Archives of Anesthesiology and Critical Care (Spring 2022); 8(2): 118-122.

Available online at http://aacc.tums.ac.ir

Research Article

Which Factors Influence on Mortality in Patients Undergoing Veno-Venous Extracorporeal Membrane Oxygenation (ECMO)?

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ARTICLE INFO

Article history:
Received 04 November 2021
Revised 26 November 2021
Accepted 09 December 2021

Keywords:
Veno-venous ECMO;
Acute respiratory distress syndrome (ARDS);
Mortality

ABSTRACT

Background: There are inconclusive data of Ven venous extracorporeal membrane oxygenation (VV-ECMO) VV-ECMO for a therapeutic strategy for acute respiratory distress syndrome (ARDS).

Methods: Totally 28 critically ill patients were included into the study between 23 September 2013 and 20 january 2020. Critically ill adult patients who were refractory to conventional therapeutic modalities were eligible for veno-venous ECMO and study inclusion.

Results: Of a total of 28 patients, 15 patients (53.6%) survived and 13 (46.42%) died. Gender frequency had no significant difference between survivors and non-survivors (P=0.07). Mean of age and BMI had no significant differences between the mentioned groups also (P>0.05). It was the same for BSA and the two groups were in the same situation (1.82±0.37 vs. 1.79±0.29; P=0.81). There were no significant differences between survivors and non-survivors regarding ECMO time (114.49±91.05 vs. 162.62±100.17 minutes; P=0.20) and ICU stays (9.65±5.11 vs. 8.93±4.96; P=0.10). The average time of ICU stay was 9.29±5.16 days. The ejection fraction in survives was significantly higher than non-survivors (52.14±6.42 vs. 57.31±4.39; P=0.02). Those patients who were in the non-survivors group had lower blood pressure (MAP<65mmHg) during the study (P=0.049), however, did not find any significant differences between the groups regarding inotropes or vasoconstrictors.

Conclusion: In this study, the mortality rate was 46.42%. Bleeding, hypotension and dialysis were the risk factors for mortality among study participants.

The authors declare no conflicts of interest.
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Extracorporeal membrane oxygenation (ECMO) is known as one of the main extracorporeal life support devices [1]. ECMO as therapeutic procedure allow temporary pulmonary support [2-3] for cardiac failure [4-5] which were resistance to routine clinical treatment [3-6]. First report of successful use of ECMO was reported during one cardiac operation in 1954 [7] and first respiratory usage of ECMO was reported in 1972 [8]. The first multicentric randomized clinical trial for ECMO usage in respiratory failure setting, was published in 1979 [6].

There were several studies which used ECMO with acute respiratory syndrome which was refractory to conventional clinical support [2-3, 9], patients with in-hospital cardiac arrest [10] and patients with refractory cardiogenic shock [11]. ECMO had capability for supporting respiratory or cardiac function, which known as primary strategies for bridging acutely deteriorating lung transplant patients. Moreover, several studies approved the overall safety and efficacy of ECMO as a means to bridge among lung transplant patients [12-16]. ECMO can be removed after a few days of use and when the patient's clinical condition is improving [17]. However, no specific strategy has been proposed to remove ECMO from patients' treatment lines [12, 17-18].

According results of previous studies, significant improvement have been made in this therapeutic procedure, patients management and consequently in the outcome of ECMO patients [19]. However, we need to clinical survey to further assess the optimal use, outcomes, and several aspects of ECMO in different clinical setting. The aim of the study was to assess and compare outcome of veno-venous ECMO among critically ill patients.

Methods

The present study is a single-centered retrospective cohort that has been conducted on the V-V ECMO cases with the approval of ethic committee Shahid Beheshti University in the Masih Daneshvari Hospital of Tehran, Iran. After receiving written consent, 28 critically ill patients were evaluated between 23 September 2013 and 20 January 2020. Inclusion criteria included critically ill patients over 18 years of age, resistant to conventional therapies, and requiring ECMO. Patients were also considered for ECMO in conditions where despite protective ventilation, PaO2 / FiO2 ratio less than 50 mmHg, FiO2 = 1 for at least three hours, or in conditions where FiO2 = 1 for more than six hours and PaO2 / ratio FiO2 less than 80 mmHg or pH less than 7.20 for more than 6 hours. Exclusion criteria include susceptibility to anticoagulants, bleeding or possible bleeding, intracranial lesions, mechanical ventilation for more than seven days, immune system problems, multiorgan failure, coma after cardiac arrest, severe and irreversible pulmonary damage, age over 70 years, body mass index greater than 35 kg / m2, and low probability of survival. Patients underwent percutaneous vascular cannulation. Also, drainage femoral cannula was RAPFV two-stage 23 out of 25 which was inserted with seldinger's maneuver in femoral vein. The return cannula was the 23F easy flow DUO arterial femoral cannula, which was inserted into the right jugular vein with seldinger's maneuver. In V-V ECMO, the consul was the centrifugal pump system (Liva Nova Deutschland Gmbh, Munich, Germany). EOS hollow fiber oxygen generator was also used (Liva Nova, Mirandola, Moden, Italy). During ECMO, patients were monitored by a team of anesthesiologists, perfusionists, ICU specialists, cardiac surgeons, and a number of nurses. When necessary, venous cannulas and extracorporeal system were removed using ELSO guidelines.

Statistical analysis

Study data including demographic (age, sex), anthropometric parameters, respiratory and ventilation characteristics, hemodynamic and vasoactive features, complete biochemical profile with lactate, complications related and unrelated to veno-venous ECMO, and status at ICU discharge were collected and analysed in SPSS V.22. Descriptive statistics are presented with frequency and percentages and continuous variables presented as mean and standard deviation (SD). Chi-square and Independent student sample t-test were used for comparing qualitative and quantitative variables. All P-values less than 0.05 were assumed as significant results.

Results

A total of 28 patients, sixteen men and twelve women, with a mean (SD) age of 40.29 (15.28) years and a mean BMI of 27.34 (6.43) kg/m2 underwent Veno-venous ECMO. Laboratory and respiratory parameters before ECMO are listed in (Table 1)

Table 1- Demographics, laboratory and respiratory parameters before ECMO.

Variables	Number of patients (%)
Total patients	28 (100)
Sex (male)	16 (57.1%)
Age, mean (SD)	40.29 (15.28)
BMI, mean (SD)	27.34 (6.43)
Mean arterial pressure (mmHg)	73.03±19.57
Heart rate (Rate/min)	105.50±19.82
Ejection fraction	54.63±6.03
Temperature (℃)	36.89±0.71
PH	7.26±0.16
Pco2 (mmHg)	68.29±3.27
PO2 (mmHg)	57.14±4.06
O2 Sat (%)	82.61±9.16
Blood Sugar(mg/dl)	151.72±80.99
INR	1.71±1.58
PTT(s)	37.12±1.79
NA (mEq/l)	139.46±5.54

K(mEq/l)	4.07±0.78
Ca(mg/dl)	8.03±1.12
BUN (mg/dl)	46.16±3.07
Cr(mg/dl)	1.69±1.38
ALT (mg/dl)	46.70±3.79
AST (mg/dl)	75.90±8.13
Hb(g/dl)	16.18±2.11
PLT (103/ul)	179.71±88.72

During the study period, 15 patients (53.6%) survived and 13 ones (46.42%) died. Gender frequency had not significant difference between survivors and non-survivors (P=0.07). Mean of age and BMI had not significant differences between the mentioned groups also (P>0.05). It was same for BSA and two groups were in the same situation (1.82±0.37 vs. 1.79±0.29; P=0.81). There were not significant differences between survivors and non-survivors regarding to ECMO time (114.49±91.05 vs. 162.62±100.17 minutes; P=0.20) and ICU stay (9.65±5.11 vs. 8.93±4.96; P=0.10). Average time of ICU stay was 9.29±5.16 days. Ejection fraction in survives was significantly higher than non-survivors (52.14±6.42 vs. 57.31±4.39; P=0.02).

Some patients received inotrope or vasoconstrictor because of mean blood pressure less than 65 mmHg, however we did not find significant differences between survivors and non-survivors (8, 53.33% vs 11, 84.62%; P=0.08).

Unfortunately, some of patients had ECMO related complications. We had hypoxia, haemolysis, clot formation, ICH, dialysis, hypertension and hypotension as ECMO related complication among study participants. We compared ECMO complications between survivors and non-survivors and found that bleeding, hypotension and dialysis were significantly higher among non-survivor participants.

Facts and figures in the current study showed that renal function was affected more in the non- survival group patients and they went undergone renal replacement therapy more than the survival ones(P=0.049). In our institute, continuous renal replacement therapy is the first choice to do in these situations, so all patients received this type of therapy if needed (Table 2).

Table 2- Frequency distribution of ECMO complications in both study groups

Complication	Total	Survivors	Non-survivors	P-value
Bleeding	11	3 (38.5%)	8 (61.5%)	0.031
Hypoxemia	2	0	2 (100%)	0.12
Haemolysis	2	0	2 (100%)	0.12
Clotting	3	2 (66.67%)	1 (33.33%)	0.63
ICH	1	0	1 (100%)	0.28
Dialysis	3	0	3 (100%)	0.049
Hypertension	4	3 (75%)	1 (25%)	0.36
Hypotension	3	0	3 (100%)	0.049

Comparing coagulation state and blood product usage showed that PTT in non-survived patients was significantly higher than the other group and patients who died during ECMO received more platelet units in order to normalised coagulopathy.

Our result signified that patient who were in the non-survivors group had lower blood pressure (MAP<65mmHg) during the study (P=0.049), however we did not find any significant differences between the groups regarding to inotropes or vasoconstrictors (Table 3).

Table 3-Coagulation state and blood product usage in both groups

ECMO Time	Survivors	Non-survivors	P value
Pre ECMO-PTT	28.11±8.59	46.12±20.24	0.007
Pre ECMO-INR	1.25±0.37	2.17±2.15	0.15
Post ECMO PTT	44.49±15.82	56.88±8.24	0.02
Post ECMO INR	1.67±1.07	1.73±0.99	0.91
PC	4.67±4.10	7.06±5.19	0.43
PLT	2.73±4.15	11.69±11.74	0.01
FFP	2.07±3.24 Units	2.92±4.11 Units	0.54

Discussion

Use of Veno-venous ECMO among critically ill patients had been reported within the present study. This procedure was successful in fifteen out of 28 patients. The mortality rate among our study participants (46.42%) was higher than that found in other studies. According to an observational study on a total of 168 patients treated

with extracorporeal membrane oxygenation for severe acute respiratory distress syndrome from January 2007 to January 2013 in Australia, the mortality rate was 29% [20].

Our study showed that among ECMO complications, bleeding from cannulation site was significantly higher among non-survivors in comparison with survivors. Similar with these results, we found that frequency of blood products especially platelet, was significantly higher among non-survivors in comparison with survivors. Bleeding was reported between 30% and 40% in the previous studies using ECMO [3, 21-23]. Based on a study in Australia [3], mechanical complications related to the techniques such as cannulation and explanation of ECMO, are responsible for remarkable bleeding [3]. However, we found that systemic bleeding had a considerable role for massive bleeding in the non-survived group during the present study. We usually use standard protocols to manage coagulation state during ECMO, but sometimes the patients had extra normal level of PTT or ACT which can be the leading factor for bleeding. Bleeding and its consequences can affect the ECMO prognosis [23-24] and because transfusions requirement was frequent feature in our ECMO patients, facing high mortality rate was not so far-fetched.

Hypotension was a risk factor for mortality in our study and nearly all of non- survived patients suffered from it [25]. Lower level of EF and higher rate of bleeding in the mentioned group can be considered as these results.

Another issue that had an important role in the mortality was renal replacement therapy [26].

Regarding to some harmful factors in the non-survived patients such as hypotension, massive bleeding and receiving huge amount of blood products, this type of complication is not non- expected.

Although, there are some mortality prediction systems for ECMO, existing validated mortality prediction tools for patients undergoing veno-venous ECMO have shown suboptimal performance [27]. We need to find prognostic factors for ECMO, and preparing risk scores for pre-ECMO mortality prediction among critically ill patients. We think that higher rate of blood products usage among non-survivors in comparison with survivors due to higher rate of bleeding might responsible for higher rate of other morbidities and also mortality among study participants so predicting and managing it may be lifesaving. Moreover, preparing suitable clinical international guideline with more specific indications and patients selection criteria can improve survival rate of patients' undergoing ECMO procedure.

Our study had some limitations; first of all, we performed a single centre study and we cannot carefully interpret our study for other ill patients in other hospitals due to small study population. Secondarily, we did not focus in specific type of disorders such as ARDS, lung transplantation or other disorders. Each of noted disorders might have some specifications which can effect on ECMO performance.

Conclusion

In our study on veno-venous ECMO, mortality rate was 46.42%. Bleeding, hypotension and dialysis were the risk factors for mortality among study participants. Our results suggest that appropriate coagulation managing system is crucial to improve ECMO outcome.

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