Original Article

Risk factors for severe acute kidney injury post complication after total arch replacement combined with frozen elephant trunk, in acute type A aortic dissection

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Background: Total arch replacement with the frozen elephant trunk (TAR + FET) technique is a challenging approach for acute type A aortic dissection (ATAAD). Severe acute kidney injury (AKI) adversely affects the prognosis of hospitalized patients. The study aims to evaluate the incidence and risk factors of severe AKI.

Methods: We conducted a retrospective cross-sectional study of the records of ATAAD patients following TAR + FET, admitted between January 2013 and December 2018. A multivariate logistic regression model was used to identify predictors of severe postoperative AKI. Severe postoperative AKI was defined using the Kidney Disease Improving Global Outcomes criteria.

Results: The whole in-hospital mortality rate was 4.3%. Among 670 patients, major adverse outcomes were present in 169 patients (25.2%), 67 patients (10.0%) required renal replacement therapy (RRT), and 80 (11.9%) developed severe postoperative AKI. In-hospital mortality in the severe AKI group (13.8%) was 4.5 times higher than in the non-severe AKI group (3.1%). Compared with the non-severe AKI patients, the severe AKI patients had a higher incidence of major adverse outcomes (100% *vs.* 15.1%, P<0.001) and more frequent use of RRT (83.8% *vs.* 0.0%, P<0.001). Multivariate analysis revealed that severe postoperative AKI was predicted by advanced age [odds ratio (OR) =1.029; 95% confidence interval (CI): 1.002–1.056; P=0.032], lower limb symptoms (OR =4.384; 95% CI: 2.240–8.582; P<0.001), coronary artery involvement (OR =2.478; 95% CI: 1.432–4.288; P=0.001), preoperative postoperative serum creatinine (SCr) (OR =1.008; 95% CI: 1.003–1.013; P=0.001), and prolonged cardiopulmonary bypass (CPB) time (OR =1.011; 95% CI: 1.006–1.015; P<0.001).

Conclusions: There was a high incidence of severe AKI and high in-hospital mortality after TAR + FET in ATAAD patients. The risk factors for severe AKI in ATAAD patients undergoing TAR + FET were determined to help identify the high-risk patients and make rational treatment decisions.

Keywords: Total arch replacement (TAR); frozen elephant trunk (FET); acute type A aortic dissection (ATAAD); severe acute kidney injury (AKI)

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Introduction

Acute type A aortic dissection (ATAAD) is an emergency and life-threatening condition with high mortality and major postoperative complications (1). Aortic arch involvement dictates a stringent surgical approach and decision-making framework. Limited aortic arch repair entails hemiarch replacement while other authorities advocate extended repair paired with frozen elephant trunk (FET) use (2). Recent studies have demonstrated that total arch replacement combined with FET [total arch replacement (TAR) + FET] yields good results through improved organ protection techniques (3). In China, this gradually became a routine surgical procedure to treat complex aortic arch disease (2-5).

Acute kidney injury (AKI) patients after aortic surgery have a considerably worse short- and long-term prognosis, resulting in a higher risk of mortality and major adverse outcomes (6). AKI incidence after thoracic aortic surgery varies between 26.0–77.6%, depending on different definitions of AKI and confounding patient selection (7-14). Severe AKI (AKI stage 3) is associated with higher postoperative mortality, more renal replacement therapy (RRT) treatments, and longer intensive care unit (ICU) stays for patients than in non-severe AKI individuals (8,15-17).

Reported series on renal outcomes of patients undergoing TAR + FET are underscored in current literature (12,18,19). However, indifferent attention has been directed to severe postoperative AKI in ATAAD patients receiving TAR + FET procedure (20). Hence, this study aims to evaluate the incidence and risk factors of severe AKI after TAR + FET procedure in ATAAD patients. We present the following article in accordance with the STROBE reporting checklist (available at https://cdt.amegroups.com/article/view/10.21037/cdt-22-313/rc).

Methods

Study design

We conducted a retrospective cross-sectional analysis of patients with ATAAD admitted to our institute, a high volume tertiary referral hospital, between January 2013 and December 2018. During this period, 670 consecutive patients with ATAAD involving the aortic arch received the traditional TAR + FET procedure (*Figure 1*). Inclusion criteria included: (I) adult patients (age >18 years); (II) ATAAD patients who received TAR + FET procedure. All the patients underwent preoperative aortic computed tomography angiography (CTA) and coronary CTA/coronary angiography.

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The Ethics Committee Institute of Fuwai Hospital approved the present study (No. 2021-1557). Because of the retrospective nature of the study, the requirement for informed consent was waived.

Data definition

We retrospectively reviewed clinical records and data on patient demographics, and preoperative risk factors, as well as intraoperative and postoperative data from the electronic medical records system of our institution. A recent classification for AKI, based on the RIFLE and AKIN criteria, was proposed by Kidney Disease Improving Global Outcome (KDIGO) (21-23). We defined AKI according to KDIGO consensus criteria to classify patients as severe AKI (AKI stage 3) or non-severe AKI (no AKI or AKI stage 1–2). Severe AKI was defined when the postoperative serum creatinine (SCr) increased more than three times baseline in the first week, or there was an increase in SCr to ≥4.0 mg/dL (353.6 μmol/L), or the initiation of RRT within 48 h postoperatively, or urine output <0.3 mL/kg/h for ≥24 h, or anuria ≥12 h. Preoperative SCr values closest to the date of surgery were chosen as baseline SCr levels. Prior cardiovascular surgery was defined as surgery on the heart or great vessels. Hypotension or shock was defined as a permanent deterioration in systolic blood pressure <90 mmHg (1). Lower limb symptoms included pain, decreased muscle strength, and sensory dysfunction. The assessment of branch vessel involvement by aortic dissection was based on preoperative imaging data by two radiologists and intraoperative exploration by surgeons. When there was an aortic root surgery, coronary ostium could be simultaneously reconstructed in the Bentall or David procedure using the button technique. We combined the variables for Bentall and David procedures into one variable for a similar procedure, including ascending aorta replacement and coronary ostium reconstruction (the button technique). According to the International Aortic Arch Surgery Study Group, major adverse outcomes were defined as events ranging from Grade III complications to death (24).

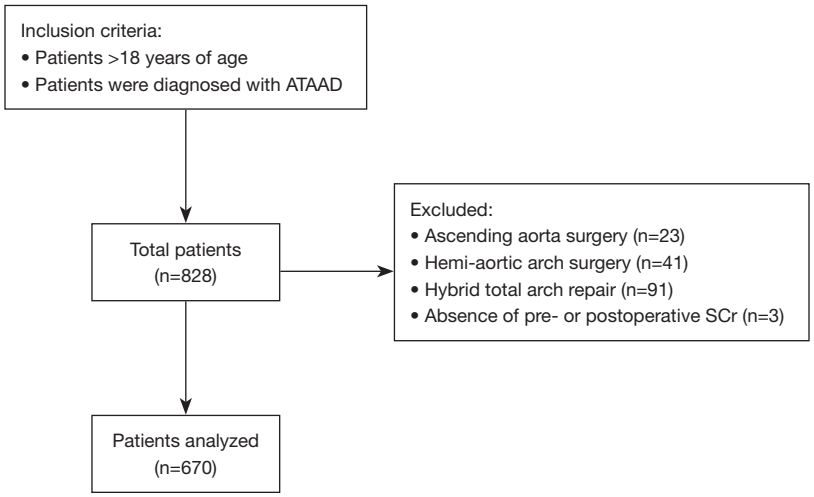

Figure 1 Flow chart of participants in the present study. ATAAD, acute type A aortic dissection; SCr, serum creatinine.

Surgical technique

It has been a complex operation to replace a total aortic arch. However, after successful operations, many patients require further treatment of the distal aorta. Repairing the descending aorta with an open surgical procedure is difficult, especially if the proximal anastomosis needs to be connected to an implanted aortic arch graft. This operation was greatly simplified when the FET was introduced. The FET technique used a stent graft to secure the distal elephant trunk section, contributing to true lumen expansion and coverage of entry tears into the false lumen. It helped diminish the risk of proximal endoleak while facilitating false lumen thrombosis to ensure aortic remodeling. Moreover, it allowed for the treatment of complex pathologies of the aortic arch and the proximal descending aorta in one step and facilitated the possibility of second-stage and more extensive repairs, if required (2).

The chest was opened via median sternotomy in all patients. Arterial cannulation was accessed through one side of the femoral artery and/or the right axillary artery. The right or left common carotid artery was cannulated to perform unilateral selective antegrade cerebral perfusion. Based on the patient's condition, management was either moderate, or deep hypothermic circulatory arrest occurred. The TAR + FET procedure has previously been described in detail (25). The entire procedure included two steps: the total aortic arch, with or without the ascending aorta, is replaced with a tetrafurcate graft (Vascutek Terumo, Tokyo, Japan), followed by a stented graft (MicroPort Medical Co, Ltd., Shanghai, China) implantation. Selective antegrade cerebral perfusion was discontinued after distal arch reconstruction, cardiopulmonary bypass (CPB) flow was resumed, and systemic warming began until body temperature reached 35 ℃.

Statistical analysis

Categorical characteristics were compared using the χ^2 test or Fisher's exact test, where appropriate. With Student's *t*-test, continuous variables were analyzed based on their mean and standard deviation. All statistical tests were 2-sided, and P values were considered statistically significant at 0.05 or below. Univariate analyses were conducted using univariate logistic regression analysis. No correction was made for multiple testing. Multiple logistic regression analysis analyzed the influence of different parameters on severe AKI. All variables including statistically significant and clinically essential variants were included in the multiple logistic regressions, and a forward stepwise selection method was then performed. The logistic regression results are presented as odds ratios (OR) with 95% confidence intervals (CI). All statistics were analyzed using SPSS version 22 (SPSS Inc., Chicago, IL, USA).

Results

Patient characteristics

A total of 670 ATAAD patients who received TAR + FET operation were enrolled in this retrospective study and divided into the non-severe AKI group and severe AKI

group (*Figure 1*). The mean age of the study patients (n=670) was 46.9±10.2 years (range, 19–77 years) and 144 (21.5%) were women. Patients' characteristics are presented in *Table 1*. After surgery, there were 80 patients (11.9%) with severe AKI. The mean ventilator time in the study cohort was 55.5±103.1 min, and the mean ICU time was 5.5±6.0 days. In total, major adverse outcomes were present in 169 patients (25.2%), and 67 patients (10.0%) required RRT. The whole in-hospital mortality rate was 4.3% (*Table 2*).

In-hospital outcomes

In-hospital mortality in the severe AKI group (13.8%) was 4.5 times higher than in the non-severe AKI group (3.1%). Compared with the non-severe AKI patients, the severe AKI patients had a longer duration of mechanical ventilation (min) (149.8±172.6 *vs.* 42.7±81.9, P<0.001), a higher incidence of major adverse outcomes (100% *vs.* 15.1%, P<0.001), and more frequent use of RRT (83.8% *vs.* 0.0%, P<0.001). Therefore, the severe AKI patients had longer ICU stays (days) (13.9±8.2 *vs.* 4.4±4.7, P<0.001) (*Table 2*).

Univariate analysis

Patients who developed severe AKI were more likely to be older (years) (49.4±11.1 *vs.* 46.5±10.0, P=0.019), were also more likely to present preoperatively with preoperative malperfusion of the organ: hypotension or shock (5.0% *vs.* 1.5%, P=0.034), and lower limb symptoms (25.0% *vs.* 6.9%, P<0.001). The proportion of branch vessel involvement by aortic dissection was significantly higher for patients with severe AKI than non-severe AKI patients: coronary artery (42.5% *vs.* 18.0%, P<0.001), innominate artery (70.0% *vs.* 56.1%, P=0.018), left subclavian artery (56.3% *vs.* 43.1%, P=0.026) and left renal artery (60.0% *vs.* 43.1%, P=0.004). Laboratory results revealed that patients with severe AKI had higher SCr (μmol/L) (125.1±51.4 *vs.* 96.9±45.3, P<0.001) and lower platelet numbers ($\times 10^9$/L) (165.6±55.8 *vs.* 182.5±62.3, P=0.021) than non-severe AKI patients. Patients with severe AKI more frequently had concomitant coronary artery bypass graft (CABG) (30.0% *vs.* 10.8%, P<0.001) than non-severe AKI patients. The severe AKI group had a significantly longer duration CPB time (min) (severe AKI 219.9±80.6 *vs.* non-severe AKI 175.8±46.2, P<0.001) than the non-severe AKI group (*Table 1*). The results of the univariate logistic regression analysis showed that age, hypotension or shock, lower limb symptoms, coronary artery involvement, innominate artery involvement, left subclavian artery involvement, left renal artery involvement, platelets, SCr, CABG, CPB time, cross-clamp time, and hypothermic circulatory arrest (HCA) time were significantly correlated with severe AKI (*Table 3*).

Multivariate analysis

The multivariable analyses of risk factors for severe postoperative AKI were carried out by including all candidate variables derived from the univariable analysis and clinically important variables (age, hypotension or shock, lower limb symptoms, coronary artery involvement, innominate artery involvement, left subclavian artery involvement, left renal artery involvement, white blood cell count, SCr, platelets, Bentall or David procedure, CABG, and CPB time). Multivariate analysis revealed that severe AKI was predicted by advanced age (OR =1.029; 95% CI: 1.002–1.056; P=0.032), lower limb symptoms (OR =4.384; 95% CI: 2.240–8.582; P<0.001), coronary artery involvement (OR =2.478; 95% CI: 1.432–4.288; P=0.001), preoperative SCr (OR =1.008; 95% CI: 1.003–1.013; P=0.001), and prolonged CPB time (OR =1.011; 95% CI: 1.006–1.015; P<0.001) (*Table 3*).

Discussion

Chinese ATAAD patients were younger than those in Europe and North America (7,9,10,26). Thus, the TAR + FET, as a one-stage repair technique, has become a routine procedure to facilitate future surgery for the distal aorta (25-31). A solid understanding of surgical therapies for ATAAD and optimal organ protection is required to perform aortic arch replacement, albeit limited versus extended. Our study used the KDIGO criteria, previously tested for predicting of AKI in the population undergoing cardiac surgery (27,28). As such, we identified the incidence, risk factors, and in-hospital outcomes for ATAAD patients undergoing TAR + FET, who are complicated with severe postoperative AKI. Some previous studies have depicted that the incidence of severe AKI and in-hospital mortality following ATAAD surgery ranged from 5.5% to 37.8% and from 4.7% to 27%, respectively, according to different diagnostic criteria (7,10,15,32). In addition, a small number of studies revealed that the incidence of severe AKI and in-hospital mortality after TAR + FET was reported to be 19.3% and 5.7%, respectively (17,18). However, few studies focused on severe AKI after TAR + FET in ATAAD

Table 1 Patient characteristics

Variables	Total (n=670)	Non-severe AKI (n=590)	Severe AKI (n=80)	P value
Demographics				
Age (years)*	46.9±10.2	46.5±10.0	49.4±11.1	0.019*
Female gender	144 (21.5)	121 (20.5)	23 (28.8)	0.092
BMI (kg/m^2)	26.5±4.3	26.4±4.3	26.9±4.5	0.338
Medical history				
Marfan syndrome	60 (9.0)	55 (9.3)	5 (6.3)	0.367
Hypertension	561 (83.7)	495 (83.9)	66 (82.5)	0.750
Diabetes	20 (3.0)	18 (3.1)	2 (2.5)	0.786
Prior cardiovascular surgery	24 (3.6)	22 (3.7)	2 (2.5)	0.579
Prior CAD	2 (0.3)	1 (0.2)	1 (1.3)	0.096
Family history of dissections or aneurysms	10 (1.5)	9 (1.5)	1 (1.3)	0.849
Current smoker	304 (45.4)	274 (46.4)	30 (37.5)	0.132
ATAAD presentation				
Chest pain	562 (83.9)	494 (83.7)	68 (85.0)	0.772
Back pain	301 (44.9)	261 (44.2)	40 (50.0)	0.331
Abdominal pain	119 (17.8)	106 (18.0)	13 (16.3)	0.706
Head or neck pain	16 (2.4)	13 (2.2)	3 (3.8)	0.395
Preoperative malperfusion of organ				
Brain ischemia	67 (10.0)	55 (9.3)	12 (15.0)	0.112
Myocardial ischemia	3 (0.4)	2 (0.3)	1 (1.3)	0.252
Cardiac failure	15 (2.2)	14 (2.4)	1 (1.3)	0.524
Hypotension or shock*	13 (1.9)	9 (1.5)	4 (5.0)	0.034*
Lower limb symptoms*	61 (9.1)	41 (6.9)	20 (25.0)	<0.001*
Echocardiography				
DAA (mm)	45.0±7.4	45.0±7.5	45.5±7.1	0.583
LVEDD (mm)	51.3±6.3	51.5±6.2	50.2±6.7	0.086
LVEF (%)	60.1±4.5	60.2±4.4	59.9±5.5	0.613
Involvement of vessel branches				
Coronary artery*	140 (20.9)	106 (18.0)	34 (42.5)	<0.001*
Innominate artery*	387 (57.8)	331 (56.1)	56 (70.0)	0.018*
Left common carotid artery	332 (49.6)	285 (48.3)	47 (58.8)	0.080
Left subclavian artery*	299 (44.6)	254 (43.1)	45 (56.3)	0.026*
Celiac trunk	283 (42.2)	249 (42.2)	34 (42.5)	0.960
Superior mesenteric artery	175 (26.1)	151 (25.6)	24 (30.0)	0.400
Right renal artery	191 (28.5)	169 (28.6)	22 (27.5)	0.832
Left renal artery*	302 (45.1)	254 (43.1)	48 (60.0)	0.004*

Table 1 (*continued*)

Table 1 (*continued*)

Variables	Total (n=670)	Non-severe AKI (n=590)	Severe AKI (n=80)	P value
Laboratory results				
White blood cell count ($\times10^9$/L)	12.6±5.0	12.5±5.0	13.6±4.8	0.052
Platelets ($\times10^9$/L)*	180.5±61.7	182.5±62.3	165.6±55.8	0.021*
SCr (μmol/L)*	100.3±47.0	96.9±45.3	125.1±51.4	<0.001*
Combined surgery				
Bentall or David procedure	173 (25.8)	149 (25.3)	24 (30.0)	0.363
CABG*	88 (13.1)	64 (10.8)	24 (30.0)	<0.001*
Duration of procedure (min)				
CPB time*	181.1±53.4	175.8±46.2	219.9±80.6	<0.001*
Cross-clamp time*	106.2±34.2	104.0±30.8	122.3±50.2	<0.001*
HCA time*	17.9±7.0	17.6±6.8	20.3±7.7	0.001*

Data are presented as the mean ± SD or n (%). *, non-severe AKI *vs.* severe AKI, P<0.05. AKI, acute kidney injury; BMI, body mass index; CAD, coronary artery disease; ATAAD, acute type A aortic dissection; DAA, diameter of ascending aorta; LVEDD, left ventricular end diastolic diameter; LVEF, left ventricular ejection fraction; SCr, serum creatinine; CABG, coronary artery bypass graft; CPB, cardiopulmonary bypass; HCA, hypothermic circulatory arrest; SD, standard deviation.

Table 2 In-hospital outcomes

Variables	Total (n=670)	Non-severe AKI (n=590)	Severe AKI (n=80)	P value
In-hospital death*	29 (4.3)	18 (3.1)	11 (13.8)	<0.001*
RRT*	67 (10.0)	0 (0.0)	67 (83.8)	<0.001*
Major adverse outcomes*	169 (25.2)	89 (15.1)	80 (100.0)	<0.001*
Perioperative myocardial infarction*	22 (3.3)	11 (1.9)	11 (13.8)	<0.001*
Cerebrovascular accident	22 (3.3)	18 (3.1)	4 (5.0)	0.359
Paraplegia*	33 (4.9)	22 (3.7)	11 (13.8)	<0.001*
Gastrointestinal ischemia or bleeding*	15 (2.2)	8 (1.4)	7 (8.8)	<0.001*
Mediastinal infection	3 (0.4)	3 (0.5)	0 (0.0)	0.523
Respiratory complications*	47 (7.0)	26 (4.4)	21 (26.3)	<0.001*
Aortic rupture	1 (0.1)	1 (0.2)	0 (0.0)	0.712
Osteofascial compartment*	5 (0.7)	0 (0.0)	5 (6.3)	<0.001*
Postoperative limb ischemia*	1 (0.1)	0 (0.0)	1 (1.3)	0.007*
Femoro-femoral artery bypass	12 (1.8)	10 (1.7)	2 (2.5)	0.610
Thoracotomy exploration*	20 (3.0)	14 (2.4)	6 (7.5)	0.011*
ICU time (days)*	5.5±6.0	4.4±4.7	13.9±8.2	<0.001*
Ventilator time (min)*	55.5±103.1	42.7±81.9	149.8±172.6	<0.001*

Data are presented as the mean ± SD or n (%). *, non-severe AKI *vs.* severe AKI, P<0.05. AKI, acute kidney injury; RRT, renal replacement therapy; ICU, intensive care unit; SD, standard deviation.

Table 3 Univariate and multivariate analysis of risk factors for severe AKI

Variables	Univariate analysis		Multivariate analysis	
	OR (95% CI)	P value	OR (95% CI)	P value
Demographics				
Age (years)*	1.028 (1.004–1.052)	0.020*	1.029 (1.002–1.056)	0.032*
Female gender	1.564 (0.926–2.641)	0.094	–	–
BMI (kg/m^2)	1.025 (0.975–1.078)	0.338	–	–
Medical history				
Marfan syndrome	0.648 (0.252–1.672)	0.370	–	–
Hypertension	0.905 (0.488–1.677)	0.751	–	–
Diabetes	0.815 (0.186–3.579)	0.786	–	–
Prior cardiovascular surgery	0.662 (0.153–2.870)	0.582	–	–
Prior CAD	7.456 (0.462–120.388)	0.157	–	–
Family history of dissections or aneurysms	0.817 (0.102–6.536)	0.849	–	–
Current smoker	0.692 (0.428–1.119)	0.133	–	–
ATAAD presentation				
Chest pain	1.101 (0.574–2.113)	0.772	–	–
Back pain	1.261 (0.790–2.012)	0.322	–	–
Abdominal pain	0.886 (0.472–1.664)	0.706	–	–
Head or neck pain	1.729 (0.482–6.205)	0.401	–	–
Preoperative malperfusion of organ				
Brain ischemia	1.717 (0.875–3.366)	0.116	–	–
Myocardial ischemia	3.722 (0.334–41.515)	0.286	–	–
Cardiac failure	0.521 (0.068–4.015)	0.531	–	–
Hypotension or shock*	3.398 (1.022–11.301)	0.046*	–	–
Lower limb symptoms*	4.463 (2.456–8.111)	<0.001*	4.384 (2.240–8.582)	<0.001*
Echocardiography				
DAA (mm)	1.009 (0.978–1.040)	0.582	–	–
LVEDD (mm)	0.967 (0.931–1.005)	0.086	–	–
LVEF (%)	0.987 (0.939–1.038)	0.612	–	–
Involvement of vessel branches				
Coronary artery*	3.375 (2.066–5.512)	<0.001*	2.478 (1.432–4.288)	0.001*
Innominate artery*	1.826 (1.102–3.026)	0.019*	–	–
Left common carotid artery	1.524 (0.949–2.447)	0.081	–	–
Left subclavian artery*	1.701 (1.062–2.724)	0.027*	–	–
Celiac trunk	1.012 (0.631–1.623)	0.960	–	–
Superior mesenteric artery	1.246 (0.746–2.081)	0.400	–	–

Table 3 (*continued*)

Table 3 (*continued*)

Variables	Univariate analysis		Multivariate analysis	
	OR (95% CI)	P value	OR (95% CI)	P value
Right renal artery	0.945 (0.561–1.593)	0.832	–	–
Left renal artery*	1.984 (1.233–3.194)	0.005*	–	–
Laboratory results				
White blood cell count ($\times10^9$/L)	1.034 (0.995–1.075)	0.091	–	–
Platelets ($\times10^9$/L)*	0.995 (0.990–0.999)	0.020*	–	–
SCr (μmol/L)*	1.009 (1.005–1.013)	<0.001*	1.008 (1.003–1.013)	0.001*
Combined surgery				
Bentall or David procedure	1.268 (0.759–2.119)	0.364	–	–
CABG*	3.522 (2.044–6.069)	<0.001*	–	–
Duration of procedure (min)				
CPB time*	1.013 (1.009–1.017)	<0.001*	1.011 (1.006–1.015)	<0.001*
Cross-clamp time*	1.013 (1.007–1.019)	<0.001*	–	–
HCA time*	1.058 (1.023–1.095)	0.001*	–	–

*, non-severe AKI *vs.* severe AKI, P<0.05. AKI, acute kidney injury; OR, odds ratio; CI, confidence interval; BMI, body mass index; CAD, coronary artery disease; ATAAD, acute type A aortic dissection; DAA, diameter of ascending aorta; LVEDD, left ventricular end diastolic diameter; LVEF, left ventricular ejection fraction; SCr, serum creatinine; CABG, coronary artery bypass graft; CPB, cardiopulmonary bypass; HCA, hypothermic circulatory arrest; SD, standard deviation.

patients. In the present study, the incidence of severe postoperative AKI and the overall in-hospital mortality was 11.9% and 4.3%, respectively. Despite the incidence of severe AKI and in-hospital mortality being high in our study, they do not seem to be high after TAR + FET compared to other thoracic aortic surgeries (7,15). To some extent, TAR + FET can be considered a relatively safe procedure.

Previous research has reported the predictive risk factors for postoperative AKI, including age, gender, body mass index, hypertension, left ventricular ejection fraction, preoperative SCr, CPB time, perioperative sepsis, thoracotomy exploration, and coronary involvement (7,9,10,28-30). Nevertheless, there is no agreement on it yet. On the one hand, most of the attention has been paid to AKI, and only a few studies have reported specifically on severe AKI, which was strongly associated with the development of adverse events and in-hospital mortality (8,15,28). Our results also found that severe AKI was associated with significantly higher in-hospital mortality and incidence of in-hospital adverse events, including longer duration of mechanical ventilation, higher incidence of major adverse outcomes, and more frequent use of RRT. On the other hand, TAR + FET with a long duration and complicated operation posed a high risk of periprocedural complications in ATAAD patients. Thus, we focused on severe AKI in ATAAD patients receiving TAR + FET. The main finding of our study was that advanced age, lower limb symptoms, coronary artery involvement, preoperative SCr, and prolonged CPB time are independent risk factors for severe AKI after TAR + FET for ATAAD. Among these, lower limb symptoms is an emerging risk factor. In clinical practice, identifying risk factors for severe postoperative AKI is meaningful to adjust or modify the treatment strategy.

Partly following these previous findings (7,9-12,18,19,28, 29,31,33,34), advanced age, preoperative SCr, and prolonged CPB time were also found to contribute to the development of severe AKI in our study. Elevated SCr indicated impaired kidney function (32). Moreover, the population in our study was younger than those conducted in Europe and North America, reflecting differences in demographics (7,10,26,35). The relatively low incidence of severe AKI and in-hospital mortality were considered to be related to the youth of our

subjects, extensive prior experience with this procedure, and meticulous perioperative management. In addition to surgical skills, high-volume centers also have greater experience with administering extracorporeal circulation, anesthetic, and intensive care. Our surgical team in TAR + FET procedure has a shorter CPB time, cross-clamp time, and hypothermic circulatory arrest time than other studies (26,36-38). Experience with this procedure may help to shorten CPB time and improve short-term outcomes (2).

Lower extremity ischemia was a risk factor for postoperative AKI in previous studies (10,39-43). Better renal and survival outcomes might be achieved with shorter lower body ischemic times. Moreover, spinal cord injury had also been demonstrated to play an important role in AKI (44,45). In our study, multivariate analysis showed preoperative lower limb symptoms were a risk factor for severe AKI. Limb ischemia or spinal cord injury might associate severe extension of the aortic dissection with renal malperfusion. We surmised that limb ischemia or spinal cord injury was the cause of lower limb symptoms, including pain, a decline of muscle strength, and sensory disturbances. In addition, it was likely that ischemia-reperfusion injury was an important pathophysiological change in severe AKI. The ischemia-reperfusion injury did not only affect the lower extremity but also the kidney, as a nearby organ (39). Rhabdomyolysis, which might be caused by ischemia-reperfusion injury, also might contribute to the development of severe AKI in previous studies (41,43,46). The results of this study confirmed the significant impact of lower limb symptoms on severe AKI for ATAAD patients receiving TAR + FET.

A previous study had correlated the risk of AKI with coronary artery involvement in patients with type A aortic dissection, which was confirmed through the results of multivariate analysis in this study (9). Based on Neri's classification (47), coronary ostium repair, coronary ostium reconstruction (the button technique), and CABG were performed in patients with coronary artery involvement. Our findings suggest that coronary artery involvement occurs in 20.9% of patients, similar to previous studies (9,48). These additional procedures required longer durations of operation, CPB time, and kidney ischemia time, which likely increases the risks of severe AKI. Moreover, even if there is no myocardial ischemia, it does not mean it will not occur. A few patients without myocardial ischemia might develop suspected myocardial ischemia during surgery preparation due to coronary malperfusion, which may be caused by low blood pressure. Acute worsening of cardiac function due to myocardial ischemia may lead to severe AKI, known as cardiorenal syndrome type 1 (49).

Limitations

This study has several potential limitations. First, it is a retrospective observational study. It is very difficult to conduct a randomized controlled trial for patients with ATAAD due to their urgent needs. Second, we used KDIGO as the diagnostic criteria for AKI, whereas some previous studies (7,20) used RIFLE or AKIN classification. This difference may be difficult to compare our results with previous research. Finally, we have not yet had access to long-term follow-up data. Therefore, we plan to conduct a further follow-up study on this topic.

Conclusions

There was a high incidence of severe AKI and high in-hospital mortality after TAR + FET in ATAAD patients. Based on our results, advanced age, lower limb symptoms, coronary artery involvement, preoperative SCr, and prolonged CPB time are the independent risk factors for severe AKI after TAR + FET in ATAAD patients. The risk factors for severe AKI in ATAAD patients undergoing TAR + FET were determined to help identify the high-risk patients and make rational treatment decisions.

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Footnote

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