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Article

Influences of V-A Mode Assisted ECMO Combined with Intra-Aortic Balloon Counterpulsation on Disease Outcome and Troponin Level in Patients with Acute Fulminant Myocarditis

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Abstract

Introduction: The acute fulminant myocarditis (AFM) is a special type of myocarditis, characterized by rapid onset, progression with abnormal hemodynamics causing high mortality. The combination of extracorporeal membrane oxygenation (ECMO) and intra-aortic balloon counterpulsation (IABP) in these cases have improved the acute phase attacks resulting in increased survival of the effected individuals. To observe the effect of vein-artery (V-A) mode assisted ECMO combined with IABP on the disease outcomes and troponin level in patients with acute fulminant myocarditis (AFM). **Methods**: A total of 45 patients with AFM were admitted to our hospital from January 2016 to December 2021, they were divided into group A (21 patients, receiving traditional treatment) and group B (24 patients, receiving V-A mode assisted ECMO and IABP based on traditional treatment) according to the treatment plan. The hypersensitive troponin (hs-cTnI), B-type natriuretic peptide (BNP), arterial blood gas analysis index, multiple organ dysfunction score (MODS), simplified acute physiology score II (SAPS II), cardiac ultrasound index, and disease outcomes were compared between the two groups. **Results**: After treatment, the hs-cTnI, BNP, blood lactic acid, MODS score and SAPS score in both groups were lower than before treatment ($p < 0.05$), the arterial oxygen saturation (SaO_2), left ventricular ejection fraction (LVEF) and cardiac index (CI) was higher than before treatment ($p < 0.05$), the hs-cTnI, BNP, blood lactic acid, MODS score and SAPS II score in group B were lower than group A ($p < 0.05$), SaO_2, LVEF and CI was higher than group A ($p < 0.05$). The in-hospital mortality of group B (9.52%, 2/21) was lower than group A (45.83%, 11/24) (χ^2 = 7.188, p = 0.007). Among the recovered discharged patients, the length of stay in group B (19 patients, 14.42 ± 4.59 days) was shorter than group A (13 patients, 18.34 ± 5.72 days) (t = 2.147, p = 0.040). **Conclusions**: V-A mode assisted ECMO combined with IABP can improve the condition and arterial blood gas analysis index and cardiac function of AFM patients, alleviate myocardial injury, reduce mortality in the hospital, and shorten the hospitalization time of the recovered patients.

Keywords

vein-artery mode; extracorporeal membrane oxygenation; intra-aortic balloon counterpulsation; acute fulminant myocarditis; disease outcome; troponin

Introduction

Acute fulminant myocarditis (AFM) is a special type of myocarditis, characterized by rapid onset, progression, abnormal hemodynamics and high mortality rates [1,2]. At present, although the pathogenesis of AFM has not been fully explained, its long-term prognosis is generally good as long as early detection, quick response and proper handling of such cases, so that patients can pass through the acute risk period smoothly. The Chinese Expert Consensus on the Diagnosis and Treatment of Adult Outbreak Myocarditis proposes to adopt a "comprehensive treatment scheme based on life support" to save lives as much as possible [3]. However, only the traditional treatment were not effective [3].

Many studies have been proposed regarding the combination of extracorporeal membrane oxygenation (ECMO), intra-aortic balloon pump (IABP) and other life support treatments to have positive impact in AFM patients, especially in the acute phase improving the survival rate of patients [4–6]. ECMO assisted by vein-artery (V-A) mode can maintain the blood perfusion ability and ensure the full rest of the heart by providing lasting life support. IABP rapidly inflates the balloon during cardiac diastole, and swiftly deflates the balloon during cardiac systole, such repeated rhythmic inflation and deflation can increase coronary blood flow and cardiac output, while reducing the left ventricular ejection resistance, and play a circulatory support role [7,8]. The above two life support treatment schemes have widely applied in treating AFM, although the mechanism of action is different. Whether the combination of these two can complement each other and further improve the clinical effect of AFM is uncertain. The current study aimed to optimize the treatment strategy of AFM by observing the effectiveness of ECMO combined with IABP assisted by V-A mode in the treatment of AFM, so as to promote the disease outcome of patients.

Methods

Study Design and Participants

The present study is a retrospective observational study which was conducted in accordance with the Declaration of Helsinki. A total of 45 patients diagnosed with AFM were selected, admitted to the Department of critical Care Medicine, The Affiliated Hospital of Qingdao University from January 2016 to December 2021. They were divided into group A (21 cases, only traditional treatment) and group B (24 cases, ECMO and IABP assisted by V-A mode based on traditional treatment) based on the different treatment strategies. Prior to recruitment, all the participants signed an informed consent after carefully reviewing the procedures, risks and precautions of the study. This study was approved by the Ethics Committee of the Affiliated Hospital of Qingdao University (NO. QYFY WZLL 28680). Inclusion and exclusion criteria were based on current reports and the clinical experience in our unit.

Inclusion criteria: ① Subjects who were in accordance with the AFM diagnostic criteria: A sudden onset of severe hemodynamic disturbances with obvious prodromal symptoms of viral infection, especially generalized malaise and loss of appetite followed by severe myocardial damage on laboratory tests and diffuse ventricular wall motion reduction on echocardiography [8]; ② Course of disease was less than 7 days; ③ Age >18 years old.

Exclusion criteria: Those who had previous history of heart diseases myocardial dysfunctions; and those who were contraindicated to the V-A mode-assisted ECMO and IABP treatment regimen; and subjects diagnosed with malignancies were all excluded.

Data Collection

Base features: gender; age; underlying diseases, including hypertension and diabetes; heart rate; pericardial effusion; electrocardiogram (ECG) characteristics, including atrioventricular block and ventricular tachycardia.

Treatment Strategies

Traditional Treatment in Group A

① The patients were placed on absolute bed rest and the number of visits was controlled; ② It was recommended to eat, digestible and nutritious food, adhering to the principle of eating less and eating more; ③ Oxygen supply was customized; ④ Phosphocreatine and other drugs were admintered timely to regulate the myocardial energy metabolism, and was combined with trimetazidine; ⑤ Vitamin supplements were given; ⑥ The liquid replenishment was measured; ⑦ Proton pump inhibitors were supplemented; ⑧ Individualized physical cooling and glucocorticoids were also given.

Group B was Given ECMO and IABP Assisted by V-A Mode on the Basis of Traditional Treatment

Mechanical circulation support: The cardiac function, arterial blood pressure, urine volume and other indicators were monitored, and timely ECMO and IABP regimen was given and assisted by V-A mode.

Indication of IABP activation [8]: ① Cardiac index <2 L/min/m^2; ② Mean arterial pressure <60 mmHg, or systolic pressure <90 mmHg; ③ Left atrial pressure monitoring results, or pulmonary capillary wedge pressure >20 mmHg; ④ Urine volume <20 mL/h. Indication of IABP withdrawal [9]: ① Hemodynamic stability; ② Cardiac index >2.5 L/min/m^2; ③ Mean arterial pressure >80 mmHg, or systolic pressure >100 mmHg; ④ Pulmonary capillary wedge pressure <18 mmHg; ⑤ Urine volume >1 mL/kg/h; ⑥ The peripheral circulation was stabilized and , the patient was clear, and the dosage of dopamine is less than 5 µg/kg/min.

Indication of ECMO activation assisted by V-A mode [9]: ① It is confirmed that there was severe heart failure and the effect of regular treatment was not good; ② The effect of using a large amount of positive inotropic drugs is not good, and the hemodynamics are abnormal; ③ Cardiac index <2 L/min/m^2 for more than 180 consecutive minutes, mean arterial pressure <60 mmHg for more than 180 consecutive minutes, lactic acid >5 mmol/L were continuously increased, and urine volume <0.5 mL/kg/h for more than 5 consecutive hours.

Indication of ECMO withdrawal assisted by V-A mode [9]: ECMO circulation support flow assisted by V-A mode is about 20% of the patient's cardiac output, and appropriate vasoactive drugs were given, if dopamine <5 µg/kg/min (Pfizer, NDC 00409-7809-22, New York, NY, USA), dobutamine <5 µg/kg/min (Pfizer Inc., New York, NY, USA), adrenaline <0.02 µg/kg/min (Pfizer, 6FM722, New York, NY, USA), with hemodynamic stability, mean arterial pressure >60 mmHg, central venous pressure <10 mmHg, left ventricular internal pressure <12 mmHg, left ventricular ejection fraction >40%. ECG examination results showed no malignant arrhythmia, venous oxygen saturation >60%, lactic acid <2 mmol/L. Immunoregulation: the glucocorticoid (methylprednisolone (Pfizer, NDC 00009-3475-01, New York, NY, USA) is selected uniformly in this study) 200 mg × 3 d, then changed to 80 mg

Table 1. Data comparison of the baseline characteristics.

Group		A group	B group	χ^2/t	p
N		21	24		
Age ($\bar{x} \pm$ s)		35.11 ± 9.35	37.09 ± 9.12	0.718	0.477
Hypertension (n)		13	12	0.643	0.423
Diabetes (n)		4	7	0.621	0.431
Heart rate ($\bar{x} \pm$ s, time/min)		109.87 ± 14.93	107.23 ± 13.79	0.616	0.514
Pericardial effusion (n)		2	4	0.070	0.792
Gender (n)	Male	11	15	0.470	0.493
	Female	10	9		
ECG characteristics	Atrioventricular block	6	4	0.918	0.338
	Ventricular tachycardia	6	9	0.402	0.526
Treatment duration ($\bar{x} \pm$ s, days)		7.00 ± 1.76	6.50 ± 1.92	0.906	0.370

ECG, electrocardiogram.

Table 2. Comparison of hs-cTnI and BNP ($\bar{x} \pm$ s).

Group	n	hs-cTnI (μg/L)		BNP (ng/L)	
		Before treatment	After treatment	Before treatment	After treatment
A group	21	29.49 ± 3.21	5.11 ± 1.68*	2352.14 ± 48.63	1100.36 ± 26.79*
B group	24	30.64 ± 3.13	1.23 ± 0.37*	2337.32 ± 46.86	773.27 ± 32.18*
t		1.215	11.030	1.040	36.740
p		0.231	<0.001	0.304	<0.001

hs-cTnI, high-sensitivity cardiac troponin; BNP, B-type natriuretic peptide. Compared with the same group before treatment $^*p < 0.05$.

× 3 d, finally changed to 40 mg × (1~2) d. Gammaglobulin (Grifols, S.A., Barcelona, Spain), intravenous injection, about 20 g × (3~5) days.

Timely start bedside blood purification treatment: Comprehensive body fluid balance assessment results, renal function status, urine volume were all monitored, *etc*.

Observation Indicators

(1) Before and after treatment, the hypersensitive troponin (hs-cTnI) and B-type natriuretic peptide (BNP) were detected.

(2) The arterial blood gas analysis index, blood lactic acid and arterial blood oxygen saturation (SaO_2) levels were detected at the pre and post treatment.

(3) The multiple organ dysfunction score (MODS) and simplified acute physiology score II (SAPS II) were evaluated by MODS and SAPS II, before and after the treatment of which the total score of MODS was 0–24 points, where the lower score indicated the better organ function; The total score of SAPS II was 0–163 points. The lower the score, the lighter was the condition.

(4) Cardiac ultrasound indexes before and after treatment, a color Doppler ultrasound diagnostic instrument (Philips SD800, Amsterdam, Netherlands) was used for cardiac ultrasound examination for detecting the left ventricular ejection fraction (LVEF) and cardiac index (CI).

(5) The mortality of the two groups was calculated according to the disease outcome, and the hospitalization time of the discharged patients was also counted.

Statistical Analysis

SPSS 23.0 (SPSS23.0 software IBM, Armonk, NY, USA) was used for data analysis. If the measurement data adheres to the normal distribution, they all were expressed by the standard deviation (SD) of the mean, and the independent sample t test was performed to compare the two different groups; The counting data was expressed in n (%) and subjected to chi-square test. The smaller samples were compared with Fisher exact probability method. The p value < 0.05 were considered statistically significant.

Results

Comparison of Baseline Characteristics of Patients

The baseline characteristics of the 2 groups before treatment are shown in Table 1. Before treatment, patients in group A (only receiving traditional treatment, n = 21) were younger and more likely to have hypertension with higher heart rate and more atrioventricular block. In contrast, patients in group B (receiving V-A mode assisted ECMO and IABP on the basis of traditional treatment, n = 24) were more often males, having diabetes with more

Table 3. Comparative arterial blood gas analysis index ($\bar{x} \pm$ s).

Group	n	Blood lactic acid (mmol/L)		SaO_2 (%)	
		Before treatment	After treatment	Before treatment	After treatment
A group	21	10.86 ± 0.63	3.52 ± 0.21*	54.68 ± 5.36	61.09 ± 4.42*
B group	24	10.92 ± 0.49	2.31 ± 0.18*	52.21 ± 6.17	68.84 ± 3.21*
t		0.359	20.817	1.423	6.788
p		0.721	<0.001	0.162	<0.001

Compared with the same group before treatment *$p < 0.05$.

Table 4. Comparison of MODS and SAPS II ($\bar{x} \pm$ s, points).

Group	N	MODS		SAPS II	
		Before treatment	After treatment	Before treatment	After treatment
A group	21	9.34 ± 1.12	7.42 ± 0.76*	42.89 ± 2.48	34.82 ± 2.13*
B group	24	9.23 ± 1.21	6.01 ± 0.68*	44.08 ± 2.54	32.13 ± 2.01*
t		0.315	6.569	1.585	4.356
p		0.754	<0.001	0.120	<0.001

MODS, multiple organ dysfunction score; SAPS II, simplified acute physiology score II. Compared with the same group before treatment *$p < 0.05$.

pericardial effusion and ventricular tachycardia. Although patients had slightly different baseline characteristics, there were no statistically significant differences between them.

Comparison of Inflammation and Heart Injury Markers after Treatment

After treatment, hs-cTnI and BNP in both groups were lower than before treatment ($p < 0.05$), and group B was lower than group A ($p < 0.05$) as shown in Table 2.

Comparison of Arterial Blood Gas Analysis Indexes after Treatment

After treatment, the blood lactic acid in both groups was lower than that before treatment ($p < 0.05$), and SaO_2 was higher than that before treatment ($p < 0.05$), and the blood lactic acid in group B was lower than that in group A ($p < 0.05$), and SaO_2 was higher than that in group A ($p < 0.05$) (Table 3).

Comparison of MODS and SAPS II after Treatment

After treatment, the scores of MODS and SAPS in both groups were lower than those before treatment ($p < 0.05$), and group B was lower than group A ($p < 0.05$) as described in Table 4.

Comparison of Cardiac Ultrasound Indexes

After treatment, LVEF and CI in both groups were higher than those before treatment ($p < 0.05$), and group B was higher than group A ($p < 0.05$) as shown in Table 5.

Comparison of Disease Outcomes

The hospital mortality rate in group B (9.52%, 2/21) was lower than that in group A (45.83%, 11/24) ($\chi^2 = 7.188$, $p = 0.007$). The cause of death in group B was multiple organ dysfunction syndrome, and the cause of death in group A was 8 cases of multiple organ dysfunction syndrome, 2 cases of cardiac arrest, and 1 case of intracranial hemorrhage.

Among the discharged patients, the hospital stay in group B (19 cases) was (14.42 ± 4.59) days shorter than that in group A (13 cases) (18.34 ± 5.72) days (t = 2.147, p = 0.040) (**Supplementary Material**).

Discussion

V-A ECMO with IABP is a promising rescue therapy for patients with cardiac AFM [10,11]. The results of this study show that ECMO combined with IABP assisted by V-A mode can alleviate myocardial injury in patients with AFM. The reason may be that IABP can reduce the burden of the heart and increase the blood supply of the heart, while ECMO combined with V-A mode does not rely on the hearts function and ability to function, and this allows the heart to rest fully and lower the biventricular preload before treatment, so it can alleviate the cardiac muscle injury of AFM patients to a certain extent [12,13].

The results in Table 3 and Table 5 show that ECMO combined with IABP assisted by V-A mode can improve the arterial blood gas analysis index and cardiac function of AFM patients. The reason for analysis may be that IABP can improve cardiac function. At the same time, in combination with ECMO assisted by V-A mode, it can lead the

Table 5. Comparison of cardiac ultrasound indexes ($\bar{x} \pm$ s).

Group	N	LVEF (%)		CI [L/(min/m^2)]	
		Before treatment	After treatment	Before treatment	After treatment
A group	21	41.08 ± 4.73	52.07 ± 6.11*	1.47 ± 0.23	2.48 ± 0.21*
B group	24	43.14 ± 4.42	56.28 ± 6.34*	1.53 ± 0.21	2.62 ± 0.18*
t		1.510	2.260	0.915	2.409
p		0.138	0.029	0.365	0.020

LVEF, left ventricular ejection fraction; CI, cardiac index. Compared with the same group before treatment $^*p < 0.05$.

right atrial venous blood to the body, and complete oxygenation and carbon dioxide excretion in the outside body with the help of external mechanical assistance device [14]. Also, it can also be infused into the arterial system through the peripheral artery, which can partially replace the heart and lung functions, so that they can rest enough, to promote the improvement of heart and lung functions. It is beneficial to regulate arterial blood gas analysis index [15].

Results of Table 4 show that ECMO combined with IABP assisted by V-A mode can improve the condition of AFM patients. It may benefit from the implementation of ECMO assisted by V-A mode to achieve circulation and oxygenation support, so that it can improve the condition. The rapid progress of AFM and the high risk of early death, the long-term prognosis of AFM is generally good as long as it is detected early, responded quickly and handled properly so that the patients can pass the acute risk period smoothly. The results of this study showed that the hospital mortality rate in group B (9.52%, 2/21) was lower than in group A (45.83%, 11/24) (χ^2 = 7.188, p = 0.007); Among the discharged patients, the hospital stay in group B (19 cases) was (14.42 ± 4.59) days shorter than that in group A (13 cases) (18.34 ± 5.72) days (t = 2.147, p = 0.040). It shows that ECMO combined with IABP assisted by V-A mode can reduce the in-hospital mortality of AFM patients and shorten the hospitalization time of discharged patients. The reason for the analysis may be that group B had adopted a "comprehensive treatment plan based on life support", multidisciplinary cooperation and complementary advantages, which can reduce the heart load, also provide pulsatile physiological blood flow, ensuring the blood flow perfusion of the body's brain, kidney and other important organs, helping the patient to escape through the dangerous period and speed up the recovery. In addition, the causes of death of the two groups were analyzed. It was found that the causes of death of the two cases in group B were multiple organ dysfunction syndrome, and the causes of death of the 11 cases in group A were 8 multiple organ dysfunction syndrome, 2 cardiac arrest, and 1 intracranial hemorrhage. It is suggested that we should pay high attention to the tendency of multiple organ dysfunction syndrome in patients with AFM and predict the condition early. With the increasing popularity of ECMO and IABP, in addition to clearly grasping the working principles of ECMO and IABP, we should also strengthen clinical monitoring, strengthen the training of modern intensive care unit nursing teams, ensuring that each team member is aware of possible complications and can take appropriate preventive strategies on time, and carry out comprehensive preventive and therapeutic care, and continuously improve the quality of care, so as to reduce the nursing defects, reduce the risk of potential complications, accelerate the improvement of the condition and shorten the hospitalization time of patients [16–18].

The results of this retrospective observational study are significant for clinical recommendations. Although there are certain limitations. First of all there may be statistical bias because the study is a retrospective single-center design with a limited sample size and a lower degree of freedom. We should also include more objective indications, such as associated complications, to enable quicker and more accurate identification of the illness outcome. Also, there was insufficient detail in the data to distinguish between death from cardiovascular and noncardiovascular causes, which could lead to statistical bias. Strictly randomized clinical trials or alternative study designs are therefore required to further minimize bias and subsequently elucidate the illness prognosis and troponin level in patients with AFM produced by V-A ECMO with IABP.

To summarize, the ECMO combined with IABP assisted by V-A mode can improve the condition, arterial blood gas analysis index and cardiac function of AFM patients, alleviate myocardial injury, reduce the in-hospital mortality, and shorten the hospitalization time of discharged patients. However, there are still shortcomings in this study. This study is a retrospective observational study with a small sample size (21 cases in group A and 24 cases in group B), and the long-term follow-up observation results are not counted, which leads to some limitations in the conclusions of this study. Therefore, in the follow-up study, it is necessary to carry out a large sample and long-term follow-up observation to further verify the effectiveness and safety of V-A mode assisted ECMO combined with IABP in the treatment of AFM.

Conclusions

The study demonstrates that V-A mode assisted ECMO combined with IABP significantly improves the clinical outcomes for patients with acute fulminant myocarditis (AFM). Key findings include a substantial reduction in hospital mortality and shorter hospitalization times for recovered patients in the combined treatment group compared to traditional treatment alone. The combination therapy enhances cardiac function, alleviates myocardial injury, and improves arterial blood gas indices, highlighting its potential as an effective intervention for managing AFM. Further research with larger samples and long-term follow-up is recommended to validate these findings.

Availability of Data and Materials

Data to support the findings of this study are available-upon reasonable request from the corresponding author.

Author Contributions

ZY were responsible for the research project, responsible for determining the direction, objectives, and Writing. XH and FW was responsible for conceptualization, methodology, investigation, formal analysis, Writing, original draft. YJ, YL were responsible for collection and assembly of data, supervision, validation, writing — review and editing. WZ and JX were responsible for conception and design of the work, formal analysis, and interpretation of data for the work. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

Prior to recruitment, all the participants signed an informed consent after carefully reviewing the procedures, risks and precautions of the study. This study was approved by the Ethics Committee of the Affiliated Hospital of Qingdao University (NO. QYFY WZLL 28680).

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Conflict of Interest

The authors declare no conflict of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.59958/hsf.7573.

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