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Analysis of Prognosis and Risk Factors for Postoperative Hepatic Dysfunction in Patients with Acute Type A Aortic Dissection

ORIGINAL INVESTIGATION

ABSTRACT

Background: To explore the prognosis and risk factors of postoperative hepatic dysfunction in patients with acute type A aortic dissection.

Methods: A total of 156 patients who underwent surgery for acute type A aortic dissection in our hospital from May 2014 to May 2018 were retrospectively enrolled. The patients were divided into 2 groups based on postoperative liver function. The postoperative model for end-stage liver disease score was used to define hepatic dysfunction. There were 35 patients with postoperative hepatic dysfunction (group hepatic dysfunction, model for end-stage liver disease score $\geq$ 15) and 121 patients without postoperative hepatic dysfunction (group non-hepatic dysfunction, model for end-stage liver disease score < 15). Univariate and multiple analyses (logistic regression) were used to identify the predictive risk factors.

Results: In-hospital mortality rate was 8.3%. Multiple logistic analysis showed that preoperative alanine aminotransferase ($P < .001$), cardiopulmonary bypass time ($P < .001$), and red blood cell transfusion ($P < .001$) were independent determinants for postoperative hepatic dysfunction. The patients were followed up for 2 years, with an average follow-up of 22.9 ± 3.2 months, and the lost follow-up rate was 9.1%. The short- and medium-term mortality in hepatic dysfunction group was higher than that in non-hepatic dysfunction group (log-rank $P = .009$).

Conclusions: The incidence of postoperative hepatic dysfunction is high in patients with acute type A aortic dissection. Preoperative alanine aminotransferase, cardiopulmonary bypass time, and red blood cell transfusion were independent risk factors for those patients. The short- and medium-term mortality in hepatic dysfunction group was higher than that in non-hepatic dysfunction group.

Keywords: Acute aortic dissection, hepatic dysfunction, risk factors, prognosis

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INTRODUCTION

The report on cardiovascular health and diseases in China shows that cardiovascular and cerebrovascular diseases are the leading causes of death in China. Aortic dissection is one of the main causes of death in patients with cardiovascular disease. Most patients with aortic dissection in China have a history of hypertension, and their average age of onset is lower than those in European and American countries. Aortic dissection usually develops suddenly and rapidly. Stanford type A aortic dissection, in particular, has a very high mortality rate when treated conservatively, increasing by 1% per hour within 48 hours of onset.[1] With the development of cerebral protection strategy and hybrid techniques in recent years, the outcome of surgical repair in type A aortic dissection in China has also made remarkable advances. The perioperative mortality rate has significantly decreased, which has dropped to less than 10% or even to about 5%.[2-4] However, the incidence of perioperative organ dysfunction in patients with aortic dissection is still higher compared with those patients undergoing other cardiac surgeries. Studies have shown that the incidence of liver failure after cardiac surgery is up to 4% and even to 10% in those patients who underwent cardiopulmonary bypass (CBP) surgery, which is significantly related to mortality and other complications after cardiac surgery.[5] A total of 156 patients with acute Stanford acute type A aortic dissection (ATAAD) undergoing surgery in our hospital were enrolled in this study retrospectively from May 2014 to May 2018. The aim of this retrospective study is to investigate the risk factors of postoperative hepatic dysfunction (HD) in ATAAD patients, provide protection and treatment for reducing the occurrence of severe postoperative complications, and further improve the surgical outcome of aortic dissection.

METHODS

Patients

A total of 156 patients who underwent surgery for ATAAD in our hospital from May 2014 to May 2018 were retrospectively enrolled. Stanford type A aortic dissection was confirmed by preoperative computed tomography angiography in 156 patients. Exclusion criteria were history of chronic liver disease, cirrhosis, or severe hepatitis. We evaluated whether the patients had previous liver pathology by history taking, blood test of hepatitis-related biomarkers, and computed tomography scan. The model for end-stage liver disease (MELD) score has been verified as an effective measuring tool for HD. In this study, we evaluated postoperative HD by using the MELD score, and the cut-off point was set as 15 points according to recent studies.[6,7] High MELD score (≥15) was defined as the HD group, and the low MELD score (<15) was defined as the non-HD group.

Surgical Procedures

Operations were performed through a standard longitudinal median sternotomy. Axillary or femoral arterial cannulation was established. Most of the patients underwent axillary arterial cannulation. Selective antegrade cerebral perfusion was performed in patients with deep hypothermic circulatory arrest, and most patients were treated with bilateral cerebral perfusion. Intraoperative cerebral oxygen monitoring was performed in all patients by using near-infrared spectroscopy device. There were 103 patients undergoing deep hypothermic circulatory arrest and 53 patients undergoing moderate hypothermia CBP. Of the 156 patients, ascending aorta replacement was performed in 30 cases, ascending aorta + hemiarch replacement in 20 cases, Bentall procedure in 20 cases, David procedure in 2 cases, ascending aorta replacement/Bentall procedure + total arch replacement + elephant trunk procedure in 79 cases, and debranching hybrid procedure in 5 cases. Twelve patients underwent concomitant coronary artery bypass grafting.

HIGHLIGHTS

- The incidence of hepatic dysfunction (HD) is high in patients with acute type A aortic dissection (ATAAD) after surgical procedure.
- Preoperative alanine aminotransferase, cardiopulmonary bypass time, and red blood cell transfusion were the independent risk factors for those patients with ATAAD.
- The short- and medium-term mortality in HD group was higher than that in non-HD group.

Data Collection and Variables

Gender, age, body mass index (BMI) [weight (kg)/height (m)]^2, preoperative alanine aminotransferase (ALT), other perioperative characteristics, and perioperative complications (stroke, acute kidney injury (AKI), hypoxemia, low cardiac output syndrome (LCOS), re-intubation, and re-exploration) were recorded and analyzed. All patients received telephone or outpatient follow-up within 2 years after discharge. They were followed up at 1 month, 6 months, 12 months, 18 months, and 24 months postdischarge.

We calculated patients' MELD scores by using the following formula: MELD = 3.8 × ln [total bilirubin (mg/dL)] + 11.2 × ln (international normalized ratio [INR]) + 9.6 × ln [creatinine (mg/dL)] + 6.4 × (cause: bilious or alcoholic 0, others 1). The MELD score was calculated according to the indexes measured every day in the early postoperative period (within 7 days), and the highest score was selected to evaluate the occurrence of postoperative HD.

Definition of important variables: Emergency surgery was defined as surgical treatment within 24 hours after admission. Acute kidney injury (AKI) was diagnosed and classified by the Acute Kidney Injury Network classification as follows: serum creatinine (SCR) increased by more than or equal to 26.4 μmol/L within 48 hours, a percentage increase in SCR of more than or equal to 50% compared with the baseline value (the most recent SCR value before surgery), or urine output is less than 0.5 mL/(kg h) for more than 6 hours.[8,9] Postoperative hypoxemia was defined as arterial partial oxygen pressure (PaO_2) (6 hours after admission to the intensive care unit (ICU))/inhaled oxygen concentration (FIO_2) less than 200 mm Hg.[10] Postoperative stroke was defined as permanent neurological dysfunction diagnosed by imaging evaluation and neurologist evaluation. Use of positive inotropic drugs was defined as a continuous infusion of dopamine, dobutamine, epinephrine, norepinephrine, or isoproterenephrine for more than 30 minutes during the operation.

Statistical Analysis

Statistical analysis was carried out by using Statistical Package for Social Sciences 19.0 software. The S-W test was used for the conformity of the continuous data to the normal distribution. Continuous data with a normal distribution were presented as mean ± standard deviation and data with nonnormal distribution as medians with an interquartile range. Categorical data were presented as percentages. Independent samples *t*-test was used to compare the means of 2 groups in normally distributed continuous data, and the chi-square test or Fisher's exact test was used for the analysis of categorical data. Univariate analysis and multiple logistic regression analysis were performed to analyze the independent risk factors of postoperative HD. The receiver operating characteristic (ROC) curve was drawn to determine the area under the ROC curve (AUC), sensitivity, and specificity of each predictor. The influence of HD on prognosis was estimated by Kaplan–Meier method and log-rank test, and the survival curve was drawn. A *P*-value of less than .05 was considered statistically significant.

RESULTS

Demographic Characteristics

The mean age of the 156 patients was 56.2 ± 8.3 (30-82) years, including 114 males and 42 females. There were 35 patients in HD group and 121 patients in the non-HD group. Preoperative clinical characteristics of the 2 groups were shown in Table 1.

Risk Factors for Postoperative Hepatic Dysfunction

Univariate analysis showed that there was no statistically significant difference in gender, BMI, hypertension, diabetes, smoking, chronic obstructive pulmonary disease, cardiac function (New York Heart Association functional classification) grade III-IV, preoperative MELD score, celiac trunk artery involvement, superior mesenteric artery involvement, preoperative left ventricular ejection fraction, and emergency surgery between the 2 groups. There were statistically significant differences in preoperative ALT, preoperative creatinine, preoperative white blood cell, preoperative D-dimer, and European cardiovascular risk factor score between the 2 groups, as shown in Table 1.

Table 1. Characteristics of Patients with Stanford Acute Type A Aortic Dissection

Characteristics	HD Group (n = 35)	Non-HD Group (n = 121)	t/χ^2-Value	*P*
Age (years, SD)	57.3 ± 8.1	55.8 ± 7.6	1.013	.313
Gender			0.034	.855
Male	26 (74.3)	88 (72.7)		
Female	9 (25.7)	33 (27.3)		
Body mass index (kg/m^2)	26.9 ± 3.8	25.7 ± 3.6	1.715	.088
Chronic obstructive pulmonary disease	2 (5.7)	5 (4.1)	0.159	.691
Hypertension	23 (65.7)	81 (66.9)	0.018	.892
Smoking	13 (37.1)	42 (34.7)	0.070	.791
Diabetes	2 (5.7)	8 (6.6)	0.036	.849
New York Heart Association functional class III-IV (%)	8 (22.9)	24 (19.8)	0.152	.697
Euroscore (SD)	8.5 ± 2.3	7.5 ± 2.1	2.428	.016
Preoperative alanine aminotransferase (U/L) (SD)	44.6 ± 9.2	29.5 ± 7.8	9.677	<.001
Preoperative hepatic dysfunction (MELD ≥ 15)	3 (8.6)	3 (2.5)	2.724	.099
Celiac trunk artery involvement	8 (22.9)	24 (19.8)	0.152	.697
Superior mesenteric artery involvement	6 (17.1)	12 (9.9)	1.389	.239
Preoperative serum creatinine (μmol/L) (SD)	125.6 ± 23.8	92.3 ± 20.7	8.099	<.001
D-Dimer (μg/mL) (SD)	28.2 ± 3.4	26.4 ± 2.9	3.108	.002
Preoperative leukocyte level (×10^9) (SD)	13.5 ± 3.2	11.7 ± 2.6	3.418	<.001
LVEF (%, SD)	54.8 ± 7.2	56.1 ± 7.9	0.874	.384
Emergency operation	33 (94.3)	115 (95.0)	0.032	.858

HD, hepatic dysfunction; LVEF, left ventricular ejection fraction; MELD, model for end-stage liver disease; SD, standard deviation.

There were statistically significant differences in CPB time, elephant trunk procedure, and intraoperative and 24 hours postoperative red blood cell transfusion volume between the 2 groups. The incidences of postoperative AKI, postoperative hypoxemia, and LCOS in HD group were significantly higher than those in non-HD group (34.3% vs. 13.2%, *P* = .004; 37.1% vs. 20.7%, *P* = .045; 11.4% vs. 1.7%, *P* = .008). Therefore, it can be seen that the incidence of postoperative complications is significantly higher in HD group. The mechanical ventilation time, ICU stay length, and in-hospital mortality in HD group were significantly higher than those in non-HD group (*P* <.05), as shown in Tables 2 and 3.

The significant risk factors of univariate analysis results were used as independent variables for multiple unconditional logistic regression analyses. The results showed that preoperative ALT level [odds ratio (OR) = 1.235, *P* < .001], CPB time (OR = 1.102, *P* < .001), and intraoperative and 24 hours postoperative red blood cell transfusion volume (OR = 4.750, *P* < .001) were independent risk factors for postoperative HD in ATAAD patients, as shown in Table 4.

Draw Receiver Operating Characteristic Curve to Evaluate the Prediction Efficiency of the Model

The probability prediction model of postoperative HD was established by drawing ROC curve through SPSS software.

Table 2. Univariate Analysis of Intraoperative and Postoperative Characteristics of Patients with Stanford Acute Type A Aortic Dissection

Characteristics	HD Group (n = 35)	Non-HD Group (n = 121)	t/χ^2-Value	*P*
Concomitant CABG	4 (11.4)	8 (6.6)	0.887	.346
Elephant trunk procedure	24 (68.6)	55 (45.5)	5.804	.016
Cardiopulmonary bypass time (min)	192.5 ± 44.2	168.7 ± 41.5	2.945	.004
Aortic occlusion time (min)	105.3 ± 24.5	97.3 ± 23.7	1.746	.083
Deep hypothermic circulatory arrest time (min)	43.2 ± 7.5	41.6 ± 6.8	1.198	.233
Mean arterial pressure during CPB (mm Hg)	64.5 ± 4.8	66.2 ± 5.1	1.759	.081
Minimum rectal/bladder temperature (°C)	24.3 ± 1.7	23.8 ± 1.6	1.606	.110
Intraoperative and 24 hours postoperative red blood cell transfusion volume (U)	11.5 ± 3.4	7.8 ± 3.1	6.084	<.001
Mean arterial pressure of 24 hours postoperatively (mm Hg)	71.6 ± 4.9	73.5 ± 5.2	1.928	.056
Drainage volume in 24 hours postoperatively (mL)	870.6 ± 102.5	837.5 ± 96.7	1.760	.089
Positive inotropic drugs	24 (68.6)	72 (59.5)	0.943	.332

CABG, coronary artery bypass grafting; CPB, cardiopulmonary bypass; HD, hepatic dysfunction.

Table 3. Comparison of Postoperative Complications and Outcomes in Patients with Stanford Acute Type A Aortic Dissection

Characteristics	HD Group (n = 35)	Non-HD Group (n = 121)	t/χ^2-Value	*P*
Stroke	2 (5.7)	3 (2.5)	0.916	.339
Postoperative acute kidney injury	12 (34.3)	16 (13.2)	8.178	.004
Postoperative hypoxemia	13 (37.1)	25 (20.7)	4.002	.045
LCOS	4 (11.4)	2 (1.7)	7.015	.008
Re-intubation	3 (8.6)	5 (4.1)	1.100	.294
Re-exploration	5 (14.3)	6 (5.0)	3.603	.058
Mechanical ventilation time (hours)	98.6 ± 15.8	49.2 ± 9.5	22.981	<.001
ICU stay length (hours)	128.5 ± 19.7	68.7 ± 11.2	23.006	<.001
In-hospital mortality (%)	7 (20.0)	6 (5.0)	8.040	.005

HD, hepatic dysfunction; ICU, intensive care unit; LCOS, low cardiac output syndrome.

A combined predictor Pre was generated in the SPSS worksheet. The AUCs of the combined predictor Pre, preoperative ALT level, CPB time, and intraoperative and 24 hours postoperative red blood cell transfusion volume of each predictor were calculated, as shown in Table 5. It can be seen that the AUC of the combined predictor is higher than those of the other predictors. The AUC was 0.928, $P \leq .001$, and the 95% confidence interval was 0.880-0.977, as shown in Figure 1. The sensitivity and specificity of each predictor and the combined predictor of the prediction model were detailed in Table 6.

Outcomes of the Postoperative Patients

Thirty-five patients (22.4%) developed HD after surgery among 156 patients, and 7 patients (20.0%) of them died during hospitalization. One hundred twenty-one patients (77.6%) did not develop HD, 6 cases (5.0%) of them died during hospitalization. Overall in-hospital mortality was 8.3% (13/156). The causes of death were multiple organ failure in 8 patients, stroke in 1 patient, hemorrhage in 2 patients, and severe septic shock in 2 patients. The early in-hospital mortality in HD group was significantly higher than that in non-HD group ($P = .005$). The patients were followed up for 2 years, the lost follow-up rate was 9.1%, and the average follow-up time was 22.9 ± 3.2 months. During the follow-up, 4 patients (14.3%) died in HD group and 3 patients (2.6%) died in non-HD group. The survival curve is shown in Figure 2. There is a significant difference (log-rank $P = .009$).

DISCUSSION

Aortic dissection is a serious life-threatening cardiovascular disease, and most patients need emergency surgery. The operation is extremely complex and difficult. Therefore, it is the "crown" of cardiovascular surgery. Aortic dissection operation has the highest incidence of complications and mortality in cardiac surgery. With the continuous effort of the Chinese cardiovascular surgeon, we have made rapid development and progress in major vascular surgery. Bentall procedure, David procedure, and Sun's procedure have already been carried out in many country hospitals. The perioperative and long-term mortality rates have decreased significantly, but the incidence of complications such as organ dysfunction was still high, especially the occurrence of postoperative HD which significantly increased the perioperative mortality rates.[11] However, there are few studies on postoperative HD in ATAAD patients. Therefore, it is of great clinical significance to investigate the risk factors of postoperative HD in ATAAD patients. The research findings may help us to reduce the occurrence of postoperative HD in those patients, shorten the length of stay in ICU, and reduce the perioperative mortality of aortic dissection patients.

So far as of now, there are 4 measures of liver function that are widely used in clinical practice: (1) biochemical index classification method, (2) Child Turcotte score; (3) Child-Turcotte-Pugh score; (4) MELD score. The data collected by MELD is objective and continuous, so it is increasingly important to evaluate liver dysfunction in surgeries other than liver surgery.[12,13] Liu et al[11] used biochemical indices to evaluate postoperative liver dysfunction, and the incidence of postoperative HD was 8.7%. Zhou et al[6] used MELD score to evaluate postoperative HD. They defined postoperative HD as MELD score ≥ 14, and the incidence of postoperative HD

Table 4. Multiple Analysis of Postoperative Hepatic Dysfunction in Patients with Stanford Acute Type A Aortic Dissection

Variable	Coefficient	Standard Error	Ward Value	Odds Ratio	95% CI	*P*
Preoperative ALT	0.211	0.064	11.062	1.235	1.091-1.399	<.001
Preoperative creatinine	0.033	0.029	1.248	1.033	0.975-1.095	.264
Preoperative leucocyte	0.622	1.125	0.305	1.862	0.205-16.897	.580
Preoperative D-dimer	1.189	0.650	3.349	3.285	0.919-11.741	.067
European cardiovascular surgery risk factor score	0.211	0.447	0.223	1.235	0.514-2.965	.637
CPB time	0.097	0.029	11.068	1.102	1.041-1.167	<.001
Elephant trunk procedure	0.409	0.636	0.414	1.506	0.433-5.241	.520
Intraoperative and 24 hours postoperative red blood cell transfusion volume	1.558	0.372	17.575	4.750	2.293-9.842	<.001
Constant	44.826	8.976	24.942	<0.001		<.001

ALT, alanine aminotransferase; CPB, cardiopulmonary bypass.

Table 5. Area Under the Curve, Standard Error, *P*-Value, and 95% Confidence Interval for Each Predictor

Variable	Area Under the Curve	Standard Error	*P*	95% CI
Preoperative ALT level	0.756	0.053	<.001	0.652-0.861
CPB time	0.781	0.048	<.001	0.687-0.876
Intraoperative and 24 hours postoperative red blood cell transfusion volume	0.830	0.039	<.001	0.753-0.907
Combined predictor Pre	0.928	0.025	<.001	0.880-0.977

ALT, alanine aminotransferase; CPB, cardiopulmonary bypass.

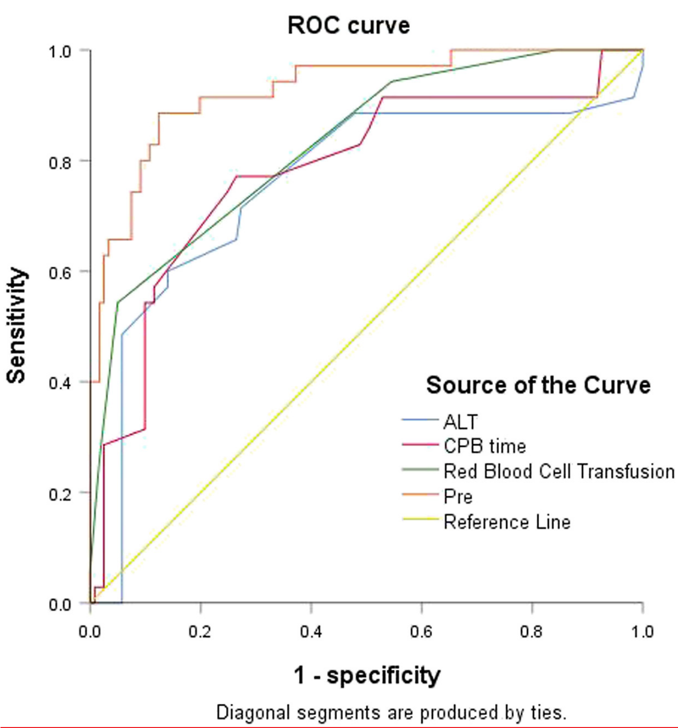

Figure 1. Area under the curve of each variable in this group.

in patients with Stanford type A aortic dissection was 60.9%, which was relatively high. Therefore, we defined postoperative HD as MELD score ≥ 15 according to the classification standard of liver dysfunction of Zhou and other studies. In this study, the incidence of postoperative HD in ATAAD patients was 22.4%, and the in-hospital mortality rate of patients with HD was 20.0%. Based on this study and other relevant studies, the mortality rate of ATAAD patients with postoperative HD is significantly higher than the overall in-hospital mortality rate of all patients. The mortality was significantly higher than that of patients without HD in the short- and medium-term follow-ups.

This study confirmed that preoperative ALT elevation, CPB time, and intraoperative and 24 hours postoperative red blood cell transfusion volume are independent risk factors for postoperative HD in ATAAD patients.

The false lumen can propagate rapidly in both directions from the tear of intima and affect most of its distal branches, including the coronary, cerebral arteries, and abdominal aorta and its important branches in ATAAD patients. Patients will have "dynamic ischemia" of true lumen collapse with obstruction of the ostium of the branching vessel owing to the pressure gradient between the false lumen (high pressure) and the true lumen (low pressure) or "static ischemia" of occlusion of the lumen owing to intimal flap extending into the ostium of the branching artery, especially when the celiac trunk artery and mesenteric artery are involved. All of these can lead to insufficient blood supply of the liver, gastrointestinal tract, and other important abdominal organs.[14] Dissection in patients with type A aortic dissection may retrogradely extend to the proximal aorta root, and this may lead to avulsion of the aortic valve commissure, which will lead to severe aortic insufficiency and acute left heart failure. Pericardial effusion or acute pericardial tamponade caused by rupture of the false lumen or hematoma exudation at the root will lead to cardiogenic shock in some patients. All of these will aggravate liver ischemia and lead to ischemic hepatitis and ischemic damage to liver function. Systemic inflammatory response syndrome (SIRS) caused by the release of inflammatory cytokines owing to the dissection of the layers of the aortic wall can also lead to hepatocyte damage. Therefore, the patients' liver function was damaged before the operation. The results of this study showed that elevated preoperative ALT level was an independent risk factor for postoperative liver dysfunction. Therefore, it is necessary to shorten the time of hepatic ischemia before operation as soon as possible in ATAAD. Patients with elevated ALT before the operation should be treated with hepatoprotective drugs in time after the operation, and other liver protection strategies should be performed as much as possible during preoperative preparation if possible.

Table 6. Sensitivity and Specificity of Each Predictor and the Combined Predictor

Variable	Sensitivity Value, 95% CI	Specificity Value, 95% CI	Youden's index
Preoperative ALT level	0.568, 0.396-0.725	0.882, 0.807-0.932	0.450
CPB time	0.610, 0.445-0.754	0.913, 0.842-0.955	0.523
Intraoperative and 24h postoperative red blood cell transfusion volume	0.760, 0.545-0.898	0.878, 0.806-0.926	0.638
Combining predictor Pre	0.705, 0.546-0.828	0.964, 0.906-0.988	0.669

ALT, alanine aminotransferase; CPB, cardiopulmonary bypass.

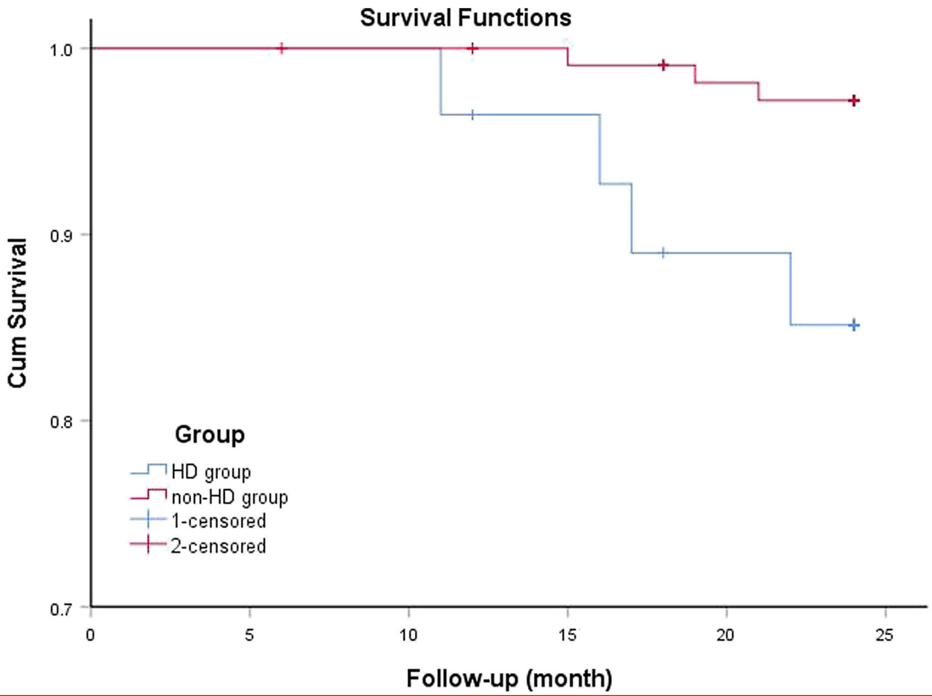

Figure 2. Comparison of 2-year survival curve between the 2 groups. HD, hepatic dysfunction.

Cardiopulmonary bypass is a milestone in the history of cardiac surgery. This technique makes open heart surgery possible and has saved lives of countless patients with heart disease. At present, the rapid development of medical technology makes CPB equipment increasingly excellent, but no technology can be perfect, it will still bring certain pathological damage to the human body. Many studies have shown that prolonged CBP is an independent risk factor for renal dysfunction, respiratory dysfunction, and prolonged ICU stay length, and even it may increase in-hospital mortality.[15-17] This study also confirmed that CBP time is an independent risk factor for postoperative HD in ATAAD patients. Nonphysiological perfusion during CBP can lead to the destruction of blood cells, denaturation of plasma proteins, low-temperature and low-flow perfusion of various tissues and organs, and subsequent reperfusion injury. Surgical stress and the endotoxemia caused by intestinal "bacterial translocation" during CBP can lead to SIRS.[18,19] It may lead to a series of chain reactions such as the activation of a variety of inflammatory factors.[20,21] This reaction can result in the injury of vascular endothelium, liver injury, and even multiple organ dysfunction. The destruction of blood cells and other blood tangible composition, microthrombosis, air embolism, and fat embolism during CBP can lead to hepatic capillary network embolism and aggravate the damage of liver cells.[22] Patients undergoing cardiac surgery with CBP are in a state of "controlled shock." Despite the stronger compensatory capacity of the liver compared with other organs such as heart, brain, and kidney, prolonged low-flow and non-pulsatile perfusion can still cause liver cell damage,[23] especially if patients have liver function abnormalities such as elevated transaminases before operation. CBP or even deep hypothermic circulatory arrest is inevitable in type A aortic dissection surgical procedures; we should try to shorten the time of CBP and deep hypothermic circulatory arrest as much as possible so as to reduce the non-physiological perfusion. This requires the surgeon to evaluate the condition comprehensively, select a reasonable operation procedure, and have skilled operative techniques. Temperature, perfusion flow, and perfusion pressure should be monitored closely during operation so as to reduce the multiple organ dysfunction caused by hypoperfusion and reperfusion and to protect liver function. Perioperative anti-inflammatory drugs such as ulinastatin can be used to inhibit the increase of elastase in vivo, so as to reduce the liver cell damage caused by systemic inflammatory reactions.

The blood consumption of cardiac surgery accounts for a large proportion of the total blood consumption, up to more than 60%, and ranks first in surgical blood consumption.[24] It is much more obvious in patients with aortic dissection than other cardiac surgeries owing to the preoperative thrombosis, consumption of platelets and other coagulation factors, complexity of surgery, and longer CPB time than other cardiac surgery. Therefore, massive hemorrhage and blood transfusion in the perioperative period are also difficult problems for cardiac surgeons. In recent years, the amount of blood transfusion in cardiovascular surgery has decreased significantly because of the continuous improvement of surgical techniques by cardiac surgeons. However, it is still a thorny problem in some grassroots hospitals in China. Blood transfusion has saved the lives of many patients with aortic dissection, but it also brings some complications to them. Many studies have confirmed that blood transfusion in patients undergoing cardiac surgery is closely related to multiple organ dysfunction and long-term prognosis.[10,17]

Blood transfusion can lead to a variety of acute and chronic immune and nonimmune reactions. It can lead to transfusion-associated acute lung injury and immunosuppression.[25] Massive transfusion of banked blood in a short time will lead to a large number of allogeneic proteins entering the body and extensive formation of cell fragments and microthrombosis, and these will lead to direct damage of hepatocytes and changes of hepatocyte autoimmunity protective mechanisms. Simultaneously, massive blood transfusion can cause disorders of coagulation mechanism and internal environment and affect blood supply and metabolism of hepatocytes.[26] All of these effects can lead to an increase in bleeding. The results of our study showed that the amount of red blood cell transfusion intraoperative and 24 hours postoperative was an independent risk factor for postoperative HD in ATAAD patients. Therefore, what we need to do is to strengthen blood conservation and reduce blood loss. Appropriate quantities of platelets and cryoprecipitated antihemophilic factors should be prepared before operation. Autologous priming technique may be performed if possible. Cardiac surgeons should master excellent vascular anastomosis techniques, and anti-hemorrhagic agents and hemostatic materials can be used appropriately. We should try to avoid excessive hemodilution. Autologous blood recovery system should be used as far as possible to wash and reinfuse the residual blood in the surgical field and in CBP circuits after CPB. We should strictly grasp the indications of blood transfusion and perform reasonable blood transfusion strategy to minimize the occurrence of postoperative HD and other organ dysfunction.

Study Limitations

There are some limitations in our study that require emphasis. First, the patient population enrolled in this study was just in a single institution, so it is relatively small; therefore, the conclusions might not be applicable to other centers. Second, some risk factors that may affect liver function are not included, such as the type and dose of intraoperative anesthetic drugs. Third, more short- and medium-term follow-up data should be analyzed after discharge, such as the incidence of complications and causes of death. Finally, our study just presented short- and medium-term outcomes; the long-term follow-up might be needed to further assess the effect.

CONCLUSION

The incidence of perioperative organ dysfunction in patients with acute Stanford A aortic dissection is relatively high owing to their complicated conditions and difficult surgical procedure. In particular, the occurrence of HD has significantly increased the mortality of patients. Therefore, we should try to shorten the time of preoperative hepatic ischemia, reconstruct the aorta, and restore the blood supply of organs as soon as possible. We should try our best to improve our own surgical skills and the cooperation experience of the whole team, select the operation mode reasonably, and shorten the CBP time as much as possible. Positive blood protection measures, strict evaluation of blood transfusion indications, and reasonable component blood transfusion should be carried out. We should avoid using drugs that can injure the liver during the perioperative period in patients with elevated transaminases before operation, and the drugs for liver protection and anti-inflammatory reaction should be used appropriately. So, therefore, we can avoid or reduce the occurrence of postoperative liver injury in ATAAD patients through the above measures and improve the short- and medium-term prognosis of patients. The long-term follow-up results need to be further studied.

Ethics Committee Approval: This study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Ethics Committee of Qingdao Municipal Hospital (No.2020-045).

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – W.S., X.L.; Design – W.S., X.L.; Supervision – H.Q., Z.N.; Materials – H.Q.; Data Collection and/or Processing – Z.W.; Analysis and/or Interpretation – W.S., Z.W.; Literature Review – W.S., Z.N.; Writing – W.S.; Critical Review – W.S., Z.N., X.L.

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