Analysis of risk factors of type A aortic dissection (TAAD) operation of frozen elephant trunk and total arch replacement

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Abstract. – OBJECTIVE: To investigate the incidence and risk factors of acute renal failure (ARF) after operation of frozen elephant trunk and total arch replacement for acute thoracic aortic aneurysm and dissection (TAAD) with mild hypothermic circulatory arrest (MHCA), and to analyze the long-term survival rate of the patients with ARF.

PATIENTS AND METHODS: From February 2009 to March 2015, patients with acute TAAD accepted operation of frozen elephant trunk and total arch replacement were enrolled. Those patients who were treated with renal replacement treatment (RRT) before the operation were excluded. The age, gender, cardiovascular disease history, preoperative serum creatinine and extracorporeal circulation duration in operation were recorded. On the basis of requiring RRT after TAAD operation, the patients were divided into ARF group and non-ARF group. The risk factors of ARF after TAAD operation were assessed by univariate and multivariate analysis. After completion of clinical follow-up, Kaplan-Meier curve was drawn to analyze five-year survival.

RESULTS: A total of 524 patients were included in the study. 51 cases of them got postoperative ARF. The incidence was 9.7%. The mortality rate of ARF group in the hospital was significantly higher than non-ARF group (25.5% *vs.* 3.6%; *p*<0.001). Univariate analysis showed that there was statistically significant difference in the age, gender, hypertension history, preoperative serum creatinine ≥200 *μ*mol/L, extracorporeal circulation duration ≥260 min and combined with coronary artery bypass surgery simultaneously (*p*<0.05). Multiple logistic regression analysis showed that there were three independent risk factors of ARF after the operation, including hypertension (*p*=0.031, OR=2.377), preoperative serum creatinine ≥200 *μ*mol/L (*p*=0.005, OR=4.451) and extracorporeal circulation duration ≥260 min (*p*=0.002, OR=3.295). The total five-year survival rate of ARF group after the operation was 56%. There was no statistically significant difference in the five-year survival rate between preoperative serum creatinine ≥200 *μ*mol/L group and <200 *μ*mol/L group (*p*>0.05).

CONCLUSIONS: The incidence of ARF after the operation was 9.7%. Preoperative serum creatinine ≥200 *μ*mol/L, hypertension history and extracorporeal circulation duration ≥260 min were independent risk factors of ARF after the operation. The five-year survival rate of ARF after the operation was 56%. The preoperative serum creatinine level had no influence on the postoperative long-term survival.

Key Words:
  Acute type A aortic dissection, Acute kidney failure, Risk factors, Survival.

Introduction

The treat and cure rate of patients with the most dangerous clinical onset acute thoracic aortic aneurysm and dissection (TAAD) significantly increased with continuous improvement in imaging techniques and surgical procedures[1]. However, due to the complexity of the surgical procedure and a long duration of extracorporeal circulation, the incidence of acute renal injury associated with cardiac surgery was higher than 30%[2,3]. In most of these patients, the renal function recovered spontaneously, while the renal functions continued to deteriorate and resulted in ARF (ARF) in some of the patients, and needed renal replacement therapy (RRT)[4-7]. ARF was a major and severe complication after TAAD operation of frozen elephant trunk and total arch replacement[8-10]. The aim of the study was to investigate the incidence and risk factors of ARF after the operation of frozen elephant trunk and total arch replacement for acute TAAD and to explore the long-term survival of patients needed RRT after the operation.

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Patients and Methods

Patients

The Ethics Committee of Anzhen Hospital approved this retrospective study and waived the need for individual patient's consent for this study. From February 2009 to March 2015, a total of 524 patients (patients treated with renal replacement before the operation were excluded) accepted TAAD operation of frozen elephant trunk and total arch replacement in our hospital were enrolled, 405 cases of them were male and 119 cases were female. The range of age was 18-85 years old, and the average age was 47.9 ± 10.9 years old. There were 362 cases with history of hypertension, 17 cases of diabetes mellitus, 8 cases of cerebral stroke, 157 cases of poor perfusion syndrome, 5 cases of chronic obstructive pulmonary disease. There were no patients with history of cardiovascular surgery, history of renal disease and chronic obstructive pulmonary disease.

A preoperative diagnosis of TAAD was confirmed by transthoracic echocardiography and/or computed tomographic angiography in all patients.

Surgical Procedure

All procedures were performed by a median sternotomy and total cardiopulmonary bypass (CPB) with low flow selective cerebral perfusion (SCP). Cannulation of the right axillary artery was used for CPB and SCP. The arterial line was bifurcated for the right axillary artery perfusion and for low flow perfusion through 1 limb of a 4-branch prosthetic graft. Cannulation for CPB was performed through the right axillary artery and the right atrium. During the cooling phase, the ascending aorta was clamped. The proximal ascending aorta was longitudinally opened, and anticoagulation perfusion of cold blood cardioplegic solution was directly infused into the coronary ostia. Aortic root procedures were performed in this cooling phase. Circulatory arrest was instituted if the nasopharyngeal temperature reached from 20°C to 25°C. Unilateral SCP was started through the right axillary artery after the brachiocephalic arteries were cross-clamped and the brain was perfused. Left carotid and left subclavian artery were also cross-clamped. A stent graft and a 4-branch prosthetic graft were used in the operation. After completion of the open distal anastomosis, the 4-branch prosthetic graft was cross-clamped, and blood perfusion of the lower body was started via the perfusion limb of the 4-branch prosthetic graft. After the anastomosis to the left common carotid artery, left subclavian artery and innominate artery were accomplished and SCP was discontinued. Then, CPB was gradually resumed to normal flow and rewarming started.

Diagnostic Criteria for Postoperative ARF

The postoperative ARF was diagnosed as a requirement of RRT after the operation. The indication of RRT were oliguria (urine output <100 ml in a 6-hour period) and unresponsive to fluid resuscitation, hyperkalaemia (serum potassium >6.5 mmol/L), metabolic acidosis, serum creatinine concentration >200 µmol/L or the presence of clinically significant organ edema (e.g., pulmonary edema). Patients with a history of preoperative RRT were excluded.

Statistical Analysis

SPSS 13.0 statistical software package (SPSS Inc., Chicago, IL, USA) was used to analyze and process the data. The measurement data were expressed by mean ± SD, and the *t*-test was used for comparison among groups. The enumeration data were expressed by the number of cases and tested by chi-square test. Multivariate logistic regression model was used to analyze the related factors of ARF. All tests were two-sided and $p<0.05$ indicated that the difference was statistically significant. Kaplan-Meier curve was drawn to analyze five-years survival of patients with ARF after the operation.

Results

Postoperative ARF was observed in 51 out of 524 cases. The incidence was 9.7% (51/524). 30 cases died in hospital, 13 cases were in AKF group and the mortality rate was 25.5% (13/51), while the mortality rate was 3.6% (17/473) in non-AKF group. The mortality rate of ARF group was statistically significantly higher than non-AKF group ($p<0.001$). One-way analysis showed there was statistically significant difference between two groups in age, gender, history of hypertension, preoperative serum creatinine ≥200 µmol/L, the duration of cardiopulmonary bypass (CPB) ≥260 min and combined with coronary artery bypass surgery simultaneously ($p<0.05$) (Table I).

Before and during the operation of frozen elephant trunk and total arch replacement for TADD, multiple Logistic regression was used to analyze the related factors of ARF. The results showed that
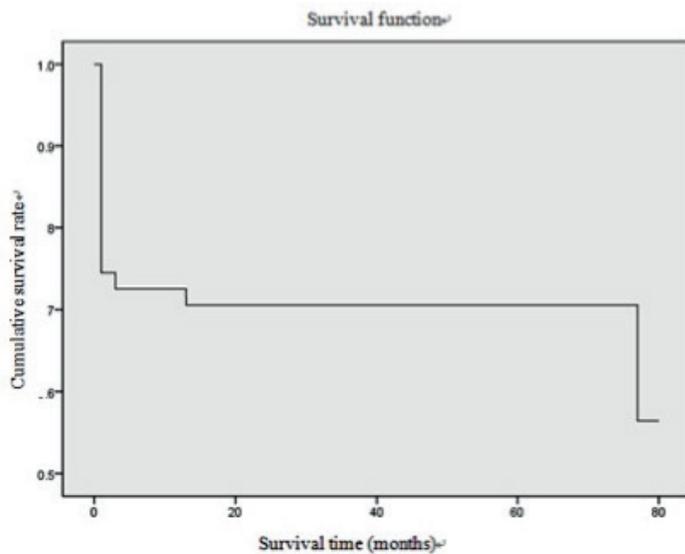
Figure 1. The Kaplan-Meier analysis of survival curve of AKF group.

preoperative serum creatinine ≥200 μmol/L, history of hypertension and the turnaround duration ≥260 min were related to onset risk of ARF after the operation (Table II). The analysis of survival curve of patients with ARF was shown in Figure 1. The average follow-up period was 30.5 months. The overall five-year survival rate was 56%. According to the preoperative serum creatinine levels, the patients were divided into two groups: Cr ≥200 μmol/L group and Cr <200 μmol/L group. The follow-up period of the two groups was identical. The actual five-year survival rate was 50% in the Cr ≥200 μmol/L group and 57% in the Cr <200 μmol/L group. There was no statistical sig-

nificant difference in actual five-year survival rate between the two groups (log rank, p =0.367) (Figure 2).

Discussion

The average age of onset of acute TADD in Chinese population was between 40 and 50 years old[11-14], and these patients had a long life expectancy. The total aortic arch replacement with trunk stent implantation during emergency operation was a good and economic treatment option in these cases. However, due to the complexities

Table I. The comparison of clinical data of acute renal failure after TAAD.

	No AKF (n=473)	AKF (n=51)	*p*-value
Age (years)	47.6±10.8	50.9±10.7	0.041
Male, n (%)	187 (75)	130 (87)	0.005
BMI (kg/m²)	26.7±3.6	25.8±3.6	0.100
Smoking, n (%)	211 (45)	28 (55)	0.161
Hypertension, n (%)	319 (67)	43 (84)	0.013
Diabetes mellitus, n (%)	15 (3)	2 (4)	0.774
Stroke, n (%)	7 (1)	1 (2)	0.790
Marfan syndrome, n (%)	5 (1)	0 (0)	0.461
MPS, n (%)	141 (30)	16 (31)	0.817
Preoperative Cr ≥200 μmol/L, n (%)	13 (2.7)	6 (11.8)	0.001
The turnaround time ≥260 min, n (%)	40 (8.5)	12 (23.5)	0.001
ASCP time ≥42 min, n (%)	46 (9.7)	6 (11.7)	0.643
Concomitant CABG, n (%)	15 (3.2)	5 (9.8)	0.019

Values are n (%). AKF, acute kidney failure; MPS, mal-perfusion syndrome; Cr, creatinine; CPB, cardiopulmonary bypass; ASCP, antegrade selective cerebral perfusion; CABG, coronary artery bypass grafting.

Table II. The analysis of risk factors of acute renal failure after TAAD.

	Odds ratio	p-values	95% confidential intervals
Preoperative Cr ≥200 umoL/L	4.451	0.005	1.562-12.681
	3.295	0.002	1.570-6.914
The turnaround time ≥260 min			
History of hypertension	2.377	0.031	1.080-5.229
Constant	0.042	0.000	

Values are n (%). AKF, acute kidney failure; MPS, mal-perfusion syndrome; Cr, creatinine; CPB, cardiopulmonary bypass; ASCP, antegrade selective cerebral perfusion; CABG, coronary artery bypass grafting.

involved in the operation, a significant increase in early postoperative ARF had been observed in recent studies[13,15,16]. Further, the circulatory arrest temperature had been changed from deep hypothermia (18-20°C) to mild hypothermia (23-25°C) in order to reduce the damage to renal vascular endothelial cells caused by hypothermia. In this study, the occurrence rate of ARF was 9.7%, which was consistent with the results of previous studies[17-19].

Although ARF was caused by multiple factors[20-23], the elevation of preoperative serum creatinine levels was one of the strongest risk factors of ARF[24]. However, in our study, preoperative serum creatinine levels were associated with the occurrence of postoperative ARF, but it did not affect the long-term survival rate of the patients. It found that preoperative serum creatinine ≥200 μmol/d increased the risk of acute renal failure 4.45 times. The serum creatinine level has been established as an effective index in evaluation of renal functions[25,26]. Moreover, in the cases of acute aortic dissection accompanied with increased preoperative serum creatinine level, the operation could improve the long-term survival rate, but perioperative renal protection should be strengthened to reduce the risk of postoperative ARF. So, elevated preoperative serum creatinine level was not the risk factor of the long-term mortality.

Extracorporeal circulation was a main factor of cardiac surgery associated ARF[27-29], which was related to reaction mechanism of ischemia/
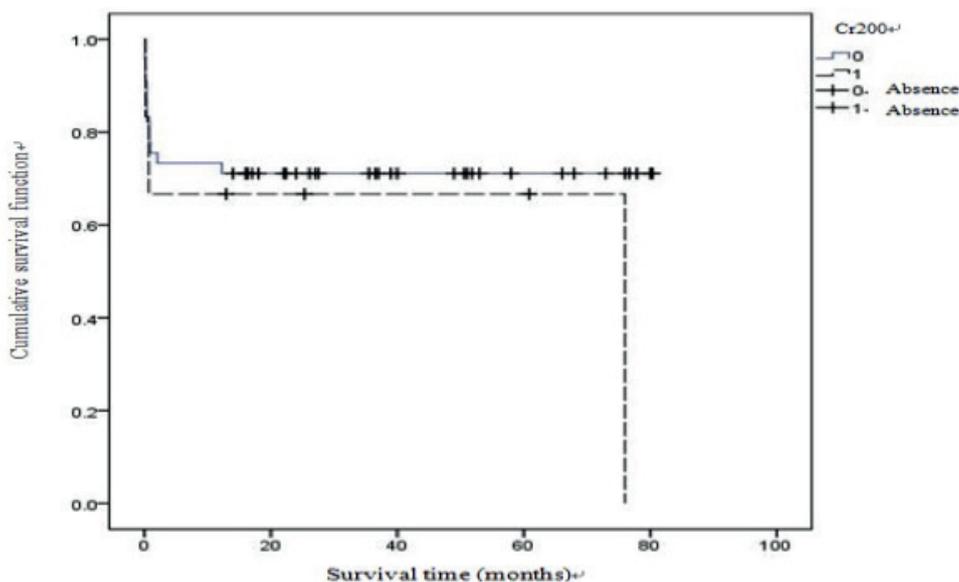

Figure 2. The Kaplan-Meier analysis of survival curve of the patients with acute kidney failure based on the level of serum creatinine.

reperfusion injury, blood dilution and inflammatory reaction mechanism[30,31]. The longer the extracorporeal circulation duration, the more serious the renal function deterioration. It showed in the earlier studies that more than 150 minutes of turnaround period would directly cause the renal tubular dysfunction and acute renal function decline[32-34]. More than 180 minutes of extracorporeal circulation would not only cause 3-4 times increase in the acute kidney injury risk, but also significantly elevate the hospital mortality[35]. Our study founds that more than 260 minutes of extracorporeal circulation was an independent risk factor for ARF (OR=3.295, 95% CI:1.570-6.914). We used the middle and low temperature circulatory arrest during the operation of the aorta replacement and found no correlation between extracorporeal circulation duration and ARF after TAAD. This might be due to the small proportion of patients with acute aortic dissection and the mean turnaround time was significantly shorter than our study. So, it was helpful to reduce the occurrence of ARF to improve the surgical skills as soon as possible and shorten the extracorporeal circulation duration.

Hypertension was another major factor of the onset of TAAD, Englberger et al[36] found that hypertension was an independent risk factor of acute kidney injury after aortic surgery. Aronson et al[34] also suggested that the risk of hypertension patients with pulse pressure greater than 80 mmHg gap who died of kidney diseases was as 3 times as patients without hypertension[37,38]. Pulse pressure was often used to measure the elasticity of blood vessel wall. High blood pressure caused atherosclerosis and decreased vascular wall elasticity. Low pressure and low perfusion in the extracorporeal circulation caused renal vascular compensatory reduction and more severe ischemia. In this study, we also found that cardiopulmonary bypass duration and hypertension were independent risk factors of ARF. High blood pressure increased the risk of postoperative ARF by 2.38 times (OR=2.377, 95% CI: 1.880-5.229).

We first reported the 5-year survival rate of patients with ARF after TAAD operation. It found that the hospital mortality was the highest at the 30th day after surgery, and the survival rate was 56% 5 years after surgery. The study also found that the survival rate of patients with ARF was not affected by the preoperative serum creatinine level. The long term survival rate of patients with serum creatinine ≥200 µmol/L and <200 µmol/L were consistent. A large scale Swiss study reported that 1/3 of 2634 patients after TAAD operation was aortic dissection surgery and the 5-year survival rate was 77%. It was higher than those with acute renal failure after acute aortic dissection. The limitation of the study was that it was a retrospective study and the sample was relatively small.

Conclusions

In a word, the ARF after TAAD operation was still a major and serious complication. To improve the preoperative renal function, keep serum creatinine level <200 µmol/L, shorten the operation duration, control the turnaround time and keep the blood pressure stable in a long term would help to reduce the risk of acute kidney function failure. Moreover, these factors could improve the surgery results of the aortic repair operation as well as the long-term postoperative survival rate.

Conflicts of interest
The authors declare no conflicts of interest.

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