Factors associated with acute kidney injury in patients undergoing transcatheter aortic valve implantation: Short-term outcomes and impact of right heart failure

Dilek Aslan Kutsal,1 Sait Terzi2
1Department of Nephrology, University of Health Sciences, Dr. Siyami Ersek Cardiovascular Surgery Training and Research Hospital, Istanbul, Türkiye
2Department of Cardiology, University of Health Sciences, Dr. Siyami Ersek Cardiovascular Surgery Training and Research Hospital, Istanbul, Türkiye

ABSTRACT

OBJECTIVE: Transcatheter aortic valve implantation (TAVI) was developed as an alternative to surgery for symptomatic, high-risk patients with severe aortic stenosis (AS). Acute kidney injury, a major complication of TAVI, is associated with a poor prognosis. In our study, we planned to investigate the effect of right heart failure on the development of acute kidney injury after TAVI and other factors contributing to the development of AKI.

METHODS: Between January 2015 and December 2020, 198 patients who underwent TAVI due to severe symptomatic aortic stenosis at Dr. Siyami Ersek Cardiovascular Surgery Hospital were screened. Local ethics committee approval was obtained (HINEAH-KAEK 2021/134-3343). Transthoracic echocardiographic findings and laboratory evaluations were recorded. Patients were evaluated according to Acute Kidney Injury Network (AKIN) criteria.

RESULTS: The rate of AKI after TAVI was found to be 41.9%. The mean age of patients who developed AKI was higher (80.90±6.8). AKI development rates were higher in the female gender (68.7%) and patients with hypertension (44.8%). It was observed that the risk of developing AKI was higher in patients who underwent TAVI and developed AKI afterwards, especially in patients with stage-3 and stage-4 advanced CKD before TAVI (p<0.01) We did not find an independent relationship between AKI and right-heart failure in our analysis.

CONCLUSION: We observed that chronic kidney disease before TAVI, advanced age, and female gender are important determinants of the development of AKI after TAVI. Although a relationship between TAVI and right heart failure has not been demonstrated, large-scale studies are needed in the future.

Keywords: Acute kidney injury; right heart failure; risk factors; transcatheter aortic valve implantation.

The incidence of degenerative aortic stenosis increases with the aging of the population. Early recognition and treatment of aortic stenosis is of great importance because untreated symptomatic severe aortic stenosis is fatal. There is no effective medical treatment for aortic stenosis. Surgical aortic valve replacement or transcatheter aortic valve implantation (TAVI) is recommended to improve survival in symptomatic patients with severe aortic stenosis.

Cite this article as: Kutsal DA, Terzi S. Factors associated with acute kidney injury in patients undergoing transcatheter aortic valve implantation: Short-term outcomes and impact of right heart failure. North Clin Istanb 2024;11(2):133–139.
TAVI is an effective and safe treatment option for patients with high surgical risk in the treatment of aortic stenosis. Despite conclusive evidence for the safety and efficacy of TAVI with respect to the prognostic benefits and outcomes of treated patients, the determinants of clinical response to TAVI are not well defined. It is known that acute kidney injury (AKI), which affects this clinical response and occurs specifically after TAVI, is a common complication and is associated with a poor prognosis. The pathogenesis of AKI after TAVI is multifactorial. The relationship between right heart failure and AKI is known, but there are very few reports on this subject. Right heart failure causes renal venous congestion and decreased renal perfusion pressure, leading to AKI and often cardiorenal syndrome. Since there is no evaluation of right heart dysfunction in the development of AKI after TAVI, we planned to investigate the development of acute renal failure in patients with right heart failure before TAVI and other factors in patients who developed AKI.

**MATERIALS AND METHODS**

It is a retrospective, single-center observational study. Patients who were diagnosed with severe aortic stenosis according to clinical, echocardiographic, and hemodynamic criteria in the cardiology clinic at Siyami Ersek Thoracic and Cardiovascular Surgery Center Training and Research Hospital between January 2015 and December 2020 and were at high risk for surgical repair were included in the study. Ethical committee approval was received from the clinical research ethics committee of the Haydarpasa Numune Training and Research Hospital, (dated: 26.04.2021, approval no: HNEAH-KAEK 2021/134-3343). The study was conducted in compliance with the principles included in the Declaration of Helsinki.

Patients who had previously received hemodialysis treatment were excluded from the study. Demographic and clinical characteristics of the patients, laboratory and echocardiographic data, as well as complications during the procedure were recorded. Acute kidney injury (AKI) was defined according to the increase in serum creatinine within the first 48 hours using the Acute Kidney Injury Network criteria. Demographic characteristics of patients classified between stage 1 and stage 3, renal functions of those whose records were available, and mortality rates were recorded. Among the transthoracic echocardiographic evaluations of the patients, the values of the tricuspid annular plane systolic excursion (TAPSE) and inferior vena cava (IVC) measurements were recorded for right ventricular dysfunction. TAPSE<17 mm was considered as the definition of right ventricular dysfunction. Since the detailed evaluation of the right ventricle was performed by different operators, two-parameter evaluations and cut-off values were taken as the basis. The relationship between these measurements and patients who developed AKI was evaluated. OpxalTM 350 (MDS Health Products Trade. Inc, Turkey) was used in all procedures. OpxalTM 350 is a low-osmolar, non-ionic, water-soluble, radiographic contrast media containing 755 mg/mL of Iohexol equivalent to 350 mg/mL of organic iodine (Osmolality 810 mOsm/kg/H2O) was used as contrast media in all patients. All patients at high risk for contrast medium-induced nephropathy were evaluated by nephrology before the procedure and precautions were taken for contrast nephropathy. Pre and post-procedural hydration was optimized. It was recommended that the amount of contrast material used during the procedure be kept to a minimum level, no unnecessary volume of contrast agent was applied to our patients.

**Statistical Analysis**

SPSS Statistics (23.0, Inc, Chigaco, Illinois 13 USA) program was used for statistical analysis. Clinical and laboratory data of the patients were expressed as±mean standard deviation and percentage (%). The distribution of quantitative data was examined with the one-sample Kolmogorov-Smirnov test. Wilcoxon test for repeated measurements, one of the non-parametric tests, was applied to data that was not normally distributed. The chi-square test was applied for independent non-parametric qualitative data. Student’s t-test was used to compare parametric variable means. Results were considered significant at the 95% confidence interval and p<0.05 level.
RESULTS

The results of a total of 198 patients were analyzed retrospectively. Demographic characteristics of the patients whose records were obtained, acute kidney injury development rates, and demographic, laboratory, and echocardiographic characteristics of patients who developed AKI and those who did not were compared. These results are shown in Table 1, Table 2 and Table 3.

DISCUSSION

The prevalence of aortic stenosis is increasing with the aging population, and despite limited data, current guidelines recommend aortic valve replacement as the only effective treatment for severe symptomatic aortic stenosis. Although surgical treatment has long been the gold standard treatment modality, transcatheter aortic valve implantation (TAVI) is now a widely used alternative for patients with native aortic valve stenosis who are not suitable or are at high risk for surgery. Initially, this technique used to be considered only in high-risk patients. Nowadays, it is increasingly preferred for intermediate-risk patients. In TAVI, a team of cardiac specialists determines the most appropriate treatment for each patient based on their comorbidities, patient preference, and the potential for improvement in quality of life. Moreover, the incidence of TAVI complications has significantly decreased with advances in patient selection, multimodal imaging, and third-generation devices. TAVI has been shown to be an effective and reliable procedure; however, despite the accumulating clinician experience and advances in technology, most studies prove that procedural complications and co-morbidities remain an important problem affecting patient outcomes [1]. Patients undergoing TAVI are usually very old. The prevalence gradually increases with age, ranging from 0.2% in the 50–59 age group to 3.9% in the 70–79 age group and 9.8% in the 80–89 age group [2]. The mean age of patients who participated in our study was 78.49±8.01 years. It was similar to the population included in the SURTAVI and NOTION trials, which included TAVI patients [3, 4]. In our study, female patients were more predominant with a mean age of 56.1%. and our patients’ EF (49.33±0.79%) was found to be normal (>40%) and their mean trans-valvular gradient was high (50.49±1.046) (Table 1). Our study included patients with more comorbidities than existing TAVI studies. Table 1 shows that 29.3% of our patients had previous cardiac operations.

<table>
<thead>
<tr>
<th>Table 1. Demographic characteristics of patients (n=198)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years, Mean±SD)</td>
</tr>
<tr>
<td>Gender (%)</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>DM (%)</td>
</tr>
<tr>
<td>HT (%)</td>
</tr>
<tr>
<td>COPD (%)</td>
</tr>
<tr>
<td>CKD (%)</td>
</tr>
<tr>
<td>Stage 1-2: GFR:≥60 ml/dk/1.73m²</td>
</tr>
<tr>
<td>Stage 3: GFR:30–59 ml/dk/1.73m²</td>
</tr>
<tr>
<td>Stage 4: GFR&lt;29 ml/dk/1.73m²</td>
</tr>
<tr>
<td>NYHA 3–4 (%)</td>
</tr>
<tr>
<td>SVD (%)</td>
</tr>
<tr>
<td>PHT (&gt;35 mmHg) (%)</td>
</tr>
<tr>
<td>TAPSE (&lt;17 mm) (%)</td>
</tr>
<tr>
<td>IVC diameter (&gt;21 mm) (%)</td>
</tr>
<tr>
<td>Left ventricular ejection fraction (%)</td>
</tr>
<tr>
<td>Aortic mean transvalvular gradient (mmHg)</td>
</tr>
<tr>
<td>Complications (%)</td>
</tr>
<tr>
<td>Death (%)</td>
</tr>
<tr>
<td>Rate of AKI (48th hour GFR) (%)</td>
</tr>
<tr>
<td>GFR (&lt;59 ml/1.73 m²)</td>
</tr>
</tbody>
</table>

DM: Diabetes mellitus; HT: Hypertension; COPD: Chronic obstructive pulmonary disease; SVD: Cerebrovascular disease; CKD: Chronic kidney disease; GFR: Glomerular filtration rate; NYHA: New York Heart Association; AKI: Acute kidney injury; TAPSE: Tricuspid annular plane systolic excursion; PHT: Pulmonary hypertension; IVC: Inferior Vena Cava Collapsing Index. Table 1 shows the overall distribution of 198 TAVI patients, most of the patients (56.1%) were female gender. HT was detected in 83.3%, and advanced stage (stage-3 and stage-4) CKD was detected in 51.5%. Our patient group had high comorbidities. The rate of patients with a history of coronary bypass was observed as 29.3%, COPD: 49.5%. In patients with a mortality rate of 11.1% and a complication rate of 29.8%, the rate of patients with TAPSE<17 mm in the echocardiographic evaluation of right heart failure was found to be 24.7%. The rate of patients with inferior vena cava diameter >21 mm was found to be 54%, and the rate of patients with PHT>35 mmHg was 68.7%.

It is also known that the prevalence of chronic kidney disease is higher in patients with aortic stenosis and there is an increase in the rate of progression of aortic stenosis, in patients with chronic kidney disease [5]. Assessment of baseline renal dysfunction is clinically more important in patients undergoing TAVI compared to surgery. This is a complication known to commonly persist and is associated with a poor prognosis [1]. Pre-TAVI assessment of renal function status is important as these patients are at increased risk for AKI following TAVI. In our study, as renal dysfunction contributes to
poor outcomes, the number of advanced-stage (Stage 3–4) CKD patients was observed to be 101 (51%). Especially, post-TAVI-associated acute kidney injury (AKI) is a common complication that is an important determinant of mortality. AKI incidence ranges between 3% and 57%, depending on the defining criteria, patient selection and characteristics, and various factors such as the experience of the clinician and peri-procedural complications [6, 7].

According to the AKIN criteria, patients with an increase in serum creatinine ≥0.3 mg/dL or ≥50% within 48 hours following TAVI compared to baseline creatinine and a concomitant decrease in eGFR values were considered AKI [8]. In our study, eGFR (estimated glomerular filtration rate) values were calculated using the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration Equation) according to the basal creatinine levels of the patients before TAVI. Among patients with increased creatinine (>0.3 mg) at the 48th hour after TAVI and decreased GFR according to CKD-EPI, AKI patients with stages 1 and 2 were accepted. In our study, the rate of AKI was 41.9% [9].

Many factors play a role in the development of AKI after TAVI. Hemodynamic changes such as the development
of hypotension during the procedure, prolonged procedure and bleeding along with inflammatory and nephrotoxic causes (amount of contrast material) are some of the factors that cause kidney damage [10]. Among other patient-specific risk factors, advanced age, female gender, diabetes mellitus, hypertension, presence of chronic kidney disease, and presence of anemia before and after the procedure are independent risk factors for development of AKI after TAVI [11–13]. In our study, in Table 2, the mean age of patients who developed AKI was higher (80.90±6.8). AKI development rates were higher in female gender (68.7%) and patients with hypertension (44.8%). In the literature, it was observed that the development of AKI was higher in patients with the same characteristics [14, 15]. We also observed that the risk of developing AKI was significantly higher in patients with lower hemoglobin levels before TAVI. Previous studies have reported that the presence of anemia before TAVI is a risk factor for the development of AKI [16]. The presence of CKD before TAVI has been found to be another important risk factor for the development of AKI and a significant predictor of clinical outcomes [17, 18]. Classification according to CKD stages before TAVI helps with the risk assessment for early and midterm clinical outcomes. Due to the high mortality rates after TAVI for patients with stage-4 CKD, it is difficult to accept patients with stage-4 and end-stage renal failure [19]. CKD staging according to GFR (based on initial eGFR): ≥60 ml/min/1.73 m² (normal or mild CKD, stage 1 and 2), 30–59 ml/min (moderate CKD, stage 3), 15–29 ml/min/1.73 m² (severe CKD), stage 4) was done. We found the rate of patients with GFR: ≥60 ml/min/1.73 m² (48.5%), the rate of patients with stage-3 (44.4%), and the rate of patients with stage-4 (7.1%). Patients with a history of dialysis or end-stage renal failure were not included in the study [20]. In Table 2, it was observed that the risk of developing AKI was higher in patients who underwent TAVI and developed AKI afterwards, especially in patients with stage-3 and stage-4 advanced CKD before TAVI (p<0.01). Additionally, in Table 2, it was determined that 16 patients who developed AKI died in the early period after the procedure. The mortality rate was statistically higher in patients who developed AKI compared to patients who did not develop AKI (19%, and 5%, respectively). In another study conducted in Turkey, when the short and mid-term results of 136 patients who underwent TAVI were evaluated retrospectively, it was observed that 12 patients (8.8%) died perioperatively, and 8 patients died within 6 months. Creatinine levels of deceased patients were found to be higher at the 48th hour compared to the living group [21]. It has been suggested that right ventricular (RV) failure has an impact on the kidney and contributes to the development of AKI. In right ventricular failure, renal function may worsen due to decreased renal perfusion and increased venous pressure, and AKI may develop due to renal congestion. The presence of right heart failure as a late marker in aortic stenosis has been associated with poor prognosis [22].

Galli et al. [23] reported the prevalence of right ventricular dysfunction in patients with severe aortic stenosis as 24%, and Cavalcante et al. [24] reported 57%. Despite these high rates, right ventricular dysfunction is not included in the evaluation of aortic stenosis, current guidelines, or risk scoring of TAVI patients [23–25]. There is not enough information in the literature about the development of right ventricular dysfunction and AKI before TAVI. A meta-analysis showed that baseline RV dysfunction is a predictor of early mortality and adverse outcomes in TAVI patients. There is no consensus on the incidence, prognostic impact, and development of right ventricular dysfunction in patients treated with TAVI. The ideal measurements of right ventricular systolic dysfunction for evaluation in the TAVI population are still unknown. The standard approach in the evaluation of aortic stenosis is echocardiographic examination. It also plays an important role in the evaluation of all structural changes due to aortic stenosis [26–28]. There is no clear information about right ventricle evaluations before TAVI due to reasons such as the different cut-off values of Tricuspid annular plane systolic excursion (TAPSE) and Peak Systolic Velocity (PSV) measurements in the evaluation of right ventricular function or echocardiograms performed by different cardiologists, or the lack of systematic and consistent imaging methods.

The prevalence of right ventricular dysfunction before TAVI is as high as its incidence, ranging from 8.7% to 29.1% in previous studies. This variability can be explained by the fact that the echocardiographic parameters (TAPSE, S’ wave, fractional area change) and threshold values used in the evaluation of RV function are highly variable depending on the study [29, 30]. A retrospective cohort study on right heart function before TAVI reported that outcomes were worse in the presence of right ventricular dysfunction compared to those without at baseline [11]. In our study, right ventricular dysfunction was defined as a TAPSE value...
below 17 mm, and right ventricular dysfunction was detected in 49 (24.7%) of a total of 198 patients (Table 1). Echocardiographic evaluation was performed by different cardiologists. When the rate of right ventricular dysfunction in patients who developed AKI was analyzed, 19 patients (38.8%) had TAPSE <17 mm. According to the baseline TAPSE IVC measurements of TAVI patients, we did not find an independent relationship between AKI and right-sided insufficiency measurements in our analysis.

Our study was a single-center, retrospective study conducted in our country to evaluate survival rates and influencing factors in patients with symptomatic aortic stenosis who developed AKI after TAVI. Although there are no studies in the literature showing a significant relationship between right ventricular dysfunction and AKI in TAVI patients, prospective, large-scale randomized controlled studies are needed on this subject.

Study Limitations

The limitations of our study are that the sample size was small, 1-year outcome data was not available, follow-up periods were less than 30 days, long-term mortality and morbidity rates were unknown, and echocardiographic imaging varied depending on operator experience and expertise, and therefore no optimum evaluation or advanced examination MRI was performed. The findings of our study should be confirmed by further prospective studies.

Conclusion

Due to the long-life expectancy of TAVI candidate patients, it is important to determine the factors affecting short- and long-term mortality rates. It is of critical importance today to identify risk factors that contribute to the development of AKI after TAVI, such as old age (>75), diabetes, pre-TAVI creatinine level, pre-TAVI left ventricular ejection fraction, and COPD. Although the relationship between contrast medium volume and toxicity and the risk of AKI development in TAVI patients is not clear, further studies are needed to predict its relationship with TAVI.

The presence of CKD before TAVI is very important in the development of AKI, which affects long-term survival and causes significant morbidity. Careful evaluation of risk factors in high-risk patients by the multidisciplinary TAVI planning team, including nephrologists along with cardiologists, will help improve outcomes.

**Ethics Committee Approval:** The Haydarpasa Numune Training and Research Hospital Clinical Research Ethics Committee granted approval for this study (date: 26.04.2021, number: HNEAH-KAEK 2021/134-3343).

**Authorship Contributions:** Concept – DAK, ST; Design – DAK, ST; Supervision – DAK; Data collection and/or processing – DAK; Analysis and/or interpretation – DAK, ST; Literature review – DAK; Writing – DAK; Critical review – DAK, ST.

**Conflict of Interest:** No conflict of interest was declared by the authors.

**Use of AI for Writing Assistance:** Not declared.

**Financial Disclosure:** The authors declared that this study has received no financial support.

**Peer-review:** Externally peer-reviewed.

**REFERENCES**

13. Kliuk-Ben Bassat O, Finkelstein A, Bazan S, Halkin A, Herz I, Sal-


