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Analysis of Risk Factors for Acute Kidney Injury after Ascending Aortic Replacement Combined with Open Placement of Triple-Branched Stent Graft in Type A Aortic Dissection: A New Technique versus the Traditional Method in a Single Chinese Center

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Background: We aimed to analyze the risk factors and prognosis of acute kidney injury (AKI) after aortic arch repair in type A aortic dissection.

Material/Methods: We included 155 patients undergoing arch repair surgery for type A aortic dissection from January 2009 to January 2014 in our hospital. Ninety-three patients underwent ascending aortic replacement combined with open placement of triple-branched stent graft and 62 underwent arch replacement with 4-branched Dacron graft combined with stented elephant trunk implantation into the descending aorta. Univariate analysis and multiple logistic regression were performed to evaluate possible parameters associated with AKI according to the AKI Network (AKIN).

Results: Postoperative AKI occurred in 56 patients, with a morbidity of 36.13%. Advanced age (OR=2.32 per decade, 95% CI; range, 1.47–3.67); aortic arch replacement with 4-branched Dacron graft combined with stented elephant trunk implantation (OR=3.29, 95% CI; range, 1.12–9.67); cardiopulmonary bypass time >180 min (OR=3.91, 95% CI; range, 1.35–11.35) and packed red blood cells >10 U (OR=4.88, 95% CI; range, 2.03–11.76) were independent risk factors.

Conclusions: AKI is a complication after arch repair in type A aortic dissection. Advanced age; aortic arch replacement with 4-branched Dacron graft combined with stented elephant trunk implantation; cardiopulmonary bypass time >180 min; and packed red blood cells >10 U were independent risk factors for AKI. Ascending aortic replacement combined with open triple-branched stent graft placement could reduce the occurrence of AKI and protect renal function.

MeSH Keywords: **Acute Kidney Injury • Aneurysm, Dissecting • Aortic Aneurysm**

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Background

Acute kidney injury (AKI) is a common complication of cardiovascular surgery and occurs more easily in patients following surgical arch repair in aortic dissection. The incidence of AKI after aortic arch surgery has been reported to be higher than after other cardiac surgery [1,2]. Renal dysfunction leads to increased postoperative morbidity and mortality. Acute kidney injury also affects long-term mortality, especially for patients after aortic arch repair surgery [1].

The conventional surgery for acute Stanford type A aortic dissection is replacement of the ascending aorta [3,4]. However, the residual dissection still exists, and it has been proven to be an essential factor in the determination of prognosis [5,6]. Therefore, for patients in whom the dissection extends into the arch and descending thoracic aorta, extensive primary repair of the thoracic aorta is desirable. This study cohort includes only patients in whom the dissection extends into the arch and descending thoracic aorta and all patients needed to undergo arch repair surgery. Many previous studies demonstrated some risk factors of AKI after cardiac surgery or cardiothoracic surgery. However, there is little data regarding AKI after aortic arch repair surgery in aortic dissection. In this study, we analyzed the risk factors related to AKI occurrence and prognosis after surgical arch repair in type A aortic dissection using the AKIN criteria to improve the prognosis of patients with AKI after aortic arch repair surgery.

Material and Methods

Patient population

The Institutional Review Board of Union Hospital approved the study and waived the requirement for informed consent for the retrospective review of medical records. Patients with a history of chronic renal dysfunction of any stage were excluded because of the difficulty in measuring the progression of renal dysfunction. The preoperative renal function was defined by the estimated glomerular filtration rate, using the Chinese Modification of Diet in Renal Disease equation [7]. Patients who died within 24 h after surgery were also excluded because the cause of death in these patients was not related with renal dysfunction even if patients' serum creatinine level progressed.

A total of 155 patients underwent arch repair surgery in type A aortic dissection from January 2009 to January 2014. Patients were classified into 2 groups according to the type of surgery: ascending aorta replacement combined with open triple-branched stent graft placement or total arch replacement with 4-branched Dacron graft combined with stented elephant trunk

implantation into the descending aorta. Ninety-three patients with the following indications were selected for the open triple-branched stent graft placement technique [8]: (1) the intimal tear located in transverse arch or proximal descending aorta that could not be resected by hemiarch replacement, (2) serious involvement of the arch vessels, (3) Marfan syndrome. Another 62 patients with type A aortic dissection with arch or proximal descending aortic aneurysm, those with history of carotid artery disease, and those in which all 3 arch branch ostia could not be seen clearly from the arch true lumen, were selected for extensive repair of the thoracic aorta with the hybrid technique of Kato et al. [8–10]. There were 116 men and 39 women; the average age was 51.65 ± 8.65 years (range, 21–62 years); 132 cases had acute aortic dissection (incidence <2 weeks) and 23 cases had chronic aortic dissection (incidence >2 weeks). There were 110 cases with chronic hypertension, 86 patients had hypertension without effective control, and 23 cases with Marfan syndrome.

Operative procedure

Ascending aortic replacement combined with open triple-branched stent graft placement

Reconstruction of the aortic root was completed first. When the nasopharyngeal temperature dropped to 20°C, selective cerebral perfusion via the right axillary artery was established, and perfusion to the lower body was discontinued. Via a transverse incision into the ascending aorta, the main portion of the triple-branched stent graft was inserted into the true lumen of the arch and proximal descending aorta, and then each sidearm graft was positioned separately into the aortic branch. Finally, continuous end-to-end anastomosis to the 1-branched Dacron tube graft was performed to complete the surgery [8].

Ascending aortic replacement and total arch replacement with 4-branched Dacron graft combined with stented elephant trunk implantation into the descending aorta

Reconstruction of the aortic root was completed first. A stent graft and 4-branched prosthetic graft were used in the total arch replacement combined with stented elephant trunk implantation. When the nasopharyngeal temperature reached 20°C, circulatory arrest was established followed by selective cerebral perfusion. The stented elephant trunk was inserted into the true lumen of the descending thoracic aorta. The 4-branched prosthetic graft and the distal aorta containing the intraluminal stented graft were anastomosed using the open aortic technique. Following anastomosis, CPB was gradually resumed to normal flow, and rewarming was begun. The innominate and left common carotid and left subclavian arteries were anastomosed to the respective limbs of the 4-branched prosthetic graft in an end-to-end style. The prosthetic graft

Table 1. AKIN criteria for AKI staging adapted from Meta et al. [7].

Stage	Change in serum creatinine during the past 48h	Urinary output
Stage 1	Increase in serum creatinine of ≥ 26.4 $\mu\text{mol/L}$ or $\geq 150\%$ but $< 200\%$ of baseline creatinine	< 0.5 $\text{ml}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$ for > 12 h
Stage 2	Greater than 200% but less than 300% increase of baseline creatinine	< 0.5 $\text{ml}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$ for > 12 h
Stage 3	At least 300% increase in baseline serum creatinine, or serum creatinine ≥ 354 $\mu\text{mol/L}$ with acute rise of ≥ 44 $\mu\text{mol/L}$	< 0.3 $\text{ml}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$ *24 h or anuria*12 h

was anastomosed to the proximal aortic stump, which had already been reconstructed [9–11].

Definition and grouping of AKI

According to AKIN standards, acute kidney injury (AKI) is defined as increased serum creatinine (Scr) ≥ 26.4 $\mu\text{mol/L}$ within 48 h, or an increase $\geq 50\%$ compared with baseline; and/or urine output < 0.5 $\text{ml}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$ up to 6 h [12]. In this study, the preoperative Scr value was used as the baseline value. AKI was defined as AKI occurring within 7 days after cardiac surgery [13]. According to AKI staging criteria recommended by AKIN, AKI was staged and the results are shown in Table 1 [12]. Based on postoperative renal function, patients were divided into an AKI group ($n=56$), and a non-AKI group ($n=99$).

Variables and definitions

Preoperative variables included sex, age, preoperative serum creatinine, hyperuricemia, proteinuria, anemia, hypertension, diabetes mellitus, and acute aortic dissection. Hyperuricemia was defined as a serum uric acid > 6.6 in women and > 7.0 mg/dl in men. Proteinuria was defined as protein > 15 mg/dl in spot urine specimens. Hypertension was defined as SBP ≥ 140 mm Hg and/or DBP ≥ 90 mm Hg.

Intraoperative variables included operation time, cardiopulmonary bypass (CPB) time, aortic cross-clamp time, deep hypothermic circulatory arrest (DHCA) time, and surgery type.

Postoperative variables included hypotension, use of metformin, use of ACEI/ARB, pneumonia, central venous pressure (CVP), and need for more than 10 units of packed red blood cells (pRBCs) intraoperatively and/or postoperatively, but before the diagnosis of AKI. Hypotension was defined as SBP < 90 mm Hg. CVP was recorded as an average value of CVP after surgery but before the diagnosis of AKI.

Statistical analysis

We used SPSS version 11.5 for Windows software for all statistical analyses (SPSS Inc., Chicago, IL, USA). Continuous variables

are expressed as mean $\pm$ SD and analyzed using the unpaired student's *t* test. Nonparametric variables are expressed as median and 25–75% percentiles and analyzed using the Mann-Whitney test. Categorical variables were analyzed using the chi-square test. A multivariate logistic regression model incorporating all factors showing a univariate *P* value < 0.05 was performed to identify risk factors associated with AKI. Risk data are presented as odds or hazard ratios with 95% CIs. *P* < 0.05 was considered statistically significant for all comparisons.

Results

A total of 155 patients were included after the exclusion of 5 patients (4 history of chronic renal dysfunction, 1 death within 24 h after surgery). Of these, 56 (36.13%) had an episode of AKI during hospitalization: 31 (20%) were stage 1; 19 (12%) were stage 2; and 6 (4%) were stage 3. Only 10 of the patients with AKI required any renal replacement therapy (RRT); 20 had partial renal recovery and 31 had complete renal recovery at the time of hospital discharge. The incidence of AKI was not different between patients with acute dissection and those with chronic dissection. Total 30-day mortality was 4.52% ($n=7$). In the group with AKI, 30-day mortality was 10.71% ($n=6$) versus 1.01% ($n=1$) in the group without AKI (*P* < 0.05) (Table 2).

Demographic and operative variables according to AKI grades are shown in Table 2. Significant differences between the 2 groups were detected for the following variables: age, surgery time, CPB time, aortic cross-clamp time, DHCA time, type of surgery, and pRBCs.

Demographic and operative variables according to type of arch repair surgery are shown in Table 3. The 2 types of surgery differed in surgery time, CPB time, aortic cross-clamp time, DHCA time, and pRBCs.

In univariate analysis, the groups with and without AKI differed in age; serum creatinine > 106 $\mu\text{mol/L}$; total arch replacement combined with stented elephant trunk implantation surgery; surgery time; CPB time > 180 min; and pRBCs > 10 units (Table 4). Multivariate logistic regression analysis identified 4

Table 2. Patient characteristics grouped according to AKI status.

Index	Non-AKI group (n=99)	AKI group (n=56)			P value
		Stage 1 (n=31)	Stage 2 (n=19)	Stage 3 (n=6)	
Preoperative variables					
Male, n	70 (71%)	25 (81%)	15 (79%)	6 (100%)	0.12
Age, years	46.13±9.21	52.45±11.54	57.16±9.58	56.17±8.33	<0.0001
Acute aortic dissection, n	87 (88%)	25 (81%)	17 (89%)	3 (50%)	0.61
Hypertension, n	66 (67%)	23 (74%)	16 (84%)	5 (83%)	0.12
Diabetes mellitus, n	8 (8%)	3 (10%)	2 (11%)	0	0.86
Anemia, n	4 (4%)	3 (10%)	2 (11%)	1 (17%)	0.20
Serum creatinine, umol/l	99.52±27.04	113.10±36.84	93.74±16.50	115.50±17.90	0.14
Intraoperative variables					
Surgery time, h	7.92±1.22	8.68±1.08	9.89±3.06	12.33±4.08	<0.001
CPB time, min	174.06±29.98	207.17±38.76	206.72±41.17	216.48±37.12	<0.01
Aortic cross-clamp time, min	98.91±32.69	108.17±37.41	113.17±37.12	114.48±47.23	0.02
DHCA, min	20.34±2.06	20.84±2.16	20.89±1.56	21.50±2.43	0.087
Open placement of triple-branched stent graft surgery, n	76 (77%)	13 (42%)	3 (16%)	1 (17%)	<0.001
Stented elephant trunk implantation surgery, n	23 (23%)	18 (58%)	16 (84%)	5 (83%)	<0.001
Postoperative variables					
Total pRBCs, U	8.91±2.24	12.77±3.85	10.74±3.63	13.67±4.08	<0.01
Hypotension,n	2 (2%)	4 (13%)	2 (11%)	2 (33%)	<0.01
Use of metformin, n	3 (3%)	1 (3%)	1 (5%)	0	0.93
Use of ACEI/ARB, n	17 (17%)	4 (13%)	2 (11%)	1 (7%)	0.87
CVP <6 cm H ₂ O, n	3 (3%)	4 (13%)	3 (16%)	1 (17%)	0.02
Pulmonary infection, n	18 (18%)	6 (19%)	4 (21%)	2 (33%)	0.15
30-day mortality, n	1 (1%)	3 (10%)	1 (5%)	2 (33%)	<0.01

independent risk factors for AKI: age (per 10 y, OR=2.32, 95% CI; range, 1.47–3.68); total arch replacement with 4-branched Dacron graft combined with stented elephant trunk implantation surgery (OR=3.29, 95% CI; range, 1.12–9.67); CPB time >180 min (OR=3.92, 95% CI; range, 1.35–11.35); and pRBCs greater than 10 units (OR=4.89, 95% CI; range, 2.03–11.76) (Table 5).

Discussion

AKI is a common complication of cardiac surgery, and the reported incidence differs due to the use of different AKI

definitions. Currently, the most common AKI criteria are the RIFLE criteria defined by the Acute Dialysis Quality Initiative Workgroup and the criteria defined by the AKI network. In this retrospective analysis of 155 arch repair surgery patients, we evaluated the prevalence and risk factors for AKI defined by the AKIN consensus definition. The incidence of AKI following arch repair surgery in type A aortic dissection was 36% in our study, which is marginally higher than the 5–30% previously reported [13–16]. This finding was not unexpected because both aortic surgery and DHCA are known to be independent risk factors for renal dysfunction. This study focused on total arch repair surgery in type A aortic dissection. Because of the

Table 3. Clinical data on the 2 types of arch repair surgery.

Index	Group with open placement of triple-branched stent graft (n=93)	Group with stented elephant trunk implantation (n=62)	P value
Preoperative variables			
Male, n	71 (76%)	45 (73%)	0.60
Age, years	48.02±10.63	50.81±10.22	0.11
Acute aortic dissection, n	78 (88%)	54 (82)	0.36
Hypertension, n	64 (69%)	46 (74%)	0.28
Diabetes mellitus, n	5 (5%)	8 (13%)	0.14
Proteinuria, n	2 (2%)	5 (8%)	0.12
Hyperuricemia, n	32 (34%)	16 (10%)	0.20
Anemia, n	4 (4%)	6 (10%)	0.20
Serum creatinine, umol/l	104.69±28.65	98.32±28.25	0.17
Intraoperative variables			
Surgery time, h	7.81±1.24	9.50±2.38	<0.01
CPB time, min	152.59±56.63	192.26±63.71	<0.01
Aortic cross-clamp time, min	92.45±20.40	118.19±36.77	0.02
DHCA, min	20.09±1.99	21.26±1.94	0.01
Postoperative variables			
Total pRBCs, U	9.23±2.61	11.39±3.64	0.01
Hypotension, n	3 (3%)	7 (11%)	<0.01
Use of metformin, n	2 (2%)	2 (3%)	1.00
Use of ACEI/ARB, n	10 (11%)	14 (23%)	0.07
Pulmonary infection, n	10 (11%)	20 (32%)	<0.01
CVP <6 cm H ₂ O, n	2 (2%)	9 (15%)	<0.01
Neurological complications	2 (2%)	2 (3%)	1.00

Table 4. Univariate analysis of risk factors for AKI.

Index	OR	95% CI	P value
Age (per 10 y)	1.37	1.19–1.59	<0.001
Serum creatinine >106 umol/L	1.02	1.00–1.05	0.03
Stented elephant trunk implantation surgery	7.58	3.63–15.82	<0.0001
Surgery time (per 1 h)	1.91	1.16–3.15	0.01
CPB time >180 min	4.03	1.06–39.05	0.001
pRBCs >10 Units	6.12	2.97–12.58	<0.0001

Table 5. Multivariate analysis of risk factors for AKI.

Index	OR	95% CI	P value
Age (per 10 y)	2.32	1.47–3.68	<0.0001
Stented elephant trunk implantation surgery	3.29	1.12–9.67	0.03
CPB time >180 min	3.92	1.35–11.35	0.01
pRBCs > 10 Units	4.89	2.03–11.76	<0.0001

rapid progression of Stanford type A aortic dissection, emergent surgery is recommended once it is diagnosed. However, surgery time and CPB time are relatively long, increasing concerns regarding brain and kidney protection and with postoperative AKI occurring more easily.

Thirty-day mortality in patients with AKI was 11%, which was higher than the previous study reported by Roh et al. (9%) [17]. The reason may be that this study focused on AKI after aortic arch repair surgery, which is more complex than cardiac surgery or thoracic aortic surgery. Some previous studies have reported that AKI after cardiac surgery worsens 30- or 90-day mortality, and even 10-year mortality [1,2,18]. The current study also had demonstrated that 30-day mortality of AKI patients was significantly higher than in the non-KI group (11% vs. 1%, Table 2). Therefore, early identification of risk factors of AKI after aortic arch repair surgery and preventing postoperative AKI are important in improving prognosis.

The logistic regression model identified age, CPB time >180 min, and pRBCs >10 units as independent risk factors for AKI, matching the findings of earlier reports [17,19,20]. The AKI incidence increased with increasing age, and Bahar et al. [21] reported that the degree of risk for postoperative AKI increased by 1.243 for every 10 years of increasing age. Englberger et al. [22] reported that the degree of risk was 1.46, with the risk increasing 1.21-fold for every 10 years of increased age.

Preoperative basic renal function and postoperative AKI were also closely related. Any preoperative impaired renal function would decrease the kidney ischemic tolerance, with surgery causing uneven postoperative distribution of renal blood flow and increased renal vascular resistance. In the univariate analysis of risk factors, baseline serum creatinine was higher in patients that developed AKI; however, baseline serum creatinine has not always been identified as an independent risk factor for AKI after aortic arch repair surgery in aortic dissection. Therefore, the results of this study suggest that baseline serum creatinine may be less important than other risk factors, such as age.

Interestingly, we found that traditional total arch replacement with 4-branched Dacron graft combined with stented elephant

trunk implantation surgery was an independent risk factor for AKI. In our cohort, 2 types of surgery were used to reconstruct the aortic arch: traditional total arch replacement with 4-branched Dacron graft combined with stented elephant trunk implantation surgery [9–11], and ascending aortic replacement combined with open placement of triple-branched stent graft to simplify the aortic arch reconstruction in type A aortic dissection [8]. We found that the AKI occurring in the group undergoing the simplified surgery was significantly less than in the group receiving the traditional surgery. The risk of postoperative AKI in patients receiving traditional surgery was increased by 3.29-fold, while the simplified surgery was not an independent risk factor. Compared with the traditional surgery, the simplified surgery had a lower surgery time, aortic cross-clamp time, DHCA time, and CPB time (Table 3), and patients therefore recovered renal perfusion earlier. Comparing the 2 surgeries, we knew that in the simplified surgery, anastomoses to 3-arch vessels were avoided, there was only 2 anastomosis, and shorter total surgery time contributed to the quick recovery of patients.

The results also showed that CPB time >180 min was an independent risk factor for AKI, which was demonstrated previously [17,20]. Studies by Roh [17] showed that the degree of risk for acute renal insufficiency in patients with CPB time >180 min was 4-fold that of patients with CPB time <120 min. In addition, patients experienced acidosis and renal ischemia more readily and had both a longer low perfusion time and a more remarkable glomerular filtration rate reduction. Therefore, in patients with type A aortic dissection, choosing the simplified surgery could shorten the surgery time and CPB time, better protect renal function, and reduce the incidence of postoperative AKI.

Total pRBCs >5 units was found by Mangano [20] et al. to be independently associated with renal dysfunction. In our study, pRBCs >10U was an independent risk factor for postoperative AKI. There is no direct causality between blood transfusion and renal dysfunction in the literature; however, there is evidence from a nonrandomized trial that increased RBC transfusion can worsen morbidity and mortality rates in a population of patients undergoing isolated coronary artery bypass grafting. Postulated explanations for the adverse outcomes related to transfusion include proinflammatory end-organ damage and an adverse immunomodulatory effect on T-cell function [23],

suggesting it is best to reduce pRBCs transfusions. Total arch repair surgery is complex and technically difficult with numerous vascular anastomoses and many opportunities for bleeding and necessitating large amounts of intraoperative and postoperative pRBC transfusions. Transfusion-related kidney injury was an independent AKI risk factor after cardiac surgery and was also a cause of increased 30-day mortality. There were only 2 anastomoses in the simplified surgery, which is much less than with the traditional surgery, and because both the chances of bleeding and blood transfusions were reduced, the incidence of AKI was also reduced.

This study had some limitations. First, this retrospective study with relatively small sample size had insufficient statistical power. However, there is scant data on AKI collected from such a homogeneous group of all patients undergoing aortic arch

repair in type A aortic dissection. Second, we selected an aggressive procedure to repair the aortic arch, which is employed in a just a few cardiac centers. However, this new technology has true advantage in shortening surgery time and reducing postoperative bleeding.

Conclusions

We found the AKIN criteria to be a useful classification system for renal failure in patients undergoing aortic arch repair in aortic dissection. Advanced age; total arch replacement combined with stented elephant trunk implantation surgery; CPB time >180 min; and pRBCs >10 units were risk factors for AKI. Future clinical trials are needed to determine whether preventative strategies can reduce AKI after aortic arch repair surgery.

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