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Research Article

Potential Role of Extracellular CIRP in Total Aortic Arch Replacement under Hypothermic Circulatory Arrest

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Objectives. To investigate the potential role of extracellular cold-inducible RNA-binding protein (CIRP) in total aortic arch replacement under hypothermic circulatory arrest. *Methods*. The serum extracellular CIRP levels at five time points in 96 patients with Stanford A aortic dissection were detected. Overall change trend of CIRP levels at five time points was described, and the risk factors for 30-day mortality after surgery were analyzed. *Results*. The serum extracellular CIRP levels increased gradually after surgery, starting to rise significantly at approximately 12 h postoperatively, reaching or approaching a peak at approximately 24 h postoperatively, and ceasing to rise significantly after approximately 48 h postoperatively. Age, troponin-I, urodilatin, cooling time, cardiopulmonary bypass time, cross-clamp time, duration of surgery, and CIRP level at the end of surgery in the death group were significantly higher than those in the survival group. Multivariable analysis indicated that CIRP level at the end of surgery, age, urodilatin, and cross-clamp time were independent risk factors for postoperative 30-day mortality. *Conclusion*. Extracellular CIRP is closely related to the perioperative condition and prognosis of hypothermic circulatory arrest.

1. Introduction

Aortic dissection is a very dangerous emergency that is classified as Stanford types A and B. Stanford type A aortic dissection (TAAD) is a lesion originating from the ascending aorta that is prone to aortic rupture and death and should be actively performed. Hypothermic circulatory arrest is a routine surgical procedure for aortic dissection [1], and moderate hypothermic circulatory arrest (MHCA) is a safe and effective circulatory strategy that is now widely used in aortic arch surgery [2]. MHCA combined with selective antegrade cerebral perfusion (SACP) can reduce the incidence of postoperative complications of aortic dissection [3]. Aortic dissection is severe and rapidly progressive, and there is no ideal biomarker to evaluate its prognosis after hypothermic circulatory arrest. Cold-inducible RNA-binding protein (CIRP) is a multifunctional protein that is widely expressed at low levels in a variety of tissues and cells. CIRP function is mainly determined by cellular localization, including intracellular CIRP (iCIRP) and extracellular CIRP (eCIRP). ICIRP is beneficial to the organism while eCIRP is detrimental, and eCIRP expression can be upregulated by stress and inflammatory conditions [4], acting as a mediator of inflammation to induce inflammatory responses and cause tissue and organ damage [5]. Studies have shown that inflammation plays an important role in the stress response period during aortic dissection [6]. However, to date, there have been no studies on the changes in CIRP levels at different time points during the perioperative period of hypothermic circulatory arrest in patients with aortic dissection and their correlation with postoperative prognosis.

This study aims to investigate the changes in serum extracellular CIRP at different time points during the perioperative period of hypothermic arrest circulation in patients with TAAD and their correlation with postoperative

prognosis, with the aim of early monitoring and intervention of CIRP as a potential biomarker to improve the prognosis of patients.

2. Methods

2.1. Patients. A total of 96 patients with Stanford type A aortic dissection admitted to the hospital from September 2019 to March 2021, were retrospectively selected for the study, including 78 males and 18 females, aged 31–65 years, with a mean age of 49.46 ± 8.72 years. All patients were diagnosed by thoracoabdominal aortic CTA and underwent total aortic arch replacement under moderate hypothermic circulatory arrest combined with selective antegrade cerebral perfusion. Patients were divided into a survival group ($n = 86$) and a death group ($n = 10$) according to the clinical prognosis at 30 days after surgery.

Inclusion criteria include the following: (i) those with Stanford type A aortic dissection confirmed by thoracoabdominal aortic CTA; (ii) those aged ≥18 years ; (iii) surgical treatment and cardiopulmonary bypass (CPB) strategy was moderate hypothermic circulatory arrest combined with selective antegrade cerebral perfusion.

Exclusion criteria include the following: (i) patients with incomplete clinical data or abandoned treatment; (ii) pregnant or lactating women; (iii) patients with chronic organ failure or end-stage malignancy.

The study complied with medical ethics standards and was approved by the hospital's Ethical Committee.

2.2. Clinical Specimens and Data Collection

2.2.1. General Data. Clinical data after admission were collected, including preoperative data: sex, age, BMI index, nature of dissection, degree of urgency, left ventricular ejection fraction, C-reactive protein, troponin-I, urodilatin, and underlying diseases. Intraoperative data: selective antegrade cerebral perfusion flow, cooling time (start to stop circulation time), minimum temperature (nasopharyngeal temperature), circulation arrest time, rewarming time (recovery of lower body antegrade perfusion to stop CPB time), CPB time, aortic cross-clamp time, CPB urine volume, and duration of surgery; CIRP levels at five time points: after admission, end of surgery, 12 h postoperatively, 24 h postoperatively, and 48 h postoperatively.

2.2.2. Assay Method. Five milliliters of venous blood specimens were routinely drawn from all patients included in the study at five time points: after admission, at the end of surgery, 12 h postoperatively, 24 h postoperatively, and 48 h postoperatively, set up as groups 1, 2, 3, 4, and 5, centrifuged at 3000 r/min for 10 min, and the serum was separated and stored at −70°C. Serum extracellular CIRP levels were determined by enzyme-linked immunosorbent assay (ELISA) provided by MyBioSource (MBS932362). Operation was performed in strict accordance with the instructions.

2.3. Statistical Analysis. SPSS 26.0 software was used for statistical analysis. Normally distributed measurement data are expressed as the mean ± standard deviation ($\overline{x} \pm s$), and two independent samples' t-test was used for comparisons between two groups. Measurement data with a skewed distribution are expressed as the median with interquartile range (M (P25 and P75)), with a nonparametric Mann–Whitney U test for comparison between two groups and a nonparametric Friedman test (correlated samples Friedman two-way by rank-variance analysis) for comparison of correlated skewed distribution data between multiple groups. Count data were expressed as the number of cases (percentage) (n (%)), and the chi-square test was used for comparisons between the two groups. Pearson correlation analysis was used to investigate the correlation between postoperative CIRP levels and cardiopulmonary bypass time or aortic cross-clamp time in TAAD patients. Multivariate logistic regression analysis was used to analyze the risk factors for 30-day postoperative mortality in TAAD patients. The receiver operating characteristic (ROC) curves of the independent risk factors for 30-day postoperative mortality in TAAD patients were drawn, and the predictive value of each index was evaluated. To calculate the area under the ROC curve (AUC) and 95% confidence interval (CI), the cutoff value, sensitivity, specificity, and Youden index were calculated. Differences were considered statistically significant when $P < 0.05$.

3. Results

3.1. General Trend in CIRP Levels at Five Time Points. A box plot of CIRP levels at five time points for all patients included in the study showed a gradually increasing trend (Figure 1). The nonparametric Friedman test was used to analyze the differences between groups, and significant differences were found in the overall distribution of CIRP levels among the five groups ($F = 72.227$, $P < 0.001$). Among them, CIRP levels were significantly higher in the 12 h, 24 h, and 48 h postoperative groups than in the preoperative group; CIRP levels were significantly higher in the 24 h and 48 h postoperative groups than in the end-of-surgery group and the 12 h postoperative group (all $P < 0.05$). There was no statistically significant difference between the preoperative group and the end-of-surgery group, the end-of-surgery group and the 12 h postoperative group, and the 24 h postoperative group and the 48 h postoperative group (all $P > 0.05$) (Table 1).

In summary, the serum extracellular CIRP levels of TAAD patients undergoing total aortic arch replacement under moderate hypothermic circulatory arrest combined with selective antegrade cerebral perfusion gradually increased in TAAD patients after hypothermic circulatory arrest compared with preoperative level, starting to rise significantly at approximately 12 h postoperatively, reaching or approaching a peak at approximately 24 h postoperatively, and ceasing to rise significantly after approximately 48 h postoperatively.

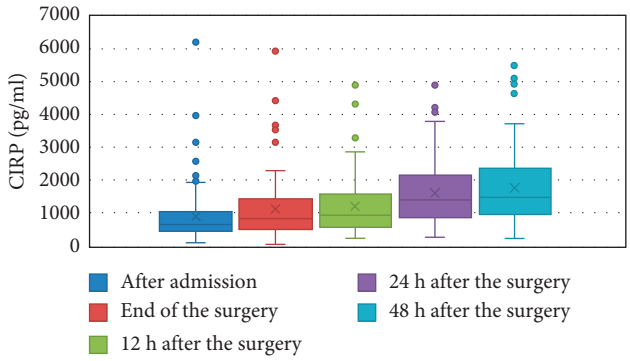

Figure 1: Box plot of CIRP levels in five groups of all patients.

Table 1: Paired comparison of CIRP levels in five groups of all patients.

CIRP levels comparison	*F* value	*P* value
CIRP1-CIRP2	−0.516	0.239
CIRP1-CIRP3	−0.724	**0.015**
CIRP1-CIRP4	−1.531	**<0.001**
CIRP1-CIRP5	−1.604	**<0.001**
CIRP2-CIRP3	−0.208	1.000
CIRP2-CIRP4	−1.016	**<0.001**
CIRP2-CIRP5	−1.089	**<0.001**
CIRP3-CIRP4	−0.807	**0.004**
CIRP3-CIRP5	−0.880	**0.001**
CIRP4-CIRP5	−0.073	1.000

CIRP: cold-inducibleRNA-binding protein. The bold values in the *P* value column are less than 0.05, which indicates statistical significance.

3.2. Comparison of Preoperative and Intraoperative Clinical Data between the Two Groups. In this study, 96 patients were included in strict accordance with the inclusion and exclusion criteria and were followed up for 30 d. Eighty-six patients (89.58%) survived (survival group) and ten patients (10.42%) died (death group). Compared with the survival group, patients in the death group were older, had higher troponin-I and urodilatin levels, and had longer cooling time, CPB time, cross-clamp time, and duration of surgery, which were risk factors for mortality at 30 d postoperatively in TAAD patients (all $P < 0.05$) (Tables 2 and 3).

3.3. Comparison of CIRP Levels at Five Time Points between the Two Groups. A higher CIRP level at the end of surgery (the second time point) in the death group than in the survival group was a risk factor for the 30-day mortality of TAAD patients after hypothermic circulatory arrest ($P < 0.05$) (Table 4).

3.4. Correlation between CIRP-2 Level and Cardiopulmonary Bypass Time or Cross-Clamp Time in TAAD Patients. According to results in section 3.2 and 3.3, compared with the survival group, the CIRP-2 level was higher, the CPB time and aortic cross-clamp time were longer in the death group, and the differences were statistically significant ($P < 0.05$). Pearson correlation analysis showed that the CIRP-2 level in TAAD patients were positively correlated with cross-clamp time ($r = 0.239$, $P = 0.019$) (Figure 2), but not with CPB time ($r = 0.131$, $P = 0.203$).

3.5. Multivariate Logistic Regression Analysis of Risk Factors for 30-Day Postoperative Mortality in TAAD Patients. The clinical indicators with statistically significant differences in the univariate analysis of results in section 3.2 and 3.3 were used as independent variables, and the prognosis of TAAD patients 30 d after hypothermic circulatory arrest was used as the dependent variable (assigned values: survival = 0, death = 1). Multivariate logistic regression analysis was performed. The results showed that age (OR = 1.248, 95% CI: 1.045–1.489, $P = 0.014$), urodilatin (OR = 1.002, 95% CI: 1.000–1.004, $P = 0.018$), cross-clamp time (OR = 1.146, 95% CI: 1.025–1.281, $P = 0.016$), and CIRP level at the end of surgery (CIRP-2) (OR = 1.001, 95% CI: 1.000–1.002, $P = 0.013$) were independent risk factors for 30-day mortality after hypothermia circulatory arrest in TAAD patients (Table 5).

3.6. Predictive Value of CIRP-2 Level, Age, Urodilatin, and Cross-Clamp Time on the Prognosis of TAAD Patients. ROC curve analysis showed that CIRP could be used as a biomarker for predicting 30-day mortality after hypothermic circulatory arrest in TAAD patients (Figure 3), with an AUC of 0.775 (95% CI: 0.648–0.902). The optimal cutoff value of the CIRP level at the end of surgery (CIRP-2) was 750.5 pg/ml when its sensitivity was 100.0% and specificity was 48.8% for predicting 30-day mortality after hypothermic circulatory arrest in TAAD patients (Table 6).

4. Discussion

Surgical reconstruction of the aortic arch with the hypothermic circulatory arrest strategy is the main treatment for Stanford type A aortic dissection, which has an acute onset, severe disease, and high mortality. Deep hypothermic circulatory arrest (DHCA) was first reported successfully for aortic arch replacement in 1975 [7], contributing to the development of modern aortic surgery. However, with the increase in surgical volume, the negative impact of deep hypothermia on patients' intraoperative and postoperative recovery has attracted clinical attention [8]. To solve the adverse effects caused by deep hypothermia, moderate hypothermic circulatory arrest (MHCA) has been widely used in clinical practice and proven to be a safe and effective circulatory strategy [2]. Selective antegrade cerebral perfusion (SACP) allows blood to be evenly distributed in the capillary bed, maintaining a near-physiological cerebral circulation, and tolerating a long period of safe circulatory arrest [9]. MHCA combined with SACP is supported clinically [10–12]. Studies have shown that MHCA combined with SACP significantly reduces intraoperative cardiopulmonary bypass time and postoperative mortality, as well as the incidence of permanent nerve damage, stroke, and renal failure compared with DHCA alone in hypothermic circulatory arrest [3, 13–15]. The surgical hypothermic circulatory arrest strategy for patients with TAAD included in this study was MHCA combined with SACP, which complied with this trend.

Table 2: Comparison of preoperative data between the two groups.

Variables	Overall ($n = 96$)	Survival group ($n = 86$)	Death group ($n = 10$)	$t/Z/x^2$ value	P value
Preoperative data					
Age (y, $\overline{x} \pm s$)	49.46 ± 8.72	48.81 ± 8.53	55.00 ± 8.79	−2.165	**0.033**
Gender (male/female)	78/18	71/15	7/3	0.927	0.336
BMI index (kg/m^2, $\overline{x} \pm s$)	24.88 ± 3.04	24.86 ± 3.02	25.06 ± 3.41	−0.201	0.841
Nature of dissection (acute/chronic)	91/5	81/5	10/0	0.613	0.434
Degree of urgency (emergency/limited)	90/6	80/6	10/0	0.744	0.388
LVEF (%, M ($P25$, $P75$))	57.00 (54.25, 58.00)	57.00 (54.00, 58.00)	56.50 (54.50, 58.25)	−0.544	0.586
C-reactive protein (mg/L, M ($P25$, $P75$))	6.55 (2.53, 12.38)	6.09 (2.53, 11.93)	12.05 (2.27, 17.15)	−1.073	0.283
Troponin-I (ng/mL, M ($P25$, $P75$))	0.02 (0.01, 0.14)	0.02 (0.01, 0.12)	0.13 (0.03, 0.44)	−2.508	**0.012**
Urodilatin (pg/mL, M ($P25$, $P75$))	375.50 (164.75, 690.75)	339.50 (156.50, 641.00)	809.50 (322.50, 2256.50)	−2.177	**0.029**
Underlying diseases (n (%))					
Preoperative renal function impairment (creatinine clearance <80)	31 (32.29)	26 (30.23)	5 (50.00)	1.601	0.206
Preoperative liver function impairment (mild)	4 (4.17)	3 (3.49)	1 (10.00)	0.951	0.329
Hypertension	64 (66.67)	58 (67.44)	6 (60.00)	0.223	0.637
Cardiovascular interventions	11 (11.46)	10 (11.63)	1 (10.00)	0.023	0.878
Pulmonary infection	4 (4.17)	4 (4.65)	0 (0.00)	0.485	0.486
Pleural effusion	14 (14.58)	12 (13.95)	2 (20.00)	0.263	0.608
Transient ischemic attack	6 (6.25)	6 (6.98)	0 (0.00)	0.744	0.388
Paresis	11 (11.46)	8 (9.30)	3 (30.00)	3.783	0.052

LVEF: left ventricular ejection fraction. The bold values in the P value column are less than 0.05, which indicates statistical significance.

Table 3: Comparison of intraoperative data between the two groups.

Variables	Overall ($n = 96$)	Survival group ($n = 86$)	Death group ($n = 10$)	$t/Z/x^2$ value	P value
Intraoperative data					
Selective antegrade cerebral perfusion flow (mL/min, M ($P25$, $P75$))	550.00 (451.25, 647.50)	550.00 (453.75, 660.00)	535.00 (397.50, 635.00)	−0.630	0.528
Cooling time (min, M ($P25$, $P75$))	80.00 (71.25, 94.00)	78.50 (71.00, 92.25)	100.50 (79.75, 110.50)	−2.010	**0.044**
Minimum temperature (nasopharyngeal temperature) (°C, M ($P25$, $P75$))	25.30 (25.00, 25.80)	25.30 (25.00, 25.80)	25.35 (25.05, 25.70)	−0.096	0.923
Circulation arrest time (min, M ($P25$, $P75$))	34.00 (32.00, 39.75)	34.50 (31.00, 39.00)	33.50 (32.00, 44.25)	−0.325	0.746
Rewarming time (min, M ($P25$, $P75$))	99.50 (89.00, 115.00)	97.50 (87.75, 114.25)	106.00 (99.75, 140.00)	−1.746	0.081
CPB time ((min, $\overline{x} \pm s$))	221.98 ± 32.60	219.05 ± 29.78	247.20 ± 45.30	−2.667	**0.009**
Cross-clamp time ((min, $\overline{x} \pm s$))	104.93 ± 17.01	103.15 ± 16.33	120.20 ± 15.70	−3.137	**0.002**
CPB urine volume (mL, M ($P25$, $P75$))	975.00 (600.00, 1500.00)	975.00 (600.00, 1500.00)	1050.00 (600.00, 1525.00)	−0.138	0.890
Duration of surgery (h, $\overline{x} \pm s$)	6.67 ± 1.00	6.59 ± 0.98	7.30 ± 0.93	−2.170	**0.033**

CPB: cardiopulmonary bypass. The bold values in the P value column are less than 0.05, which indicates statistical significance.

Table 4: Comparison of CIRP levels at five time points between the two groups.

Variables	Overall ($n = 96$)	Survival group ($n = 86$)	Death group ($n = 10$)	Z value	P value
CIRP-1 (pg/mL, M ($P25$, $P75$))	650.50 (432.25, 1037.50)	613.50 (429.25, 1006.25)	1307.50 (559.50, 2449.25)	−1.721	0.085
CIRP-2 (pg/mL, M ($P25$, $P75$))	837.50 (519.50, 1442.00)	762.50 (482.00, 1313.75)	1661.00 (899.25, 2610.25)	−2.837	**0.005**
CIRP-3 (pg/mL, M ($P25$, $P75$))	955.50 (587.25, 1585.50)	940.00 (585.75, 1506.00)	1564.50 (940.00, 2592.50)	−1.943	0.052
CIRP-4 (pg/mL, M ($P25$, $P75$))	1398.00 (883.50, 2152.25)	1379.50 (878.00, 2121.50)	1635.00 (849.00, 2726.75)	−0.708	0.479
CIRP-5 (pg/mL, M ($P25$, $P75$))	1463.00 (940.25, 2361.25)	1424.00 (944.75, 2195.25)	2707.50 (735.50, 3290.00)	−1.475	0.140

CIRP: cold-inducibleRNA-binding protein. The bold values in the P value column are less than 0.05, which indicates statistical significance.

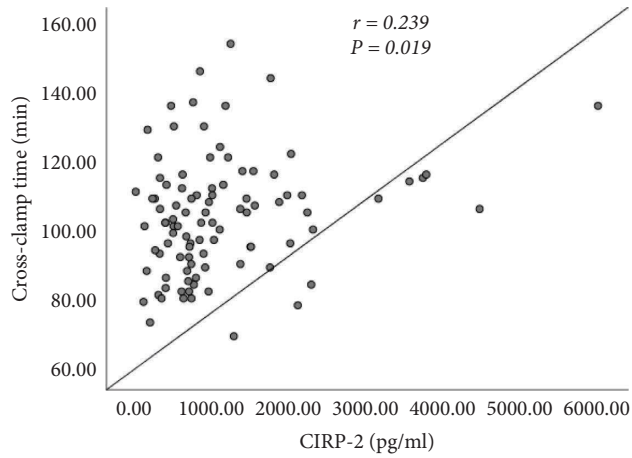

Figure 2: Scatter plot of correlation between CIRP-2 level and cross-clamp time in TAAD patients. Abbreviations: CIRP—cold-inducible RNA-binding protein.

Table 5: Multivariate logistic regression analysis of risk factors for 30-day postoperative mortality in TAAD patients.

Variables	β	SE	Wald χ^2	P value	OR	95% CI
Age	0.221	0.090	5.994	**0.014**	1.248	(1.045~1.489)
Troponin-I	−0.311	1.012	0.095	0.758	0.732	(0.101~5.327)
Urodilatin	0.002	0.001	5.591	**0.018**	1.002	(1.000~1.004)
Cooling time	−0.025	0.035	0.509	0.475	0.975	(0.910~1.045)
CPB time	−0.001	0.035	0.002	0.968	0.999	(0.933~1.069)
Cross-clamp time	0.136	0.057	5.770	**0.016**	1.146	(1.025~1.281)
Duration of surgery	1.348	1.081	1.553	0.213	3.850	(0.462~32.061)
CIRP-2	0.001	0.000	6.132	**0.013**	1.001	(1.000~1.002)
Constant	−39.754	13.261	8.987	0.003	—	—

CPB: cardiopulmonary bypass; CIRP: cold-inducible RNA-binding protein. The bold values in the P value column are less than 0.05, which indicates statistical significance.

CIRP was first discovered in hibernating animal cells in the 1990s, and its main role is to regulate the cell cycle [16]. It is widely expressed at low levels in a variety of tissues and cells, and its expression can be upregulated in response to cellular stress and inflammation [4]. CIRP function is mainly determined by cellular localization, including iCIRP and eCIRP. ICIRP stabilizes specific mRNAs to promote cell survival; eCIRP acts as an endogenous proinflammatory mediator and induces the production of multiple inflammatory mediators [4]. During cellular stress, iCIRP can be transferred from the nucleus to the cytoplasm and released outside the cell [17], becoming eCIRP to induce an inflammatory response that causes tissue and organ damage. A study [6] showed that inflammation plays an important role in aortic dissection, the body experiences a stress response period during aortic dissection, and the inflammatory factors and immune response generated by the stress response can cause a series of adverse effects on the organism. Therefore, it can be reasonably deduced that CIRP is released in large quantities to participate in the inflammatory response during aortic dissection, which will adversely affect the perioperative condition and prognosis of patients with aortic dissection. However, no specific study prior to this study has investigated the changes in CIRP levels during the perioperative period of hypothermic circulatory arrest in aortic dissection and their correlation with the postoperative prognosis.

The results of this study showed that age was an independent risk factor for 30 d postoperative mortality in TAAD patients, and for TAAD patients, the older they were,

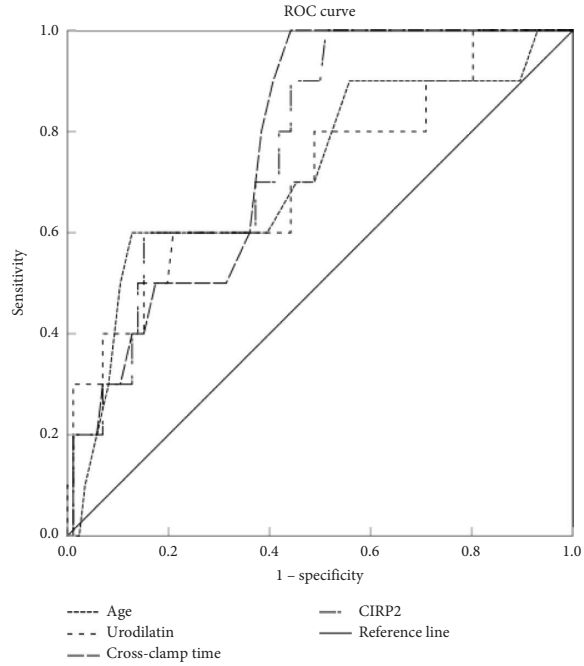

Figure 3: ROC curves for CIRP-2, age, urodilatin, and cross-clamp time to predict 30-day postoperative mortality in TAAD patients. Abbreviations: CIRP—cold-inducible RNA-binding protein.

Table 6: Predictive value of CIRP-2, age, urodilatin, and cross-clamp time for 30-day postoperative mortality in TAAD patients.

Variables	AUC	Sensitivity (%)	Specificity (%)	Youden index	95% CI	Cutoff value
CIRP-2	0.775	100.0	48.8	0.488	0.648–0.902	750.5 pg/mL
Cross-clamp time	0.773	100.0	55.8	0.558	0.655–0.892	105.0 min
Age	0.717	60.0	87.2	0.472	0.534–0.900	58.5 years
Urodilatin	0.711	60.0	79.1	0.391	0.527–0.895	686.5 pg/mL

CIRP: cold-inducibleRNA-binding protein.

the higher the 30 d postoperative mortality, which may be related to the decreased function of the organism and the combination of more complications in elderly patients; urodilatin was an independent risk factor for mortality at 30 d postoperatively in TAAD patients, indicating that the worse preoperative renal function, the higher postoperative mortality, and the worse prognosis in TAAD patients, so early identification of patients with poor preoperative renal function is of positive significance for preventing poor prognosis. The aortic cross-clamp time is an independent risk factor for 30-day postoperative mortality in TAAD patients, indicating that the longer the aortic cross-clamp time during surgery is, the worse the postoperative prognosis of TAAD patients. Furthermore, the Pearson correlation analysis showed that the CIRP level at the end of surgery in TAAD patients were positively correlated with aortic cross-clamp time, but not with CPB time. There are many aspects of cardiopulmonary bypass that are not necessarily associated with the elevated CIRP level. It is acceptable that there is no correlation between CPB time and CIRP level. Therefore, aortic arch replacement should be completed as soon as possible to minimize the aortic cross-clamp time under the premise of ensuring the quality of surgery. Meanwhile, this study also found that the serum extracellular CIRP level at the end of surgery was an independent risk factor for 30 d postoperative mortality after hypothermic circulatory arrest in TAAD patients; CIRP could be used as a biomarker to predict 30 d postoperative mortality in TAAD patients; the serum CIRP levels of TAAD patients undergoing total aortic arch replacement under moderate hypothermic circulatory arrest combined with selective antegrade cerebral perfusion gradually increased in TAAD patients after hypothermic circulatory arrest compared with preoperative levels, starting to rise significantly at approximately 12 h postoperatively, reaching or approaching a peak at approximately 24 h postoperatively, and ceasing to rise significantly after approximately 48 h postoperatively. In this study, most of the patients in the death group died of postoperative multiple organ failure, which was largely caused by excessive inflammatory response. It can be speculated that anti-CIRP therapy given early after surgery may be beneficial to improve the prognosis of patients.

Previous clinical studies have found that elevated CIRP expression can be caused by multiple traumas and is highly correlated with patient prognosis [18]. CIRP is associated with increased disease severity in patients with rheumatoid arthritis and osteoarthritis [19], peripheral blood CIRP levels

can be used as a potential biomarker of prognosis in patients with sepsis [5], and serum CIRP levels are significantly higher in patients with a poor prognosis of severe acute pancreatitis than in those with a good prognosis [20]. Previous animal experimental studies have found that a large amount of CIRP was released into the blood circulation in animal models of septic shock or hemorrhagic shock, which could promote the release of TNF-α, IL-6, HMGB1, and other inflammatory mediators from macrophages to induce inflammatory responses, leading to corresponding tissue and organ damage, while anti-CIRP serum could alleviate the adverse outcomes induced by shock [5]. The above mentioned studies suggest that CIRP, as a novel inflammatory factor, may be a potential clinical biomarker to predict the prognosis of TAAD patients after hypothermic circulatory arrest. The results of the present study confirmed this.

There are limitations in this study, such as limited sample size, lack of multicenter large sample data, and no long-term follow-up of discharged patients to assess long-term complications and prognosis. However, this study confirmed the correlation between CIRP and prognosis after hypothermic circulatory arrest in patients with TAAD, which can be used as a predictor of postoperative prognosis and provides a direction for future studies. The next step could be to further clarify the correlation between CIRP and prognosis through the administration of anti-CIRP treatment in a rigorously designed multicenter prospective randomized controlled study.

In conclusion, the serum extracellular CIRP is closely related to the prognosis of hypothermic circulatory arrest during the perioperative period, and can be used as a potential biomarker to evaluate the prognosis of patients. The CIRP level at the end of surgery is an independent risk factor for 30-day mortality after hypothermic circulatory arrest in TAAD patients. Early intervention can be performed to improve the prognosis of patients with high CIRP levels.

Data Availability

All relevant data are included within the paper. The data are not publicly available due to privacy or ethical restrictions.

Ethical Approval

The procedures used in this study adhere to the tenets of the Declaration of Helsinki. This study was approved by the Medical Ethics Committee (No. Y(2022)080).

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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