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Effect of Xingnaojing Injection on Neurological Outcomes in patients with Extracorporeal cardiopulmonary resuscitation: A single-center retrospective cohort study

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ABSTRACT

Background: Patients undergoing extracorporeal cardiopulmonary resuscitation (ECPR) have poor neurological prognoses and low survival rates. Xingnaojing injection (XNJ) is widely used in the acute phase of ischemic stroke. This study aimed to investigate the effects of XNJ on neurological outcomes in patients receiving ECPR.

Methods: Medical data of all patients who underwent ECPR at Zhongshan People's Hospital from January 2023 to March 2024 were collected. In this retrospective cohort study, patients were divided into XNJ and non-XNJ groups according to whether or not they used XNJ. Baseline data of patients were collected, including serum neuron-specific enolase (NSE) S-100 protein, TNF-α and IL-6 at 1 h, 24 h, 48 h and 72 h after extracorporeal membrane oxygenation (ECMO). The optimal Glasgow Coma Scale (GCS)at 24 and 72 hours after ECMO and the outcomes of neurological function and prognosis at discharge were evaluated. Univariate and multivariate logistic regressions were used to analyze the risk factors affecting patient prognosis.

Results: A total of 44 patients were included in this study; 22 in each group. The patients were 47 (38.0, 57.5) years old, the CPR time before ECMO was 30 (22, 50) min, and the APACHE II score was 28 (20, 31) points. ECMO assisted 96 (72,144) hours, ICU 7.5 (5, 12) days, 14.5 (6.3, 24) days in the hospital, 50% survived discharge, and 40.9% of patients had favorable neurological outcome at discharge. The GCSscores at 24 and 72 hours after ECMO were (9(3, 13) vs 9(3, 15), p=0.68), (12.5 (3, 15) vs 10 (3, 15), p=0.13), respectively. There was no statistically significant difference in Cerebral Performance Category (CPC) scores at discharge, p=0.68. The rate of favorable neurological outcomes at discharge between the XNJ and non-XNJ groups was 40.9% vs 40.9%, p=0.62, and there was no significant difference between the two groups in terms of survival and discharge (45.6% vs 54.5%, p=0.76). Serum S100 and NSE proteins, which are markers of brain injury, increased within 24 hours and decreased 48 hours later in both groups. The expression of S100 protein in the XNJ group at 24, 48, and 72 hours was lower than that in the non-XNJ group ($p<0.05$). The expression of NSE protein in the XNJ group at 48 and 72 hours was lower than that in the non-XNJ group ($p<0.05$). Serum TNF-α and IL-6, *markers of inflammation in both groups, showed a decreasing trend at 24 hours after ECMO.* The expression of serum TNF-α at 24 and 48 hours was lower in the XNJ group ($p<0.05$). The expression of IL-6 *at 48 and 72 hours was lower in the XNJ group* ($p<0.05$). The lactate level before ECMO (1.353 [1.020-1.796], p=0.036) was an independent risk factor for the prognosis of ECMO-assisted patients. ROC curve of pre-ECMO lactate level (AUC=0.75 (0.61-0.91), $p<0.01$.

Conclusion: XNJ may alleviate brain injury and inhibit the inflammatory response in patients undergoing ECPR but may not improve the neurological function and survival of patients at discharge.

Keywords: ECPR; Extracorporeal cardiopulmonary resuscitation; Brain injury; CPC; Cerebral performance category; Neurological outcome.

List of Abbreviations

Extracorporeal membrane oxygenation, ECMO
Extracorporeal cardiopulmonary resuscitation, ECPR
Xingnaojing, XNJ
End-tidal carbon dioxide, ETCO2
Intra-aortic balloon pump, IABP
Cerebral performance category, CPC
Acute Physiology and Chronic Health Evaluation II, APACHE II
Glasgow Coma Scale, GCS
Highest GCS after ECMO, H-GCS
Procalcitonin, PCT
Highest PCT after ECMO, H-PCT
Neuron-specific enolase, NSE

Introduction

Sudden cardiac death is a common cause of death, accounting for approximately 50% of all cardiac deaths and 15% of total mortality [1, 2]. Despite the widespread use of cardiopulmonary resuscitation, survival rates for cardiac arrest remain low [3]. The use of extracorporeal membrane oxygenation (ECMO) during cardiopulmonary resuscitation for cardiac arrest, defined as ECPR, is a recognized option for refractory cardiac arrest and is increasingly used worldwide [4]. Compared with traditional cardiopulmonary resuscitation, ECPR reduces in-hospital mortality and improves long-term neurological function outcomes and survival after cardiac arrest, especially in patients with in-hospital cardiac arrest [5, 6]. Although ECPR strategies have improved neurological outcomes in patients, the outcomes are unsatisfactory. Therefore, further improvement in the neurological function of patients receiving ECPR is still a problem worthy of attention. There are many reasons for impaired neurological function in patients, and it is currently believed that there are two mechanisms of acute brain injury after cardiac arrest. The first is primary brain injury caused by the cessation of oxygen supply to the brain during cardiac arrest, and the other is secondary brain injury caused by reperfusion and/or spontaneous circulatory recovery (ROSC) after resuscitation [7]. For the former, it is most important to ensure high-quality cardiopulmonary resuscitation before ECMO and establish ECMO as early as possible to shorten the time of low blood flow to brain tissue. For secondary brain injury, it is mainly for the brain injury caused by ischemia-reperfusion injury and ECMO extracorporeal circulation inflammatory response. Xingnaojing Injection (XNJ) is composed of musk (Moschus), turmeric (ginger family), gardenia (Rubiaceae), and Borneolum [8]. Approved by the China Food and Drug Administration, it is widely used in the acute stage of ischemic stroke [9]. Previous studies have suggested that XNJ can improve cerebral ischemia-reperfusion injury by inhibiting inflammation through the SIRT1 pathway and may be a useful target for the treatment of cerebral ischemia-reperfusion injury [10]. Therefore, this study aimed to investigate the effects of XNJ on neurological outcomes in patients receiving ECPR.

Materials And Methods

This study was approved by the Ethics Committee of Zhongshan People's Hospital (No:K2022-082), and informed consent was obtained from the patients or their family members.

1. STUDY SUBJECTS

All patients who underwent ECPR at Zhongshan People's Hospital between January 2023 and March 2024 and met the inclusion criteria were selected to participate in the study.

1.1 The inclusion criteria were: (1) age > 18 years, (2) patients with cardiac arrest, (3) no cardiopulmonary resuscitation time <5 min, (4) no flow to ECMO time <60 min, and (5) $ETCO_2$ >20 mmHg before ECMO.

1.2 The exclusion criteria were: (1) Disturbance of consciousness due to other causes (trauma, cerebrovascular accident). (2) Terminal disease (malignant tumor); (3) Age > 75 years. (4) Bleeding disorder that cannot be corrected, (5) multiple organ failure, and (6) ECMO time <24 h.(7)previous neurologic impairment.

2. RESEARCH METHODS

The patients enrolled in this study were retrospectively analyzed and divided into XNJ and non-XNJ groups according to whether or not they received XNJ intravenously.Whether to use Xingnaojing injection was determined according to the experimental group.
ECMO establishment: All patients underwent ECMO establishment via the femoral artery and femoral vein. The ECMO flow rate was 2.2 L/cm^2* body surface area, and the mean arterial pressure was > 70 mmHg.

Data Collection

General data were collected on all patients (sex, age, weight, disease history, compression duration, ECMO duration, ICU stay, length of stay, clinical outcome). Serum concentrations of neuron-specific enolase (NSE), S-100 protein, TNF-a, and IL-6 were collected 1, 24, 48, and 72 hours after ECMO.

3. PRIMARY STUDY ENDPOINTS

Optimal GCS were determined at 24 and 72 hours after ECMO and neurological outcomes at discharge in both groups. The CPC scale was used to assess neurological outcomes in the ICU. If the CPC score was 1 or 2, the neurological prognosis was considered favorable. If the CPC score was 3-5, the prognosis was unfavorable. The CPC score is shown in Table 1.

Table 1: Cerebral Performance Category (CPC) Scoring System

Level	Neurological Function
CPC 1	Optimal Neurological Function: Patient is alert and cognizant, capable of normal life and work activities.
CPC 2	Moderate Neurological Disability: Patient is alert, capable of part-time work or independent daily activities within a specified environment.
CPC 3	Severe Neurological Disability: Patient is alert, yet reliant on external assistance for daily activities, retaining limited cognitive function.

Level	Neurological Function
CPC 4	Coma and Vegetative State: Patient lacks awareness, unconscious to the environment, devoid of cognitive function.
CPC 5	Death: Patient is confirmed as brain-dead or deceased according to conventional criteria.

4. SECONDARY ENDPOINT:
The secondary endpoint of the study was the analysis of factors affecting the prognosis of patients who received ECPR.

5. STATISTICAL ANALYSIS
Descriptive statistics were computed for all the variables of interest. Continuous variables are expressed as medians along with their corresponding interquartile ranges, while categorical variables are presented as counts and percentages. To conduct a univariate analysis, Fisher's exact test was used to assess categorical variables, whereas the Mann-Whitney U test was used for continuous variables. Chi-square test was used for categorical variables. Factors affecting survival at hospital discharge were analyzed using multivariate logistic regression analysis. All p-values were two-tailed, and statistical significance was set at values < 0.05. Statistical computations were performed using SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, NY).

Results

Sixty patients were included in the study; 16 were excluded, and 44 were eventually included. There were 22 patients each in the XNJ and non-XNJ groups. The study flow chart is shown in Figure 1.

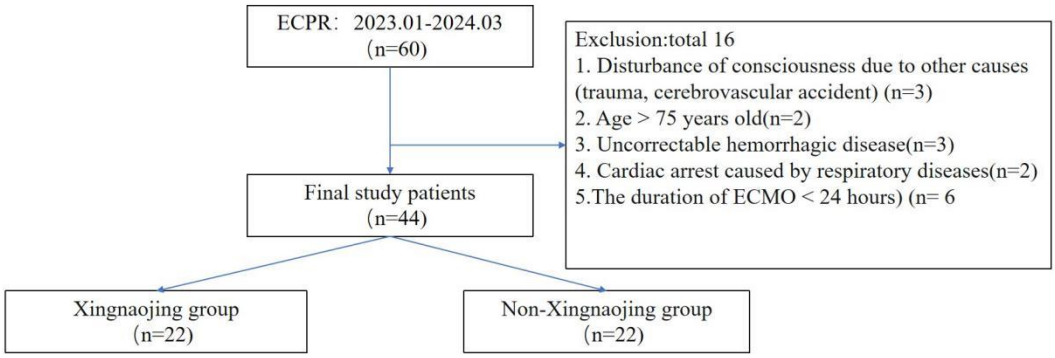

Figure 1. The study flow chart

The baseline data of the patients in the two groups are shown in Table 2; there was no statistically significant difference between the two groups. There were 47 (38.0, 57.5) years old, CPR time before ECMO was 30 (22, 50) minutes, and the APACHE-II score was 28 (20, 31).

Table2. Comparison of characteristics between the XNJ group and Non-XNJ group

Variable	Overall, N = 44[1]	XNJ group N = 22[1]	Non-XNJ group N = 22[1]	p-value[2]
Sex				0.69
Female	8(18%)	3 (13.6%)	5 (22.7%)	
Male	36(82%)	19 (86.4%)	17 (77.3%)	
Age, years	47(38.0, 57.5)	50 (31.75, 57.25)	45 (40.75, 59.25)	0.82
Disease				0.62
Myocardial infarct	23 (52.3%)	12 (54.5%)	11 (50%)	
Valvular heart disease	5 (11.4%)	2 (9.1%)	3 (13.6%)	
Fulminant myocarditis	9(20.5%)	6(27.3%)	3(13.6%)	
Other primary diseases	7(15.8%)	2 (9.1%)	5 (22.8%)	
History of disease				
Hypertension				0.50
Yes	11 (25%)	5(22.7%)	6 (27.3%)	
No	33 (75%)	17(77.3%)	16 (72.7%)	
Diabetes				0.66
Yes	6 (27.3%)	3 (13.6%)	3 (13.6%)	
No	38(72.7%)	19(86.4%)	19 (86.4%)	
Before ECMO				
CPR duration, minutes	30 (22, 50)	31 (20.7, 65.0)	30(23.7, 50.0)	0.58
APACHE-II score	28 (20, 31)	28.5 (19.7, 32.0)	27.5 (20.7, 31.2)	0.82
Lactate level, mmol/L before ECMO	12.65(8.0, 15.0)	12.4 (7.9, 15.0)	12.6 (8.1, 15.0)	0.86
After ECMO				
ECMO flow, L/min on the first day	3.00 (2.60, 3.30)	2.90 (2.61, 3.22)	3.00 (2.57, 3.35)	0.86

Variable	Overall, N = 44[1]	XNJ group N = 22[1]	Non-XNJ group N = 22[1]	p-value[2]
ECMO flow, L/min on the second day	2.50 (2.20, 3.01)	2.50 (2.20, 2.93)	2.50 (2.00, 3.15)	0.63
ECMO flow, L/min on the third day	2.35 (2.00, 2.95)	2.30(2.00, 2.78)	2.50 (2.00, 3.05)	0.37
MAP, mmHg on the first day	78.0 (71.3, 87.0)	80 (76.0, 87.5)	75 (67.0, 86.3)	0.09
MAP, mmHg on the second day	86.0 (75.0, 92.0)	86 (79.0, 92.3)	81(66.5, 90.5)	0.16
MAP, mmHg on the third day	85.5(76.0, 90.0)	85.5(80.3, 93.0)	85.5 (68.3, 90.0)	0.24
Lactate level, mmol/L 24 hours after ECMO	2.15(1.50,4.00)	2.3 （1.75,7.05）	8.9(3.90,15)	0.83
Lactate level, mmol/L 48hours after ECMO	1.65(1.20,2.95)	1.60(1.20,3.05)	1.85(1.20,2.95)	0.93
Lactate level, mmol/L 72 hours after ECMO	1.45(1.00,2.15)	1.50(1.02,2.30)	1.30(0.97,1.85)	0.54
IABP				0.50
Yes	13 (29.5%)	6(27.2%)	7 (31.8%)	
No	31(70.5%)	16 (72.8%)	15 (68.2%)	
Infections				0.62
Yes	28(63.6%)	14 (63.6%)	14 (63.6%)	
No	16(36.4%)	8(36.4%)	8 (36.4%)	

[1]n (%), median (IQR). [2]Pearson's chi-squared test; Wilcoxon rank-sum test; Fisher's exact test.

1. NEUROLOGICAL OUTCOME

A total of 40.9% of patients had good neurological function at discharge. The Glasgow scores at 24 and 72 hours after ECMO were (9 [3, 13] vs 9 [3, 15], p=0.68), (12.5 [3, 15] vs 10 [3, 15], p=0.13), respectively. There was no statistically significant difference in CPC scores at discharge, p=0.68. The rate of favorable neurological outcome at discharge between the XNJ group and non-XNJ group was 40.9% vs 40.9%, p=0.62), and there was no difference between them, as shown in Table 3 and Figure 2. There was no statistically significant difference in survival and discharge rates between the two groups (45.6% vs 54.5, p=0.76), as shown in Table 3.

Table3: Neurological outcomes and clinical outcomes between the XNJ group and Non-XNJ group

Variable	Overall N = 44	Xingnaojing group N = 22	Control group N = 22	p-value
Duration of ECMO, days	96 (72, 144)	96 (72, 150)	88 (72, 120)	0.13
ECMO Weaning				0.50
Yes	33(75%)	17 (77.3%)	16 (72.7%)	
No	11 (25%)	5 (22.7%)	6 (27.3%)	
Length of ICU stay,days	7.5 (5.0, 12.0)	7.5 (4.7, 12.0)	7.5 (5.0, 12.0)	0.94
Length of hospital stay, days	14.5 (6.2, 24)	13.5 (5.7, 25.0)	17.0 (6.5, 25)	0.61
GCS 24 hours after ECMO	9 (3, 13)	9(3, 13)	9(3, 15)	0.68
GCS 72 hours after ECMO	10.5 (3, 15)	12.5 (3, 15)	10(3, 15)	0.13
CPC score				0.63
1 score	15 (34.1%)	8 (36.4%)	7 (31.9%)	
2 score	3 (6.8%)	1 (4.5%)	2 (9.1%)	
3 score	1 (2.3%)	0 (0%)	1 (4.5%)	
4 score	1 (2.3%)	0 (0%)	1 (4.5%)	
5 score	24 (54.5%)	13 (59.1%)	11 (50%)	
Neurological outcomes at discharge				0.62
Favorable outcome	18 (40.9%)	9(40.9%)	9 (40.9%)	
Unfavorable outcome	26 (59.1%)	13(59.1%)	13 (59.1%)	
Survival to discharge				0.76
Yes	22(50%)	10 (45.6%)	12 (54.5%)	
No	22 (50%)	12 (54.4%)	10 (45.5%)	

[1]n (%), median (IQR). [2]Pearson's chi-squared test; Wilcoxon rank-sum test; Fisher's exact test. GCS(24 hours after ECMO) refers to the highest Glasgow Coma Scale score at the 24th hour of ECMO support. ECMO Weaning was defined as weaning from ECMO for 48 hours. A CPC score of 1 or 2 was considered indicative of a good neurological prognosis, whereas a score ranging from 3 to 5 was considered indicative of a poor neurological prognosis.

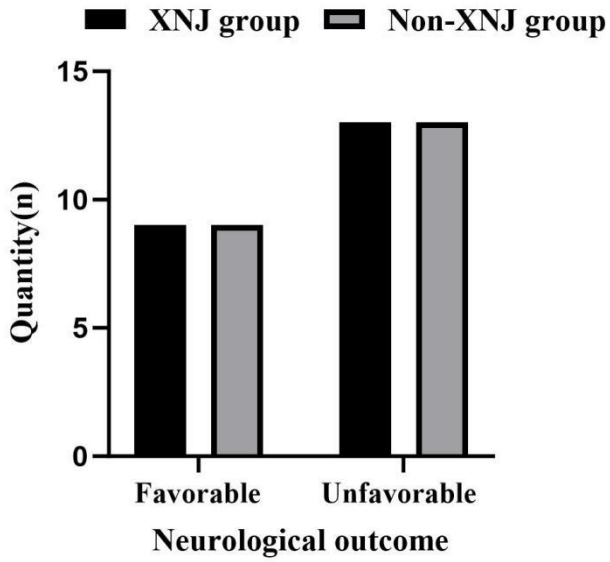

Figure 2. Comparison of neural function between XNJ group and non-XNJ group
A CPC score of 1 or 2 was considered indicative of a favorable neurological outcome, whereas a CPC score ranging from 3 to 5 was considered indicative of an unfavorable neurological outcome.

Serum S100 protein, a marker of brain injury, increased within 24 hours and decreased after 48 hours, and its expression in the XNJ group was lower than in the non-XNJ group at 24, 48, and 72 hours ($p<0.05$). The expression of brain injury marker serum NSE protein was increased within 24 hours and decreased after 48 hours, and the expression in the XNJ group was lower than that in the non-XNJ group at 48 and 72 hours ($p<0.05$); The expression of inflammation marker serum *TNF-α* in both groups decreased 24 hours after ECMO, and the expression in the XNJ group was lower than that in the non-XNJ group at 24 and 48 hours ($p<0.05$). The inflammatory marker *IL-6* showed a decreasing trend at 24 hours after ECMO, and the expression at 48 and 72 hours was lower in the XNJ group ($p<0.05$), as shown in Figure 3.

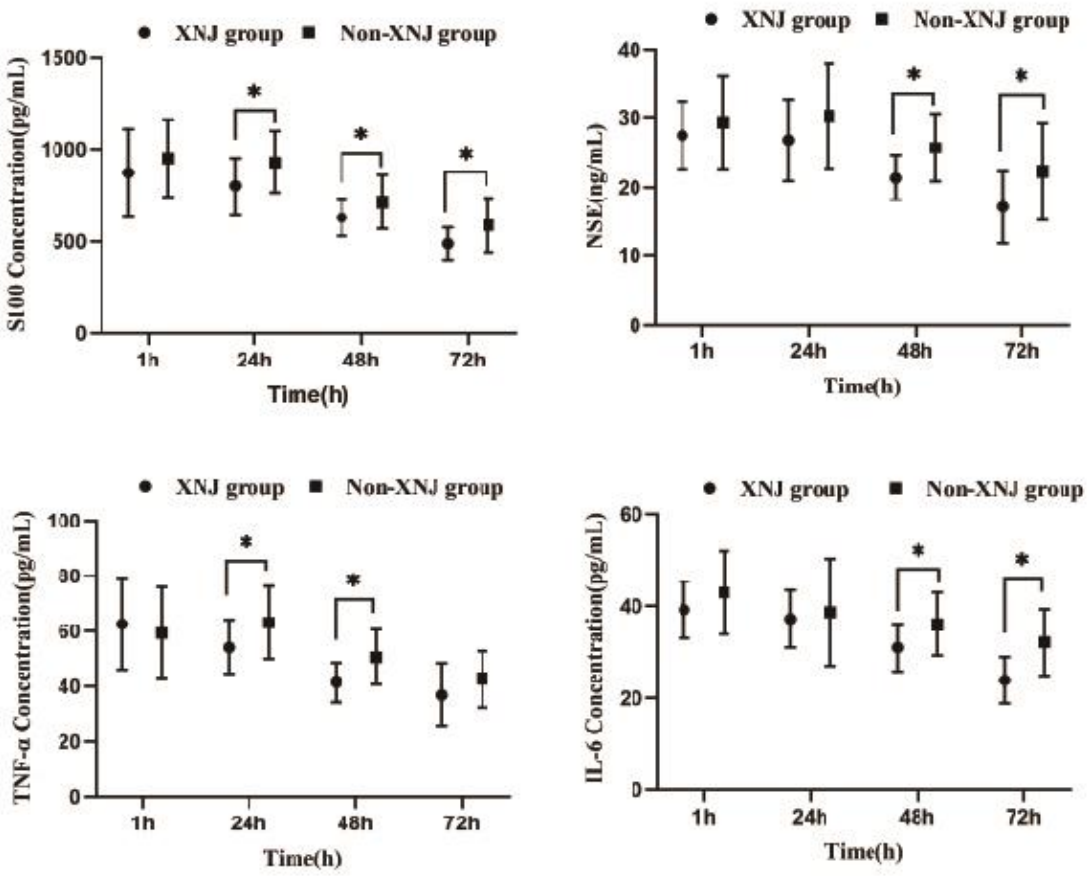

Figure 3. Expression of brain injury markers S100 protein, NSE and inflammation markers TNF-α and IL-6 at 1 h, 24 h, 48 h and 72 h after ECMO in the XNJ and non-XNJ groups

2. CLINICAL OUTCOME

ECMO assistance was provided for 96 (72,144) hours, ICU 7.5 (5, 12) days, hospitalization 14.5 (6.3, 24) days, 50% of patients survived discharge. Univariate analysis showed that sex, length of stay, lactate level before ECMO, lactate level 24 h after ECMO, occurrence of infection, and H-PCT level were risk factors affecting prognosis and were not related to whether XNJ was used, as shown in Table 4.

Multivariate logistic regression analysis showed that the pre-ECMO lactate level (1.353 [1.020-1.796], p=0.036) was an independent risk factor for the prognosis of ECMO-assisted patients, as shown in Table 5. The ROC curve of pre-ECMO lactate level (AUC=0.75 [0.61-0.91], p<0.01) is shown in Figure 4.

Table 4: Univariate analysis of prognosis of patients at discharge

Variable	**Overall**, N = 44[1]	**Survival**, N = 22[1]	Non-Survival, N = 22[1]	p-value[2]
Sex				0.046
Female	8 (18.2%)	7 (31.8%)	1(4.5%)	
Male	36 (81.8%)	15 (68.2%)	21(95.5%)	
Age	47 (38, 57.8)	45 (28.5, 57.2)	50(42, 60.5)	0.20
Disease				0.12
Myocardial infarct	23 (52.3%)	8(36.4%)	15 (68.2%)	
Valvular heart disease	5 (11.4%)	2(9%)	3 (13.6%)	
Fulminant myocarditis	9(20.5%)	8 （36.4%）	1 （4.5%）	
Other primary diseases	7(15.8%)	4 (18.2%)	3 (13.7%)	
Interventions				0.76
XNJ group	22(50%)	10(45.5%)	12(54.5%)	
Non-XNJ group	22(50%)	12(54.5%)	10(45.5%)	
IABP				0.51
Yes	13 (29.5%)	5(22.7%)	8 (36.4%)	
No	31 (70.5%)	17(77.3%)	14 (63.6%)	
Hypertension				0.16
Yes	11 (25%)	3 (13.6%)	8 (36.4%)	
No	33 (75%)	19(86.4%)	14 (63.6%)	
Diabetes				0.18
Yes	6 (13.6%)	1 (4.5%)	5 (22.7%)	
No	38 (86.4%)	21 (95.5%)	17(77.3%)	
CPR duration, minutes	30(22, 50)	30(20, 53)	33.5 (30, 50)	0.10
APACHE-II score	28 (20, 31)	26(19.7, 30)	30 (20, 35)	0.23
Duration of ECMO, hours	96(72,144)	96 （72,120）	108(72,168)	0.20
Length of ICU stay, days	7.5 (5, 12)	7 (5, 12)	7.5 (3.75, 12.25)	0.53
Length of hospital stay, days	14.5 (6.3, 24)	18.5 (11.50, 32)	12 (4.75, 18.25)	0.03
Lactate level, mmol/L before ECMO	12.65 (8.03, 15.0)	9.25(6.75, 12.8)	14.6 (12.17, 15.0)	0.003
Lactate level, mmol/L 24 hours after ECMO	2.15 （1.5,4.0）	1.65 （1.30， 3.57）	2.7 （1.9， 5.17）	0.012
ECMO flow, L/min on the first day	3.0(2.6, 3.3)	2.8(2.5, 3.2)	3.2 (2.68, 3.35)	0.06
MAP, mmHg on the first day	78 (71.3, 87)	85 (75, 87.5)	77 (67, 82.5)	0.13
Infections				0.027
Yes	28(63.6%)	10 (45.4%)	18 (81.8%)	
No	16(36.4%)	12(54.6%)	4 (18.2%)	
H-PCT, ng/ml	16.4 (6.58, 30.75)	8.1(3.82, 18.01)	23.63 (7.11, 40.86)	0.006

[1]n (%), median (IQR). [2]Pearson's chi-squared test; Wilcoxon rank-sum test; Fisher's exact test.
CPR, cardiopulmonary resuscitation; APACHE II,Acute Physiology and Chronic Health Evaluation II ; PCT, procalcitonin ;H-PCT, highest PCT after ECMO.

Table5: Multivariate logistic regression analysis of prognostic factors of Survival at hospital discharge

	OR[1] (95% CI[1])	p-value
Lactate level before ECMO	1.353(1.020-1.796)	0.036

[1]OR = Odds Ratio, CI = Confidence Interval.

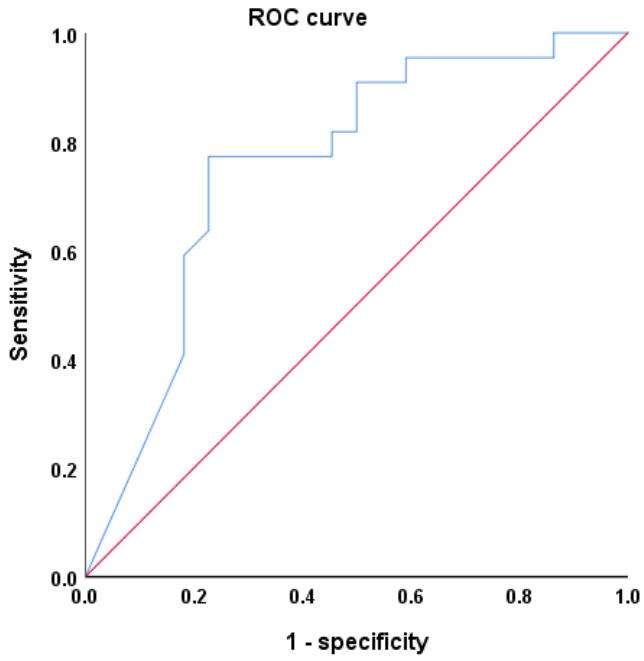

Figure 4. ROC curve

Discussion

The results of this study suggest that brain damage in ECPR patients was most impaired at 24 hours, gradually reduced after 48 hours, and 40.9% of patients had favorable neurological outcomes at discharge. The expression of brain injury markers and inflammatory response were reduced in the XNJ group, but there was no difference in the rate of favorable neurological outcomes and survival at discharge between the two groups.

Acute brain injury remains common after ECPR) [11], leading to poor neurological prognosis [12]. Primary acute brain injury is caused by global cerebral ischemia during cardiac arrest. In contrast, secondary acute brain injury results from ECMO support, and immediate cerebral blood flow recovery leads to reperfusion injury [13]. In this study, the rate of favorable neurological outcomes at discharge was 40.9%, which was higher than that of other centers (28.5%-30.2%) [12, 14]. The possible reasons are: 1. All the ECPR patients in this study were hospitalized for cardiopulmonary resuscitation; 2. 2. An $ETCO_2$ >20 mm Hg before ECMO was performed to ensure high-quality CPR. Many previous studies have confirmed the role of $ETCO_2$-oriented compressions in good neurological prognosis [15, 16]. $ETCO_2$ values are correlated with cardiac output during CPR [17]. The results of this study showed that ECPR patients had the highest serum S-100 protein levels and the most severe brain injury after 24 hours, consistent with the results of Song et al. [18]. Previous studies have suggested that S-100 protein could be used as a predictor of neurological prognosis within 24 h of cardiac arrest [19]. The NSE level 48 hours after ECPR also correlates with the prognosis of neurological function [20]. In patients with elevated serum S-100 protein levels after cardiac arrest and CPR, S-100 protein may induce nerve cell damage via inflammatory factors, thereby aggravating post-resuscitation brain injury [21].

XNJ is one of the neuroprotectants approved by the China Food and Drug Administration for the treatment of acute stroke and is widely used in China [22]. In this study, we found that the secretion of brain injury markers and inflammatory mediators decreased in the XNJ group. Studies suggest that XNJ can improve cerebral ischemia-reperfusion injury by inhibiting inflammation through the SIRT1 pathway and may be an effective target for the treatment of cerebral ischemia-reperfusion injury [23]. Some studies have suggested that XNJ may reduce cell apoptosis by regulating the endoplasmic reticulum stress-induced apoptotic pathway, making it a potential treatment for ischemic stroke [24]. The results of this study suggest that XNJ does not significantly improve the neurological function or survival of patients at discharge. This may be related to the fact that the patients in this study were on ECPR, and primary injury may be the main factor affecting their prognosis. When a patient experiences cardiac arrest, cerebral blood flow is immediately reduced, resulting in reduced oxygen delivery to the brain and leading to cerebral ischemia (primary brain injury). After cardiac arrest begins, the reduced cerebral oxygen delivery reduces neuronal aerobic metabolism and cellular ATP production, leading to cell death [25]. Although XNJ alleviates brain injury in patients by inhibiting the inflammatory response and anti-apoptotic mechanisms, the degree of primary injury may determine neurological function and prognosis. Many factors affect the neurological function and prognosis of ECPR patients, such as a history of hypertension, high lactate level on day 1, low pH value, intubation technique, decrease in PaCO2 during the peri-intubation period, and early low pulse pressure [26]. Severe hyperoxia (≥300 mm Hg) in the early ECMO period is a significant risk factor for acute brain injury and high mortality [27].

The lactic acid assay is routinely used to assess the severity of hypoperfusion and tissue hypoxia [28]. In this study, the univariate analysis showed that the lactate level 24 hours after ECMO was a prognostic risk factor. Dusik et al. showed that the serum lactate concentration within 24 h after admission was correlated with the prognosis of patients treated with ECPR [29], which was

consistent with the results of this study. Multifactor analysis showed that the lactate level before ECMO (1.353 [1.020-1.796], p=0.036) was an independent risk factor affecting the prognosis of ECMO-assisted patients. The high lactate level before ECMO reflects the degree of tissue hypoxia; the higher the lactate level, the more serious the tissue ischemia and hypoxia in patients, which ultimately affects organ function and leads to patient death. Previous studies have also suggested that lactic acid and lactate clearance can be used as prognostic indicators [30]. Therefore, hypoperfusion and hypoperfusion time should be reduced [31].

This study has several limitations. First, the sample size was relatively small, which could have created a bias in the results due to the small sample size. Second, the treatment of patients undergoing ECPR is complicated, and many interfering factors may have affected the outcome of the study. In addition, it is recommended that a multicenter, large-sample, independent cohort study be conducted to validate the results of this study.

Conclusion

XNJ may alleviate brain injury and inhibit inflammatory responses in ECPR patients but may not improve neurological function and survival at discharge.

Declaration

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Zhongshan People's Hospital. *Written informed consent was obtained from* either patients or their family members *in this study for the publication of any potentially identifiable images and data included in this article.*

Declaration of interests

The authors declare that they have no competing interests.

Declaration of Generative AI in scientific writing

No artificial intelligence writing was applied.

Disclosure instructions

AI and AI-assisted technologies were not used.

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Authors' contributions

Xiaozu Liao, Article drafting

Zhou Cheng, Data collection

Shi Zhong, Data analysis

Binfei Li, Design

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