Original Article

Incidence and risk factors of acute kidney injury after maze operation in patients with rheumatic mitral valve disease

Hee Ju Hong[1]^, Yeiwon Lee[2#]^, Sue Hyun Kim[2]^, Suk Ho Sohn[1]^, Jae Woong Choi[1]^, Kyung Hwan Kim[1]^, Ho Young Hwang[1#]^

[1]Department of Thoracic and Cardiovascular Surgery, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Korea; [2]Department of Critical Care, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Korea

Contributions: (I) Conception and design: HY Hwang; (II) Administrative support: Y Lee, HY Hwang; (III) Provision of study materials or patients: SH Kim, SH Sohn, JW Choi, KH Kim, HY Hwang; (IV) Collection and assembly of data: HJ Hong, Y Lee; (V) Data analysis and interpretation: Y Lee, HY Hwang; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to the work.

Correspondence to: Ho Young Hwang. Department of Thoracic and Cardiovascular Surgery, Seoul National University Hospital, Seoul National College of Medicine, 101 Daehak-ro, Jongno-gu, Seoul 03080, Republic of Korea. Email: scalpel@snu.ac.kr; Yeiwon Lee. Department of Critical Care, Seoul National University Hospital, Seoul National University College of Medicine, 101 Daehak-ro, Jongno-gu, Seoul 03080, Republic of Korea. Email: ywlee415@naver.com.

Background: Acute kidney injury (AKI) is one of the most common complications after cardiac surgery. While current guidelines indicate that surgical ablation does not increase the risk of renal failure, recent studies have produced conflicting results. This study was conducted to evaluate the incidence of AKI after maze procedure in patients with rheumatic mitral valve disease and atrial fibrillation, and to elucidate risk factors associated with postoperative AKI.

Methods: Between 2011 and 2020, 203 patients with rheumatic mitral valve disease and atrial fibrillation (61.4±8.7 years, male:female =67:136) who underwent concomitant maze procedure and mitral valve replacement were retrospectively reviewed. Other combined procedures included aortic valve operations (n=64, 31.5%) and tricuspid valve procedures (n=149, 73.4%). The AKI was defined as an increase of serum creatinine level by 1.5 times after surgery based on the RIFLE (Risk, Injury, Failure, Loss, and End stage) criteria. A multivariable logistic regression analysis was performed to evaluate risk factors associated with postoperative AKI.

Results: Postoperative AKI developed in 76 patients (37.4%). The multivariable analysis demonstrated that age [odds ratio (OR), 95% confidence interval (CI): 1.065, 1.025–1.107; P=0.001], cardiopulmonary bypass (CPB) time (1.007, 1.002–1.013; P=0.009) and nadir hematocrit during CPB (0.854, 0.740–0.985; P=0.031) were associated with postoperative AKI.

Conclusions: Postoperative AKI occurred in more than one thirds of patients with rheumatic mitral valve disease and atrial fibrillation who underwent combined mitral valve replacement and maze procedure. Optimization of CPB management might be needed to prevent postoperative AKI after maze procedure.

Keywords: Maze operation; atrial fibrillation (AF); acute kidney injury (AKI)

Submitted May 01, 2022. Accepted for publication Aug 19, 2022.
doi: 10.21037/jtd-22-600
View this article at: https://dx.doi.org/10.21037/jtd-22-600

^ ORCID: Hee Ju Hong, 0000-0001-7541-4169; Yeiwon Lee, 0000-0003-3342-1381; Sue Hyun Kim, 0000-0002-7414-5232; Suk Ho Sohn, 0000-0001-7391-3415; Jae Woong Choi, 0000-0002-0921-756X; Kyung Hwan Kim, 0000-0002-2718-8758; Ho Young Hwang, 0000-0002-8935-8118.

Introduction

Previous studies demonstrated the safety and efficacy of concomitant maze procedure in atrial fibrillation (AF) patients undergoing cardiac surgery (1-3). Current guidelines suggest that surgical ablation does not increase the risk of renal failure or dialysis (4). However, the rate of postoperative acute kidney injury (AKI) was increased in previous studies (5,6). A previous study also showed that the development of postprocedural AKI is associated with an increase mortality (7). A recent study showed that concomitant maze procedure increased the risk of postoperative AKI, which was offset by the significant survival benefit of the maze procedure (8). This study was conducted to evaluate the occurrence rate and risk factors of postoperative AKI after concomitant maze procedure in patients with rheumatic mitral valve (MV) disease and AF. We present the following article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-600/rc).

Methods

Patient characteristics

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study protocol was approved by the Institutional Review Board of Seoul National University Hospital as a minimal risk retrospective study (approval no.: 2112-111-1284), which did not require individual consent. Between 2011 and 2020, 203 patients underwent MV replacement (MVR) and concomitant maze procedure due to rheumatic MV disease and AF at our institution. None of the patients had preoperative end-stage renal disease requiring dialysis. All patients were enrolled in the present study. The mean age was 61.4±8.7 years (male:female ratio =67:136). Hypertension, previous history of stroke, and diabetes mellitus were the most common co-morbidities (*Table 1*).

Operative data and surgical procedure

The operations were performed under cardiopulmonary bypass (CPB) with moderate hypothermia and cold cardioplegic arrest. CryoProbe (Cryoflex, Medtronic Inc., Minneapolis, MN, USA) was used, and all patients underwent complete biatrial lesion sets following original Cox maze III procedure including coronary sinus ablation described by Cox and his colleagues (9). Left atrial appendage (LAA) elimination was performed at the discretion of the operating surgeons. MVR was performed using mechanical (n=159) or bioprosthetic (n=44) valves. Combined procedures included aortic (n=65) and tricuspid (n=149) valve procedures (*Table 2*).

Evaluation of renal dysfunction

The primary endpoint of the present study was the occurrence rate of AKI after surgery. Preoperative serum creatinine was measured on the day before surgery. Postoperative serum creatinine was measured immediately and 6 hours after surgery, and once a day thereafter until 7 days after surgery. Based on the RIFLE (Risk, Injury, Failure, Loss, and End stage) criteria (10), postoperative AKI was defined as ≥1.5-fold increase in serum creatinine from the baseline value within 7 days. The glomerular filtration rate (GFR) was calculated using the Modified Diet in Renal Disease formula as $175 \times (\text{serum creatinine})^{-1.154} \times (\text{age})^{-0.203} \times 0.742$ (if female) × 1.210 (if African-American).

Evaluation of other clinical outcomes

Early mortality was defined as death within 30 days or during the same hospitalization. Low cardiac output syndrome (LCOS) was defined as cardiac index <2.0 L/min/m^2 or systolic arterial pressure <90 mm Hg for which the patient required mechanical assistance or high inotropic support, such as dopamine or dobutamine, at >5 μg/kg/min. The postoperative respiratory complications included pneumonia or prolonged ventilator support for more than 48 hr.

Statistical analysis

The statistical analyses were performed using SPSS (version 23.0; IBM Corp., Armonk, NY, USA) and SAS (version 9.4; SAS Institute Inc., Cary, NC, USA) statistical software. Data are expressed as proportions for categorical variables, means ± standard deviations for normally distributed variables, and median with interquartile range (IQR) for non-normally distributed variables. There were no missing values. Patients with and without AKI were compared using the χ^2 test or Fisher's exact test for categorical variables and Student's *t*-test for continuous variables.

Factors associated with the occurrence of AKI were analyzed using logistic regression. All preoperative variables shown in *Table 1* and intraoperative variables such as CPB time, nadir hematocrit level and transfusion of red blood

Table 1 Study characteristics

Variables	Total (n=203)
Age (years), mean ± SD	61.4±8.7
Male/Female	67/136
Body surface area (m^2), mean ± SD	1.57±0.16
Risk factors, n (%)	
Smoking	44 (21.7)
Hypertension	48 (23.6)
Diabetes mellitus	35 (17.2)
Dyslipidemia	31 (15.3)
Overweight (BMI >25 kg/m^2)	42 (20.7)
History of stroke	41 (20.2)
Chronic kidney disease (GFR <60 mL/min)	22 (10.8)
COPD	12 (5.9)
Peripheral vascular disease	5 (2.5)
LV dysfunction (EF <0.50)	31 (15.3)
EuroSCORE II, mean ± SD	3.94±2.27

SD, standard deviation; BMI, body mass index; GFR, glomerular filtration rate; COPD, chronic obstructive pulmonary disease; EF, ejection fraction; LV, left ventricle; EF, ejection fraction; EuroSCORE, European System for Cardiac Operative Risk Evaluation

Table 2 Operative data of the study patients

Variables	Total (n=203)
Concomitant procedures, n (%)	
Aortic valve operation	65 (32.0)
Tricuspid valve operation	149 (73.4)
Coronary artery bypass grafting	5 (2.5)
Replacement of aorta	4 (2.0)
Closure of atrial septal defect	6 (3.0)
Intraoperative IABP insertion, n (%)	8 (3.9)

IABP, intra-aortic balloon pump

cell (RBC) were included in the analyses. The linearity of continuous variables was checked using restricted cubic splines. Associated factors were identified in a multivariable model using the stepwise selection method; variables with a P value <0.2 in univariate logistic analysis were included. The results of the multivariable analysis are expressed as P values and odds ratios (ORs) with 95% confidence intervals (CIs). A P value <0.05 was considered statistically significant.

Table 3 Changes in renal function and occurrence rate of acute kidney injury

Variables	Values
Preoperative creatinine (mg/dL)	0.89±0.23
Peak postoperative creatinine (mg/dL)	1.35±0.64
Ratio of peak postoperative to preoperative creatinine	1.52±0.68
*Occurrence of acute kidney injury	76 (37.4)

*, defined as ≥1.5-fold increase in serum creatinine from baseline within 7 days.

Results

Operative data

The mean CPB and aortic cross-clamp times were 233.8±57.8 min and 165.5±43.7 min, respectively. During CPB, the lowest hematocrit level was 21.1%±2.61% and the median number of RBC packs transfused was 1 (IQR: 0–1.5). The CPB times were 278.5±54.4 min and 214.6.5±47.8 min in patients with concomitant aortic valve replacement and those without, respectively. The lowest hematocrit levels were 21.3%±2.6% and 21.0%±2.6% in patients with concomitant aortic valve replacement and those without, respectively. The LAA was eliminated using staple excision, internal obliteration, and external ligation in 43, 78, and 70 patients, respectively. LAA was not eliminated in the remaining 12 patients. The peak postoperative level of creatine kinase-MB isoenzyme (CKMB) was 278.0±135.7 ng/mL.

Occurrence rate of acute kidney injury

Creatinine increased from a preoperative level of 0.89±0.23 mg/dL to a peak of 1.35±0.64 mg/dL on postoperative day 1 (IQR: 1.0–2.0). The ratio of postoperative to preoperative creatinine was 1.52±0.68. AKI occurred in 76 patients (37.4%) (*Table 3*). Univariate analyses demonstrated that age (P=0.001), CPB duration (P=0.006), number of RBC packs transfused (P=0.001), and the nadir hematocrit level during CPB (P=0.002) and concomitant aortic valve replacement (P=0.018) were associated with AKI occurrence, while the LAA elimination technique (P=0.327) and peak CKMB after surgery (P=0.085) were

Table 4 Univariate and multivariable risk factor analysis for the occurrence of acute kidney injury

Variables	Univariate analysis			Multivariable analysis		
	OR	95% CI	P value	OR	95% CI	P value
Age (years)	1.060	1.023–1.098	0.001	1.067	1.028–1.107	0.001
Sex	0.902	0.491–1.655	0.738			
Body surface area (m^2)	0.166	0.026–1.074	0.059	–	–	–
Smoking	1.206	0.609–2.385	0.591			
Hypertension	1.771	0.918–3.413	0.088	–	–	–
Diabetes mellitus	0.985	0.464–2.092	0.968			
Dyslipidemia	1.461	0.675–3.165	0.336			
Body mass index	0.980	0.893–1.075	0.667			
History of stroke	1.237	0.615–2.487	0.552			
CKD (GFR <60 mL/min)	1.452	0.595–3.543	0.413			
COPD	1.729	0.537–5.565	0.359			
Peripheral vascular disease	1.117	0.182–6.841	0.905			
LV dysfunction (EF <0.50)	1.003	0.966–1.042	0.862			
EuroSCORE II	1.235	1.076–1.418	0.003	–	–	–
CPB (minutes)	1.007	1.002–1.012	0.006	1.008	1.002–1.013	0.004
ACC (minutes)	1.006	0.999–1.012	0.082	–	–	–
Red blood cell transfusion	1.762	0.937–3.315	0.079	–	–	–
Nadir Hematocrit during CPB	0.832	0.740–0.935	0.002	0.831	0.734–0.942	0.004

Variables with P value <0.2 were entered into multivariable analysis. OR, odds ratio; CI, confidence interval; CKD, chronic kidney disease; GFR, glomerular filtration rate; COPD, chronic obstructive pulmonary disease; LV, left ventricle; EF, ejection fraction; EuroSCORE, European System for Cardiac Operative Risk Evaluation; CPB, cardiopulmonary bypass; ACC, aortic cross clamping.

not. The multivariable analysis showed that age (OR, 1.067; 95% CI: 1.028–1.107; P=0.001), CPB duration (OR, 1.008; 95% CI: 1.002–1.013; P=0.004), and the nadir hematocrit level during CPB (OR, 0.831; 95% CI: 0.734–0.942; P=0.004) were significantly associated with postoperative AKI (*Table 4*). The AKI with RIFLE criteria of Injury (≥2.0-fold increase in serum creatinine) and Failure levels (≥3.0-fold increase in serum creatinine) occurred in 29 and 9 patients, respectively. Risk factor analyses showed that smoking (P=0.035) was associated with the AKI with RIFLE criteria of Injury. Regarding the AKI with RIFLE criteria of Failure, only EuroSCORE II showed a trend of association in the univariate analyses (*Table 5*).

Other clinical outcomes

The early mortality occurred in 1 patient (1 out of 203 patients, 0.49%) who had postoperative AKI. Common postoperative complications included respiratory complications (n=16, 7.9%), LCOS (n=11, 5.4%) and bleeding requiring reoperation (n=12, 5.9%) (*Table 6*).

Discussion

This study had two main findings. First, the occurrence rate of AKI was relatively high after maze procedure performed concomitantly with MVR in patients with rheumatic MV disease. Second, perfusion parameters, such as CPB duration and the nadir hematocrit level during CPB were associated with AKI occurrence.

AKI is one of the most common complications of cardiac surgery and also associated with increase mortality in cardiac procedures (7). Among many factors, the use of CPB is a major contributor to AKI after cardiac surgery:

Table 5 Univariate and multivariable risk factor analysis for the occurrence of acute kidney injury with RIFLE criteria of injury and failure

Variables*	Univariate analysis			Multivariable analysis		
	OR	95% CI	P-value	OR	95% CI	P Value
RIFLE criteria of injury						
Age (years)	1.037	0.989–1.087	0.129	–	–	–
Smoking	2.167	0.924–5.083	0.075	2.608	1.072–6.346	0.035
Nadir Hct during CPB	0.889	0.762–1.038	0.137	0.859	0.731–1.010	0.066
RIFLE criteria of failure						
EuroSCORE II	0.521	0.259–1.047	0.067	–	–	–

*, All variables shown in table 4 were analyzed and variables with P<0.2, which were entered into multivariable analysis, are shown. OR, odds ratio; CI, confidence interval; RIFLE, Risk, Injury, Failure, Loss, and End stage; Hct, hematocrit; CPB, cardiopulmonary bypass; EuroSCORE, European System for Cardiac Operative Risk Evaluation.

Table 6 Early clinical outcomes

Variables	Total (n=203)
Early mortality, n (%)	1 (0.49)
Postoperative complications, n (%)	
Respiratory complications	16 (7.9)
Bleeding reoperation	12 (5.9)
Low cardiac output syndrome	11 (5.4)
Stroke	4 (2.0)
Mediastinitis	1 (0.49)
Infective endocarditis	1 (0.49)

it predisposes the patient to the systemic inflammatory response, ischemia-reperfusion injury, and pigment nephropathy due to rhabdomyolysis and hemolysis (8,11). Because postoperative AKI is associated with worse early and long-term outcomes after cardiac surgery (12,13), identification and treatment of factors associated with postoperative AKI may improve surgical outcomes.

Previous studies have demonstrated the benefits of concomitant AF ablation during cardiac surgery, including MV surgery (1-3); current guidelines make a class I recommendation to perform concomitant surgical ablation of AF during cardiac surgery (4). Although previous studies reported a higher occurrence rate of AKI in cardiac surgery patients who underwent concomitant maze procedure (2,6), recent guidelines state that concomitant maze procedure does not increase the incidence of postoperative dialysis or renal failure (14). This may be partly due to the lack of standardized criteria for the diagnosis of AKI. A recent propensity score matching study (8) divided 874 patients with cardiac disease and AF into 308 pairs of maze and non-maze patients; a higher AKI rate was observed in the maze compared to non-maze group patients [32% (99/308 patients) *vs.* 16% (49/308 patients)]. That study confirmed that the maze procedure, rather than AF, was associated with the occurrence of AKI after surgery. However, the authors did not proffer explanations for this finding. The increased risk of AKI after surgery with concomitant maze procedure cannot be explained solely by prolonged CPB duration. To minimize confounding factors, the present study only enrolled patients with rheumatic MV disease and AF; in addition, postoperative AKI was determined on the basis of the RIFLE criteria (10). Our results showed that postoperative AKI occurred in 37.4% of patients, which was very high considering that the study population consisted of relatively young rheumatic patients with low surgical risk. However, we failed to identify risk factors for postoperative AKI associated with the maze procedure, such as an LAA elimination strategy or peak postoperative level of CKMB, which reflects the degree of injury of the left atrial muscle caused by cryoablation. We found that age and the nadir hematocrit level during CPB were associated with AKI after concomitant maze procedure; these risk factors have been well-described in previous literature (15,16). Further studies, such as those based on biomarkers, may identify specific risk factors for AKI after the maze procedure.

This study had several limitations. First, this was a retrospective study conducted at a single institution. Second, the number of enrolled patients was relatively small. Third, comparative analyses with patients who underwent MVR without concomitant maze procedure

were not performed because almost all of the patients with rheumatic MV disease and AF underwent combined maze procedure.

In conclusion, age, CPB duration, and the nadir hematocrit level were associated with an increased risk of postoperative AKI in patients with rheumatic MV disease who underwent concomitant MV surgery and the maze procedure.

Acknowledgments

Funding: None.

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-600/rc

Data Sharing Statement: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-600/dss

Peer Review File: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-600/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-600/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study protocol was approved by the Institutional Review Board of Seoul National University Hospital as a minimal risk retrospective study (approval No. 2112-111-1284), which did not require individual consent.

References

1. Ad N, Holmes SD, Massimiano PS, et al. Long-term outcome following concomitant mitral valve surgery and Cox maze procedure for atrial fibrillation. J Thorac Cardiovasc Surg 2018;155:983-94.
2. Badhwar V, Rankin JS, Ad N, et al. Surgical Ablation of Atrial Fibrillation in the United States: Trends and Propensity Matched Outcomes. Ann Thorac Surg 2017;104:493-500.
3. Yao MH, Ren CL, Zhang L, et al. Short-term and mid-term effects of radiofrequency ablation in mitral valve surgery in patients with different left atrial sizes. J Thorac Dis 2020;12:6030-8.
4. Badhwar V, Rankin JS, Damiano RJ Jr, et al. The Society of Thoracic Surgeons 2017 Clinical Practice Guidelines for the Surgical Treatment of Atrial Fibrillation. Ann Thorac Surg 2017;103:329-41.
5. Malaisrie SC, McCarthy PM, Kruse J, et al. Ablation of atrial fibrillation during coronary artery bypass grafting: Late outcomes in a Medicare population. J Thorac Cardiovasc Surg 2021;161:1251-1261.e1.
6. Churyla A, Andrei AC, Kruse J, et al. Safety of Atrial Fibrillation Ablation With Isolated Surgical Aortic Valve Replacement. Ann Thorac Surg 2021;111:809-17.
7. Zahid S, Ullah W, Khan MU, Salama A, Krupica T, Khan MZ. Predictors of acute kidney injury after transcatheter aortic valve implantation (from national inpatient sample [2011-2018]). Am J Cardiol 2021;151:120-2.
8. Bakir NH, Khiabani AJ, MacGregor RM, et al. Concomitant surgical ablation for atrial fibrillation is associated with increased risk of acute kidney injury but improved late survival. J Thorac Cardiovasc Surg 2021. [Epub ahead of print]. doi: 10.1016/j.jtcvs.2021.01.023.
9. Cox JL, Churyla A, Malaisrie SC, et al. When Is a Maze Procedure a Maze Procedure? Can J Cardiol 2018;34:1482-91.
10. Mehta RL, Kellum JA, Shah SV, et al. Acute Kidney Injury Network: report of an initiative to improve outcomes in acute kidney injury. Crit Care 2007;11:R31.
11. Laffey JG, Boylan JF, Cheng DC. The systemic inflammatory response to cardiac surgery: implications for the anesthesiologist. Anesthesiology 2002;97:215-52.
12. Wang Z, Ge M, Chen T, et al. Risk factors and long-term outcomes of elderly patients complicating with acute kidney injury after type A acute aortic dissection surgery: a

retrospective study. J Thorac Dis 2020;12:5833-41.
13. Elmistekawy E, McDonald B, Hudson C, et al. Clinical impact of mild acute kidney injury after cardiac surgery. Ann Thorac Surg 2014;98:815-22.
14. Ad N, Damiano RJ Jr, Badhwar V, et al. Expert consensus guidelines: Examining surgical ablation for atrial fibrillation. J Thorac Cardiovasc Surg 2017;153:1330-1354.e1.
15. Wang YS, Chen DX, Yan M, et al. Prediction of the severity of acute kidney injury after on-pump cardiac surgery. J Clin Anesth 2022;78:110664.
16. Brescia AA, Wu X, Paone G, et al. Effect of sex on nadir hematocrit and rates of acute kidney injury in coronary artery bypass. J Thorac Cardiovasc Surg 2019;158:1073-1080.e4.

Cite this article as: Hong HJ, Lee Y, Kim SH, Sohn SH, Choi JW, Kim KH, Hwang HY. Incidence and risk factors of acute kidney injury after maze operation in patients with rheumatic mitral valve disease. J Thorac Dis 2022;14(9):3408-3414. doi: 10.21037/jtd-22-600