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Original Article

The association between postoperative complications and prognosis in patients receiving extracorporeal membrane oxygenation in cardiac care unit

Liwen Liang, Liyuan Liu, Yamin Zhang, Xiaoying Fan, Ling Tao

Department of Cardiovascular Medicine, The First Affiliated Hospital of Airforce Military Medical University, Xi'an 710032, Shaanxi, China

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Abstract: Objective: To investigate the association between postoperative complications and prognosis in critically illed patients receiving extracorporeal membrane oxygenation (ECMO), so as to improve the survival rate of patients in cardiac care unit (CCU). Methods: 43 patients who received adjuvant therapy with ECMO in our hospital were retrospectively collected and divided into survival group (n=23) and death group (n=20) according to their survival and death during hospitalization. Patients in both groups were treated with ECMO adjuvant therapy. The levels of serum total bilirubin (STB), alanine transaminase (ALT), creatine (Cr), lactic acid (Lac) and urine volume in two groups were evaluated, and the postoperative complications of two groups were observed. Results: ECMO was performed as adjuvant therapy in both groups. The serum levels of STB, ALT, Cr and Lac in survival group were significantly lower than those in death group ($P < 0.05$). The number of complications such as hemorrhage, infection, renal failure, multiple organ failure (n>3) and ischemic necrosis of lower extremities in survival group was significantly less than that in death group. Conclusion: ECMO can significantly improve the survival rate of patients in CCU. When the serum levels of STB, ALT, Cr and Lac decrease and urine volume increases, liver and kidney function injury is mild, with less postoperative complications and good prognosis. Therefore, monitoring STB, ALT, Cr, Lac and urine volume is able to adjust treatment plan in time, reduce postoperative complications and improve prognosis quality, thus has great positive clinical significance.

Keywords: Cardiac care unit, ECMO, liver and kidney injury, complications, prognosis

Introduction

Extracorporeal membrane oxygenation (ECMO) originates from cardiopulmonary bypass and can artificially replace part or all cardiopulmonary function of patients [1]. As the fundamental principle, it drains human venous blood out of the body, oxygenates venous blood by artificial pulmonary bypass and then injects into venous or arterial system. In 1971, Hill et al. successfully applied ECMO in a 24-year-old patient with respiratory failure caused by multiple traumas for the first time [2]. In recent years, ECMO has more and more indications with its growing development, including fulminant myocarditis, low cardiac output syndrome, acute respiratory failure and septic shock. Despite some insurmountable shortcomings, ECMO has still won valuable time for disease treatment in increasing numbers of patients [3-5].

The equipment used in ECMO mainly includes vascular catheter, connecting pipe, oxygen supply pipe, power pump, oxygenator and control and monitoring system. At present, ECMO mainly has two modes: veno-venous ECMO (VV-ECMO) and venous-arterial ECMO (VA-ECMO). VV-ECMO conducts partial gas exchange of the draining venous blood and sends it back into the vein. This pathway only provides respiratory assistance and oxygenation for patients with respiratory failure who are ineffective to traditional mechanical ventilation [6, 7]. VA-ECMO conducts oxygenation of the draining venous blood, remove the inside CO_2 and then injects it into the artery again to substitute partial cardiopulmonary function, which is mainly used to provide cardiopulmonary support for patients [8, 9].

As a rapidly established cardiopulmonary auxiliary method, ECMO has high cost performance and good clinical effect, and can significantly improve the survival rate of patients, which has attracted the attention of more and more medical workers. ECMO requires multidisciplinary cooperation including intensive care unit (ICU), vascular surgery, cardiopulmonary bypass, etc. The key to its success lies in determining the accurate beginning time, skilled operation of medical workers and reducing the incidence of complications during treatment.

By introducing ECMO into the treatment of patients in cardiac care unit (CCU), we aimed to observe the association between postoperative complications and prognosis, evaluate the clinical effect of ECMO and provide a theoretical basis for the use of ECMO to improve the therapeutic effect. The details are as follows:

Material and methods

The clinical data of 43 patients who received adjuvant therapy with ECMO in our hospital from May 2016 to May 2018 were collected retrospectively, including 26 males and 17 females. This study has been approved by the Ethics Committee of the First Affiliated Hospital of Airforce Military Medical University. All study participants provided written informed consent before participating in the study.

Inclusion criteria: Complete case data; complete records of relevant parameters before using ECMO; patients with reversible cardiopulmonary failure; ECMO adjuvant therapy was expected to improve disease and weaning could be performed in a short time; no pneumothorax; and patients with the high setting condition of mechanical ventilation < 7 days.

Exclusion criteria: Incomplete case data; treatment abandoning midway; serious injury of other organs; serious ventilator-related complications, etc.

According to the survival and death during hospitalization, the patients were divided into survival group (n=23) and death group (n=20).

The personal files of 43 patients were collected. The indices of gender, age, body weight and results of liver and kidney function and blood routine tests were recorded.

Methods

Patients in both groups received adjuvant therapy with ECMO (Medtronic, Inc). 35 patients used Doppler ultrasound to evaluate vascular condition and were punctured according to the evaluation results. They all used peripheral femoral VA-ECMO catheterization. 15F or 17F arterial infusion tube was used in femoral artery, and 19F or 21F venous drainage tube was used in femoral vein. Normal saline and heparin were used for pre-filling and exhaust. After ECMO system was started, heparin was used for anticoagulation. According to the real-time monitoring results, the dosages of heparin and ventilator parameters were adjusted in time.

During the treatment, patients' normal body temperature was maintained, and analgesic drugs were used appropriately. Ensuring the basically restored cardiopulmonary function, auxiliary flow was gradually reduced. When the auxiliary flow was reduced to about 10%, ECMO weaning could be performed, and the patient's blood vessels could be repaired.

ECMO system management

After ECMO system was started, heparin was used for anticoagulation. ACT was monitored every 1-4 hours, and the heparin dosage was adjusted according to the ACT value to keep ACT at 150-200 s. If the patient had a large amount of exudation or bleeding, heparin should be reduced and even stopped to reduce ACT. Upon ECMO weaning, heparin dosage should be increased to maintain a high level of ACT to prevent embolism in patients.

During ECMO intervention, the dosage of vasoactive drugs should be reduced according to patients' hemodynamic index in order to ensure the fully recovery and contractility of heart and prevent blood clots formation. Ultrasound and electrocardiograph (ECG) monitoring were performed every other day.

Ventilator parameters adjustment adopted protective ventilation strategy, with PEEP < 10 mmHg, tidal volume of 5-6 ml/kg, platform pressure < 25 cmH_2O. Blood gas analysis was monitored every 1-4 hours, and ventilator parameters were adjusted in time according to

Table 1. Comparison of indices between two groups before ECMO intervention ($\overline{x}$ ± s)/n (%)

General clinical material		Survival group (n=23)	Death group (n=10)	t/X^2	*P*
Gender	Male	15	8	1.800	0.323
	Female	6	4		
Average age (year)		49.87 ± 8.32	47.56 ± 10.64	0.792	0.489
Average weight (kilogram)		59.87 ± 6.32	58.64 ± 7.61	0.189	0.836
STB (umol/L)		15.32 ± 7.84	23.96 ± 14.18	1.236	0.289
ALT (U/L)		38.06 ± 32.76	65.47 ± 45.37	1.405	0.167
PaO_2 (mmHg)		51.03 ± 4.87	46.32 ± 3.45	0.147	0.932

the monitoring situation so as to avoid hypoxemia or hypercapnia.

Observation index and evaluation standard

Liver function of patients in two groups after ECMO intervention: Serum total bilirubin (STB) is the sum of direct and indirect bilirubin [10]. Liver plays an important role in bilirubin metabolism. It participates in the process of bilirubin uptake, binding and excretion. Liver injury will hinder the above process and lead to blood bilirubin accumulation. Therefore, STB can be used as an evaluation factor for ECMO prognosis [11-13]. And the increasing STB indicates patient's abnormal liver function.

Alanine transaminase (ALT) mainly exists in liver cells. The injured live is able to release a large amount of ALT into blood. And 1% of necrotic liver cells can lead to doubled serum ALT level, which therefore can be used as a sensitive factor for liver injury [14, 15]. Increased serum ALT level reflects liver injury.

Renal function indices of patients in two groups after ECMO intervention: Serum creatinine (Cr) is the product of creatine metabolism. When glomerular dysfunction happens, serum Cr level will increase significantly. Early renal function injury is manifested as reduced urine volume. And increased serum Cr level and decreased urine volume reflect renal injury.

Serum lactic acid of patients in two groups after ECMO intervention: Lactic acid (Lac) is the product of anaerobic metabolism and can reflect Lac balance. Besides, Lac is regarded as an important predictor in the prognosis analysis of critically ill patients [16-18]. Increased serum Lac level indicates imbalanced oxygen supply and consumption. When the patient's Lac level rises, it reflects circulatory failure.

Complications of patients in two groups after ECMO intervention: After ECMO intervention, critically ill patients are prone to postoperative complications such as hemorrhage, infection, organ failure and ischemic necrosis of lower extremities [19, 20]. Postoperative complications may reduce the recovery quality of patients and even endangers their life. The number of postoperative complications in two groups was evaluated.

Statistical analysis

SPSS 22.0 software was performed for statistical analysis. Measurement data were expressed as mean ± standard deviation ($\overline{x}$ ± s). The differences between groups were compared by *t* test. A $P < 0.05$ was considered as statistical significance.

Results

Comparison of indices between two groups before ECMO intervention

Among the 43 patients, there were 15 males and 8 females in survival group, with an average age of (49.87 ± 8.32) years, and 11 males and 9 females in death group, with an average age of (47.56 ± 10.64) years. General material (including gender, age, and biochemical indices on admission) between two groups before ECMO showed no significant difference (P>0.05) and thus were comparable (**Table 1**).

Comparison of serum STB and ALT changes between two groups after ECMO intervention

After ECMO intervention, the serum levels of STB and ALT in survival group increased 1-3 days after operation, reached the maximum on the 3rd day (STB: 30.93 ± 14.15 umol/L, and ALT: 109.73 ± 24.53 U/L), and gradually decreased from the 4th day. While the serum levels of STB and ALT in death group continued to increase after operation. The level of serum

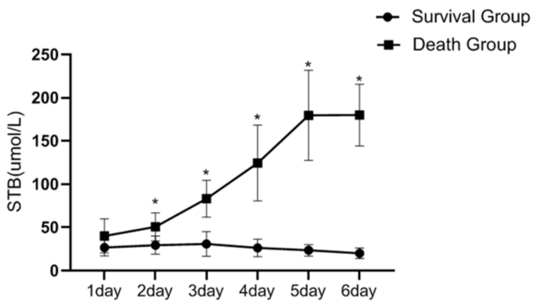

Figure 1. Comparison of serum STB changes between two groups after ECMO intervention. At the same timepoint, patients in survival group have lower serum levels of STB than those in death group. From the 2nd day after intervention, survival group shows significantly lower serum STB level than death group (*P* < 0.05). * refers to significant difference between two groups at the same timepoint.

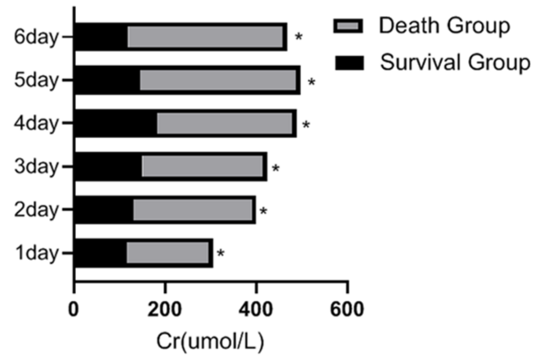

Figure 3. Comparison of serum Cr changes between two groups after ECMO intervention. At the same timepoint, the serum Cr level in survival group is significantly lower than that in death group (*P* < 0.05). * refers to significant difference between two groups at the same timepoint.

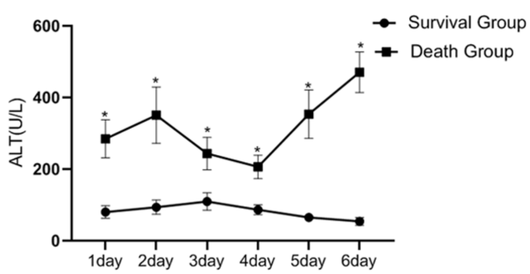

Figure 2. Comparison of serum ALT changes between two groups after ECMO intervention. At the same timepoint, patients in survival group have lower serum levels of ALT than those in death group. From the 2nd day after intervention, survival group shows significantly lower serum ALT level than death group (*P* < 0.05). * refers to significant difference between two groups at the same timepoint.

STB in death group was higher than that in survival group, and there was no significant difference between two groups on the 1st and 2nd day (P>0.05), but there was significant difference between two groups from the 3rd day (*P* < 0.05, **Figure 1**). Death group showed higher serum ALT level than survival group, with the significant difference between two groups (*P* < 0.05, **Figure 2**).

Comparison of serum Cr and urine volume changes between two groups after ECMO intervention

After ECMO intervention, the level of serum Cr in survival group increased slightly, and reached the maximum on the 4th day (182.54 ± 32.17) umol/L. While Cr in death group was kept in high level and increased continuously and reached the maximum on the 5th day (352.46 ± 73.84) umol/L, Serum Cr level in death group was significantly higher than that in survival group, and there was significant difference between two groups (P < 0.05, **Figure 3**).

After ECMO intervention, death group had significantly lower urine volume than survivors at the same timepoint. Patients in both groups had increased gradually urine volume from the 1st to 3rd day after operation. The urine volume of patients in survival group remained stable from the 4th day after operation, while the urine volume of patients in death group remained at a low level from the 4th day after operation. Significant difference in urine volume between two groups did not exist on the 1st-3rd day (P>0.05) but did exist on the 4th-6th day (P < 0.05, **Figure 4**).

Comparison of serum Lac changes between two groups after ECMO intervention

After ECMO intervention, the serum Lac level in survival group decreased gradually and approached the normal value on the 4th day after operation, while the serum Lac level in death group remained at a high level. Death group was significantly higher than survival group in serum Lac level at the same timepoint, with significant difference between two groups (*P* < 0.05, **Figure 5**).

Comparison of complications between two groups after ECMO intervention

After ECMO intervention, survival group had significantly lower incidence of complications

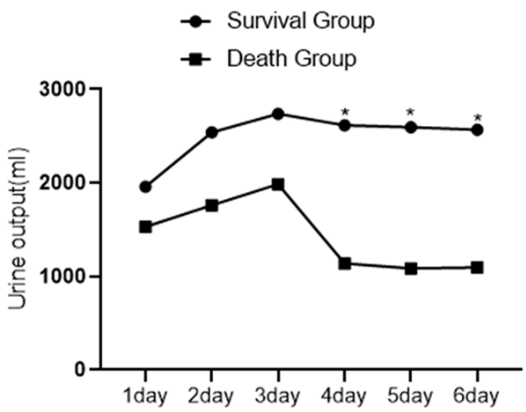

Figure 4. Comparison of urine volume changes between two groups after ECMO intervention. Survival group is higher than death group in urine volume at the same timepoint. From the 4th day after intervention, the urine volume in survival group is significantly higher than that in death group ($P < 0.05$). * refers to significant difference between two groups at the same timepoint.

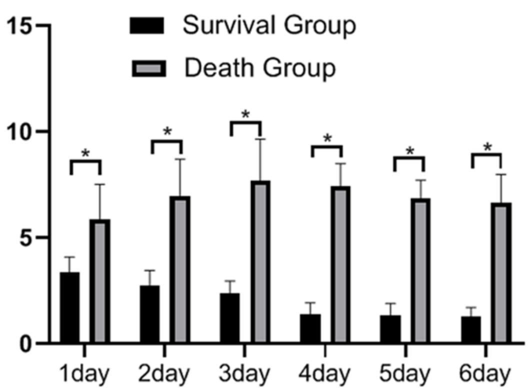

Figure 5. Comparison of serum Lac changes between two groups after ECMO intervention. Survival group has significantly lower serum Lac level at the same timepoint compared with death group ($P < 0.05$). * refers to significant difference between two groups at the same timepoint.

than death group, including hemorrhage, infection, renal failure, multiple organ failure (n>3) and ischemic necrosis of lower extremities (**Figure 6**).

Discussion

As an extracorporeal circulation mechanism, ECMO can significantly increase oxygen supply and stabilize hemodynamics. Recently, more and more medical researchers have recognized ECMO application in the treatment of critical cardiac diseases. The main indications of ECMO are acute, severe and reversible cardiopulmonary failure diseases which are difficult to be treated by routine treatment. Patients with the expected mortality rate more than 50% may potentially benefit from ECMO adjuvant therapy.

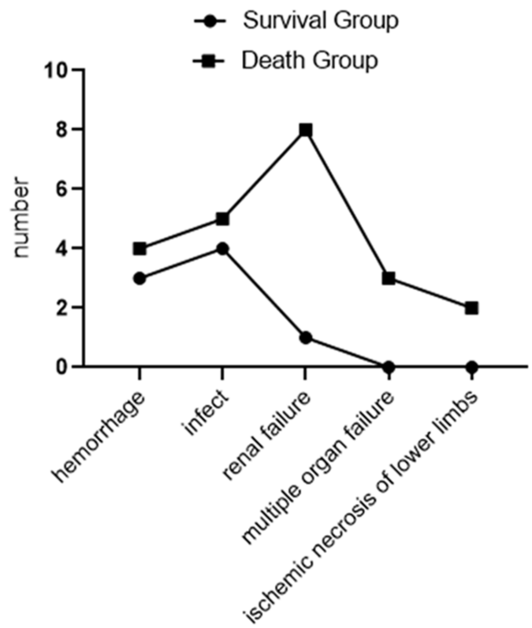

Figure 6. Comparison of complications between two groups after ECMO intervention. The incidence of complications (such as hemorrhage, infection, renal failure, multiple organ failure (n>3), ischemic necrosis of lower extremities, etc.) is significantly lower in survival group than in death group.

ECMO displays good therapeutic effect in the treatment of acute diseases while with rapid functional recovery, such as fulminant myocarditis, myocardial infarction, viral pneumonia, etc. With the continuous improvement of medical level, the survival rate of patients with various diseases treated with ECMO has been increasing to 35-57% [21, 22]. Among the 43 patients in this study, 23 survived and discharged, with an overall discharge rate of 53.5%. According to the comparison of indices before ECMO intervention, age, gender and body weight had no association with prognosis.

Both domestic and foreign studies have shown that bilirubin and ALT are closely related to the prognosis of patients [5]. In addition, renal injury can reduce the excretory capacity of the kidney, and a large amount of body fluid may cause edema in the tissue space, which will reduce the diffusion capacity of oxygen in the tissues and lead to a higher postoperative fatality rate in CCU patients [23]. After ECMO intervention, the high level of serum Lac indicates the imbalanced oxygen supply and the enhanced anaerobic glycolysis in glucose metabolism, and when Lac excesses 4 mmol/L, the mortality rate of patients increases by 6 times within 3 days [24]. Common complications (including acute renal injury, hemorrhage, infection, ischemic necrosis of lower extremities, nervous system injury, etc.) are important factors affecting the prognosis of patients [25, 26].

In this study, the serum STB, ALT, Cr, Lac and urine volume of two groups were measured 1-6 days after ECMO intervention, and the association between each index and prognosis was analyzed. The results showed that after ECMO intervention, survival group had significantly lower serum levels of STB, ALT, Cr and Lac, higher urine volume and smaller case number of complications than death group at the same timepoint, which was the same as the reported study.

To conclude, when ECMO was used to treat CCU patients, the serum levels of STB, ALT, Cr, Lac decreased and urine volume increased in survival group, indicating a good prognosis. Therefore, serum STB, ALT, Cr, Lac and urine volume can be used as factors affecting the prognosis of patients. According to the incidence of complications, patients' mortality was predicted, and there was a positive correlation between them.

This study has some limitations. First, this retrospective study included limited patients due to the high cost of ECMO treatment, thus the following results lacked universality. Secondly, the biochemical indices after ECMO intervention were not comprehensive and could not fully reflect the association between these indices and prognosis. In view of the above limitations, we next need to conduct researches with large sample size and more comprehensive detection indicators, aiming to obtain more representative and scientific conclusions and to provide a more detailed theoretical basis for ECMO application in the treatment of critical cardiac diseases.

Disclosure of conflict of interest

None.

Address correspondence to: Ling Tao, Department of Cardiovascular Medicine, The First Affiliated Hospital of Airforce Military Medical University, No. 127, Changle West Road, Xi'an 710032, Shaanxi, China. Tel: +86-15829037110; E-mail: 15829037110@163.com

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