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Peer-reviewed Original Research

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Abstract

Transcatheter aortic valve replacement (TAVR) has been recommended as the standard treatment for elderly patients with severe aortic stenosis (AS) and those at increased risk for conventional surgical procedures. Recently, TAVR has been recognized as the treatment of choice for intermediate-risk patients or even low-risk populations with AS. Our study aimed to identify factors influencing adverse events after TAVR procedures. This single-center, retrospective cohort study involved patients with severe AS treated with TAVR from 2016 to 2019. The patient's electronic medical record was reviewed, and those with valve-in-valve replacements and missing demographical data were excluded. We analyzed risk factors related to in-hospital adverse outcomes after the TAVR procedure. Among 953 screened patients, 889 were included in the study. The complication rates were relatively low. Factors that significantly influenced the outcome included age, chronic kidney disease (CKD), dialysis, mitral stenosis, Katz test for frailty, surgical risk score, and calculated operability. Multivariate logistic regression analysis showed that only CKD predicts the likelihood of the composite adverse outcome in TAVR patients during hospitalization. Our study showed that TAVR is an effective and safe option for aortic valve replacement. Perioperative complications depend on different risk factors, particularly CKD, and the results of the Katz test. Identification of risk factors influencing the TAVR outcome is crucial to prevent perioperative complications and mortality.

Keywords: aortic stenosis, transcatheter aortic valve replacement, outcomes, heart failure

Introduction

Aortic stenosis (AS)—a major health problem in the elderly population of developed countries—affects more than 5% of people over 65 years.[1] AS is a progressive, chronic disease with poor outcomes if inadequately treated. Conservative treatment[2] and balloon valvuloplasty[3] do not prolong the life of symptomatic patients. Surgical aortic valve replacement (SAVR) has been established as a treatment of choice for those with severe AS. However, there is a growing number of patients with a high surgical risk. Despite advances in cardiac surgery, up to one-third of patients with AS are not potential candidates for SAVR.[4]

Transcatheter aortic valve replacement (TAVR) is a less invasive procedure recommended as the standard treatment for severe AS in the aging population and those with an increased surgical risk.[2] Over the last decade, TAVR has been recognized as the treatment of choice for intermediate-risk patients[5] and low-risk patients with AS.[6,7] Thus, patient preference now plays an important role in treatment decisions.

Despite the lower procedural risk of TAVR in comparison to SAVR, this promising alternative option still carries the risk of several complications, which include cerebrovascular accidents, vascular complications, coronary obstruction, acute myocardial infarction, valve regurgitation, valve malposition or migration, conduction system defects, and acute kidney injury.[8] Complications can affect up to one-third of patients treated with TAVR.[4] Identifying risk factors influencing TAVR outcome is crucial to prevent perioperative complications. Our study aimed to analyze the success rate of the TAVR procedure, particularly in intermediate- and high-risk patients, and to identify factors that correlate with in-hospital adverse events.

Methods

A waiver of informed consent was obtained from the institutional review board to conduct this single-center, retrospective cohort study that involved patients with severe AS who underwent TAVR at a large, urban hospital from 2016 to 2019. Exclusion criteria were valve-in-valve replacement and missing demographical data.

Institutional Procedures

Patients were selected for the TAVR procedure based on a multidisciplinary team assessment that included an interventional cardiologist and a cardiovascular surgeon.

Before any procedure, a thorough patient history was obtained, and a complete physical examination was performed. A preoperative transthoracic echocardiogram (TTE) was performed on each patient to determine the anatomical and hemodynamical characteristics of the valve. Criteria for the severity of AS were met by reaching a valve area < 1.0 cm^2, a peak aortic velocity ≥ 4.0 m/s, and/or a mean valve gradient ≥ 40 mm Hg.[9] Per the American College of Cardiology and American Heart Association (AHA/ACC) recommendations,[10] the perioperative risk was evaluated by using the Society of Thoracic Surgeons Predicted Risk of Mortality (STS PROM) score and considering the patient's comorbidities, rehab potential, and frailty.[10] The STS PROM score serves as an excellent tool to predict a 30-day risk of mortality of SAVR. A score of < 3% classifies patients into the low-risk category; a score of 4-8% refers to intermediate risk; and patients with a score > 8% are considered high risk. Those with > 50% risk score are considered inoperable.

The main criteria for TAVR approval included severe, symptomatic AS, New York Heart Association (NYHA) class ≥ II, and anatomical suitability for the replacement based on the echocardiographic findings,[11] computed tomography angiography,[12] and preprocedural coronary angiogram.[11] The majority of patients had intermediate (3-8%) or high (> 8%) surgical risk, but there were also some patients with low surgical risk. Other important criteria were frailty, poor rehabilitation potential, other comorbidities, history of previous open-heart surgery, and age.

Patients' frailty was evaluated as recommended by the AHA/ACC[10] by using the albumin level (values < 3.5 g/dL considered as frailty),[13] 15-foot walk test (values were distributed into quartiles since data on patients' body height were not available),[10] handgrip strength test (frailty cut-off values are based on their body mass index [BMI]) and range between 29-32 kg for men and 17-21 kg for women),[14] and Katz Activities of Daily Living, with < 4 points out of 6 considered as frailty.[15]

The TAVR procedure was mainly performed under monitored anesthesia care, and the transfemoral approach was used in most cases. To reduce the risk of cerebrovascular events, a Sentinel cerebral protection device has been implemented in most cases since mid-2017.

Data Collection and Analysis

The patient's electronic medical record was reviewed, and the following data were collected: demographics, comorbidities, procedural details, and safety outcome metrics. A composite outcome within the hospitalization period was defined as developing the following: all-cause death, stroke or transient ischemic attack (TIA), complete heart block requiring a pacemaker, major or life-threatening bleeding, postprocedural acute renal failure, or a major vascular complication.

IBM SPSS Statistics 25.0.0 (IBM) was used for statistical data processing. Descriptive variables were presented as a number of units and shares. In the case of continuous variables, the normality of the distribution was checked by the Kolmogorov-Smirnov test. Normally distributed variables were interpreted by their mean and standard deviation, and asymmetrically distributed variables were explained by their median and range between the 1st and 3rd quartiles. Differences between groups were analyzed with the chi-square test in the case of descriptive variables, while the Student t-test for independent samples was used for variables with a normal distribution. The Mann-Whitney test was used for independent samples in the case of asymmetrically distributed continuous variables. The Kruskal-Wallis test was used to analyze variance. The logistic regression method determined possible prognostic factors for the composite adverse outcome; only the statistically significant variables were considered.

Results

Among the 953 patient files screened, 889 fulfilled the inclusion criteria and were enrolled in the study (Figure 1). Most patients had intermediate or high STS PROM scores (87.4%); 56.6% of the TAVR procedures were classified as elective, 42.1% as urgent, and 1.3% were emergently performed.

The baseline characteristics of patients, their functional status before TAVR, and surgical risk scores are presented in Table 1. The mean age of patients was 77.0 ± 9.0 years. Most patients had one or more risk factors for atherosclerosis, particularly dyslipidemia and arterial hypertension. Approximately a quarter of the patients (23.6%) had chronic kidney disease (CKD), as defined by a glomerular filtration rate of less than 60 mL/min/1.73 m^2 or persistent evidence of

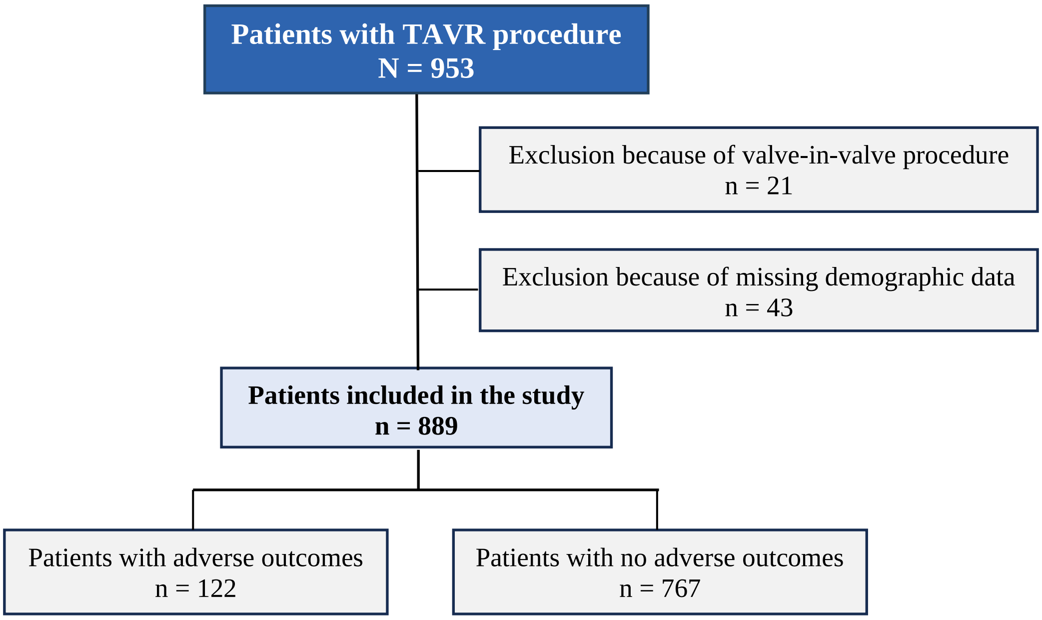

Figure 1. Study screening, enrollment, and outcomes.
Abbreviation: TAVR, transcatheter aortic valve replacement

kidney damage on imaging, biopsy, or urinalysis. A total of 92.5% of patients had limited functional capability (NYHA III and NYHA IV). Functional capability was measured by the Katz, 15-foot walk, and grip tests.

Echocardiography findings are presented in Table 2. On average, the left ventricular ejection fraction (LVEF) was only moderately reduced (mean = 57.5%). In most patients, mild aortic, mitral, and tricuspid regurgitation were present.

During hospitalization, 165 adverse events occurred in 122 patients (13.7%) (Figure 2). We evaluated the possible influence of all the observed parameters on the composite outcome. NYHA class and preoperative echocardiographic characteristics were not significantly related to the outcome. Comorbidities such as diabetes mellitus, peripheral arterial disease, atrial fibrillation, and prior history of stroke or myocardial infarction also proved no statistical association with the in-hospital adverse events. Patients with adverse outcomes were older and had a lower BMI and body surface area (BSA). They were less likely to have chronic obstructive pulmonary disease and more likely to have CKD and mitral stenosis. Patients on dialysis were more likely to develop the composite outcome. Composite adverse events were also closely related to STS PROM score, 15-foot walk test, Katz test, and operability risk (Table 1).

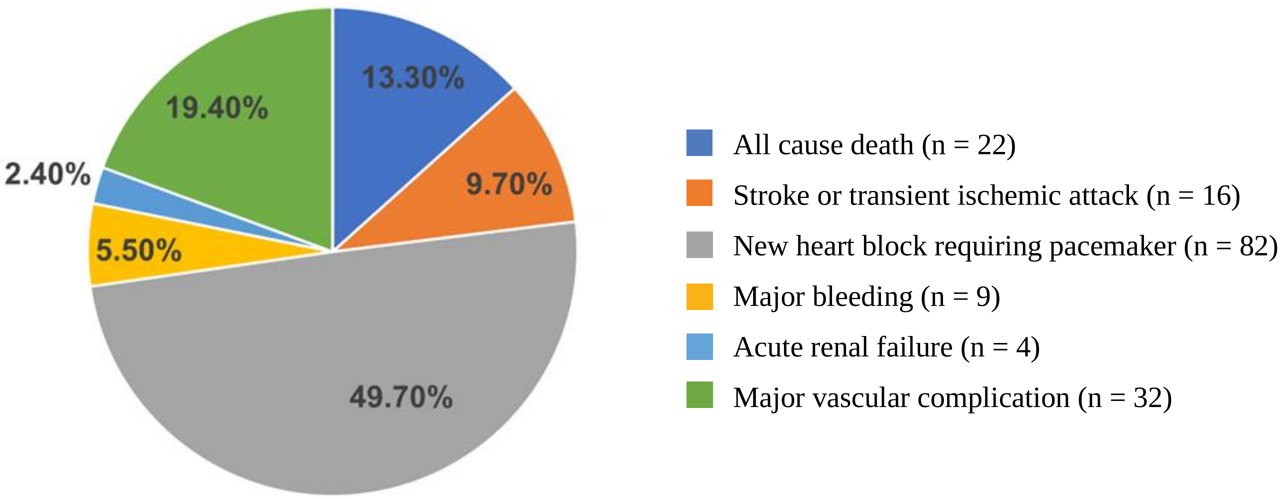

Figure 2. Periprocedural adverse events are summarized. Data are expressed as number (n) and percentage (%) of adverse events.

Table 1. Patients' baseline characteristics, frailty assessment, and surgical risk scores are presented. Data are expressed as number and percentage of patients. The mean and standard deviation are presented for age. As the remaining variables' data were not normally distributed, the median and interquartile range are reported.

Patients' Characteristics	All Patients (N = 889)	Adverse Outcome (n = 122)	No Adverse Outcome (n = 767)	P Value
Clinical variables				
Sex (male)	469.0 (52.8)	66.0 (54.1)	403.0 (52.5)	.749
Age (years)	77.0 ± 9.0	79.0 ± 10.0	77.0 ± 9.0	.020
Body mass index[a]	28.3 (24.9-33.0)	27.0 (24.3-31.0)	28.4 (25.1-33.3)	.013
Body surface area[b]	1.9 (1.7-2.1)	1.9 (1.7-2.1)	1.9 (1.7-2.1)	.037
Atrial fibrillation	248.0 (27.9)	36.0 (29.5)	212.0 (27.6)	.669
History of cancer	194.0 (21.8)	23.0 (18.9)	171.0 (22.3)	.393
COPD	283.0 (31.8)	29.0 (23.8)	254.0 (33.1)	.040
Diabetes mellitus	368.0 (41.4)	45.0 (36.9)	323.0 (42.1)	.276
Chronic kidney disease	210.0 (23.6)	40.0 (32.8)	170.0 (22.2)	.010
Dialysis	53.0 (6.0)	13.0 (10.7)	40.0 (5.2)	.018
Dyslipidemia	564.0 (63.4)	75.0 (61.5)	489.0 (63.8)	.627
Arterial hypertension	777.0 (87.4)	110.0 (90.2)	667.0 (87.0)	.322
History of myocardial infarction	134.0 (15.1)	21.0 (17.2)	113.0 (14.7)	.477
History of stroke or TIA	129.0 (14.5)	24.0 (19.7)	105.0 (13.7)	.081
Peripheral arterial disease	225.0 (25.3)	32.0 (26.2)	193.0 (25.2)	.801
Abdominal aortic aneurysm	13.0 (1.5)	3.0 (2.5)	10.0 (1.3)	.404
Mitral stenosis	79.0 (8.9)	17.0 (13.9)	62.0 (8.1)	.035
Functional status				
Serum albumin < 3.5 g/dL	390.0 (49.3)	56.0 (52.3)	334.0 (48.8)	.500
Katz test frailty[c]	161.0 (21.5)	34.0 (33.7)	127.0 (19.6)	.001
15-foot walk test frailty				
< Q1	135.0 (18.9)	15.0 (15.6)	120.0 (19.4)	
Q1–Q2	135.0 (18.9)	14.0 (14.6)	121.0 (19.5)	
Q2–Q3	140.0 (19.6)	16.0 (16.7)	124.0 (20.0)	.021
> Q3	139.0 (19.4)	19.0 (19.8)	120.0 (19.4)	
Weak/frail	167.0 (23.3)	32.0 (33.3)	135.0 (21.8)	
Grip test frailty[d]	642.0 (91.2)	93.0 (94.9)	549.0 (90.6)	.163
Operability[e]				
Low	12.0 (1.4)	2.0 (1.6)	10.0 (1.3)	
Intermediate	244.0 (27.5)	22.0 (18.0)	222.0 (29.0)	.019
High	632.0 (71.1)	98.0 (80.3)	534.0 (69.7)	
NYHA class[f]				
II	66.0 (7.4)	10.0 (8.2)	56.0 (7.3)	
III	453.0 (51.1)	58.0 (47.5)	395.0 (51.6)	.624
IV	368.0 (41.4)	54.0 (44.3)	314.0 (41.0)	
STS PROM score[g]				
Low (< 3%)	111.0 (12.6)	13.0 (10.7)	98.0 (12.9)	
Intermediate (3-8%)	410.0 (46.4)	45.0 (36.9)	365.0 (48.0)	.012
High (> 8%)	362.0 (41.0)	64.0 (52.5)	298.0 (39.2)	

Abbreviations: COPD, chronic obstructive pulmonary disease; N, number; NYHA, New York Heart Association; STS PROM, Society of Thoracic Surgeons Predicted Risk of Mortality; TIA, transient ischemic attack
[a]missing 9, [b]missing 14, [c]missing 140, [d]missing 185, [e]missing 1, [f]missing 2, [g]missing 6

Table 2. Preoperative echocardiography findings. Data are expressed as number (n) and percentage (%) of patients. As data were not normally distributed, the median and interquartile range are reported for the remaining variables.

Patients (N = 889)	
Left ventricular ejection fraction (%)[a]	57.5 (47.5-62.5)
AV mean gradient[b]	44.0 (40.2-50.0)
AV peak velocity[c]	4.3 (4.1-4.6)
AV area[d]	0.7 (0.5-0.8)
AV index[e]	0.3 (0.3-0.4)
Aortic insufficiency/regurgitation[f]	
Mild	470.0 (64.6)
Moderate	95.0 (13.0)
Severe	11.0 (1.5)
Mitral Regurgitation[g]	
Mild	546.0 (61.4)
Moderate	99.0 (12.9)
Severe	25.0 (2.8)
Tricuspid regurgitation[h]	
Mild	575.0 (64.7)
Moderate	113.0 (14.7)
Severe	19.0 (2.5)
Left ventricular outflow tract[i]	2.0 (1.9-2.0)
Aortic annulus area[j]	448.1 (386.7-522.4)

Abbreviation: AV, aortic valve
[a]missing 12, [b]missing 29, [c]missing 43, [d]missing 27, [e]missing 120, [f]missing 161, [g]missing 124, [h]missng 118, [i]missing 341, [j]missing 126

The univariate logistic regression analysis indicates the relationship between these variables and the composite outcome (Table 3). However, multivariate regression analysis showed a significant correlation of composite outcome only with CKD (P = .026), and borderline significance was indicated with Katz test frailty (P = .050) (Table 4). The STS surgical test and operability were not included in the multivariate analysis since their equations are included as risk factors already considered in the multivariate model. The same applies to dialysis and CKD, as patients on dialysis were included in the number of patients with CKD.

Discussion

TAVR is a minimally invasive procedure that reduces the complication risk and the length of a hospital stay.[16] The reports of clinical trials showed the beneficial outcomes of TAVR in those with a high risk for surgical complications.[17] Improvement in procedural techniques and advances in patients' imaging led to a dramatic decrease in procedural complications. TAVR has been accepted as safe, supporting the rationale for expanding indications to treat patients at lower surgical risk.[18] With expanding TAVR indication to low-surgical-risk patients, TAVR volume surpassed SAVR in 2019 (72,991 vs. 57,626).[19]

Our retrospective study demonstrated that most candidates who underwent TAVR at our institution were at a high or intermediate surgical risk, as only 12.6% of enrolled patients had low surgical risk scores. Despite the increased level of risk, the 2.5% all-cause in-hospital mortality rate in our patients is comparable to other studies. A study by Stachon et al. reported a 2.2% all-cause in-hospital mortality rate for self-expandable valves.[20] A recent study by Amgai et al. reported mortality rates of 3.1% in men and 4.2% in women.[21]

Bleeding complications, particularly life-threatening bleeding, are independently associated with in-hospital and later mortality.[8,22] In our study, major bleeding affected 1.0% of patients, representing a low complication rate. In the study by Khan et al., 34,752 patients with TAVR were included, and 6.6% of them had a major bleed. Predictors of major bleeding were end-stage renal disease, liver disease, peripheral arterial disease, chronic heart failure, age, and coagulopathy.[23] Our study's lower rate of major bleeding was probably caused by a stricter selection of patients and improved surgical techniques.

The incidence of stroke and TIA 30 days after the TAVR varies between 3 and 7%.[24] Most of the complications were recorded in the first 24 hours after the implantation,[24] and neither the type of bioprosthetic valve nor the access site was

Table 3. Univariate regression analysis for the association between the composite outcome and patients' baseline characteristics, frailty assessment, and surgical risk scores.

Risk Factor	Odds Ratio	95% Confidence Interval	P value
Age	1.026	1.004–1.048	**.020**
Sex	0.939	0.640–1.378	.939
Body mass index	0.968	0.939–0.997	**.033**
Chronic obstructive pulmonary disease	0.629	0.404–0.981	**.041**
Chronic kidney disease	1.712	1.131–2.592	**.011**
Mitral stenosis	1.841	1.036–3.267	**.037**
Katz test	0.480	0.304–0.758	**.002**
15-foot walk test	1.195	1.025–1.393	**.023**
STS PROM score	1.429	1.061–1.925	**.019**
Operability	1.623	1.043–2.526	**.032**

Abbreviation: STS PROM, Society of Thoracic Surgeons Predicted Risk of Mortality

Table 4. Multivariate logistic regression model to predict the likelihood of composite outcome during hospitalization based on patients' baseline characteristics and frailty assessment.

Risk Factor	Odds Ratio	95% Confidence Interval	P value
Age	1.001	0.974–1.029	.939
Sex	0.857	0.536–1.371	.519
Body mass index	0.988	0.954–1.024	.517
Chronic obstructive pulmonary disease	0.629	0.375–1.054	.079
Chronic kidney disease	1.757	1.070–2.881	**.026**
Mitral stenosis	1.934	0.994–3.773	.052
Katz test	0.546	0.298–0.999	**.050**
15-foot walk test	1.064	0.876–1.293	.532

influenced by the incidence of cerebrovascular events.[25] In our study, the 1.8% rate of stroke and TIA was comparable to or lower than that in other studies. This low rate was probably a result of Sentinel cerebral protection use in most patients and the cooperation among the heart team members—vascular surgeons, radiologists, and anesthesiologists—to provide appropriate patient selection recommendations.

Vascular complications are a common adverse event of the TAVR procedure. Major vascular complications usually cause tissue malperfusion that requires transfusions and/or surgical procedures.[26] Rupture of the device landing zone is a very rare complication overall (< 1%) but carries a high mortality risk.[27] Even less frequent are other device landing-zone complications, such as injury or dissection of the aorta, ventricular septal defect, and aorto-ventricular fistula.[28] According to the Placement of Aortic Transcatheter Valves (PARTNER) trial, the rate of major complications was 15.3%, while minor complications accounted for 11.9%. The incidence of complications was associated with a high mortality rate.[29] However, recent data from the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy (STS/ACC TVT) Registry reported an annual rate of vascular complications of 4.2%.[30] In our study, the periprocedural major vascular complications rate was 3.2%, which is relatively low and is probably because of careful preoperative risk assessment that involved detailed radiological and clinical preoperative work-up and detailed analysis of patients' anatomy, vessel diameter, and calcification patterns.

The composite outcome factors were high BMI, mitral stenosis, CKD, and dialysis. While obesity (depicted by BMI) can potentially cause a longer operation time, larger blood loss, and more frequent wound infection,[31] some studies reported significantly worse complications and mortality rates for underweight patients.[32] In our study, BMI was lower among patients with composite outcomes than among those without adverse outcomes.

CKD is another important risk factor for perioperative complications, particularly in patients undergoing cardiac surgery. In a large meta-analysis of 4,992 individuals with CKD who received TAVR, moderate and severe kidney disease increased the risk for acute kidney insufficiency, stroke, and cardiovascular mortality at 1- year.[33] In our study, CKD was the only observed variable that showed a significant correlation with the composite outcome in multivariate regression. In general, patients with CKD are at a higher risk of developing cardiovascular disease. Experts believe that the hormones, enzymes, and cytokines released from the injured kidneys lead to vasculature changes. Such changes may affect TAVR procedures.[34-40]

As risk assessment of TAVR is complex and surgical risk scores are not always the best correlation with outcomes, other prognostic markers are needed. Some studies have shown that patients presenting with albumin < 3.5 g/dL have higher in-hospital and 1-year mortality.[13] Koifman et al. showed that serum albumin level is independently related to peri-TAVR mortality.[13] In our study, albumin levels < 3.5 g/dL were seen in almost half of the patients but were not associated with the adverse outcome.

As with all retrospective studies, there are inherent limitations to the results collected. Long-term analysis is difficult as many patients are lost to follow-up in retrospective collection. Further investigations on the link between CKD and TAVR are needed to elucidate how it may contribute to TAVR complication rates. Future prospective studies should subclassify patients with CKD and whether they have received dialysis.

Conclusions

TAVR is an effective, safe, and minimally invasive procedure for treating symptomatic patients with severe AS. Importantly, TAVR enables the treatment of high- and intermediate-risk patients. Our population's most frequent perioperative complications included major bleeding and a new high-degree AV or complete heart block requiring a pacemaker. Our retrospective study showed that perioperative mortality is noninferior or even lower than all-cause mortality compared to SAVR. The all-cause in-hospital mortality rate was 2.5%. Risk factors related to in-hospital composite outcome were CKD, dialysis, mitral stenosis, functional capability determined by the Katz test, and the STS PROM score. In multivariate analysis, only CKD remained significantly associated with the composite outcome. Therefore, risk factors should be carefully identified to reduce perioperative complications and mortality, and the operability risk should be properly determined before the TAVR procedure.

Ethics Approval

A waiver of informed consent was obtained from the Institutional Review Board.

Disclosures

None.

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