

Original Article

Analysis of poor prognostic factors of cerebral nerve after deep hypothermic circulatory arrest in patients with type A aortic dissection

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Abstract: Objective: To investigate the influences of deep hypothermic circulatory arrest (DHCA) on postoperative cranial nerve function in patients undergoing surgery for type A aortic dissection. Methods: A total of 100 patients undergoing DHCA during the surgery for type A aortic dissection in our hospital were selected as the study subjects. After surgery, 32 patients with neurological complications were assigned to Group A, and 68 patients without neurological complications were assigned to Group B. The clinical outcomes were compared between the two groups, and the risk factors of postoperative neurological complications were analyzed by univariate and multivariate logistic regression analysis. Results: During the surgery, patients underwent cerebral perfusion at 5 min and 10 min during DHCA had remarkably decreased cerebral oxygen saturation (rSO₂) and VmMCA than those before anesthesia induction ($P<0.05$). After recovery of CPB, rSO₂ and mean velocity in middle cerebral artery (VmMCA) recovered to the preoperative levels. The correlation analysis revealed a positive correlation between rSO₂ and VmMCA ($P<0.05$). The univariate analysis suggested that the history of hypertension, hydropericardium, surgical duration, duration of cardiopulmonary bypass (CPB), aortic occlusion, ICU, and ventilator-assisted respiration, and hypoxemia significantly affected postoperative cranial nerve function ($P<0.05$). The logistic multivariate regression analysis demonstrated that the duration of CPB and aortic occlusion and hypoxemia were independent risk factors for postoperative cranial nerve dysfunction ($P<0.05$). Conclusion: There were noticeable changes in hemodynamic and blood oxygen parameters in patients with type A aortic dissection undergoing DHCA during the perioperative period. The long duration of CPB and aortic occlusion and preoperative hypoxemia are the independent risk factors leading to postoperative impaired cranial nerve function.

Keywords: Deep hypothermic circulatory arrest, type A aortic dissection, postoperative, cranial nerve function, study of influences

Introduction

Aortic dissection (AD) is the surging of blood through a tear in the aortic intima with separation of the intima and media and creation of a false lumen [1]. AD is characterized by acute onset, critical conditions and high mortality. Overseas reports have shown that the delayed intervention can lead to a mortality rate of 22.7% within 6 h, 50% within 48 h and 68% within 7 d in acute AD patients [2, 3]. With the in-depth studies of AD in these years, the pathogenesis of AD has been gradually revealed. Investigations have shown that AD can be induced by hereditary connective tissue diseases, inflammatory mechanisms, hyperten-

sion, trauma or sudden external force, hypertension is the most significant cause of AD, and about 80% of the patients suffer from hypertension to varying degrees [4, 5].

Type A AD, a subtype of AD, is more prone to rupture and has a higher mortality rate than other types of AD. Generally, once AD is diagnosed clinically, emergency surgery is required [6]. Deep hypothermic circulatory arrest (DHCA) is a surgical technique to reduce the oxygen consumption of the body, especially the cerebral metabolic oxygen consumption. That is, it involves cooling the body to the core temperature of 18-20°C through the establishment of CPB, stopping the CPB and completing surgery

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of the heart and great vessels, and the restoration of CPB and normal temperature of the body [7, 8]. Deep hypothermic circulatory arrest (DHCA), which was initially used in the treatment of complex cardiac abnormalities in infants, has been validated by clinical practices to play an irreplaceable role. Recently, DHCA has been widely promoted and implemented in multiple aortic surgeries, and has achieved satisfactory clinical outcomes [9]. However, with the widespread implementation of DHCA, more and more scholars have found that patients undergoing DHCA suffer from varying degrees of impaired cranial nerve function, which may be related to reversible or irreversible damage of nervous system caused by relative anoxia of brain tissue during DHCA [10]. A study on patients with Stanford type A AD has shown that the ratio of patients with asymptomatic or slightly neuropsychiatric manifestations after surgery is about 30%-70%, the incidence rates of stroke and epilepsy are about 5%-8% and 1%-2%, respectively, and the mortality rate of the patients is 0.3%-2% [11]. An investigation has suggested that after DHCA, neurological complications seriously affect the prognosis, increase the postoperative hospital stay and medical expenses, and reduce the postoperative quality of life and long-term survival rate of the patients, and active preventive intervention is highly recommended [12].

This study was designed to explore the risk factors of postoperative cranial nerve injury in patients with type A AD undergoing DHCA, thus providing a clinical reference for improvement of the prognosis of the patients through performing logistic regression analysis on the factors.

Materials and methods

General data

A total of 100 patients with type A AD undergoing DHCA admitted to our hospital from January 2017 to December 2020 were selected as the study subjects.

Inclusion criteria: (1) patients in line with the diagnostic criteria for type A AD [12] and diagnosed by aortic CT angiography (CTA); (2) those treated with emergency DHCA; (3) those with complete clinical data; and (4) those with clear consciousness without cognitive disorders. The

investigation has been submitted to Ethics Committee of Ganzhou People's Hospital for approval and implementation. Informed consent form was voluntarily signed by the patients or their families.

Exclusion criteria: (1) patients complicated by mental illness; (2) drug or alcohol abusers; (3) those complicated by severe audio-visual impairment; (4) those recently treated with nervous system drugs; (5) those complicated by adrenalopathy or history of related surgeries; (6) those complicated by immune system diseases or diseases requiring hormone therapy; (7) those complicated by HIV; (8) those with a history of drug abuse; (9) those complicated by preoperative cerebral infarction or coma.

Intervention methods

All patients underwent DHCA under general anesthesia and CPB. During the surgery, different treatment measures for the proximal dissection were implemented based on the conditions regarding the proximal dissection involving the antra, aortic valve leaflet and valve ring, and coronary ostia of the patients. All the patients received inhalation and intravenous general anesthesia. During circulatory arrest (CA), the patients were placed in the head-down position, and the temperature was lowered by ice-cap. The actual conditions of patients were closely observed during the surgery, efforts were made to prevent the occurrence of complications, the patients' decisions on the use of hormones, trophic nerve and hemostatic drugs were sought, and hyperbaric oxygenation intervention was conducted whenever necessary.

Observational indices and assessment criteria

The observational therapy in this study mainly included the following aspects. (1) The hemodynamic and blood oxygen indices of the patients were recorded and longitudinally compared during the perioperative period. The time points for observation were after anesthesia induction, 10 min after CPB, 10 min after aortic occlusion, 5 min and 10 min after antegrade selective cerebral perfusion (ASCP), 5 min after full flow recovery, 10 min after rewarming, 10 min after re-beating and after shut down. (2) According to the data of the subjects recorded

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Table 1. Comparison of general clinical indices between the two groups ($\bar{x}\pm s$)/[n (%)]

General clinical data	Group A (n=32)	Group B (n=68)	t/ χ^2	P
Average age (year)	45.98±4.33	46.01±4.29	0.033	0.974
Average weight (kg)	64.29±3.91	64.34±3.89	0.06	0.952
Average BMI (kg/m ²)	23.98±2.33	23.99±2.31	0.02	0.984
Hypertension				
Y	14	28	0.059	0.808
N	18	40		
Diabetes				
Y	13	27	0.008	0.93
N	19	41		

at the time points for observation, the correlation between mean arterial pressure (MAP) and mean velocity in middle cerebral artery (VmMCA) and cerebral oxygen saturation (rSO₂) and SVO₂ (venous oxygen saturation) was calculated during the perioperative period. (3) The univariate and multivariate factors affecting the prognosis of patients with type A AD undergoing DCHA were explored using the logistic regression analysis. (4) The clinical outcomes were compared between patients with and without postoperative complications.

Statistical method

The collected data were input into an EXCEL table, and SPSS 22.0 was adopted for statistical analysis. The collected data were detected using normal distribution. The data conforming to normal distribution were expressed as [n (%)]. The differences between groups were analyzed using *Chi-square* test. The measurement data were expressed as mean \pm standard deviation. The differences between groups were analyzed using *t* test, and Spearman's correlation analysis was performed. $P < 0.05$ indicated a statistically significant difference, and the study graphs were plotted using GraphPad Prism 8 [13].

Results

Comparison of differences in baseline data between the two groups

The baseline data such as gender, age, weight, and underlying health condition were collected from 100 patients. The baseline data were compared between Groups A and B. The results exhibited that there was no statistically significant

difference in the baseline data between the two groups ($P > 0.05$), which were comparable (Table 1).

Analysis of changes in hemodynamic and blood oxygen indices in the two groups during the perioperative period

The changes in MAP, VmMCA, rSO₂, and SVO₂ in 100 patients undergoing DHCA were recorded during the perioperative period. The results revealed that there was no marked difference

in cerebral function parameters (e.g., cerebral oxygen saturation and VmMCA) from anesthesia induction to the establishment of CPB. During the surgery, the patients underwent cerebral perfusion at 5 min and 10 min during DHCA had remarkably decreased rSO₂ than that before anesthesia induction, and the patients underwent cerebral perfusion at 5 min and 10 min during DHCA exhibited significantly decreased VmMCA than that before anesthesia induction and after termination of pumping ($P < 0.05$). There was marked changes in MAP and SVO₂ of the subjects during the perioperative period. The MAP was at a low level from 10 min after CPB, and recovered to the pre-induction level after shut down. SVO₂ was at a low level at 5 min and 10 min after ASCP (Figure 1 and Table 2).

Analysis of correlations between hemodynamic and blood oxygen parameters

Spearman's correlation analysis was performed to investigate the correlation between MAP and VmMCA and rSO₂ and SVO₂. The results demonstrated that MAP and VmMCA were positively correlated with rSO₂ and SVO₂ ($r = 0.9296$, $r = 0.9545$, $r = 0.7944$, $r = 0.8632$, $P < 0.05$) (Figure 2).

Analysis of univariate logistic regression results

The gender, age, hospital stay, history of hyperlipidemia, coronary heart disease, cerebrovascular accident, diseases of respiratory system, hypertension, hydropericardium, surgical duration, duration of CPB, aortic occlusion, ICU, and ventilator-assisted respiration, and hypoxemia in Groups A and B were analyzed. The

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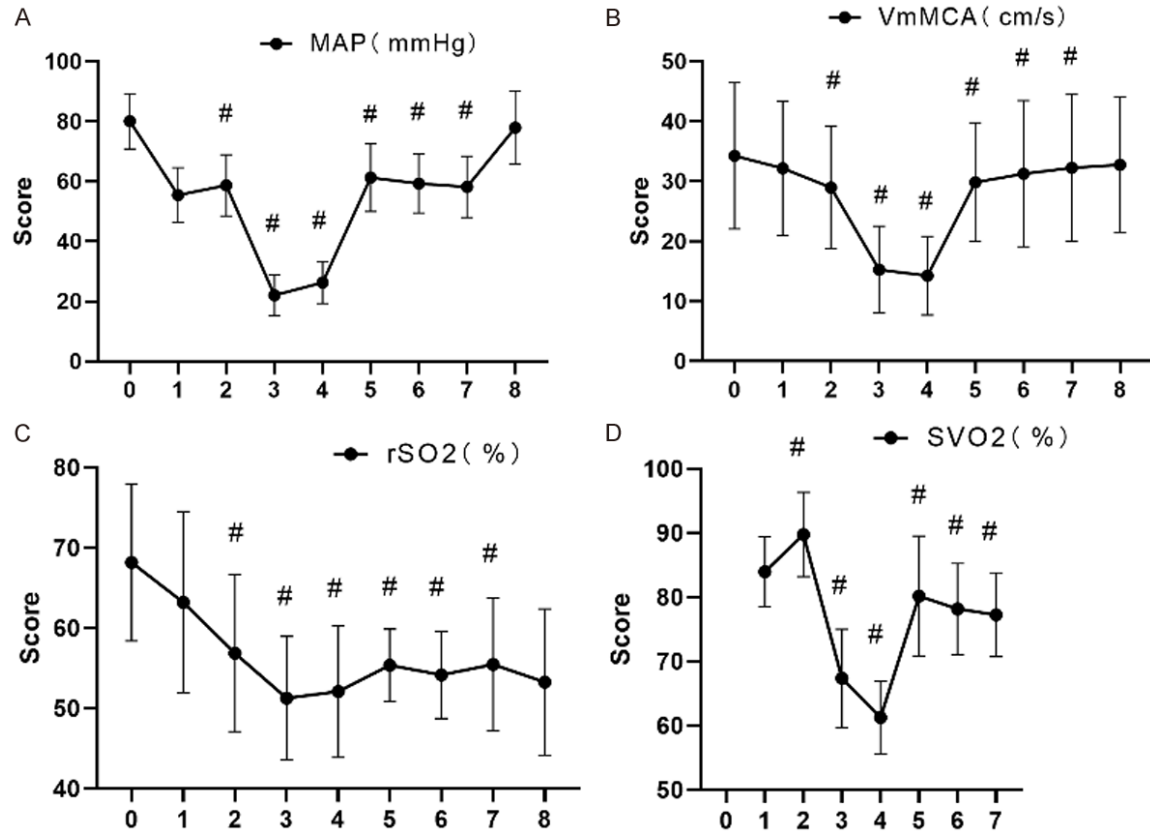


Figure 1. Analysis of changes in hemodynamic and blood oxygen indices during the perioperative period. There were statistically significant differences in VmMCA (B) and rSO2 (C) at 5 min and 10 min after ASCP between before induction and after shutdown ($P<0.05$). MAP (A) was always at a low level from 10 min after CPB to 10 min after re-beating, and there were noticeable differences in MAP between before induction and after shutdown ($P<0.05$). SVO2 (D) was at a low level from 5 min after ASCP to 10 min after ASCP, and there were remarkable differences in SVO2 between before induction and after shutdown ($P<0.05$). #Indicates the comparison between before induction and after shutdown, and the differences were statistically significant.

Table 2. Analysis of changes in hemodynamic and blood oxygen indices in the two groups during the perioperative period

Time points for monitoring	MAP (mmHg)	VmMCA (cm/s)	rSO2 (%)	SVO2 (%)
After anesthesia induction	80.11±9.21	34.29±12.20	68.19±9.77	-
10 min after CPB	55.43±9.11*#	32.19±11.21	63.22±11.29	83.98±5.44
10 min after aortic occlusion	58.67±10.21*#	28.98±10.21	56.89±9.78	89.78±6.59
5 min after ASCP	22.08±6.78*#	15.29±7.21*#	51.29±7.68*	67.38±7.65*#
10 min after ASCP	26.29±6.98*#	14.28±6.55*#	52.11±8.19*	61.28±5.66*#
5 min after full flow recovery	61.29±11.29*#	29.87±9.88	55.39±4.49	80.18±9.32
10 min after rewarming	59.29±9.87*#	31.29±12.18	54.19±5.44	78.18±7.11
10 min after rebeating	58.18±10.22*#	32.28±12.11	55.49±8.27	77.29±6.53
After shut down	77.98±12.19	32.79±11.29	53.28±9.10	-

*Indicates comparison with after induction ($P<0.05$), #indicates comparison with after shut down ($P<0.05$).

results revealed that the history of hypertension, hydropericardium, surgical duration, duration of CPB, aortic occlusion, ICU, and ventila-

tor-assisted respiration, and hypoxemia significantly affected postoperative cranial nerve function of the patients ($P<0.05$) (Table 3).

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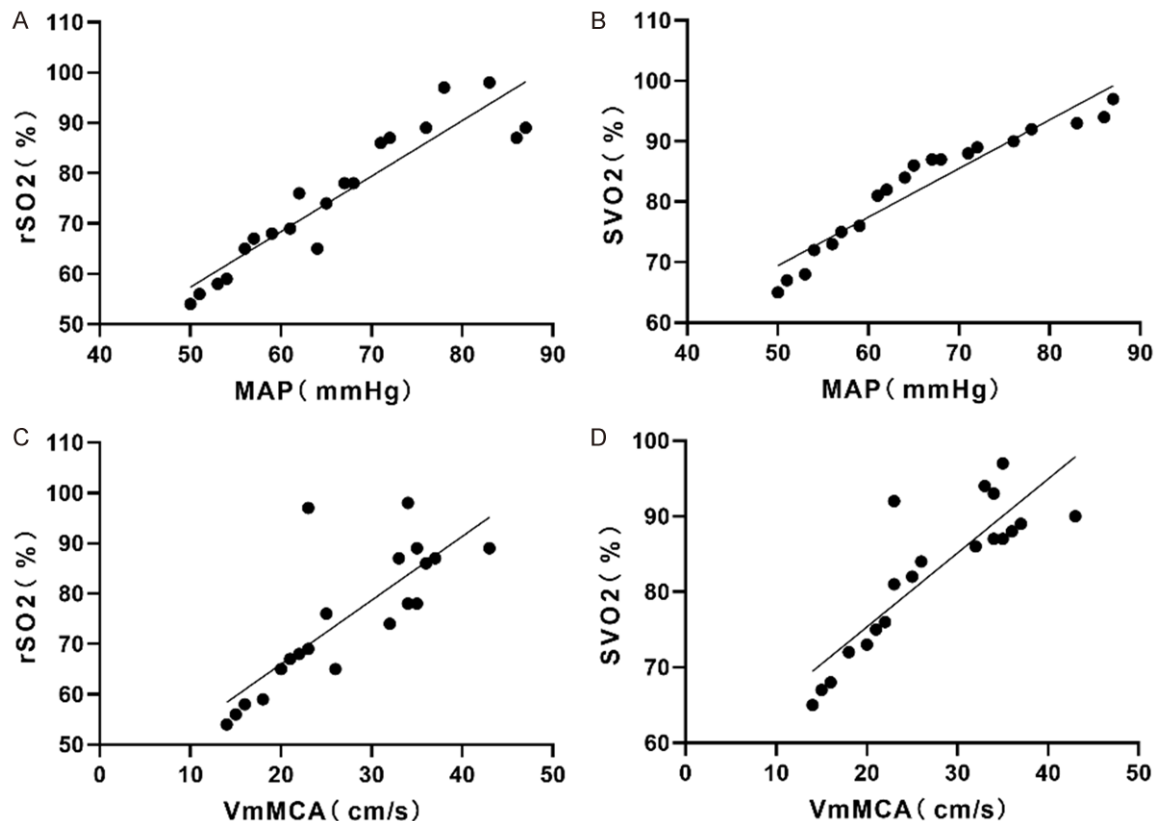


Figure 2. Analysis of correlations between hemodynamic and blood oxygen parameters. Spearman's correlation analysis was performed to investigate the correlation between MAP and VmMCA and rSO2 and SVO2. The results demonstrated that MAP and VmMCA were positively correlated with rSO2 and SVO2 ($r=0.9296$, $r=0.9545$, $r=0.7944$, $r=0.8632$, $P<0.05$).

Table 3. Analysis of univariate logistic regression results

Risk factors	β	SE	Wald	P	OR	95% CI
History of hypertension	0.881	0.231	6.891	0.01	0.782	0.671-0.981
Hydropericardium	0.912	0.199	21.229	<0.01	2.334	1.287-3.229
Surgical duration	0.189	0.024	1092.821	<0.01	1.298	1.221-1.321
Duration of CPB	0.189	0.015	8.981	<0.01	2.981	1.879-2.938
Duration of aortic occlusion	0.198	0.032	9.981	<0.001	4.391	1.982-3.019
Duration of ICU	0.121	0.089	3.433	0.005	1.290	1.001-1.023
Duration of ventilator-assisted respiration	0.221	0.091	3.443	0.004	1.323	0.981-1.211
Hypoxemia	0.321	0.043	6.544	0.012	1.001	1.001-1.043

Analysis of multivariate logistic regression results

The multivariate logistic regression analysis showed that the duration of CPB and aortic occlusion and hypoxemia significantly affected the postoperative cranial nerve function of patients with type A AD undergoing DHCA, exhibiting that the aforementioned indices were the independent risk factors for postop-

erative cranial nerve complications ($P<0.05$) (Table 4).

Comparison of clinical outcomes between the two groups

The hospital stay, rate for insertion of the second tracheal cannula, in-hospital mortality rate, duration of mechanical ventilation, and surgical duration in Groups A and B were statis-

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Table 4. Analysis of multivariate logistic regression results

Risk factors	β	SE	Wald	<i>P</i>	OR	95% CI
History of hypertension	0.023	0.011	5.112	0.023	1.201	0.989-1.044
Hydropericardium	0.013	0.004	6.556	0.012	1.004	0.891-1.032
Surgical duration	0.022	0.009	4.390	0.005	1.021	0.999-1.035

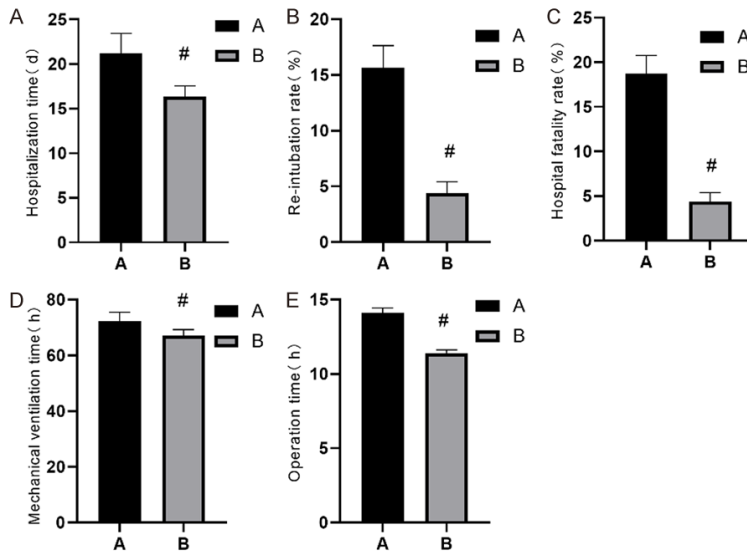


Figure 3. Comparison of clinical outcomes between the two groups. The differences in hospital stay (A), rate for insertion of the second tracheal cannula (B), in-hospital mortality rate (C), duration of mechanical ventilation (D), and surgical duration (E) were compared between the two groups. The results exhibited that Group A had a remarkably longer hospital stay, duration of mechanical ventilation, duration for insertion of the second tracheal cannula, and surgical duration, and a markedly higher in-hospital mortality rate than Group B ($P < 0.05$). #Indicates a statistically significant difference in the same indices between the two groups before and after surgery.

tically analyzed, and the differences among the aforementioned indices were compared. The results showed that Group A had a remarkably longer hospital stay, duration of mechanical ventilation, duration for insertion of the second tracheal cannula, and surgical duration, and a markedly higher in-hospital mortality rate than Group B ($P < 0.05$) (Figure 3).

Discussion

AD, especially type A AD involving aortic arch [14], has the characteristics of the extensive lesion range, involves multiple important organs, and usually requires surgery treatment. The statistics have shown that the mortality rate of such patients reaches 33% within 24 h and 50% within 48 h at the acute stage [15]. Regarding patients with type A AD involving ascending aorta and aortic arch, aortic replace-

ment, aortic root plasty, and wheat surgery are recommended. The main purpose of the surgeries is to rebuild the aortic blood supply and strengthen the aortic wall tissue [16, 17].

Clinical practices have shown that since the aortic arch is often involved in patients with type A AD, surgery should be performed during CPB and hypothermic circulatory arrest (HCA), namely, the patients' body temperature should be reduced to 18-20°C during the surgery [18]. Clinically, HCA plays a fundamental role in aortic arch surgery. HCA can provide a static and bloodless surgical field during vascular replacement in aortic arch, and improve the tolerance of patients' vital organs to ischemia and anoxia through hypothermia, which is of great significance for the protection of patients' cranial nerves during the surgery [19, 20]. However, with the widespread promotion and implementation of HCA, more and more studies have reported that DHCA inevitably affects the prognosis of patients with AD [21]. A study on 90 patients with AD undergoing DHCA has exhibited that 23.33% of the patients experience postoperative neurological impairment, and 12.22% of the patients experience postoperative coagulation disorder [22]. Scholars believe that an increase in the temperature for circulatory arrest may improve the prognosis of patients, but this assumption has not been clinically validated [23].

The study was designed to explore the risk factors affecting postoperative cranial nerve function in patients with type A AD undergoing DHCA, thereby providing a clinical reference for

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improvement of the prognosis of such patients to formulate targeted strategies for clinical intervention. The results exhibited that there were marked changes in hemodynamic and blood oxygen indices of 100 subjects during the perioperative period, especially at 5 min and 10 min after ASCP. Additionally, the MAP, VmMCA, rSO₂ and SVO₂ were decreased significantly. This suggested that DHCA reduced the cerebral oxygen consumption and improved the hemodynamic indices of patients during surgery. Some scholars have indicated that rSO₂ level is an important indicator for the level of oxyhemoglobins in cerebral tissue during CPB in cardiovascular surgery, and can reflect the cerebral oxygen supply-consumption balance, and thus can be used as an indicator for evaluation of the intraoperative status of patients [24]. A study has shown that hemodynamic and blood oxygen assessment during DHCA can help physicians determine the clinical strategies, and such monitoring is recommended for patients undergoing surgery for aortic dissection [25]. The authors believe that the decreased cerebral oxygen saturation is a main contributor leading to the impaired cranial nerve function. Currently, multiple clinical studies have indicated that when the rSO₂ level is lower than 30%, circulatory failure, severe metabolic acidosis and significant decrease in EEG amplitude occur, signaling that individuals have seriously impaired cerebral function. The study results suggested that patients had a significant decrease in rSO₂ during DHCA, indicating such patients were likely to have impaired cranial nerve function.

In this study, the risk factors affecting the prognosis of patients with type A AD undergoing DHCA were further analyzed. The univariate analysis revealed that the history of hypertension, hydropericardium, surgical duration, duration of CPB, aortic occlusion, ICU, and ventilator-assisted respiration, and hypoxemia obviously affected postoperative cranial nerve function of the patients, and the multivariate analysis demonstrated that duration of CPB and aortic occlusion and hypoxemia remarkably affected postoperative cranial nerve function of the patients. Currently, clinical studies have confirmed that the duration of DHCA significantly affects the prognosis of patients. When the duration of CA is over 40 min, the complications of individual nervous system

increase. When the duration of CA is over 65 min, the postoperative mortality rate increases significantly [26]. The authors believe that DHCA can reduce the cerebral oxygen consumption and metabolic rate, but long-term ischemia and anoxia inevitably lead to postoperative complications. Therefore, the duration of CA should be shortened to improve the prognosis of patients. A longer duration of hypothermic maintenance indicates a higher incidence of cerebral injuries. Similarly, the duration of aortic occlusion is an indicator for individual blood supply. A long-term aortic occlusion significantly increases the degree of vascular endothelial injury, leads to an increase in the incidence rate of microthrombosis in patients, and induces abnormal coagulation function, thereby affecting the prognosis of patients.

In summary, there were noticeable changes in hemodynamic and blood oxygen parameters in patients with type A aortic dissection undergoing DHCA during the perioperative period. The long duration of CPB and aortic occlusion and preoperative hypoxemia were the independent risk factors leading to postoperative impaired cranial nerve function. Clinically, the active intervention should be performed for patients with the aforementioned risk factors, so as to reduce the incidence rate of postoperative complications and expedite the postoperative outcome of the patients. The innovation of this study lies in the exploration of the risk factors affecting the postoperative cranial nerve function of patients with type A AD undergoing DHCA through grouping and comparisons, providing a theoretical reference for follow-up studies and clinical treatment. The innovation of this study is to explore the risk factors affecting the postoperative cranial nerve function of patients with type A aortic dissection and deep hypothermic circulation arrest from the perspectives of single factor and multiple factors by means of grouping and analogy, which provides a detailed theoretical reference for the development of follow-up research and clinical treatment. The deficiencies of this study include that the in-depth study on improvement of the prognosis of such patients were not conducted and only the preliminary analysis of the risk factors was performed. It is planned to perform the clinical studies on the improvement of the prognosis of such patients.

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Disclosure of conflict of interest

None.

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