Original Article

Risk Factors and Outcomes of Acute Kidney Injury after Type A Aortic Dissection Surgery at A Tertiary Care Hospital

Thavat Chanchayanon, M.D., Jutarat Tanasansuttiporn, M.D., Garnphipak Heerungeeragon, M.D., Maliwan Oofuwong, M.D., Ph.D.

Department of Anesthesiology, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkla 90110, Thailand.

Abstract:

Objective: This study aimed to determine the risk factors predisposing to postoperative acute kidney injury (AKI) after type A aortic dissection repair; regarding patient-related, surgery-related and anesthesia-related factors.

Material and Methods: A retrospective cohort study was conducted in patients who underwent type A aortic dissection repair under cardiopulmonary bypass (CPB), during the periods from January 2008 and December 2019. Patient-related, surgery-related and anesthesia-related factors were evaluated for association with AKI. AKI was defined by the Kidney Disease: Improving Global Outcomes criteria. The outcomes and mortality of AKI were also investigated.

Results: Included were 95 patients, and the incidence of AKI was 65.3%. The 30-day mortality resulted only in the AKI group (14.9%). From multivariate logistic regression analysis, receiving intraoperative cryoprecipitate (odd ratio; OR 14.18; 95% confidence interval (CI), 3.27-61.5) and PRC transfusion (OR 1.001; 95% CI, 1.0005-1.002) in ICU were the risk factors for AKI. The protective factors were: higher preoperative serum bicarbonate levels (OR 0.83; 95% CI, 0.70-0.99), higher volume of urine output during CPB (OR 0.71; 95% CI, 0.55-0.91) and higher immediate postoperative mean arterial pressure (OR 0.95; 95% CI, 0.92-0.98). Thirty-day mortality was significantly higher in the AKI group (14.5% vs 0%; p-value=0.025), and 15.0% of patients required renal replacement therapy.

Conclusion: The higher level of three factors including preoperative serum bicarbonate levels (>23 mmol/l), volume of urine output during CPB and immediate postoperative mean arterial pressure (>81 mmHg) are likely to be the protective factors of AKI.

Keywords: acute kidney injury, aortic dissection surgery, risk factor

Contact: Jutarat Tanasansuttiporn, M.D.
Department of Anesthesiology, Faculty of Medicine, Prince of Songkla University,
Hat Yai, Songkhla 90110, Thailand.
E-mail: takiangjutarat@gmail.com

Introduction

Acute kidney injury (AKI) is a major and morbid complication after type A aortic dissection surgery. It increases mortality, progression of chronic kidney disease (CKD), renal replacement therapy (RRT) and cost.[1,2] Incidence of AKI after type A aortic dissection surgery has been reported to be higher than any other cardiac surgery. Numerous pathophysiologies of AKI in cardiac settings; including, complexity of diseases, hemodynamic changes during the procedure and surgical correction of type A aortic dissection in a high-risk operation are mentioned. The mechanisms of cardiac surgery related to AKI include perioperative renal ischemia, reperfusion injury, cardiopulmonary bypass induced hemolysis, oxidative stress and inflammation.[3] Atheroemboli to the kidney can occur after aortic cannulation and cross clamping, that further potentiate ischemia and inflammation.[4,5]

A number of previous studies have evaluated risk factors associated with postoperative AKI; in aspects of patient-related and surgical-related factors.[4,6–8] However, few studies have paid attention to anesthetic-related factors.[9–11] Hence, this study is dedicated to examine the risk factors predisposing to postoperative acute kidney injury; regarding patient-related, surgery-related and anesthesia-related factors in type A aortic dissection repair.

Material and Methods

The study was approved by the Human Research Ethic Committee of the faculty of Medicine, Prince of Songkla University. A retrospective cohort study was conducted and reviewed patients who underwent type A aortic dissection repair; between 2008 and 2019, at Songklanagarind Hospital, a tertiary care hospital in southern Thailand. Patients who had preexisting end stage renal disease (glomerular filtration rate <15 mL/min/1.73 m^2), preoperative dialysis or died in the operating room were excluded. AKI was defined by Kidney Disease: Improving Global Outcomes (KDIGO) classification was proven to be a more predictive tool with excellent prognostic abilities, than Risk Injury Failure Loss of kidney function and End-stage kidney disease (RIFLE) criteria.[12] KDIGO classification can be classified into 3 categories: stage 1 happens when an increase of serum creatinine (sCr) goes beyond its baseline level by 1.5 times. Once it becomes 2 times higher than baseline, it reaches stage 2. Stage 3 can be detected if sCr increases by 3 times over baseline, or upon initiation of RRT. The variables collected were categorized into patient-related, surgical-related and anesthesia-related risk factors. The patient-related risk factors; including, demographic characteristics, co-existing disease, medications, preoperative laboratory results, preoperative hemodynamic data and aortic dissection related complications were obtained. Types of operation and surgical techniques were reviewed from representative surgeons. The cardiopulmonary bypass (CPB) time and aortic cross clamp time were collected from the perfusionist recorded data. Anesthetic details, consisting of: American Society of Anesthesiologist (ASA) classification, colloids, blood components, urine output, blood sugar, hemodynamic data and medication for hemodynamic support, were reviewed. Intraoperatively, blood transfusion protocols are decided by the anesthesiologist with the blood product being in a 1:1:1 ratio of PRC:FFP:Platelets are administered. If the surgical site still continues bleeding or oozing after administering the blood transfusion protocol, cryoprecipitate will be administered. Postoperative outcomes and complication data were taken from the intensive care unit (ICU) admissions and progress notes. Immediate postoperative mean arterial pressure was defined as: the mean arterial pressure being initially recorded within 15 minutes after the patient was transferred to the intensive care unit. Outcome of interest was acute kidney injury defined by KDIGO and the factors affecting AKI were divided into patient-related, surgical-related and anesthesia-related factors.

The sample size was calculated using binary data Formula of Cohort study. A probability of outcome occurring in the AKI group was 0.1 and the non–AKI group was 0.3613. A total of 108 patients were required. After patients were separated into AKI group and non–AKI groups, by KDIGO criteria, preoperative and intraoperative factors were analyzed to determine their relevance to the possible factors for AKI. Continuous values were numerically presented as mean (standard deviation), or median (interquartile range). Categorical values were demonstrated as percentage of frequency. Univariate analysis, with chi–squared test or Fisher's exact test for categorical variables along with Kruskal–Wallis test for continuous variables was applied in order to compare the baseline characteristics of the patients among the study sites. Only those variables for which the p–value<0.050 were considered for potential factors. After which, multivariate stepwise logistic regression analysis was used to identify independent risk factors of AKI; presented by odds ratio (OR) and 95% confidence interval (CI). The outcomes and mortality of AKI were also investigated. R statistics version 3.6.2 was used for all statistical analysis.

Results

A total of 95 patients were included, after exclusion criteria were applied, as Figure 1. AKI developed in 62 of the 95 patients. Among those with AKI, 32 patients (51.6%) were in stage 1, 14 (22.6%) in stage 2 and 16 (25.8%) in stage 3.
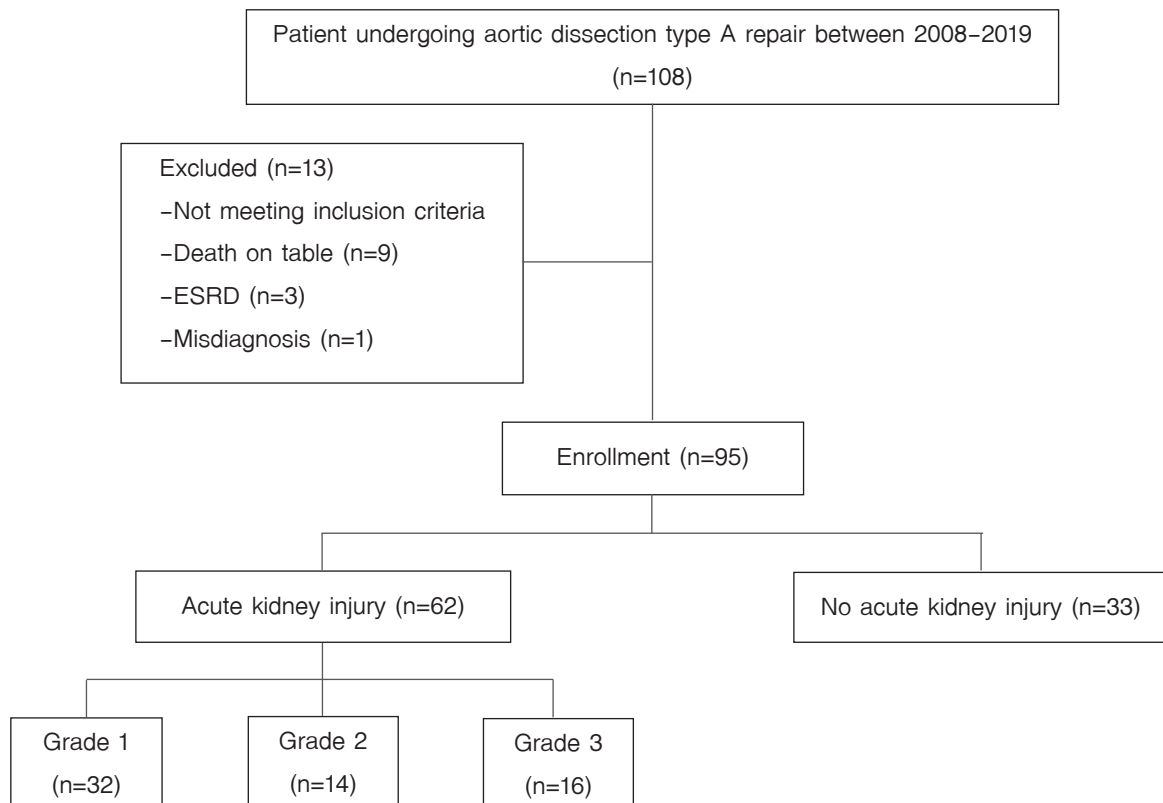
ESRD=end stage renal desease

Figure 1 Flow of the study and participate enrollment

Demographic data and clinical characteristics data are demonstrated in Table 1. From univariate analysis, the AKI group had slightly higher preoperative blood urea nitrogen (BUN) and serum creatinine (sCr) levels in addition tolower levels of serum bicarbonate than patients without AKI. There were no significant differences between the two groups in terms of demographic characteristics, co-existing diseases, medications and disease-related complications. Diastolic blood pressure (DBP) tended to be higher in the AKI group; p-value=0.035. In addition, partial time (PT) and

international normalized ratio (INR) were also higher in the AKI group (p-value=0.003, p-value=0.002, respectively).

The surgery and CPB related factors are shown in Table 2. The volume of urine output during CPB was significantly higher in the non-AKI group (p-value=0.001). The lowest hematocrit during CPB was higher in the non-AKI group (p-value=0.029). In the intensive care unit, total blood loss in the AKI group was greater than in the non-AKI group (p-value=0.039), and the requirement of blood component transfusion; including, PRC (pack red

Table 1 Demographic data and clinical characteristics among postoperative patients with and without acute kidney injury

Factors	AKI (n=62)	No AKI (n=33)	p-value
Demographics			
Age (years), mean (S.D.)	54.9 (12.8)	51.6 (12.3)	0.231
Gender			
Male	45 (72.6)	18 (54.5)	0.123
Female	17 (27.4)	15 (45.5)	
BMI, kg/m^2			
<30	55 (90.2)	32 (97.0)	0.415
≥30	6 (9.8)	1 (3.0)	
Co-existing disease			
Diabetes mellitus	5 (8.1)	3 (9.1)	1.000
Hypertension	36 (58.1)	19 (57.6)	1.000
Chronic kidney disease	10 (16.1)	2 (6.1)	0.206
Peripheral arterial disease	2 (3.2)	1 (3.0)	1.000
Cerebrovascular accident	3 (4.8)	1 (3.0)	1.000
Chronic heart failure	2 (3.2)	0 (0.0)	0.542
Chronic obstructive pulmonary disease	3 (4.8)	0 (0.0)	0.549
Anemia	26 (41.9)	16 (48.5)	0.693
Smoking	13 (21.0)	4 (12.1)	0.430
Current medications			
Aspirin	23 (37.1)	9 (27.3)	0.461
Metformin	0 (0.0)	1 (3.0)	0.347
ACEI/ARBs	12 (19.7)	9 (27.3)	0.531
Diuretics	4 (6.5)	4 (12.1)	0.443
Statins	9 (14.5)	5 (15.2)	1.000
Laboratory data at admission			
BUN (mg%), mean (S.D.)	19.1 (7.4)	15.6 (5.9)	0.019
Creatinine (mg%), median (IQR)	1.2 (0.9, 1.7)	1.0 (0.8, 1.2)	0.031
Sodium (mmol/l), mean (S.D.)	138.4 (4.1)	137.6 (4.7)	0.402
Potassium (mmol/l), median (IQR)	4.0 (3.7, 4.4)	3.8 (3.5, 4.2)	0.161
HCO$_3$ (mmol/l), median (IQR)	21.0 (18.0, 23.0)	23.0 (21.0, 25.0)	0.040
Albumin (g%), mean (S.D.)	3.8 (0.5)	3.7 (0.5)	0.354
Platelet (*10^9/l), median (IQR)	204.5 (150.7, 258.5)	206.0 (161.0, 255.0)	0.702
Prothrombin time (seconds), median (IQR)	13.6 (12.2, 14.7)	12.3 (11.9, 13.5)	0.003
Partial thromboplastin time (seconds), median (IQR)	28.0 (25.7, 30.9)	26.8 (25.7, 28.9)	0.320
INR, median (IQR)	1.2 (1.1, 1.3)	1.1 (1.0, 1.1)	0.002

Table 1 (continued)

Factors	AKI (n=62)	No AKI (n=33)	p-value
Preoperative hemodynamic data			
Systolic blood pressure (mmHg), mean (S.D.)	126.8 (26.2)	127.5 (18.3)	0.905
Diastolic blood pressure (mmHg), mean (S.D.)	71.5 (16.6)	64.4 (13.4)	0.035
Mean arterial pressure (mmHg), mean (S.D.)	90.0 (17.3)	85.4 (12.6)	0.183
Heart rate (bpm), mean (S.D.)	87.8 (19.6)	81.5 (17.8)	0.125
Use of inotropic drug	11 (17.7)	4 (12.1)	0.675
Use of vasodilator	9 (14.5)	3 (9.1)	0.533
Use of calcium channel blocker	32 (51.6)	19 (57.6)	0.735
Disease-related complication			
Renal involvement			
Unilateral involvement	17 (73.9)	9 (100)	0.150
Bilateral involvement	6 (26.1)	0 (0.0)	
AKI malperfusion syndrome	25 (73.5)	5 (55.6)	0.417
Cardiac tamponade	8 (12.9)	1 (3.0)	0.156
Coronary dissection	3 (4.8)	2 (6.1)	1.000
Aortic regurgitation	15 (24.2)	11 (33.3)	0.478

Data are presented as number (%), unless indicated otherwise
IQR=interquartile range, S.D.=standard deviation, BMI=body mass index, ACEI=angiotensin-converting enzyme inhibitors, ARBs=angiotensin II receptor blockers, BUN=blood urea nitrogen, HCO_3=bicarbonate, AST=aspartate aminotransferase, ALT=Alanine aminotransferase, ALP=alkaline phosphatase, s=second, INR=international normalized ratio, bpm=beats per minute, AKI=acute kidney injury

Table 2 Surgery-related factors and cardiopulmonary bypass-related factors among postoperative patients with and without acute kidney injury

Factors	AKI (n=62)	No AKI (n=33)	p-value
Operation			
Ascending aortic replacement	50 (80.6)	27 (81.8)	0.677
Aortic arch replacement	10 (16.1)	4 (12.1)	
Ascending + aortic arch replacement	2 (3.2)	2 (6.1)	
Additional operation			
Valve replacement	9 (14.5)	9 (27.3)	0.217
Coronary artery bypass graft	2 (3.2)	2 (6.1)	0.608
Cardiopulmonary bypass time (min), median (IQR)	240.5 (187.5, 303.8)	239.0 (215.0, 267.0)	0.659
Aortic cross clamp time (min), median (IQR)	98.0 (73.0, 144.0)	101.0 (63.0, 135.0)	0.680
Technique			
Moderate hypothermia circulatory arrest (min), median (IQR)	41.0 (30.5, 55.2)	57.0 (51.0, 72.5)	0.194
Deep circulatory arrest time (min), median (IQR)	44.5 (40.0, 53.2)	48.0 (38.8, 56.5)	0.383
During Cardiopulmonary bypass			
Volume of urine output (ml/kg/hr), median (IQR)	1.5 (0.7, 2.4)	2.7 (1.6, 3.8)	0.001
<0.5	9 (14.5)	0 (0.0)	0.025
≥0.5	53 (85.5)	33 (100)	
Lowest Hematocrit, mean (S.D.)	22.4 (3.7)	24.3 (4.3)	0.029
Lowest Mean arterial pressure (mmHg), median (IQR)	40.0 (40.0, 50.0)	40.0 (40.0, 50.0)	0.756
Blood component in ICU, median (IQR)			
PRC (ml)	1,542 (936.0, 2,219.0)	736 (542.0, 1,365.0)	<0.001
FFP (ml)	1,045 (541.5, 1,718.0)	543 (0.0, 1,054.0)	0.001
Platelet concentration (ml)	410 (289.5, 727.5)	0 (0.0, 388.0)	0.001
Cryoprecipitate (ml)	0 (0.0, 50.0)	0 (0.0, 0.0)	<0.001
Total blood loss in ICU (ml)	1,915 (1,042.5, 3,152.5)	1,400 (850.0, 2,500.0)	0.039

Data are presented as number (%), unless indicated otherwise
IQR=interquartile range, S.D.=standard deviation, PRC=pack red cell, FFP=fresh frozen plasma, AKI=acute kidney injury

cell), fresh frozen plasma (FFP), platelet concentration and cryoprecipitate in the AKI group was higher than in the non-AKI group (p-value<0.001, p-value=0.001, p-value=0.001, p-value<0.0001, respectively). There was no significant different between the two groups in terms of types of operation, techniques, CPB time and aortic cross clamp time.

Anesthesia-related and intraoperative factors are shown in Table 3. Higher volumes of FFP were administered in the AKI group (p-value=0.007). The use of cryoprecipitate was also significantly higher in the AKI group (p-value= 0.004). Systolic blood pressure (SBP), DBP and immediate mean arterial pressure (MAP) at the ICU were significantly higher in patients without AKI (SBP 109.9 (22.4) mmHg versus 123.4 (23.0) mmHg, p-value=0.007, DBP 57.9 (10.7) mmHg versus 65.3 (11.3) mmHg, p-value=0.002, MAP 75 (13.3) mmHg versus 84.2 (14.6) mmHg p-value=0.002). There were no significant differences between the two groups regarding; ASA classification, fresh gas flow, colloid and medication for hemodynamic support.

Table 3 Anesthesia-related and intraoperative-related factors among postoperative patients with and without acute kidney injury

Factors	AKI (n=62)	No AKI (n=33)	p-value
ASA classification			
3E	20 (32.2)	12 (36.4)	0.922
4E	38 (61.3)	19 (57.6)	
5E	4 (6.5)	2 (6.1)	
Dexamethasone	59 (95.2)	32 (100)	0.549
Fresh gas flow during use sevoflurane			
<2 LPM	43 (69.4)	23 (69.7)	1.000
≥2 LPM	19 (30.6)	10 (30.3)	
During cardiopulmonary bypass			
Mean blood sugar (mg/dl), median (IQR)	191.0 (155.0, 267.0)	220.0 (200.5, 271.5)	0.238
Vasopressor infusion during CPB	28 (45.2)	15 (45.5)	1.000
Colloid			
Use of gelofusine	6 (9.7)	1 (3.0)	0.415
Use of voluven	7 (11.3)	2 (6.1)	0.489
Blood component			
PRC (ml), median (IQR)	829.0 (583.0, 1,293.0)	1,000.0 (710.5, 1,341.5)	0.514
FFP (ml), median (IQR)	1,080.0 (1,015.0, 1,680.0)	1,020.0 (850.0, 1,073.0)	0.007
Platelet concentration (ml), median (IQR)	518.0 (351.2, 613.8)	383.0 (344.8, 605.0)	0.416
Use of cryoprecipitate	27 (43.5)	4 (12.1)	0.004
Medication for hemodynamic support after separation CPB			
Use of inotrope	45 (72.6)	25 (75.8)	0.928
Use of vasodilator	15 (24.2)	7 (21.2)	0.942
Use of calcium channel blocker	5 (8.1)	5 (15.2)	0.309
Hemodynamic data after transfer to ICU, mean (S.D.)			
Systolic blood pressure (mmHg)	109.9 (22.4)	123.4 (23)	0.007
Diastolic blood pressure (mmHg)	57.9 (10.7)	65.3 (11.3)	0.002
Mean arterial pressure (mmHg)	75.0 (13.3)	84.2 (14.6)	0.002
Heart rate (beat per minute)	96.7 (22.3)	90.9 (18.2)	0.204

Data are presented as number (%), unless indicated otherwise

IQR=interquartile range, S.D.=standard deviation, ASA=American Society of Anesthesiologist, LPM=liter per minute, PRC=pack red cell, FFP=fresh frozen plasma, CPB=cardiopulmonary bypass

Univariate analysis was used first to identify possible risk factors for AKI, as above, and then the multivariate model was used to include variables that were significant in univariate analysis. The results of multivariate logistic analysis of significant risk factors are shown in Table 4. Preoperative elevated serum bicarbonate levels (OR 0.83; 95% CI, 0.70, 0.99), higher volume of urine output during CPB (OR 0.71; 95% CI, 0.55, 0.91) and higher postoperative MAP (OR 0.95; 95% CI, 0.92, 0.98) were likely to be protective factors of AKI. In contrast, administration of intraoperative cryoprecipitate (OR 14.18; 95% CI, 3.27, 61.5) and receiving PRC transfusion in the ICU (OR 1.001; 95% CI, 1.0005, 1.002) tended to be a risk factor for AKI. The final model is illustrated in Figure 2. The area under the receiver operating characteristic (ROC) curves was 0.88, sensitivity 80.7% (95% CI, 68.6–89.6%), specificity 84.9% (95% CI, 68.1–94.9%); confirming the power of the best model for predictor risk factors of AKI.

The 30-day mortality occurred only in the AKI group (14.5% vs 0, p-value=0.025). Renal replacement therapy was required in 9 (14.5%) AKI patients. There was a significantly higher duration of intensive care unit stay (7 days [4, 10] versus 4 days [2, 6], p-value=0.003) in the AKI group. Postoperative outcomes are shown in Table 5.

Discussion

This retrospective study examined the risk factors and outcomes of AKI, following type A aortic dissection regarding patient-related, surgical-related and anesthetic-related factors. AKI was diagnosed by the KDIGO criteria[12], which is a more predictive tool for mortality, and has a higher incidence of AKI diagnosed than RIFLE criteria. Incidence of AKI in our study was 65.3% (62/95), which was higher than previous reports using RIFLE criteria[6,13–15] and 15.0% of patients required RRT. The 30-day mortality rate was 14.5% in the AKI group. There was a significant

Table 4 Multivariate analysis of risk factors and protective factors for acute kidney injury

| Factors	Odds ratio [OR] (95%CI)	p-value
Preoperative serum bicarbonate level	0.83 (0.70, 0.99)	0.037
Volume of urine output during CPB	0.71 (0.55, 0.91)	0.044
Use of Cryoprecipitate	14.18 (3.27, 61.50)	<0.001
MAP after transfer to ICU	0.95 (0.92, 0.98)	0.047
PRC transfused in ICU	1.001 (1.0005, 1.002)	<0.001

CPB=cardiopulmonary bypass, MAP=mean arterial pressure, PRC=pack red cell, ICU=intensive care unit

Table 5 Postoperative outcomes and complication

Outcomes	AKI (n=62)	No AKI (n=33)	p-value
30 days mortality	9 (14.5)	0	0.025
ICU stay (days), median (IQR)	7 (4.0, 10.0)	4 (2.0, 6.0)	0.003
Renal replacement therapy	9 (14.5)	0	0.025
CKD progression	4 (6.5)	0	0.365

Data are presented as number (%), unless indicated otherwise
IQR=interquartile range, ICU=intensive care unit, CKD=chronic kidney disease.
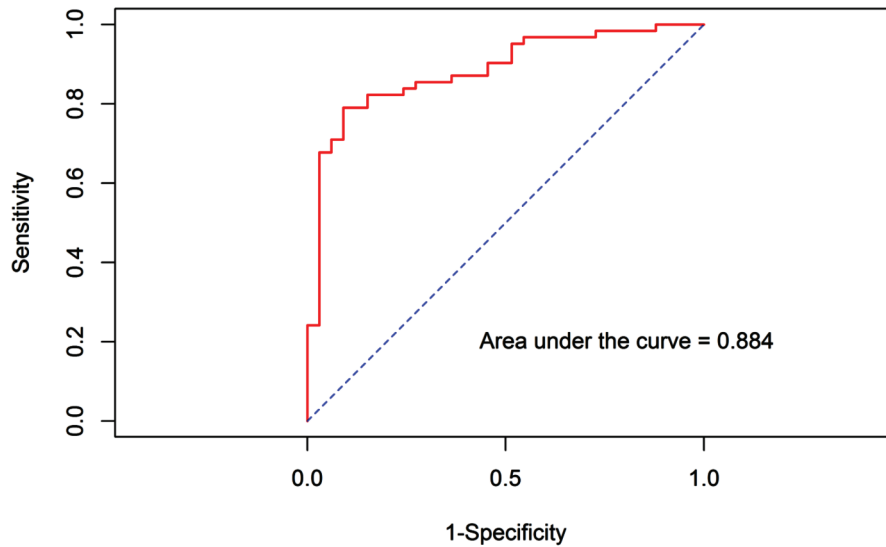
AUC=0.88, sensitivity 80.7% (95% CI, 68.6–89.6%), specificity 84.9% (95% CI, 68.1–94.9%)

Figure 2 Receiver operating characteristic curves of the final model for predictor acute kidney injury

trend toward 30–day mortality along with the severity of AKI (stage 1, 9.0%; 2, 14.0%, 3; 25.0%), which was comparable to previous studies.[14–16]

To date, many studies have documented risk factors of AKI in type A aortic dissection surgery; such as, hypertension, preoperative elevated serum creatinine[13,15,17], prolonged CPB time and red blood cell transfusion.[2,18] Several risk factors have also been differentiated, depending on patient characteristics and perioperative care. In our multivariate logistic regression analysis results, administration intraoperative cryoprecipate after CPB separation and received PRC transfusion in the intensive care unit, tended to be a risk factor for AKI. Generally, aortic dissection is associated with an intense activation of coagulation, the fibrinolytic system and platelets[18]; resulting in high rates of reoperation for postoperative bleeding that require a lot of blood component transfusions in the postoperative period. Moreover, the outcomes found in the study agree with the findings that receiving PRC

transfusions are considered as a risk factor of AKI stage 3.[19] The situation is probably explained by the effect of a great deal of RBC transfusions; such as, impaired oxygen delivery, and lowered red blood cell deformability.

A recent study has also reported that type A aortic dissection is at high risk for perioperative coagulopathy.[18] Therefore, clotting factors and fibrinogen concentration should be further increased to mitigate consumption coagulopathy. Thus, the rapid and sufficient supplementation of clotting factors and fibrinogen, after hypothermic circulatory arrest, should be considered.[20] According to the Tomita et al. study, patients administered with cryoprecipitate, plus FFP experienced significantly less blood loss, and required significantly fewer units of FFP than FFP alone.[21] Cryoprecipitate contains fibrinogen and other coagulation factors; particularly factor VIII, fibrinogen, Von Willebrand factor along with high concentrations of platelet microparticles. Additionally, it effectively stops bleeding and promotes wound healing. The potential

mechanism for cryoprecipitate transfusion causing AKI is still unknown. Some evidences show immune factors might also play an important role in the increased risk of AKI with cryoprecipitate.[22] Platelet and leukocyte interactions appear to be a critical step in inflammation.[23] Additionally, local and systemic inflammation plays a significant part in the initiation and extension phases of AKI.[24] Platelet microparticles make up one component in cryoprecipitate, having 50- to 100-fold higher specific procoagulant activity than activated platelets, and are strongly immunogenic.[25] Thus, cryoprecipitate might have a potentially strong ability of promoting thrombosis. Liu et al. study demonstrated the incidence of AKI in patients with cryoprecipitate transfusions was significantly higher than in patients without cryoprecipitate transfusions (15.9 vs. 7.8%; p-value=0.012), after orthotopic liver transplants.[26] Currently, there have been very few studies on the efficacy and complications of cryoprecipitate in the cardiac perioperative settings, because most centers are less likely to administer perioperative cryoprecipitate than red blood cells, FFP and platelet transfusions in open cardiac surgery; including type A aortic dissection surgery.[27] Thus, the administration of cryoprecipitate should be guided by viscoelastic monitoring, or clinical settings when the complications and efficacy of cryoprecipitate are still not delineated. Further investigation on possible mechanisms for the development of AKI following cryoprecipitate is required.

The common protective factors of AKI were elevated preoperative serum bicarbonate level, higher volume of urine output during CPB, and higher MAP.

Our results demonstrated a higher preoperative serum bicarbonate (HCO₃) level was likely to be a protective factor for AKI. However, it is in a normal range. In our study, we further analyzed what the optimal cut-off point of preoperative serum HCO₃ level contributing to AKI should be. We found that a preoperative serum HCO₃ level lower than 23 mmol∕L was associated with AKI. Our

results support that a below normal levels of serum HCO₃ (<23 mmol∕L) was associated with higher incidence of AKI, and a prolonged ICU stay.[28] Furthermore, a higher serum HCO₃ level is associated with a lower risk of CKD progression, and may be effective for prevention.[29] However, a multicenter double-blinded randomized controlled trial has demonstrated prophylactic perioperative sodium bicarbonate is not recommended for postoperative AKI prevention following cardiac surgery, and possibly increases mortality.[30] However, preoperative serum HCO₃ levels may be used as a predictor for the early detection of postoperative AKI.

Another protective factor for AKI, in our study, was a higher volume of urine output during CPB. Urine output usually represents renal function, and is used as part of the KDIGO criteria for AKI diagnosis. There are several mechanisms that alter renal homeostasis during CPB; including hypothermia and hemodilution. Evidences related to urine flow during CPB associated with AKI are still controversial. Some studies, investigating the predictors of AKI, have reported urine output as insignificance.[31,32] In our multivariate analysis, higher urine output was associated with AKI as being one of the protective factors. This is in accord with a previous study that reported the possible relevance of urine output during CPB to the risk of postoperative AKI.[33] An amount of urine output lower than 1.7 ml∕kg∕hour during CPB was associated with AKI. Although, some studies demonstrated that urine output is not associated with AKI, assessment of urine volume during CPB is important as guidance for CPB management, so as to ensure renal perfusion. Additionally, it is currently the only available test for kidney function during this period, also it is a simple and the fastest tool.

Higher MAP was also inclined to be a protective factor for AKI. Evidence related to blood pressure targets, before and after CPB during cardiac surgery, is still lacking and controversial.[34] Some practitioners use the considerations for non-cardiac surgery as a reference. From previous studies,

maintaining MAP within 70–100 mmHg, were still within a wide range.[35–37] Some studies report that the incidence of AKI was not significantly different between different MAP (75–85 versus 50–60 mmHg) during normothermic CPB, based on different, randomized controlled trials.36 Kidney perfusion is regularly autoregulated. For example, glomerular filtration is maintained until the mean arterial blood pressure falls below 80 mmHg. However, mean arterial blood pressure during cardiac surgery is often below the limits of autoregulation. Moreover, cardiac surgery patients have impaired autoregulation, due to existing comorbidities or a proinflammatory, ischemia–reperfusion injury and endotoxemia.[38,39] Interestingly, the lower limit of renal autoregulation is in accordance with our results. Our study showed a MAP lower than 81 mmHg was associated with postoperative AKI. Hence, it might be reasonable to maintain higher MAP in cardiac settings. Although, a MAP higher than 81 mmHg was likely to be a protective factor of AKI in our study, high blood pressure–related postoperative bleeding is one of the surgeons' concerns. Therefore, both anesthesiologists and surgeons need to discuss what level of acceptable blood pressure should be maintained. The determination of blood pressure targets in perioperative care should consider the patient's baseline, types of surgery, risk of hypotension–related organ ischemia and hypertension–related bleeding.[34] So, organ ischemia monitoring should be measured for the optimal blood flow to vital organs.

The strengths of this study were that the use of multivariate logistic regression analysis takes into account the adjustment for potential independent predictors, and using the ROC curve, which has a high prediction ability (area under the curve=0.88).

The limitations of this study are as follows. In addition to this being a retrospective cohort study; there were only a small number of patients to investigate for other factors each year. There were also differences in surgical techniques and blood transfusion protocols each year. The protective factors should be considered altogether, rather than as single factors; because individual AUC was not relatively high. Future prospective studies are required to control confounding factors, and identify the potential risk factors for AKI, following type A aortic dissection surgery.

Conclusion

In summary, our study found that administration intraoperative cryoprecipitate was associated with postoperative AKI, following type A aortic dissection repair under CPB. Avoidance of this risk factor may prevent AKI, and reduce mortality in this high–risk open–heart surgery. Higher preoperative serum bicarbonate levels, higher volume of urine output during CPB and higher immediate postoperative mean arterial pressure were likely to be protective factors of AKI.

Conflict of interest

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

References

1. Sasabuchi Y, Kimura N, Shiotsuka J, Komuro T, Mouri H, Ohnuma T, et al. Long-term survival in patients with acute kidney injury after acute type A aortic dissection repair. Ann Thorac Surg 2016;102:2003–9.

2. Ko T, Higashitani M, Sato A, Uemura Y, Norimatsu T, Mahara K, et al. Impact of acute kidney injury on early to long-term outcomes in patients who underwent surgery for type A acute aortic dissection. Am J Cardiol 2015;116:463–8.

3. Kumar AB, Suneja M. Cardiopulmonary bypass–associated acute kidney injury. Anesthesiology 2011;114:964–70.

4. O'Neal JB, Shaw AD, Billings FT. Acute kidney injury following cardiac surgery: current understanding and future directions. Crit Care 2016;20:187.

5. Vives M, Hernandez A, Parramon F, Estanyol N, Pardina B, Muñoz A, et al. Acute kidney injury after cardiac surgery: prevalence, impact and management challenges. Int J Nephrol Renovasc Dis 2019;12:153–66.

6. Wang X, Ren HM, Hu CY, Que B, Ai H, Wang CM, et al. Predictors and in-hospital outcomes of preoperative acute kidney injury in patients with type A acute aortic dissection. J Geriatr Cardiol 2016;13:679–84.

7. Kim WH, Park MH, Kim HJ, Lim HY, Shim HS, Sohn JT, et al. Potentially modifiable risk factors for acute kidney injury after surgery on the thoracic aorta. Medicine (Baltimore) 2015;94:e273.

8. Karkouti K, Wijeysundera DN, Yau TM, Callum JL, Cheng DC, Crowther M, et al. Acute kidney injury after cardiac surgery: focus on modifiable risk factors. Circulation 2009;119:495–502.

9. Goren O, Matot I. Perioperative acute kidney injury. Br J Anaesth 2015;115(Suppl 2):ii3–14.

10. Borthwick E, Ferguson A. Perioperative acute kidney injury: risk factors, recognition, management, and outcomes. BMJ 2010;341:c3365.

11. Motayagheni N, Phan S, Eshraghi C, Nozari A, Atala A. A review of anesthetic effects on renal function: potential organ protection. Am J Nephrol 2017;46:380–9.

12. Howitt SH, Grant SW, Caiado C, Carlson E, Kwon D, Dimarakis I, et al. The KDIGO acute kidney injury guidelines for cardiac surgery patients in critical care: a validation study. BMC Nephrol 2018;19:149.

13. Roh GU, Lee JW, Nam SB, Lee J, Choi J, Shim YH. Incidence and risk factors of acute kidney injury after thoracic aortic surgery for acute dissection. Ann Thorac Surg 2012;94:766–71.

14. Tsai HS, Tsai FC, Chen YC, Wu LS, Chen SW, Chu JJ, et al. Impact of acute kidney injury on one-year survival after surgery for aortic dissection. Ann Thorac Surg 2012;94:1407–12.

15. Arnaoutakis GJ, Bihorac A, Martin TD, Hess PJ, Klodell CT, Ejaz AA, et al. RIFLE criteria for acute kidney injury in aortic arch surgery. J Thorac Cardiovasc Surg 2007;134:1554–61.

16. D'Onofrio A, Cruz D, Bolgan I, Auriemma S, Cresce GD, Fabbri A, et al. RIFLE criteria for cardiac surgery–associated acute kidney injury: risk factors and outcomes. Congest Heart Fail 2010;16(Suppl 1):S32–6.

17. Bove T, Calabrò MG, Landoni G, Aletti G, Marino G, Crescenzi G, et al. The incidence and risk of acute renal failure after cardiac surgery. J Cardiothorac Vasc Anesth 2004;18:442–5.

18. Liu Y, Han L, Li J, Gong M, Zhang H, Guan X. Consumption coagulopathy in acute aortic dissection: principles of management. J Cardiothorac Surg 2017;12:50.

19. Li CN, Ge YP, Liu H, Zhang CH, Zhong YL, Chen SW, et al. Blood transfusion and acute kidney injury after total aortic arch replacement for acute Stanford type A aortic dissection. Heart Lung Circ 2021;S1443-9506(21)00549-7.

20. Lee SH, Lee SM, Kim CS, Cho HS, Lee JH, Lee CH, et al. Fibrinogen recovery and changes in fibrin-based clot firmness after cryoprecipitate administration in patients undergoing aortic surgery involving deep hypothermic circulatory arrest. Transfusion 2014;54:1379–87.

21. Tomita Y, Shimode N, Ide T, Ueki R, Tatara T, Tashiro C. Efficacy of cryoprecipitate transfusion for coagulopathy after cardiopulmonary bypass in thoracic aortic surgery. Masui 2011;60:830–4.

22. Callum JL, Karkouti K, Lin Y. Cryoprecipitate: the current state of knowledge. Transfus Med Rev 2009;23:177–88.

23. Gameiro J, Lopes JA. Complete blood count in acute kidney injury prediction: a narrative review. Ann Intensive Care 2019;9:87.

24. Radi ZA. Immunopathogenesis of acute kidney injury. Toxicol Pathol 2018;46:930–43.

25. Sinauridze EI, Kireev DA, Popenko NY, Pichugin AV, Panteleev MA, Krymskaya OV, et al. Platelet microparticle membranes have 50- to 100-fold higher specific procoagulant activity than activated platelets. Thromb Haemost 2007;97:425–34.

26. Liu S, Wang X, Lu Y, Li T, Gong Z, Sheng T, et al. The effects of intraoperative cryoprecipitate transfusion on acute renal failure following orthotropic liver transplantation. Hepatol Int 2013;7:901–9.

27. Kindzelski BA, Corcoran P, Siegenthaler MP, Horvath KA. Postoperative acute kidney injury following intraoperative blood product transfusions during cardiac surgery. Perfusion 2018;33:62–70.

28. Jung SY, Park JT, Kwon YE, Kim HW, Ryu GW, Lee SA, et al. Preoperative low serum bicarbonate levels predict acute kidney injury after cardiac surgery. Medicine (Baltimore) 2016;95:e3216.

29. Shah SN, Abramowitz M, Hostetter TH, Melamed ML. Serum bicarbonate levels and the progression of kidney disease: a cohort study. Am J Kidney Dis 2009;54:270–7.

30. Haase M, Haase-Fielitz A, Plass M, Kuppe H, Hetzer R, Hannon C, et al. Prophylactic perioperative sodium bicarbonate to prevent acute kidney injury following open heart surgery: a multicenter double-blinded randomized controlled trial. PLoS Med 2013;10:e1001426.

31. Palomba H, de Castro I, Neto ALC, Lage S, Yu L. Acute kidney injury prediction following elective cardiac surgery: AKICS Score. Kidney Int 2007;72:624–31.

32. Hori D, Katz NM, Fine DM, Ono M, Barodka VM, Lester LC, et al. Defining oliguria during cardiopulmonary bypass and its relationship with cardiac surgery–associated acute kidney injury. Br J Anaesth 2016;117:733–40.

33. Song Y, Kim DW, Kwak YL, Kim BS, Joo HM, Ju JW, et al. Urine output during cardiopulmonary bypass predicts acute kidney injury after cardiac surgery: a single-center retrospective analysis. Medicine (Baltimore) 2016;95:e3757.

34. Meng L, Yu W, Wang T, Zhang L, Heerdt PM, Gelb AW. Blood pressure targets in perioperative care. Hypertension 2018;72:806–17.

35. Gold JP, Charlson ME, Williams-Russo P, Szatrowski TP, Peterson JC, Pirraglia PA, et al. Improvement of outcomes after coronary artery bypass. A randomized trial comparing intra-operative high versus low mean arterial pressure. J Thorac Cardiovasc Surg 1995;110:1302–14.

36. Charlson ME, Peterson JC, Krieger KH, Hartman GS, Hollenberg JP, Briggs WM, et al. Improvement of outcomes after coronary artery bypass II: a randomized trial comparing intraoperative high versus customized mean arterial pressure. J Card Surg 2007;22:465–72.

37. Vedel AG, Holmgaard F, Rasmussen LS, Langkilde A, Paulson OB, Lange T, et al. High-target versus low-target blood pressure management during cardiopulmonary bypass to prevent cerebral injury in cardiac surgery patients: a randomized controlled trial. Circulation 2018;137:1770–80.

38. Paparella D, Yau TM, Young E. Cardiopulmonary bypass induced inflammation: pathophysiology and treatment. An update. Eur J Cardiothorac Surg 2002;21:232–44.

39. Laffey JG, Boylan JF, Cheng DCH. The systemic inflammatory response to cardiac surgery: implications for the anes-thesiologist. Anesthesiology 2002;97:215–52.