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Clinical Research

The Impact of Surgical versus Transcatheter Aortic Valve Replacement on Postprocedural Acute Kidney Injury in Patients with Chronic Kidney Disease

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Background: This study aimed to evaluate the impact of the treatment modality on post-procedural acute kidney injury (AKI) and other clinical outcomes in patients with advanced chronic kidney disease who underwent surgical or transcatheter aortic valve replacement (AVR).
Methods: A total of 147 patients with advanced chronic kidney disease (stage 3 to 5) who underwent isolated surgical AVR (SAVR group; n=70) or transcatheter AVR (TAVR group; n=77) were retrospectively studied. Postprocedural AKI was defined according to the RIFLE definition (an acronym corresponding to the risk of renal dysfunction, injury to the kidney, failure of kidney function, loss of kidney function, and end-stage kidney disease). Factors associated with postoperative complications and mortality were analyzed using multivariable logistic regression models and Cox proportional hazard models.
Results: Postprocedural AKI occurred in 17 (24.3%) and 6 (7.8%) patients in the SAVR and TAVR groups, respectively (p=0.006). Multivariable analyses demonstrated that the SAVR group had higher risks of AKI (odds ratio [OR], 5.63; 95% confidence interval [CI], 1.85–17.73; p=0.002) and atrial fibrillation (OR, 16.65; 95% CI, 4.44–62.50; p<0.001), whereas the TAVR group had a higher risk of permanent pacemaker insertion (OR, 5.67; 95% CI, 1.21–26.55; p=0.028). The Cox proportional hazard models showed that the occurrence of AKI, contrary to the treatment modality, was associated with overall survival.
Conclusion: In patients with chronic kidney disease, the risk of postprocedural AKI might be higher after SAVR than after TAVR.

Keywords: Aortic valve, Surgery, Transcatheter aortic valve replacement, Chronic renal insufficiency, Acute kidney injury

Introduction

Aortic valve stenosis (AS) is the most common valvular heart disease, particularly in the elderly [1]. Although surgical aortic valve replacement (SAVR) has been the treatment of choice for patients with AS, transcatheter aortic valve replacement (TAVR) has rapidly evolved, and its indications have been expanded to low-risk patients for SAVR [2-4].

Because AS is degenerative in nature and progresses with aging, a substantial proportion of patients with AS also have chronic kidney disease (CKD) [5]. These 2 conditions have also been proven to interact with each other; AS leads to renal hypoperfusion and dysfunction, while CKD leads to progression of aortic valve calcification and AS [6,7]. When treating AS in patients with CKD, both SAVR and TAVR could theoretically result in further aggravation of CKD. Acute kidney injury (AKI) is a common complication after cardiac surgery, including SAVR [8]. On the contrary, TAVR needs application of an ionized contrast agent that could damage renal function [9].

Therefore, the present study aimed to evaluate the impact of the treatment choice for AS on peri-procedural renal dysfunction in patients with concomitant AS and CKD.

Methods

Patient characteristics

From January 2015 to December 2020, primary isolated SAVR and TAVR were performed in 345 and 281 patients, respectively, at Seoul National University Hospital, and these patients were assessed for study eligibility. Among these, 147 patients suffering from aortic steno-insufficiency and advanced CKD staged between 3 and 5 (estimated glomerular filtration rate [eGFR] <60 mL/min/1.73 m^2) [10] but not dependent on dialysis were enrolled in the present study. Seventy patients underwent SAVR and 77 patients underwent TAVR (Fig. 1). The mean age at the procedure was 78.7±3.6 years, and 69 patients (46.9%) were men. Patients in the SAVR group were younger and had fewer comorbidities than those in the TAVR group. The Society of Thoracic Surgeons score was also lower in the SAVR group than in the TAVR group (2.6±1.7 versus 4.8±3.2, p<0.001) (Table 1).

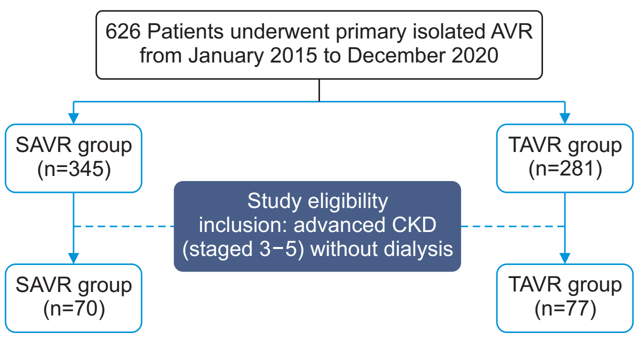

Fig. 1. Summary flow diagram for study patient enrollment. AVR, aortic valve replacement; SAVR, surgical aortic valve replacement; TAVR, transcatheter aortic valve replacement; CKD, chronic kidney disease.

Operative data

All SAVR procedures were performed through full (n=68) or upper partial median sternotomy (n=2) under moderate hypothermia and cold cardioplegic arrest. A tissue valve was implanted in 62 patients (88.6%), while a mechanical valve was used in 8 patients (11.4%). The mean cardiopulmonary bypass (CPB) and aortic cross-clamp (ACC) times were 135±39 and 89±27 minutes, respectively. All TAVR procedures were performed under general anesthesia. The mean procedural time of TAVR was 88±45 minutes. Balloon-expandable, self-expanding, and mechanically expandable valves were used in 40 (51.9%), 26 (33.8%), and 11 (14.3%) patients, respectively.

The study protocol was reviewed by the institutional review board (IRB) and was approved as a minimal-risk retrospective study (IRB approval no., H-2112-050-1281) that

Table 1. Baseline characteristics of the patients

Characteristic	SAVR group (n=70)	TAVR group (n=77)	p-value
Age (yr)	72.9±8.4	81.5±5.2	<0.001
Female sex	36 (51.4)	42 (54.5)	0.705
Society of Thoracic Surgeons score (%)	2.6±1.7	4.8±3.2	<0.001
NYHA class ≥3	13 (18.6)	45 (58.4)	<0.001
Body surface area (m^2)	1.6±0.2	1.6±0.2	0.506
Body mass index ≥25 (kg/m^2)	29 (41.4)	37 (48.1)	0.420
Diabetes mellitus	23 (32.9)	31 (40.3)	0.352
Hypertension	42 (60.0)	64 (83.1)	0.002
Dyslipidemia	28 (40.0)	61 (79.2)	<0.001
History of stroke	5 (7.1)	5 (6.5)	>0.999
Coronary artery disease	8 (11.4)	30 (39.0)	<0.001
Atrial fibrillation	3 (4.3)	24 (31.2)	<0.001
Baseline serum creatinine (mg/dL)	1.3±0.4	1.5±0.6	0.200
Baseline eGFR (mL/min/1.73 m^2)	47.9±9.5	43.5±12.0	0.034
Left ventricular ejection fraction (%)	58.0±9.8	58.7±10.9	0.354

Values are presented as mean±standard deviation or number (%).
SAVR, surgical aortic valve replacement; TAVR, transcatheter aortic valve replacement; NYHA class, New York Heart Association classification of heart failure; eGFR, estimated glomerular filtration rate.

did not require individual consent.

Evaluation of clinical outcomes

The primary endpoint of the study was the occurrence rate of AKI after operation, which was defined according to the RIFLE definition (an acronym corresponding to the risk of renal dysfunction, injury to the kidney, failure of kidney function, loss of kidney function, and end-stage kidney disease) [11] as a rise in serum creatinine (Cr) level equal or more than 50% of baseline value within 7 days after the procedure.

The secondary endpoints were operative mortality and postoperative complications. Operative mortality was defined as death from any cause during hospitalization or within 30 days after the procedure. The patients were continuously monitored with postoperative electrocardiography during their stay in the intensive care unit and in the general ward until discharge. A standard 12-lead electrocardiogram was checked daily thereafter during the hospital stay. An occurrence of atrial fibrillation that lasted for at least 30 seconds was defined as postprocedural atrial fibrillation [12]. Respiratory complications included postoperative pneumonia or prolonged ventilator support lasting longer than 48 hours. Low cardiac output syndrome (LCOS) was defined as a cardiac index lower than 2.0 L/min/m^2 or a systolic arterial pressure lower than 90 mm Hg requiring support from inotropic agents such as dopamine or dobutamine infused at more than 5 μg/kg/min or the use of epinephrine or norepinephrine at any dose. Perioperative stroke was defined as stroke occurring in the first 30 days after the procedure with a focal neurological deficit of central origin lasting over 24 hours with or without confirmation with neuroimaging [13]. Postprocedural bleeding was defined following the Valve Academic Research Consortium-2 (VARC-2) criteria of major bleeding, such as a need for massive transfusion or re-operation. Vascular damage was also defined in conformity with the VARC-2 criteria as major vascular complications, such as aortic dissection, and minor vascular complications, such as access-related vascular injury not leading to life-threatening or major bleeding.

Statistical analysis

The statistical analyses were performed using SAS ver. 9.4 (SAS institute Inc., Cary, NC, USA). The data are expressed as means±standard deviations, medians with interquartile ranges or proportions. Comparisons of categorical and continuous variables were performed with the chi-square test or the Fisher exact test and the Student t-test or the Wilcoxon rank sum test, respectively. Factors associated with AKI were identified using the backward elimination method in a multivariable logistic model including variables with a p-value <0.2 in the univariate logistic analysis and adjusted for the baseline Cr level. Comparisons of the effect of the treatment modality on postoperative complications were also conducted using logistic regression models. Overall survival was estimated using the Kaplan-Meier method, and univariate and multivariable risk factor analyses were performed using Cox proportional hazard models. A p-value less than 0.050 was considered to indicate statistical significance.

Results

Primary endpoint: occurrence rate of postoperative acute kidney injury

Seventeen patients in the SAVR group (24.3%) and 6 patients in the TAVR group (7.8%) experienced postoperative AKI (p=0.006). The renal function of more than half of these patients had recovered by discharge (n=10, 14.3% and n=4, 5.2%, respectively). Postoperative dialysis was required in 6 (8.6%) and 2 (2.6%) patients in the SAVR and TAVR groups, respectively. Among these, 1 of 6 patients in the SAVR group was free from constant dialysis on discharge, while 1 of 2 patients who received dialysis after TAVR recovered from dialysis on discharge (Table 2). The multivariable logistic regression model revealed that SAVR

Table 2. Occurrence rate of postoperative acute kidney injury

Variable	SAVR group (n=70)	TAVR group (n=77)	p-value
AKI	17 (24.3)	6 (7.8)	0.006
Restored renal function on discharge	10 (14.3)	4 (5.2)	0.086
AKI requiring dialysis	6 (8.6)	2 (2.6)	0.151
Requiring dialysis on discharge	5 (7.1)	1 (1.3)	0.103

Values are presented as number (%).
SAVR, surgical aortic valve replacement; TAVR, transcatheter aortic valve replacement; AKI, acute kidney injury.

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Table 3. Multivariable risk factor analysis adjusted for preoperative creatinine levels for the occurrence of acute kidney injury after the procedure

Variable	Univariate analysis	Multivariable analysis	
	p-value	Odds ratio (95% CI)	p-value
SAVR vs. TAVR group	0.009	5.62 (1.79–17.58)	0.003
Baseline eGFR (mL/min/1.73 m^2)	0.072	1.01 (0.93–1.10)	0.811

All variables demonstrated in Table 1 were analyzed, and only variables that were entered into the multivariable model are shown.
CI, confidence interval; SAVR, surgical aortic valve replacement; TAVR, transcatheter aortic valve replacement; eGFR, estimated glomerular filtration rate.

Table 4. Early clinical outcomes

Variable	SAVR group (n=70)	TAVR group (n=77)	p-value
Early mortality	3 (4.3)	1 (1.3)	0.347
Length of stay (day)	9.5 (7–14)	7.0 (6–8)	<0.001
Complications			
Atrial fibrillation	34 (48.6)	4 (5.2)	<0.001
Complete atrioventricular block	3 (4.3)	13 (16.9)	0.014
Permanent pacemaker insertion	2 (2.9)	11 (14.3)	0.015
Respiratory complications	5 (7.1)	12 (15.6)	0.110
Low cardiac output syndrome	6 (8.6)	2 (2.6)	0.151
Bleeding complication	4 (5.7)	3 (3.9)	0.605
Stroke	0	5 (6.5)	0.060
Vascular damage	0	8 (10.4)	0.010
Paravalvular leakage			
Mild	4 (5.7)	12 (15.6)	0.055
≥Moderate	0	1 (1.4)	>0.999

Values are presented as number (%) or median (interquartile range).
SAVR, surgical aortic valve replacement; TAVR, transcatheter aortic valve replacement.

(odds ratio [OR], 5.62; 95% CI, 1.79–17.58) was the only significant factor associated with post-procedural AKI (Table 3).

Secondary outcomes: early clinical outcomes

The operative mortality rate was 4.3% (n=3) and 1.3% (n=1) in the SAVR and TAVR groups, respectively, without a significant intergroup difference (p=0.347). The causes of death observed in the SAVR group included LCOS combined with pneumonia occurring on postoperative day 5, sudden cardiac arrest following bradyarrhythmia on postoperative day 6, and septic shock with disseminated intravascular coagulation that lasted for 17 days, whereas 1 patient in the TAVR group died of peri-procedural aortic dissection. Common postoperative complications included new-onset atrial fibrillation (n=38, 25.9%), respiratory complications (n=17, 11.6%) and LCOS (n=8, 5.4%). Permanent pacemaker (PPM) implantation was needed in 13 patients (8.8%) (Table 4).

The SAVR group patients had a higher risk of postoperative atrial fibrillation (OR, 16.65; 95% CI, 4.44–62.50; p<0.001), whereas TAVR was related to an increased risk of PPM insertion after the procedure (OR, 5.67; 95% CI, 1.2–26.55; p=0.028) in each multivariable analysis for secondary outcomes.

Secondary outcomes: mid-term survival

The median follow-up duration was 34 months (interquartile range, 21–48 months). Late death occurred in 2 and 2 patients in the SAVR and TAVR groups, respectively. The 1- and 5-year survival rates were 89.8% and 88.0%, respectively, in the SAVR group, and 97.2% and 95.5%, respectively, in the TAVR group (Fig. 2). The Cox proportional hazard models showed that the occurrence of AKI and the presence of coronary artery disease were associated with overall survival in the multivariable analysis, while the treatment modality (p=0.494) and paravalvular leak (p=0.513) were not in the univariate analyses (Table 5).

Discussion

The present study demonstrated that SAVR has a greater

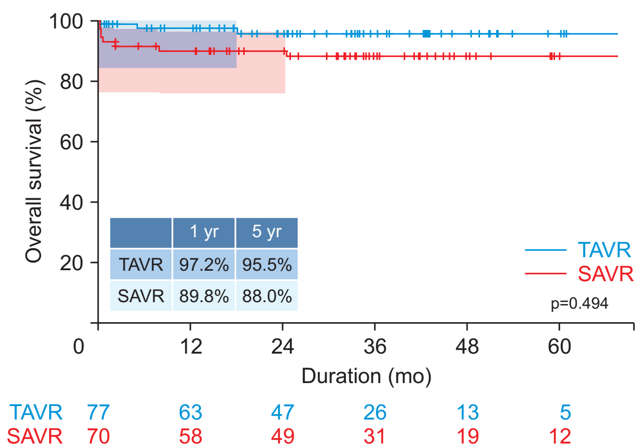

Fig. 2. Kaplan-Meier survival curves in the surgical aortic valve replacement (SAVR) and transcatheter aortic valve replacement (TAVR) groups.

Table 5. Cox proportional hazard model analyzing risk factors for mid-term survival

Variable	HR (95% CI)	p-value
AKI after procedure	2.28 (1.56–3.32)	<0.001
Coronary artery disease	2.84 (1.01–7.97)	0.047
Dyslipidemia	0.49 (0.18–1.35)	0.167
Body mass index ≥25 kg/m^2	0.43 (0.14–1.36)	0.151

All variables demonstrated in Table 1 and postoperative complications such as AKI and paravalvular leak were analyzed, and variables that were entered into the multivariable model are shown.
HR, hazard ratio; CI, confidence interval; AKI, acute kidney injury.

risk of AKI compared to TAVR in patients with advanced CKD. As procedural skills have evolved and the clinical outcomes of TAVR have improved, the indications of TAVR have been expanded to low-risk SAVR patients [2-4]. Both SAVR and TAVR could theoretically cause postprocedural AKI, particularly in patients with advanced CKD; in the SAVR group, multiple factors such as the detrimental effects of CPB and postoperative vasoplegia and bleeding could result in AKI after surgery [14]. When the patient's blood components come into contact with the artificial surface of the CPB circuit, a proinflammatory response occurs, resulting in a systemic inflammatory response causing ischemic kidney injury [15]. In addition, combined hypotension and anemia, which can easily result from postoperative bleeding, increase the risk of AKI [16]. On the contrary, TAVR has the potential hazard of inducing AKI by contrast-induced nephropathy, which depends on the contrast volume used [9,17]. Other periprocedural factors affecting AKI after TAVI include atherosclerotic emboli to the renal vessels and renal hypoperfusion related to rapid pacing during valve implantation and hypoperfusion related to vascular complication and bleeding [17,18].

Despite these factors, previous studies have proclaimed that TAVR is superior to SAVR in preserving patients' renal function. One randomized clinical trial revealed the incidence of postoperative AKI was higher after SAVR than after TAVR (6.7% versus 0.7%, p=0.01) [19]. Another prospective multicenter study comparing SAVR with TAVR conducted to intermediate-risk patients with AS and CKD demonstrated that AKI was more common after SAVR than after TAVR (26.3% versus 10.3%, p<0.001) [20]. These results are in agreement with those of the present study. In the present study, 17% of the patients in the SAVR group experienced postoperative AKI, whereas 6% of the patients in the TAVR group developed postoperative AKI. This difference was also statistically significant in the multivariable analysis, which was performed to overcome the retrospective nature of the present study. Moreover, 5 of 17 patients with postoperative AKI in the SAVR group needed dialysis even on discharge, whereas dialysis was required in only 1 of 6 patients in the TAVR group. Although this difference was not statistically significant, the lack of statistical significance might have been due to the relatively small number of the study patients.

The ACC and CPB times in the SAVR group of the present study were relatively long, although they were within the ranges presented in the literature [21]. A high calcium burden in cardiovascular system, including a diseased aortic valve leaflet and root, might be the reason for these long ACC and CPB times [22], which might affect the high occurrence rate of AKI in the SAVR group.

One of the weak points of TAVR in patients with CKD was a high rate of PPM insertion after the procedure. Although a higher risk of advanced conduction abnormalities, including new-onset left bundle branch block and high-grade atrio-ventricular block requiring pacemaker assistance, after TAVR than after SAVR has been well demonstrated in previous studies [23,24], the PPM insertion rate of 14.3% in the TAVR group was relatively high considering recent studies reporting PPM insertion rates of 4.0% to 12.7% [25,26]. In addition, a previous study at our institution reported that 5.8% of 206 patients underwent PPM insertion after a TAVR procedure [27]. This might be attributed to the fact that patients with CKD have a high burden of calcium in the cardiovascular system including a diseased aortic valve [28], which is vulnerable to conduction block after the TAVR procedure. Therefore, a multidisciplinary team discussion including the risks of AKI and conduction abnormality might be mandatory in the decision-making process when treating patients with both AS and CKD to optimize patients' outcomes.

Limitations

The present study has several limitations that should be recognized. First, this was a retrospective observational study conducted at a single center. Second, the number of patients might not have been large enough to draw definitive conclusions. Third, the patients' characteristics were different between the 2 groups, and patients who underwent mechanical SAVR were included, although the number of patients was small; therefore, selection bias might have affected the results of the present study.

Conclusion

In AS patients with CKD, the risk of postprocedural AKI might be higher after SAVR than after TAVR. Therefore, this risk after SAVR and the risk of PPM insertion after TAVR should be discussed by the heart team to determine the optimal treatment strategy for individual patients.

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Conflict of interest

No potential conflict of interest relevant to this article was reported.

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