indications of mechanical support were refractory cardiogenic shock (36%), post cardiotomy (28%), early graft failure (12%), refractory cardiac arrest (11%). One-year survival rate was 13% in group 1, 36% in group 2, 43% in group 3 respectively (p<0.001). Death mainly occurred within the first month. The strong correlation between pH and lactates led to propose a simple "three seven rule": pH<7 and lactate >7 was associated with <7% survival.

Conclusion

Extracorporeal veno-arterial membrane oxygenation should be considered with caution in patients with pH<7. Lactates and pH level might be important parameters to elaborate a new score to predict survival in this population. The simplicity of the "three seven rule" can be very relevant when facing emergency situations.

Keywords: Veno-arterial extracorporeal membrane oxygenation, critically-ill, survival, blood pH, critical care

INTRODUCTION

Extracorporeal membrane oxygenation (ECMO) is a validated technique for the temporary treatment of circulatory and/or respiratory failure(1). Although the indications are well defined(2), contraindications are not as clear and should be assessed on a patient-specific reasoning based on the clinical presentation. Apart from the obvious and irreversible multi-organ failure, the decision to not implement Veno-Arterial ECMO (VA-ECMO) is the result of a multi-disciplinary assessment between health professionals including the heart surgeon and the intensivist physician. Moreover, the decision-making process has to be extremely quick considering the high instability of such critically ill patients.

Acidosis with a blood pH<7 is in real life recognized by most physicians as a contraindication to VA-ECMO placement, but without strong evidence to support this statement. In the SAVE score, serum bicarbonate

level ([?]15 mmol/L) was identified as a poor prognostic factor(3), but without any mention to blood pH specifically. We previously explored that pH<7 appeared to be a poor prognostic factor but at that time we had much less patients in our series (1). Data in the literature of VA-ECMO using these simple biological parameters to play a role in the decision-making process are scarce (4,5).

We sought to investigate the proportion of patients implanted with low pH to compare the survival between groups according to pH levels at cannulation in our VA-ECMO cohort.

MATERIALS AND METHODS

Patients and data collection

Since the beginning of the ECMO program at our institution in 2005, all data regarding patients receiving veno-arterial support for hemodynamic failure have been prospectively entered in an electronic database registry by dedicated research nurses. This database is regularly checked for completeness and consistency. In December 2020, we performed a retrospective analysis of patients included in the registry (n = 951) over the January 2005 to December 2020 period. The indication for VA-ECMO therapy was established in compliance with the current recommendations(2) by a multidisciplinary team including two intensivists and a heart surgeon in all cases. The indication was decided when the chances of success were believed to outweigh the risks and the use of hospital resources. Patients had to present an expected good quality of life and either potential for recovery or possible candidacy to transplantation or long-term mechanical support. When VA-ECMO was judged to prolong the course of illness without a realistic chance of survival or acceptable quality of life in case of recovery, ECMO support was not instituted. VA-ECMO was implanted for refractory circulatory failure with isolated one-organ insufficiency or before severe multiorgan failure developed. Patients were evaluated using the Simplified Acute Physiology Score (SAPS) version 2 immediately before VA-ECMO cannulation [5], using the calculator available online at www.sfar.org (French Society of Anesthesia and Intensive Care website). All patients receiving VA-ECMO at our institution were included in the present study.

Ethics statement

Our database was approved by the French data protection authority: *Commission Nationale de l'Informatique et des Libertes(CNIL, reference 1685088, July, 25th 2013)* . The need for written consent was waived because of the observational design.

This study was approved by the ethics committee of Rennes University Hospital (IRB ndeg 22.70).

Classification according to blood pH

Arterial blood gases (ABG) were drawn at cannulation in the vast majority of cases. Then, ABG were performed regularly during the follow-up. We classified patients into 3 groups depending on the first arterial pH level at cannulation of VA ECMO: pH<7 (Group 1), pH between 7 and 7.2 (Group 2) and pH>7.2 (Group 3). We chose these cut-off points according to articles published in literature(4,6) and with consultation of the authors.

Surgical technique

The cannulation of VA-ECMO was performed under general anesthesia and mechanical ventilation in 99% of cases. The implanting team included two surgeons (senior and resident), a scrub-nurse, a perfusionist and an anesthetist. All required material was available on a dedicated trailer, allowing full autonomy for prompt displacement of the team within-hospital facilities wherever ECMO support was needed, including operative theatre, intensive care units (ICUs) and catheterization room.

Peripheral cannulation through the femoral access was most commonly employed (94.4%). The anterior surface of the right common femoral artery and vein was exposed through groin incision and cannulated using the Seldinger technique (16–20 Fr for the inflow cannula and 18–32 Fr for the drainage cannula, according to the patient's body surface area, vessels quality and surgeon's preference) (Edwards Lifesciences, Inc., Irvine,

CA, USA). In all peripheral VA cases, a reperfusion catheter was introduced in the superficial femoral artery to prevent limb ischaemia (5–10 Fr). The left groin was accessed in case of unsuitable vascular access on the right side. VA-ECMO cannulation was performed in the cardiac surgery operating theatre if the patient could be safely transported (71.2%). In case of unstable haemodynamics or cardiac arrest, cannulation was done at the patient's bed (18.0%) Removal of the VA-ECMO cannulae was performed in the operating theatre (except in case of death under support) to allow optimal vessel repair. A few post-cardiotomy patients (n = 32, 5.6%) received central ECMO with a left atrial vent through median sternotomy.

Follow-up

Patients who were discharged alive from the hospital were periodically contacted by dedicated mechanical circulatory support nurses. An inquiry over vital status, functional conditions and occurrence of complications was performed. If patients could not be contacted, the referring general practitioners or cardiologists were contacted. Data were prospectively entered in the Rennes ECMO Registry database.

Statistical analysis

Study population was described according to pH groups. Counts and proportions were reported for categorial variables, and means +/- standard deviations (SD) for continuous variables. Normality for continuous variables was explored both in a graphical way with histogram. Groups were compared using Chi-squared test for qualitative variables (unless expected counts were less than 10, in which case Fisher's exact test was used) and ANOVA for normal continuous variable (homogeneity of variance was analyzed using Bartlett's test) or non-parametric Kruskal Wallis test for non-normal variables.

Correlation between lactates rate distribution and blood pH rate was explored with Spearman's Rho correlation test.

The date of initiation of VA-ECMO cannulation was chosen as the date of origin for survival outcomes. Survival data were described with Kaplan-Meier survival curves. Median survival time of the study population was reported with a 95% confidence interval (95%CI). Log-rank test was used to assess comparison between pH groups. Survival rates at 30 days and one year were estimated for each group. Cox proportional hazard models were used for the assessment of the association between pH groups and overall survival and a backward stepwise selection was performed for variable selection. The final model selected covariates with significance level 0.10. Two covariates considered as potential confounders were forced into the model: sex and ECMO indication. Interaction with initial diagnosis was tested. We checked the collinearity between the covariates in the multivariable analysis using the variance inflation factor (VIF) for diagnostic for multicollinearity. A decision curve analysis was performed to graphically analyze the relationship between pH and the futility of the procedure.

Statistical analyses were performed with R version 4.0.1.

Results

Since 2005, a total of 951 patients received ECMO support in our institution. 572 patients under VA-ECMO with ABG available at cannulation were finally included in the present study (*Figure A*). Ninety-nine patients were excluded because they had no pH at cannulation, 190 because they were veno-venous ECMO and 90 because they were duplicates in the database.

Patients characteristics are presented in *Table1* . Most of the patients were male (68%) and mean age at cannulation was 54.8 (14.0) years. Mean SAPS II score was 46 (19.0).

Three groups were established considering the pH level at cannulation: Group 1 (pH<7) = 60 patients, group 2 (pH 7-7,2) = 115 patients and group 3 (pH>7,2) = 397 patients.

The three groups were significantly different for the age at cannulation (p<0.001). Patients from group 1 seemed to be younger patients (49.3 (14.0) years vs 52.5 (13.0) and 56.3 (14.0) years respectively for group 1, 2 and 3; p<0.001).

Main indication for group 1 was refractory cardiac arrest (40.7%) while predominant indications for groups 2 and 3 were post-cardiotomy (23.7 and 31.6% respectively) and refractory cardiogenic shock (22.8 and 42.2% respectively). In group 1 mean pH level was 6.86 (0.14) while mean pH level in groups 2 and 3 were 7.13 (0.06) and 7.38 (0.11) respectively ($p<0.001$).

Table 1 compares the main baseline characteristic between the three groups. We also compared ECMO's complications between groups 2 and 3 (Table 4 in supplementary data).

At cannulation, doses of vasopressor amines were different ($p<0.001$). Patients in group 1 seemed to receive higher doses of vasopressor amines than the other 2 groups, respectively 78% vs 48 and 31%. Both groups differed in term of infectious complications ($p<0.001$). We described less thrombotic or hemorrhagic complications in group 1 had also: for thrombotic complications, 15 patients were affected in group 1 (25.9%), whereas 64 (55.7%) and 239 (58.1%) patients in groups 2 and 3. Considering hemorrhagic complications, it was observed in only 1 patient (4.5%) in group 1, 17 (23.9%) and 42 (18.8%) patients in groups 2 and 3.

The survival rate at 30 days for the overall population was 42.9%, 95%CI= [0.39-0.472]. Median of survival was respectively 1 day [1-2], 14 [6-27] and 33 days [18-NR] for group 1, 2 and 3. The very vast majority of deaths occurred within the 30 days after cannulation (*Figure B*). Indeed, after the first month survival curves were roughly stable until 12 months. The survival rate 30 days post cannulation was significantly different ($p<0.001$) between the three groups; in the group 1: 15.0%, 95%CI = [0.082-0.274], in group 2 37.8%, 95%CI= [0.298-0.480] and in group 3 48.8%, 95%CI= [0.4407-0.5410]. The Kaplan Meyer estimated survival rate at 1 year were 13.3 % (95%CI = [7.0 – 25.4]) for group 1, 36.0 % (95%CI = [28.1 – 46.1]) for group 2, 43.2 % (95%CI = [38.5 – 48.6]) for group 3. These rates were significantly different ($p<0.001$) and are summarized in the *Table 2* .

Lactate level was correlated with the blood pH rate (*Figure C*). Low blood pH was associated with high rates of lactates as illustrated with -0.66 Spearman's Rho coefficient which is in favor of a strong correlation between these 2 variables.

Figure D corresponded to the realization of subgroups according to the blood lactates level (<3; 3-7 and >7), and the curves joined those of pH with a probability of survival that decreased strongly in the first 30 days and then stayed stable. Association of low pH level (<7) and high level of lactate (>7) predicted a low chance of survival at one year (5.9% CI95 = [5.5-6.4]).

In multivariable analysis (*Table 3*), there were 5 major criteria that emerged as significant at cannulation: pH level (group 2: HR=1.42, 95% CI = [1.02 – 1.97]; group3: HR=5.07, 95% CI = [3.02 – 8.04]), age (for an increase of 10 years HR = 1.36, 95% CI = [1.22 – 1.50]), VA-ECMO implantation under external cardio pulmonary resuscitation (HR = 1.63, 95% CI = [1.13 – 2.35]), diastolic blood pressure at implantation (40mmHg or more, HR = 0.56, 95% CI = [0.39 – 0.81]) and kidney failure (HR = 1.56, 95% CI = [1.19 – 2.06]).

The decision curve analysis is presented in supplementary material.

Discussion

To our knowledge, we report the largest study focusing on outcomes of VA-ECMO treatment considering blood pH at VA-ECMO initiation. Our findings suggest: 1) the survival at one year of patients with a blood pH at cannulation <7 is low but does exist. However, patients were younger and treated mainly for refractory cardiac arrest, but after adjustment blood pH remains associated with mortality. 2) The lactate level is highly correlated with the pH level.

The use of ECMO has been used exponentially since the early 2000s in western countries, allowing to treat even patients in refractory out-of-hospital cardiopulmonary arrest with better results than standard resuscitation (43% vs 7% at discharge and 43% vs 0% at 3 months)(7). VA-ECMO might become in a near future the standard treatment for refractory cardiorespiratory arrest, however clinical results remain questionable in many centers. Mork and al. recently reported a thirty day survival rate of 26% after ECMO

initiation for out of hospital refractory cardiac arrest(8). Predicted scores have been proposed but the optimal tool remains an unmet need (9). We believe pH and lactates may represent interesting parameters to consider to

help in this goal research.

The survival rate in group 1 (lowest pH) was significantly lower than in the other 2 groups ($p<0.001$). In our experience, having a pH lower than 7 at implantation multiplies the risk of death by four (Table 3). In the literature, survival in the adult population treated with VA-ECMO for cardiogenic shock is similar than in our study(10). However, we do report here our real-life daily practice without excluding patients with high acidity, even those who were supported for a few hours. Interestingly, Mork et al. reported good outcomes on a population similar to our group 1(8). In our study, the survival rate, in group 1 although very low, is not negligible. Indeed, in this group one patient out of 6 has been discharged alive from the hospital despite the extreme acidity at cannulation.

It is important to note that the high mortality rate occurs within the first 30 days post-cannulation and that the median survival is respectively 1, 14 and 33 days for groups 1, 2 and 3. These results indicate that financial and human resources require to manage such patients, although important, might not last for a long time of mechanical support, especially for group 1 patients. The most critically-ill ones die promptly, mainly within the first days. An ongoing study (ECMONOMY) at the Rennes's University Hospital, aims to accurately study the cost of a hospital stay for a patient treated with VA ECMO (**NCT03686540**). This study will eventually help to explore the financial ratio in order to avoid unnecessary expenses.

Patients in group 1 had fewer complications, whether thrombotic or infectious, than the others groups. One may consider it is because these patients die more quickly and did not have time to develop such complications.

As in daily life practice we demonstrated a strong correlation between the blood pH level and the lactate level (-0.66). This strong correlation is interesting as one or both parameters might be part of a new decision-making algorithm at cannulation. There are already scores such as the SAVE score which predicts the survival rate in patients with refractory cardiogenic shock requiring ECMO(3). This score requires a blood sample to get serum creatinine or bicarbonate levels, excluding its easy use out of hospital and requiring a minimal delay. We believe pH and lactates dosage can be obtained almost instantaneously, even outside hospital with small ambulatory biological samples devices. Such strategy may allow to help in the difficult decision-making process, especially in high emergent cases, out of hospital or in the emergency room. Indeed, our study showed that when blood pH level is low (<7) and blood lactate level is high (>7) the survival prognosis is low ($<7\%$). This simple algorithm with "the three seven rule" may be very helpful for emergent real-life clinical.

Moreover Mungan et al. indicate that in addition to the lactate level at ECMO initiation, the evolution of lactate clearance is also important as these 2 factors allow to estimate a reliable prognosis of the patient's outcome(11). To be more precise, Li et al. indicate from their univariate and multivariate analyses that the important factors are the mean lactate concentration and lactate clearance at 6 and 12 hours after the initiation of ECMO(12). This approach integrating pH and lactates levels at ECMO initiation seems logical as the elevation of lactate levels is related to tissue damage and that lactate clearance therefore indicates a restoration of tissue oxygenation and hemodynamic circulation. In our study low pH and high lactate rates are mortality's predicting factors as demonstrated by Seeger and al(6).

We believe our study pleads strongly for further investigations to precise utility or futility of ECMO treatment using pH and lactates level. These additional investigations seem to be essential because new indications of short-term assistance (ECMO or Impella(r)) may develop such as High Risk Percutaneous Coronary Indication (HR PCI), Transcatheter Aortic Valve Implantation (TAVI) or Mitraclip(r). Moral and ethical obligations will require careful evaluation of these possible new indications to avoid futile results. Heart team approach will be even more essential to define possible new indications in a very severe population.

Our study has some limitations, including its retrospective nature and the heterogeneity of its cohort. The retrospective character is somewhat mitigated by the fact that the data in the database are entered prospectively by nurses dedicated to the database. Moreover, our study compares survival outcomes between different subgroups of patients in a tertiary high-volume ECMO center. Our database does not contain the data of all the requests for ECMO procedure but only the patients implanted; it is therefore possible that a selection was made at the discretion of the surgical team when managing the call for ECMO patient, especially given the patient's age and comorbidities.

Conclusion

We classically learned at medical school that survival is impossible with pH<7 but this dogma seems, in very selected cases, challenged considering the rapid development of ECMO programs. Although survival is possible with an extremely low pH in ECMO patients, it remains rare. A strong correlation between pH and lactate level as prognosis factors leads to integrate such parameters to build a new score to help in the decision-making process of ECMO cannulation. We observed a survival rate lower than 7% when pH was lower than 7 and lactates level more than 7. We believe such simple easy reminder rule might be useful waiting for a better and more appropriate survival score in this very severe population.

References

1. Flecher E, Anselmi A, Corbineau H, Langanay T, Verhoye JP, Felix C, et al. Current aspects of extracorporeal membrane oxygenation in a tertiary referral centre: Determinants of survival at follow-up. Eur J Cardio-thoracic Surg. 2014;46(4):665–71.

2. Beckmann A, Benk C, Beyersdorf F, Haimerl G, Merkle F, Mestres C, et al. Position article for the use of extracorporeal life support in adult patients. Eur J Cardio-thoracic Surg. 2011;40(3):676–80.

3. Schmidt M, Burrell A, Roberts L, Bailey M, Sheldrake J, Rycus PT, et al. Predicting survival after ECMO for refractory cardiogenic shock: The survival after veno-arterial-ECMO (SAVE)-score. Eur Heart J. 2015;36(33):2246–56.

4. Daou O, Winiszewski H, Besch G, Pili-floury S, Belon F, Guillon B, et al. Initial pH and shockable rhythm are associated with favorable neurological outcome in cardiac arrest patients resuscitated with extracorporeal cardiopulmonary resuscitation. J Thorac Dis. 2020;12(3):849–57.

5. Okada Y, Kiguchi T, Irisawa T, Yoshiya K, Yamada T, Hayakawa K. Association between low pH and unfavorable neurological outcome among out-of-hospital cardiac arrest patients treated by extracorporeal CPR : a prospective observational cohort study in Japan. J intensive care. 2020;1–9.

6. Seeger FH, Toenne M, Lehmann R, Ehrlich JR. Simplistic approach to prognosis after cardiopulmonary resuscitation — value of pH and lactate. J Crit Care [Internet]. 2013;28(3):317.e13-317.e20. Available from: http://dx.doi.org/10.1016/j.jcrc.2012.05.004

7. Yannopoulos D, Bartos J, Raveendran G, Walser E, Connett J, Murray TA, et al. Advanced reperfusion strategies for patients with out-of- hospital cardiac arrest and refractory ventricular fibrillation (ARREST): a phase 2 , single centre , open-label , randomised controlled trial. Lancet [Internet]. 2020;6736(20):1–10. Available from: http://dx.doi.org/10.1016/S0140-6736(20)32338-2

8. Mork SR, Stengaard C, Linde L, Moller JE, Jensen LO, Schmidt H, et al. Mechanical circulatory support for refractory out - of - hospital cardiac arrest : a Danish nationwide multicenter study. Crit Care. 2021;1–13.

9. Muller G, Flecher E, Lebreton G, Luyt CE, Trouillet JL, Brechot N, et al. The ENCOURAGE mortality risk score and analysis of long-term outcomes after VA-ECMO for acute myocardial infarction with cardiogenic shock. Intensive Care Med. 2016;42(3):370–8.

10. Thiagarajan RR, Barbaro RP, Rycus PT, McMullan DM, Conrad SA, Fortenberry JD, et al. Extracorporeal Life Support Organization Registry International Report 2016. ASAIO J. 2017;63(1):60–7.

11. Mungan I, Kazancl D, Bektaş Ş, Ademoglu D, Turan S. Does lactate clearance prognosticates outcomes in ECMO therapy: A retrospective observational study. BMC Anesthesiol. 2018;18(1):1–8.

12. Li CL, Wang H, Jia M, Ma N, Meng X, Hou XT. The early dynamic behavior of lactate is linked to mortality in postcardiotomy patients with extracorporeal membrane oxygenation support: A retrospective observational study. J Thorac Cardiovasc Surg [Internet]. 2015;149(5):1445–50. Available from: http://dx.doi.org/10.1016/j.jtcvs.2014.11.052

Table 1: Baseline characteristics according to blood pH level at cannulation (n=572)

Variables Mean (SD) or n (%)	Group 1 (pH [?]7) n=60 (10.48%)	Group 2 (pH=]7.0-7.2]) n=115 (20.11%)	Group 3 (pH>7.2) n=397 (69.41%)	p-value
Simplified acute physiology score II	57.60 (23.96)	48.90 (18.79)	43.67 (18.41)	<0.001
Age, years	49.26 (13.98)	52.53 (13.29)	56.33 (14.05)	<0.001
Male	44 (73.3)	74 (64.9)	270 (68.5)	0.518
Co-morbidities	4 (6.7) 0 (0.0) 3	4 (3.5) 1 (0.9) 7	16 (4.0) 5 (1.3) 32	0.276 0.665 0.473
Diabetes	(5.0)	(6.1)	(8.1)	
Arteriopathy				
Hypertension				
Reason for ECMO	5 (8.5) 1 (1.7) 13	27 (23.7) 2 (1.8) 26	125 (31.6) 2 (0.5)	<0.001
implantation	(22.0) 3 (5.1) 2 (3.4)	(22.8) 6 (5.3) 24	167 (42.2) 7 (1.8) 40	
Post-cardiotomy	24 (40.7) 6 (10.2) 5	(21.1) 22 (19.3) 3	(10.1) 19 (4.8) 13	
cardiogenic shock	(8.5)	(2.6) 4 (3.5)	(3.3) 23 (5.8)	
Septic shock				
Medical cardiogenic shock RV dysfunction during ARDS Post-heart transplantation cardiogenic shock Refractory cardiac arrest Drug intoxication Other				
Other support at	5.6 (9.9) 14 (23.7)	8.7 (10.0) 68	10.0 (10.2) 299	0.009 <0.001
ECMO	46 (78.0)	(59.6) 56 (48.7)	(75.7) 123 (31.1)	<0.001
implantation				
Number of days with mechanical ventilation				
Dobutamine				
Norepinephrine				
ECMO localization	3 (5.1) 56 (94.9)	7 (6.1) 108 (93.9)	22 (5.6) 372 (94.4)	0.961
Central Periphery				
Biological	15.22 (4.79) 6.86	9.42 (4.38) 7.13	5.06 (4.11) 7.38	<0.001 <0.001
measurement	(0.12)	(0.06)	(0.11)	
Serum lactates				
Blood pH				

Table 2: Kaplan Meyer survival rate and Median of survival

	[?]7.0 N = 60	**]7.0-7.2] N = 115**	**>7.2 N = 3**
Number of events	**52**	**71**	**215**
Median of survival (days (CI 95))	**1 (1- 2)**	**14 (6 – 27)**	**33 (18 – NR**
Kaplan Meier estimated survival rate at 1 year (CI 95)	**13.3 (7.0 – 25.4)**	**36.0 (28.1 –46.1)**	**43.2 (38.5 –**

CI 95: Confidence Interval 95%

Table 3: Survival analysis: univariable and multivariable models

	Univariate Analysis	Univariate Analysis	Multivariate Analysis	Multivariate Analysis
Variable	HR (CI 95)	p-value	Adjusted HR (CI 95)	p-value
Sex: Male vs Female (Ref)	0.92 (0.73 – 1.16)	0.479	0.92 (0.69 – 1.21)	0.533
Age (10-year period increase)	1.35 (1.15 – 1.36)	<0.001	1.36 (1.22 – 1.50)	<0.001
Group of pH		<0.001		
>7.2	Ref			
7.0 – 7.2	1.39 (1.06 – 1.82)	0.016	1.42 (1.02 – 1.97)	0.038
<7.0	3.85 (2.83 – 5.23)	<0.001	5.07 (3.20 – 8.04)	<0.001
Implantation site				
Central	Ref		Ref	
Peripheral	3.88 (0.48 – 1.17)	0.202	0.63 (0.35 – 1.12)	0.069
ECMO indication				
Refractory cardiac arrest	Ref		Ref	
Refractory cardiogenic shock	0.55 (0.39 – 0.78)	0.001	1.36 (0.82 – 2.25)	0.229
Post-cardiotomy	0.72 (0.51 – 1.03)	0.069	1.18 (0.69 – 2.01)	0.554
Post-transplantation	0.40 (0.25 – 0.63)	<0.001	0.99 (0.53 – 1.85)	0.976
ECMO implantation under external CPR	2.12 (1.68 – 2.70)	<0.001	1.63 (1.13 – 2.35)	0.009
Resuscitated cardiac arrest	2.25 (1.29 – 3.92)	0.005		
Kidney (failure vs normal)	2.05 (1.63 – 2.58)	<0.001	1.56 (1.19 – 2.06)	0.001
DBP [?]40 vs <40	0.56 (0.40 – 0.79)	<0.001	0.56 (0.39 – 0.81)	0.009
Bicarbonates (>15 vs [?]15)	0.41 (0.20 – 0.83)	0.013		
Plateau pressure (>20 vs [?]20)	1.08 (0.85 – 1.37)	0.520		
Lactates [?]7 vs < 7	1.84 (1.47 – 2.31)	<0.001		
Liver failure	1.49 (1.15 – 1.92)	0.002		

CPR: cardio pulmonary resuscitation

DBP: Diastolic blood pressure

Ref: Reference

CI 95: Confidence Interval 95%

Figures

Central Image : Survival curve taking account blood pH level

Figure A: Study workflow for Venous-Arterial ECMO

Figure B: Survival curve in function of blood pH level

Figure C: Graph expressing pH by lactate

Figure D: Survival curve in function of blood lactate level