Venoarterial Extracorporeal Membrane Oxygenation in Severe Drug Intoxication: A Retrospective Comparison of Survivors and Nonsurvivors

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Selecting patients most likely to benefit from venoarterial extracorporeal membrane oxygenation (V-A ECMO) to treat refractory drug-induced cardiovascular shock remains a difficult challenge for physicians. This study reported short-term survival outcomes and factors associated with mortality in V-A ECMO-treated patients for poisoning. Twenty-two patients placed on V-A ECMO after drug intoxication from January 2014 to December 2020 were retrospectively analyzed. The primary endpoint of this study was survival at hospital discharge. Univariate descriptive analysis was performed to compare survivors and nonsurvivors during hospitalization. The overall survival at hospital discharge was 45.4% (n = 10/22). Survival rate tended to be higher in patients treated for refractory shock (n = 7/10) compared with those treated for refractory cardiac arrest (n = 3/12, $p = 0.08$). Low-flow duration and time from admission to ECMO cannulation were shorter in survivors ($p = 0.02$ and $p = 0.03$, respectively). Baseline characteristics before ECMO, including the class of drugs involved in the poisoning, between survivors and nonsurvivors were not statistically different except pH, bicarbonate, serum lactate, Sequential Organ Failure Assessment, and Survival After Veno-arterial-ECMO (SAVE) score. All patients with SAVE-score risk classes II/III survived whereas 85.7% (n = 12/14) of those with SAVE-score risk classes IV/V died. A lactic acid >9 mmol/L predicts mortality with a sensitivity/specificity ratio of 83.3%/100%. V-A ECMO for severe drug intoxication should be reserved for highly selected poisoned patients who do not respond to conventional therapies. Shortening the timing of V-A ECMO initiation should be a key priority in improving outcomes. Low-flow time >60min, lactic acid >9mmol/L, and SAVE-score may be good indicators of a worse prognosis. *ASAIO Journal* 2022; 68;907–913

Key Words: extracorporeal membrane oxygenation, cardiogenic shock, cardiac arrest, drug poisoning, cardiotoxicity, toxicology

Cardiovascular collapse remains a leading cause of death in severe acute drug intoxication.[1] Despite improvements in the specific treatment of poisoning exposures, the management of these patients relies mainly on symptomatic and supportive care. One of the most aggressive supportive treatments available is veno-arterial extracorporeal membrane oxygenation (V-A ECMO). In patients who are refractory to conventional medical therapy, V-A ECMO maintains organ perfusion and allows time for elimination of the offending drug, providing a bridge to recovery. Although recent data suggest that the use of V-A ECMO for poisoning increases,[2,3] rigorous data supporting its use are limited,[4] and most of the published studies in this setting are case reports and case series.[5–10] In addition, temporary mechanical support reveals a high rate of specific and unspecific side effects associated with V-A ECMO including infections, bleeding, neurologic complications, acute kidney injury, and lower limb ischemia.[11,12] Even so, V-A ECMO has proven its clinical interest (improvement in hemodynamics and acid-base status) in drug poisoning in a recent large retrospective study.[3] However, selecting patients with refractory shock as well as patients with refractory cardiac arrest most likely to benefit from V-A ECMO remains a keystone issue for physicians.

Since January 2014, our institution has expanded the role of V-A ECMO in drug-induced refractory shock and cardiac arrest and we sought to describe our experience. The purpose of this study was to investigate the clinical utility of V-A ECMO and report short-term survival outcomes and factors associated with mortality.

Methods

Study Design

We retrospectively analyzed all the patients placed on peripheral V-A ECMO for drug intoxication between January 2014 and December 2020. In accordance with the ethical standards of our hospital's institutional review board, informed consent was not necessary for data analyses. This database was registered at the Commission Nationale de l'Informatique et des Libertés (CNIL, registration no. DEC18-348).

Patient Population

We included the patients treated with V-A ECMO for refractory cardiogenic shock or mixed shock involving a significant

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cardiogenic component, and patients suffering from refractory cardiac arrest after drug intoxication. Cardiogenic shock was defined as hypotension (systolic blood pressure <90 mmHg) with markers of hypoperfusion despite adequate management of hypovolemia.[13] Refractory cardiogenic or mixed shock involving a significant cardiogenic part was defined as persistent hypotension (systolic blood pressure <90 mmHg) despite high-dose catecholamine infusion (epinephrine >1 µg/kg/min or dobutamine >20 µg/kg/min with norepinephrine >1 µg/kg/min) and optimal conventional treatment,[14] associated with altered left ventricular ejection fraction (LVEF) (<25%), low cardiac output and persistent tissue hypoxia (anuria, or acute renal failure, extensive skin mottling, elevated blood lactate, hepatic cytolysis, and neurologic impairment) despite adequate management of hypovolemia.[15] Refractory cardiac arrest was defined as the absence of a return to spontaneous circulation within a period of at least 30 min of cardiopulmonary resuscitation (CPR) under medical direction in the absence of hypothermia.[16] Age >65 years was a relative contraindication to V-A ECMO implantation while pre-existing irreversible neurologic damages or major comorbidities compromising life expectancy were absolute contraindications.

V-A ECMO Implantation and Management

Because of hemodynamic instability, all V-A ECMO implantations were performed at the bedside by cardiovascular surgeons, using a modified Seldinger technique after surgical exposure of the vessels. To prevent homolateral leg ischemia, an additional perfusion catheter (7 Fr) was implanted in the distal part of the superficial femoral arteria. Fluids and vasopressors (norepinephrine and epinephrine) were used to maintain a mean blood pressure of at least 60 mmHg. Extracorporeal blood flow was adjusted to maintain adequate systemic blood flow and oxygen supply as monitored by mean arterial pressure, urine output, and lactate concentration. In the case of prolonged ventricular asystole with no opening of the aortic valve, inotropic support was used to prevent left ventricle blood stasis, pulmonary edema, and intracardiac clotting. An unfractionated heparin bolus (50 IU/kg) was injected at V-A ECMO initiation, and then all patients were continuously infused with unfractionated heparin. The withdrawal of V-A ECMO was taken in case of the futility of the treatment retained by multidisciplinary medical and surgical teams. Stable patients at minimal V-A ECMO flow with LVEF >25% and time–velocity integral > 10 cm were weaned from V-A ECMO.[17]

Data Collection

Data collected by the computerized medical charts of our intensive care unit (ICU) included patient demographic information (age and gender), time from admission to V-A ECMO initiation, pre-V-A ECMO cannulation support/intervention and clinical assessment – acid-base markers, hemodynamic data – complication during V-A ECMO support, and clinical outcomes. Measured physiologic variables were used to calculate the Sequential Organ Failure Assessment (SOFA) score, which quantifies the number and severity of failed organs (respiration, coagulation, liver, cardiovascular, central nervous system, and renal) and predicts mortality risk for patients[18] and the SAVE-score, that assists prediction of survival for adult patients undergoing V-A ECMO for refractory cardiogenic shock.[19] Five risk classes, namely class I (SAVE-score: ≥5), class II (SAVE-score: 1 to 5), class III (SAVE-score: −4 to 0), class IV (SAVE-score: −9 to −5), and class V (SAVE-score: ≤−10) were identified with their corresponding survival rate (75%, 58%, 42%, 30%, and 18%, respectively). An initial electrocardiogram was collected and severe conduction abnormalities were defined as sino-atrial block or high degree atrioventricular block. The drugs involved in poisoning were classified as cardiovascular, opioids, antidepressants, and others. The presence of a membrane-stabilizing activity was also recorded. In patients, who had undergone cardiac arrest, we recorded no-flow time, initial cardiac rhythm, and low-flow time. No-flow time was defined as the time between the cardiac arrest and initiation of CPR by a medical provider. Low-flow time was defined as time with active CPR by a medical provider.

Outcomes and Statistical Analysis

The primary endpoint of our study was survival at hospital discharge. We evaluated the neurologic outcome at discharge through the Cerebral Performance Categories (CPCs) score. Good neurologic recovery was defined as a CPC score of 1 (good cerebral performance) or 2 (moderate cerebral disability) on a five-point scale. The secondary endpoints were initial V-A ECMO flow rate, successful weaning rate from V-A ECMO, days on V-A ECMO, ICU and total hospital length of stay, and complications during V-A ECMO support. Quantitative variables were expressed as medians (interquartile range). The normality of their distributions was assessed using histograms and Shapiro-Wilk tests. Categorical variables were expressed as numbers (percentages). Baseline characteristics were compared between survivors and nonsurvivors by Fisher exact tests for categorical variables and Mann-Whitney U tests for continuous variables. The ability of serum lactate level before V-A ECMO to predict mortality was assessed using receiver operating characteristics (ROCs) curves. The best cutoff of pre-V-A ECMO lactic acid was determined using Youden's index that provides the highest ratio sensitivity/specificity. Graphpad Prism 6 software (San Diego, CA) was used for data analysis. All tests were two-sided, and a p value less than 0.05 was considered statistically significant.

Results

During the study period, 22 acutely poisoned patients received V-A ECMO; 12 for a refractory cardiac arrest (all these patients collapsed in front of medical provider and received immediate CPR), and 10 for a refractory shock (Figure 1). Refractory cardiac arrest occurred out-of-hospital in five cases and in-hospital in seven cases. The initial rhythms were mostly asystole (91.7%). In patients with refractory shock, the median heart rate, mean arterial pressure, and LVEF before V-A ECMO support were, respectively, 87 (69–134) beats per minute, 55 (50–64) mmHg, and 20 (15–35%). Ten patients were excluded from ECMO because of age more than 65 years (n = 4), pre-existing irreversible neurologic damages (n = 3), and major comorbidities (two patients with liver cirrhosis Child-Pugh C and another one with disseminated neoplasia).

Demographic, clinical, and biologic characteristics between survivors and nonsurvivors were not statistically different except pH, bicarbonate, serum lactate, time from admission to V-A ECMO support, SOFA, and SAVE score (Table 1). The drugs involved in poisoning were similar between the two groups

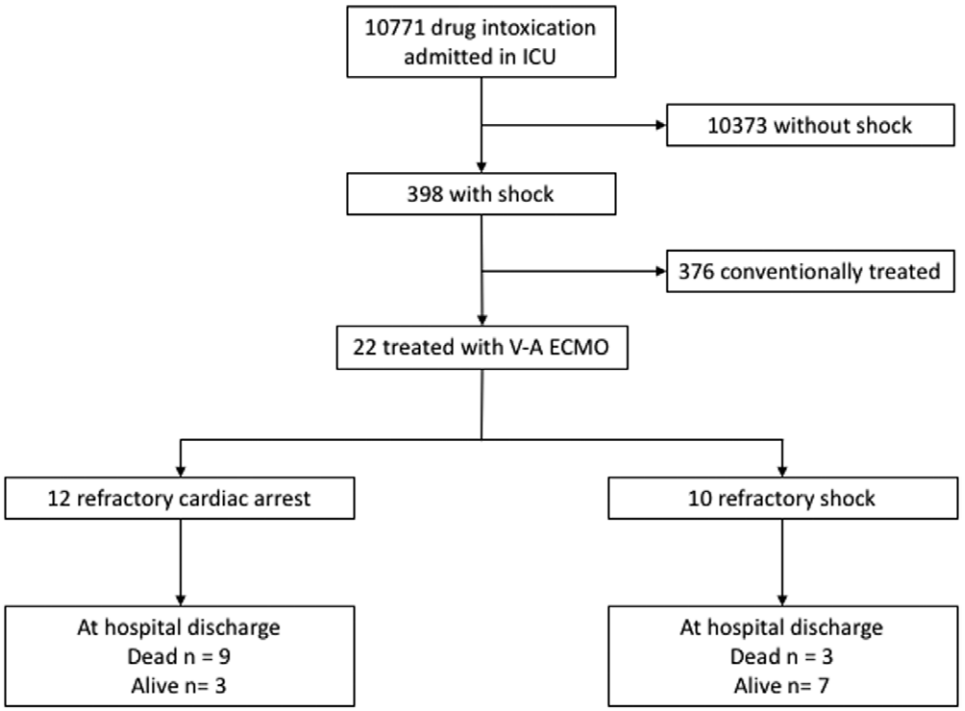

Figure 1. Flowchart of the study. ICU, intensive care unit; V-A ECMO, venoarterial extracorporeal membrane oxygenation.

and are detailed for each patient in Table 2. Pre-V-A ECMO support/intervention was also similar between groups. All the patients were mechanically ventilated and received vasoactive drugs infusion; 72.7% (n = 16) of the patients received two or more agents, and 63.6% (n = 14) 3 or more agents. The vasopressor/inotropic agents infused were epinephrine (86.4%), norepinephrine (72.7%), dobutamine (54.5%), and isoprenaline (36.4%). Because of severe conduction defects, 10 patients (45.4%) received molar sodium lactate infusion, and 3 others required external pacing. Continuous venovenous

Table 1. Demographic, Clinical, and Biologic Characteristics of Cases That Received V-A ECMO for Drug-induced Cardiovascular Toxicity

Variables	Patients (n = 22)	Survivors (n = 10)	Nonsurvivors (n = 12)	*p* value
Age, years	52 (40–64)	50 (20–59)	56 (41–65)	0.32
Men, n (%)	4 (18)	1 (10)	3 (25)	0.59
Weight, kg	64 (54–70)	64 (59–68)	64 (50–90)	0.76
Type of agent in poisoning, n (%)				
Cardiovascular	19 (86.4)	9 (90)	10 (83.3)	–
Opioid	2	2 (20)	0	–
Antidepressant	6 (27.3)	3 (30)	3 (25)	–
Other	2 (9.1)	0	2 (16.7)	–
Multiple drugs intoxication, n (%)	16 (72.7)	8 (80)	8 (66.7)	0.65
Severe conduction trouble*	15 (68.2)	5 (50)	10 (83.3)	0.17
Refractory cardiac arrest	12 (54.5)	3 (30)	9 (75)	0.08
Time from admission to V-A ECMO#, hours	9 (4.8–18.5)	5.2 (4.3–9.5)	18.2 (9.2–23.7)	0.03
Biological parameters				
ASAT, U/l	167 (35–451)	91 (32–237)	249 (63–576)	0.21
ALAT, U/l	125 (28–345)	56 (28–132)	206 (52–689)	0.17
BUN, mmol/l	6.6 (5–8.9)	5 (5–8.3)	7.5 (5.4–10)	0.11
pH	7.23 (7.11–7.32)	7.32 (7.22–7.37)	7.18 (6.99–7.25)	0.01
HCO_3, mmol/l	14 (11–19)	18 (15–25)	11 (8–14)	0.003
Lactate, mmol/l	7.8 (4.5–12.9)	4.6 (3.1–6.3)	13.6 (9.5–16.7)	0.0004
SOFA	12 (9–15)	9 (7.5–12)	14 (11–16)	0.003
SAVE-score	–8.5 (–16, –3)	–3 (–6.5, –1.25)	–14.5 (–17, –9.25)	0.0002
SAVE-score risk classes, n (%)				
II–III	8 (36.4)	8 (80)	0	0.0001
IV–V	14 (63.6)	2 (20)	12 (100)	0.0001

Data are expressed as median (interquartile range) and percentage, depending on the variable of interest.

ASAT, aspartate aminotransferase; ALAT, alanine aminotransferase; BUN, blood urea nitrogen; SAVE-score, the Survival After Veno-arterial-ECMO-score; SOFA, Sequential Organ Failure Assessment; V-A ECMO, venoarterial extracorporeal membrane oxygenation.

*Sino-atrial block or high degree atrioventricular block.

#The five patients with out-of-hospital cardiac arrest were excluded (four nonsurvivors and one survivor).

Table 2. Patients and Drugs Used

Patients	Drugs	Outcomes
1	Diltiazem 9 g	Died
2	Metoprolol* 1425 mg–Quinine* 1080 mg–Felodipine 150 mg–Colchicine 20 mg–Escitalopram–Clorazepate	Died
3	Propanolol* 19 g	Survived
4	Propafenone* 5 g–Venlafaxine* 750 mg–Oxazepam 200 mg–Zolpidem 600 mg	Survived
5	Flecainide*–Paracetamol–Diazepam–Paroxetine	Died
6	Propanolol*–Verapamil–Lorazepam	Died
7	Chloroquine* 5 g	Died
8	Morphine 3220 mg–Tramadol 4 g–Bisoprolol 300 mg–Loprazolam 30 mg–Pregabaline 8 g–Perindopril 150 mg	Survived
9	Verapamil	Died
10	Venlafaxine* 5 g–Lorazepam 60 mg	Died
11	Perindopril 204 mg–Amlodipine 416 mg	Survived
12	Tramadol 3 g	Survived
13	Perindopril 611 mg–Amlodipine 1248 mg	Died
14	Bisoprolol 300 mg–Verapamil 300 mg–Clorazepate 70 mg–Cyamemazine 800 mg	Survived
15	Flecainide*–Atenolol–Perindopril–Amlodipine	Survived
16	Flecainide*–Propanolol*–Fluoxetine–Laudanosine–Sotalol	Survived
17	Bisoprolol 225 mg–Verapamil 3750 mg–Bromazepam 180 mg–Escitalopram 140 mg	Survived
18	Amlodipine 300 mg–Perindopril 300 mg	Survived
19	Diltiazem 6 g	Died
20	Flecainide* 3 g–Apixaban 95 mg	Died
21	Colchicine–Paracetamol–Perindopril–Diazepam	Died
22	Verapamil–Perindopril–Amlodipine	Died

*Drugs with membrane-stabilizing activity.

hemofiltration was used in three patients. Before or just after V-A ECMO initiation, 14 patients (63.6%) underwent gastric lavage and received activated charcoal. During ECMO support, glucagon, 10% calcium chloride, and high-dose insulin were initiated or continued in 5 (22.7%), 10 (45.4%), and 9 (40.9%) patients, respectively, without significant difference between survivors and nonsurvivors.

Outcomes are reported in Table 3. Ultimately, 10 (45.4%) patients were discharged alive from the hospital with good neurologic outcomes and a CPC score of 1. All the survivors were seen by the psychiatrist before leaving the ICU. Three patients were directly discharged home from the ICU and seven patients were transferred from ICU to a psychiatric (n = 3) or a medicine department (n = 4). As the nonsurvivors died with a median delay of 3 (2–5) days after ICU admission, the ICU and hospital length of stay were significantly longer in survivors. Refractory cardiac arrest before V-A ECMO cannulation tended to be associated with worse outcomes ($p = 0.08$), and only three patients survived (25%). Four patients with out-of-hospital cardiac arrest (OHCA) (80%) and five patients with in-hospital cardiac arrest (IHCA) (71.7%) died. Among these patients, eight died while on V-A ECMO during the first 48 hours of support (brain death, n = 3; multiple organ failure and withdrawal of life-sustaining treatment, n = 5), and one died weaned from V-A ECMO after the withdrawal of life-sustaining treatment because of severe hypoxic-ischemic brain injury. The low-flow duration was longer in nonsurvivors (77.5 [65–100] min) compared with survivors (45 [40–60] min; $p = 0.02$). Among the patients with refractory drug-induced cardiovascular shock, three died of multiple organ failure after the withdrawal of life-sustaining treatment (30%) and seven survived (70%). At the time of cannulation, the LVEF was significantly higher in survivors (20 [15–25] %) compared with nonsurvivors (10 [5–15] %, $p = 0.03$). During the weaning process, the median LVEF was estimated at 60 (50–60) % indicating the myocardial recovery.

Table 3. Outcomes

Variables	Patients (n = 22)	Survivors (n = 10)	Nonsurvivors (n = 12)	*p* value
Initial V-A ECMO flow rate, l/min	4 (3.4–4.6)	4.3 (3.9–4.7)	3.7 (2.9–4.1)	0.03
Initial mean arterial pressure, mmHg	70 (59–82)	80 (65–89)	68 (55–76)	0.06
V-A ECMO weaning, n (%)	11 (50)	10 (100)	1 (8.3)	<0.0001
Days on V-A ECMO	3 (2–5)	4 (3–6)	2 (1–4.5)	0.04
Days requiring vasopressors	4.5 (3–6)	6 (4–10)	3 (2–5)	0.01
Days requiring mechanical ventilation	3.5 (3–8.5)	7 (3–18)	3 (2–5)	0.02
Days in ICU	5 (3–17)	13 (8–23)	3(2–5)	0.002
Days in hospital	6 (3–22)	19 (8–32)	3 (2–5)	0.0003
Cannulation-related injuries, n (%) (limb ischemia, venous thrombosis, severe bleeding at the site of cannulation)	14 (63.6)	4 (40)	10 (83.8)	0.07
Others complications, n (%)	18 (81.8)	7 (70)	11 (91.7)	0.29
Neurologic	2 (9.1)	1 (10)	1 (8.3)	–
Renal	12 (54.5)	2 (20)	10 (83.3)	–
Hemorrhagic	5 (22.7)	2 (20)	3 (25)	–
Infectious	12 (54.5)	7(70)	5 (41.7)	–

Data are expressed as median (interquartile range) and percentage, depending on the variable of interest.
ICU, intensive care unit; V-A ECMO, venoarterial extracorporeal membrane oxygenation.

Vascular complications related to femoral cannulation included five cases of limb ischemia (all in nonsurvivors; three patients had no specific interventions because they died during the first 48 hours of support, two developed a compartment syndrome requiring longitudinal fasciotomy, and one of them was amputated above the knee), two venous thrombosis (all in survivors; one inferior vena cava and one common femoral vein thrombosis), and seven cases of severe cannulation site's bleeding requiring transfusion (groin hematoma in two survivors and three nonsurvivors, and bleedings requiring surgical re-exploration at the V-A ECMO insertion site in two nonsurvivors). Moreover, five patients required a massive transfusion for substantial bleeding (three gastrointestinal bleedings, one epistaxis, and one muscle hematomas). Twelve patients (54.5%) required renal replacement therapy during V-A ECMO support. Seven (31.8%) patients had ventilator-associated pneumonia and 5 (17.6%) developed septicemia during V-A ECMO support and ICU stay.

The Whisker plot in Figure 2 shows the relationship between serum lactate level before V-A ECMO and in-hospital mortality. Area under the ROC curve was 0.916 (95% confidence interval: 0.79–1.04, $p = 0.001$). The best cutoff to predict mortality was a serum lactate level above 9 mmol/L, with a sensitivity/specificity ratio of 83.3%/100%.

Discussion

We report here the largest retrospective, single-institution experience regarding drug-induced refractory shock and cardiac arrest managed with V-A ECMO. The most important finding was the worse outcome of patients with poor perfusion, particularly those suffering from cardiac arrest with low-flow time >60 min, and the potential interest of a lactic acid >9 mmol/L and a SAVE-score risk class IV/V as predictors of poor prognosis. As no formal clinical guidelines on VA-ECMO in drug poisoning exists, our findings could be helpful for clinicians.

The overall survival in our study (45.4%) is comparable to the recent retrospective study of the Extracorporeal Life Support Organizations involving adult cases that received V-A ECMO for cardiac support,[3] even if other studies found a wide range of survival rates (26–86%).[6,12,20–23] Because of a broad age range of patients, diverse demographic/clinical characteristics, and a variety of pharmaceutical and nonpharmaceutical exposures, extrapolation from these studies is hazardous. Moreover, it is essential to distinguish V-A ECMO in poisoned patients with refractory shock from V-V ECMO in acute respiratory distress syndrome caused by intoxication or exposure. Ramanathan et al[24] published data on poisoning cases in the ELSO database and found an overall survival rate significantly higher for VV-ECMO (69%) than V-A ECMO (39%). Finally, the use of V-A ECMO could be an option in the management of circulatory failure refractory to maximal therapy.[25,26] A retrospective study found that patients admitted for drug-induced circulatory shock or cardiac arrest and treated with V-A ECMO have an increased survival rate compared with patients without extracorporeal assistance (86% *vs.* 48%, $p = 0.02$).[21] Although the indiscriminate use of V-A ECMO could lead to a reduction in mortality rate, the univariate analysis of our study highlighted two patient profiles and simple useful indicators to discriminate patients who will not benefit from V-A ECMO.

First, we identified the patients with a refractory cardiac arrest before V-A ECMO initiation. In our study, only 25% of the 12 patients who had V-A ECMO placed during active CPR survived compared with 70% in the 10 patients who did not have a cardiac arrest. Implantation of V-A ECMO during cardiopulmonary arrest is known to be associated with a higher risk of death.[5,22] The initiation of V-A ECMO during cardiac arrest requires periods without effective chest compression that could worsen morbidity and mortality.[27] Nevertheless, extracorporeal CPR (ECPR) might procure a survival benefit over conventional CPR in selected patients with refractory IHCA[28] or refractory OHCA[29] unrelated to a drug overdose. Low-flow time is an independent predictor of mortality with a negative linear correlation between time to V-A ECMO and survival in the ECPR population.[30] In our study, low-flow time was significantly shorter in survivors compared with nonsurvivors, and no patient with low-flow time above 60 min survived. This is in line with the recent ELSO guidelines recommending that the goal of ECPR is to establish adequate ECMO flow within 60 min of onset of cardiac arrest.[31] The selection of patients that should benefit from fast cannulation in case of cardiac arrest and logistic organization of a quick procedure if needed are key challenges.

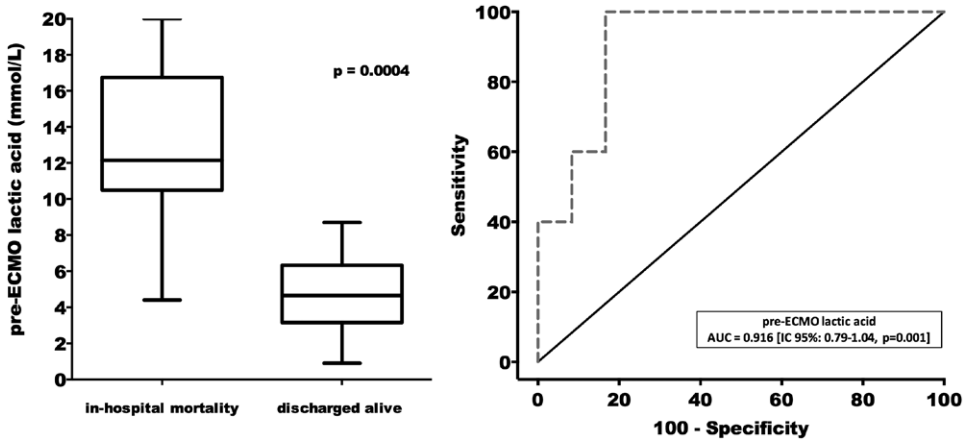

Figure 2. The Whisker plot illustrates the relationship between pre-V-A ECMO lactic acid and in-hospital mortality. The receive operator curve on the right demonstrates the ability of pre-V-A ECMO lactic acid to predict mortality. V-A ECMO, venoarterial extracorporeal membrane oxygenation.

Second, the patients had a long time from admission to V-A ECMO cannulation. Although the initiation of V-A ECMO before cardiovascular collapse may lead to improve overall survival,[20] delays to V-A ECMO initiation could be linked with the development of organ failure, and poor prognosis.[32] Daubin et al[6] reported 17 cases of refractory cardiogenic shock in adults with an overall survival rate of 76%. Interestingly, the meantime from hospital admission to initiation of V-A ECMO (6.4 ± 7.0 hours) was close to our survivor group (7 ± 4.3 hours). Unfortunately, the refractory characteristic of conventional treatment is difficult to define and prognostic factors able to predict nonresponse to conventional treatment of cardiotoxic drugs are unknown, except for digitalis.[33] Every poisoned patient is not a good candidate for V-A ECMO, and V-A ECMO does not come without risks. The implantation and management of V-A ECMO are still strongly challenging with significant morbidity.[11] As in studies of poisoned patients managed with V-A ECMO,[6,12,34] we report numerous complications including ischemia, acute kidney injury, infections, and severe bleeding. The femoral vessels injuries related to cannulation were the most frequent complication, particularly in nonsurvivors. Several factors could explain this disproportionate rate of complications: (1) the low mean arterial pressure with peripheral hypoperfusion; (2) the high level of vasoconstrictor support caused by the frequent ingestion of cardiovascular drugs (86.4%); (3) the presence of a nearly occlusive cannula in the femoral artery could contribute to lower limb ischemia; and (4) the presence of an underlying coagulopathy could promote excessive bleeding. Finally, great caution is warranted when considering V-A ECMO in poisoned patients because it should be available as fast as possible for selected patients refractory to conventional treatment, both in case of cardiac arrest and refractory shock. Thus, we need reliable indicators to discriminate patients who will benefit from extracorporeal CPR compared with patients for whom ECMO could be useless or futile.

Lastly, our study highlighted simple indicators that may be useful for selecting patients who will not benefit from V-A ECMO. In fact, patients with a serum lactate level >9 mmol/L should be carefully evaluated before considering V-A ECMO. In our study, plasma lactate concentration >9 mmol/L predicted mortality with a sensitivity of 0.83 and a specificity of 1. To note, the very high serum lactate levels in patients with a prolonged cardiac arrest may have influenced this finding. Moreover, prognostic scores could also be helpful. In our study, all the patients with SAVE-score risk classes II and III survived whereas 85.7% (12/14) of the patients with SAVE-score risk classes IV and V died.

The limitations of the study result from its retrospective nature and the absence of standardized criteria for V-A ECMO use. The small sample size could minimize the statistical power of our analysis. The single-center retrospective observational design may undermine the external validity. As prognostic factors are specific for a drug or a class of drugs, the heterogeneity of toxicant-combinations ingested may limit the interpretation and relevance of our data. Moreover, the suspected ingested doses were not always known, and we were not able to provide data on the plasma concentration of the drugs to evaluate the intensity of the ingestion. Nevertheless, because of the absence of large prospective randomized clinical trials because of ethics, we believe these data to provide important information about V-A ECMO used as a last resort treatment in patients with drug-induced cardiac arrest and severe cardiovascular failure.

Conclusions

In severe drug intoxication, V-A ECMO is reserved for highly selected poisoned patients not responding to conventional therapies. Shortening the timing of V-A ECMO initiation and low-flow duration as much as possible to limit tissue damages should be key priorities in improving outcomes. In our study, no patients with low-flow time >60 min or lactic acid >9 mmol/L survived. Further studies are warranted to clarify prognosis-associated factors of cardiotoxic drug poisonings and, therefore, indications and usefulness of V-A ECMO.

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