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Device Failure in Bicuspid Aortic Stenosis Following Transcatheter Aortic Valve Implantation

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Recent studies showed the favorable outcomes of transcatheter aortic valve implantation (TAVI) in patients with bicuspid aortic valve (BAV) stenosis. However, data on the relation between BAV morphology and optimal transcatheter heart valve (THV) selection are limited. This study sought to evaluate the determinants of device performance in patients with BAV who underwent TAVI. Consecutive patients with BAV who underwent TAVI with the SAPIEN 3 from multicenters were evaluated. Outcomes were the incidence and predictors of device failure. Device failure was defined as peak aortic velocity >3.0 m/s, mean pressure gradient >20 mm Hg, moderate or severe paravalvular leakage and/or procedure mortality. A total of 187 patients with BAV were identified, aged 77 years, and 38.0% were women. A total of 37 patients (19.8%) were treated with 23-mm valve, 58 (31.0%) with 26-mm valve, and 92 (49.2%) with 29-mm valve. Predischarge echocardiogram demonstrated 37 patients (19.8%) with device failure. BAV with excessive leaflet calcification plus calcified raphe (EC-BAV) (OR 16.7, 95% CI 1.99 to 39.6) and smaller THV (OR 4.41, 95% CI 1.43 to 13.6) were independently associated with increased risk of device failure. In addition, 4.0%, 5.1%, and 11.1% of device failures were observed in patients without EC-BAV who underwent TAVI with 23-, 26- and 29-mm THV (p = 0.47), respectively, and 91.7%, 31.6% and 23.2% in those with EC-BAV, respectively (p <0.001). In conclusion, EC-BAV morphology was the major determinant of a device failure after TAVI. Moreover, TAVI in patients with EC-BAV requiring small SAPIEN 3 could be challenging. Further data on device and treatment selection in patients with BAV are still warranted. **(Am J Cardiol 2022;176:96−104)**

Bicuspid aortic valve (BAV) is the most common congenital valvular abnormality in 0.5% to 2.0% of the general population.[1,2] During the past few years, the clinical practice turned toward treating BAV with transcatheter aortic valve implantation (TAVI) in lower risk and younger patients with aortic stenosis (AS).[3] Accordingly, extended knowledge of TAVI for BAV is essential because the proportion of BAV is higher in those patients. Observational studies demonstrated favorable outcomes in patients with BAV comparable to TAVI in tricuspid aortic valves.[4] Although hostile BAV anatomy is known to be associated with poor prognosis after TAVI,[5] data on the association between optimal device selection and BAV morphology remain unknown. Therefore, detailed real-world data on device failure because of BAV morphology after TAVI with specific transcatheter heart valve (THV) are now emerging. In the current registry, we sought to investigate (1) the immediate valve performance along with clinical outcomes after TAVI with the balloon-expandable SAPIEN 3/Ultra (Edwards Lifesciences, California) and to assess (2) the factors associated with device failure.

Methods

A total of 187 consecutive patients with BAV who underwent TAVI with the SAPIEN 3 or Ultra in 3 centers (Shonan Kamakura General Hospital, Japan; Helsinki University Hospital, Finland; Oulu University Hospital, Finland) between February 2016 and March 2021 were retrospectively reviewed. TAVI procedures were planned after evaluating contrast-enhanced multidetector computed tomography (MDCT) and coronary angiography. All patients were evaluated as eligible for TAVI by a multidisciplinary heart team.[6] The decision of the THV sizing was left to the operators. The study protocol conformed to the Declaration of Helsinki. This study was approved by the institutional review boards of each participating center. Data were collected into a dedicated electronic case report form by cardiologists. Data underwent robust checking for its completeness and quality.

All MDCT examinations were reviewed by experienced interventional cardiologists and surgeons using 3 mensio Structure Heart software (3mensio Medical Imaging B.V., Bilthoven, The Netherlands) and Syngo.via (Siemens

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See page 103 for disclosure information.

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Healthineers, Germany). Planimetry of the annulus contours yielded area, major diameter, and minor diameter. Annulus area was measured by manually tracking the luminal contours on the double-oblique transverse plane. The percentage of oversizing (positive percentage) (%OS) was calculated using the following formula: % OS = (THV nominal area/MDCT annular area − 1) × 100. The nominal external valve areas of an expanded THV are 328 mm^2 (20 mm), 409 mm^2 (23 mm), 519 mm^2 (26 mm), and 649 mm^2 (29 mm), according to the manufacturer. The leaflet and annulus were analyzed for the degree of calcification. If present, the distribution of calcification and extension into the left ventricular outflow tract were also assessed in a semiquantitative fashion as follows: mild, moderate, or severe.[7,8]

Diagnosis and assessment of BAV were performed based on the classification described by Sievers et al[9] according to the presence and number of raphes (no raphe as type 0, 1 raphe as type 1, and 2 raphes as type 2) and spatial position of the raphe. For BAV type 1 or 2, if calcification was observed on raphe, it was defined as calcified raphe. BAV with severe leaflet calcification having calcified raphe was defined as excessively calcified BAV (EC-BAV) (Figure 1). The configurations of the landing zone were defined as tube, taper, and flare in the relation between intercommissure distance at 4 mm above annulus and perimeter-derived diameter of the annulus as described in previous research.[10] The formula to determine the annulus ellipticity index was defined by the ratio of maximum and minimum annulus diameters ($D_{max.}/D_{min.}$).

Pre− and post−TAVI transthoracic echocardiography were performed by echocardiographers who are independent from TAVI operators at each participating center. Paravalvular leakage (PVL) was graded as none-trace, mild, moderate, and severe according to the Valve Academic Research Consortium 2 (VARC-2) criteria.[11]

All patients had severe AS defined by standard criteria. The operative risk of the patients was evaluated according to the Society of Thoracic Surgeons risk scoring methods.[12] Chronic kidney disease was defined as an estimated glomerular filtration rate ≥60 ml/min/1.73 m^2 according to the Modification of Diet in Renal Disease equation.[13] Clinical outcomes were registered based on VARC-2 criteria.[11] Device success was defined accordingly as the proper implantation of the first THV used, with the intended performance of the valve (peak aortic flow velocity <3 m/s, mean pressure gradient <20 mm Hg and no moderate or severe PVL) and absence of intraprocedural mortality. Vice versa, device failure was as without intended performance of the valve and/or intraprocedural mortality.

The primary outcome of this study was to elucidate the incidence of device failure after TAVI using SAPIEN 3/Ultra in patients with BAV. The secondary outcomes were

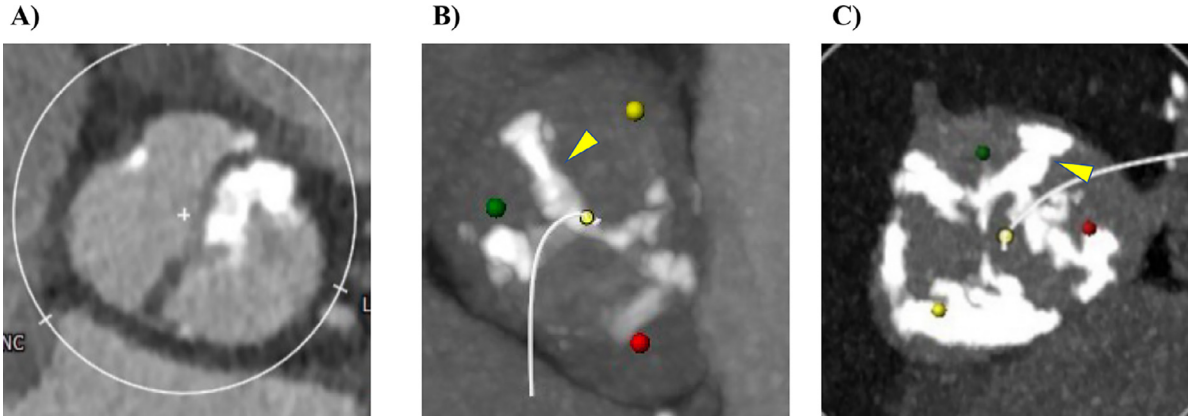


Figure 1. BAV morphology and degree of calcification. *(A)* Type 0 BAV with moderate leaflet calcification. *(B)* Type 1 BAV with calcified raphe and moderate leaflet calcification. *(C)* Type 1 BAV with calcified raphe and excessive leaflet calcification. EC-BAV is defined as in *(C)*. Yellow arrow head = calcified raphe.

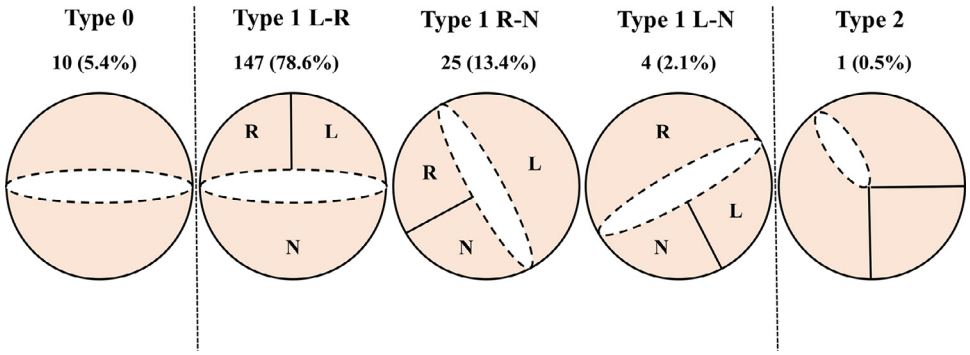
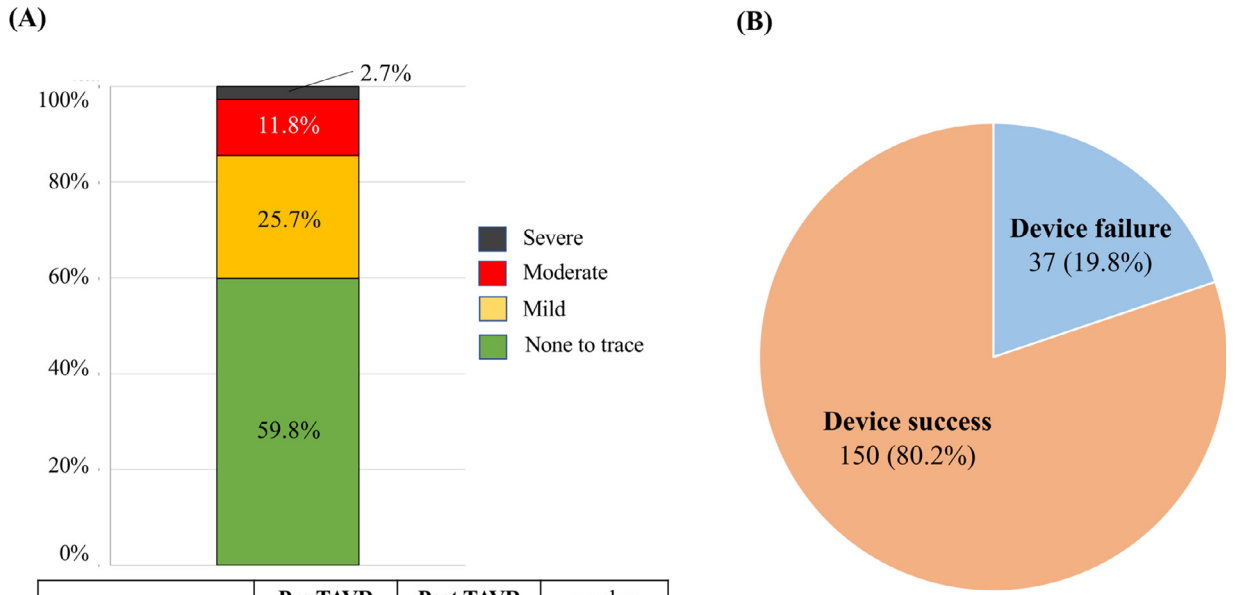


Figure 2. BAV classification. BAV was classified based on Sievers' definition.[9] L = left coronary sinus; N = non-coronary sinus; R = right coronary sinus.



	Pre TAVR	Post TAVR	*p* value
Peak AV m/s	4.3 ± 0.68	2.2 ± 0.54	< 0.001
Mean PG mmHg	48.5 ± 15.7	11.3 ± 5.2	< 0.001

Figure 3. Post-TAVI hemodynamics and device failure. *(A)* Post-TAVI hemodynamics.*(B)* Device failure: device failure was defined as peak aortic flow velocity >3 m/s, mean pressure gradient >20 mm Hg and/or moderate or severe PVL and/or intraprocedural mortality. AV = aortic velocity; PG = pressure gradient; TAVR = transcatheter aortic valve replacement.

to identify the predictors of device failure and to assess the 30-day clinical outcomes based on VARC-2 criteria.

Categorical variables are presented as counts and/or percentages and were compared using the chi-square test. Continuous variables are presented as the mean ± SD and were compared using the Student's *t* test or the Wilcoxon rank-sum test based on their distributions. To determine the adjusted odds ratio (OR) of device failure, a Cox regression analysis including baseline clinical, MDCT data, and procedural covariates was used, and 95% confidence interval (CI) for the development of end points. A p value <0.1 on univariate analysis was selected for the multivariate model. Two multivariable models were created, including (1) preprocedural variables and (2) preprocedural and intraprocedural variables. A p value <0.05 was considered statistically significant. All statistical tests were 2-tailed and performed using JMP Version 16.0 (SAS Institute Inc., Cary, North Carolina).

Results

A total of 187 patients with BAV who underwent TAVI with SAPIEN 3 were the subjects of this analysis. Type 0 BAV was observed in 10 patients (5.4%), type 1 in 176 patients (94.1%) and type 2 in 1 patient (0.5%) (Figure 2). Hemodynamics improved after TAVI, with a significant decrease in peak aortic velocity (4.3 ± 0.68 vs. 2.2 ± 0.54 m/s, p <0.001) and mean pressure gradient (48.5 ± 15.7 vs 11.3 ± 5.2 mm Hg, p <0.001). The incidence of moderate or severe PVL after TAVI was 14.5%. Device failure was observed in 37 patients (19.8%) (Figure 3).

There were no significant differences in the baseline clinical characteristics between patients with and without device failure. In preprocedural echocardiogram, patients with device failure had higher peak aortic velocity and mean pressure gradient in comparison to those without (peak aortic velocity: 4.7 ± 0.80 vs 4.3 ± 0.63 m/s, mean pressure gradient: 54.2 ± 18.9 vs 47.1 ± 14.5 mm Hg, respectively) (Table 1). In MDCT evaluation, 63.1% and 46.5% of patients have calcified raphe and EC-BAV morphology in the total cohort. The patients with device failure had significantly more frequent incidence of calcified raphe, EC-BAV, and moderate to severe left ventricular outflow tract calcification than those with device success (Table 2).

In terms of THV size, 20-mm SAPIEN 3 was in 0 patient (0%), 23-mm in 37 patients (19.8%), 26-mm in 58 patients (31%), and 29-mm in 92 patients (42.9%). No significant differences were observed in procedural characteristics between the 2 groups (Table 3).

Post-TAVI echocardiography demonstrated a higher incidence of moderate or severe PVL, high peak velocity, and mean gradient in patients with device failure. There were no significant differences in all-cause mortality between the 2 groups at 30-day follow-up. The incidence of bleeding and vascular complications was significantly higher in patients with device failure than in those without (Table 4).

The multivariable analysis was performed to identify predictors of device failure (Table 5). In model 1, higher mean aortic gradient (OR 1.03, 95% CI 1.02 to 1.06), EC-BAV (OR 16.7, 95% CI 2.87 to 79.1), and smaller aortic annulus (OR 3.87, 95% CI 1.29 to 12.2) were significantly associated with device failure. Similarly, in model 2, EC-

Table 1
Baseline clinical characteristics

Variable	Total BAV cohort(n = 187)	Device failure(n = 37)	Device success(n = 150)	p value
Age (years)	77.0 ± 6.7	76.8 ± 5.9	77.1 ± 6.9	0.74
Women	71 (38.0%)	13 (35.1%)	58 (38.7%)	0.69
BMI (kg/m^2)	26.4 ± 4.9	25.8 ± 4.7	26.5 ± 5.0	0.41
BSA (m^2)	1.86 ± 0.23	1.84 ± 0.29	1.87 ± 0.21	0.41
Hypertension	152 (81.3%)	32 (86.5%)	120 (80.0%)	0.36
Diabetes mellitus	52 (27.8%)	11 (29.7%)	41 (27.3%)	0.77
CKD*	61 (32.6%)	8 (21.6%)	53 (35.3%)	0.11
Atrial fibrillation	59 (31.6%)	12 (32.4%)	47 (31.3%)	0.90
Peripheral artery disease	26 (13.9%)	8 (21.6%)	18 (12.0%)	0.13
Prior PCI	44 (23.5%)	13 (35.1%)	31 (20.7%)	0.06
Prior CABG	10 (5.4%)	2 (5.4%)	8 (5.3%)	0.99
Prior CVA/TIA	19 (10.2%)	4 (10.8%)	15 (10.0%)	0.88
Prior PMI	15 (8.0%)	2 (5.4%)	13 (8.7%)	0.51
NYHA class ≥ III	124 (66.3%)	26 (70.3%)	98 (65.3%)	0.57
STS-PROM (%)	3.2 ± 2.2	3.2 ± 2.6	3.2 ± 2.1	0.82
Hemoglobin (g/L)	125.9 ± 28.2	121.4 ± 35.8	127.0 ± 26.0	0.29
Creatinine (μmol/L)	88.2 ± 33.6	81.3 ± 38.4	89.8 ± 32.3	0.17
Right bundle branch block	16 (8.6%)	2 (5.4%)	14 (9.3%)	0.44
Left bundle branch block	15 (8.0%)	1 (2.7%)	14 (9.3%)	0.19
LVEF (%)	54.9 ± 12.4	56.0 ± 14.5	54.7 ± 11.8	0.55
Peak aortic velocity (m/s)	4.4 ± 0.67	4.7 ± 0.80	4.3 ± 0.63	0.002
Aortic valve area (cm^2)	0.67 ± 0.18	0.63 ± 0.20	0.68 ± 0.17	0.17
Mean pressure gradient (mm Hg)	48.5 ± 15.5	54.2 ± 18.9	47.1 ± 14.5	0.015
Aspirin	80 (42.8%)	18 (48.7%)	62 (41.3%)	0.42
ADP receptor blocker	21 (11.2%)	6 (16.2%)	15 (10.0%)	0.28
OAC	59 (31.6%)	11 (29.7%)	48 (32.0%)	0.79

* Estimated glomerular filtration rate <60 ml/min/1.73 m^2.

Values are n (%) or mean ± SD.

ADP = adenosine-diphosphate; BAV = bicuspid aortic valve; BMI = body mass index; BSA = body surface area; CABG = coronary artery bypass graft; CKD = chronic kidney disease; CVA/TIA = cerebrovascular attack/transient ischemic attack; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; OAC = oral anticoagulant; PCI = percutaneous coronary intervention; PMI = pacemaker implantation.

BAV (OR 16.7, 95% CI 1.99 to 39.6) and smaller SAPIEN 3 (OR 4.41, 95% CI 1.43 to 13.6) were significantly associated with device failure.

There were 7.0% of patients with device failure in patients without EC-BAV, and there were 34.5% of patients with device failure in those with EC-BAV (p <0.001). Hemodynamic and clinical outcomes are listed in Supplementary Table 1. Regarding predischarge hemodynamics, although there were no significant differences in peak aortic velocity and mean pressure gradient between patients with or without EC-BAV, the incidence of moderate or severe PVL was higher in patients with EC-BAV than in those without. One annulus rupture and 3 cases of cardiac tamponade were observed in patients with EC-BAV.

According to implanted SAPIEN 3 size, although no significant difference was observed in the incidence of device failure in patients without EC-BAV, the mean pressure gradient was significantly higher in those who received SAPIEN 3 23 mm. In patients with EC-BAV, the incidence of device failure was significantly different between THV sizes (23 mm: 91.7%, 26 mm: 31.6%, 29 mm: 23.2%, p <0.001) (Table 6). Details of device failure according to THV size in patients with EC-BAV are shown in Figure 4. In total, 64.5% of device failures in patients with EC-BAV were caused by moderate or severe PVL. In patients who underwent TAVI with 29-mm THV, all cases of device failure were caused by moderate or severe PVL alone. In contrast, in those with 23-mm THV, cases of device failure were caused by high aortic velocity and gradient alone in 63.6%, moderate or severe PVL alone in 18.2%, and both in 18.2%.

In 3 centers, patient selection and the incidence of device failure were significantly different (Supplementary Table 2). Although the number of patients with BAV who underwent TAVI with SAPIEN3 tends to increase over time, no significant time effect was observed in patient characteristics and clinical outcomes except for Society of Thoracic Surgeons-Predicted Risk of Mortality (Supplementary Figure 1).

Discussion

We performed a multicenter study of outcomes in patients with BAV who underwent TAVI using SAPIEN 3/Ultra. Our main findings are as follows: (1) the incidence of device failure was 19.8%, (2) EC-BAV morphology and small aortic annulus requiring small THV were significantly associated with device failure, (3) 64.5% of device failure in patients with EC-BAV were caused by PVL ≥moderate, and (4) in patients without EC-BAV, the incidence of device failure appeared to be acceptable, whereas 91.7%, 31.6%, and 23.3% of device failures were observed in those with EC-BAV who were using SAPIEN 3/Ultra 23-, 26-, and 29-mm. In patients with EC-BAV who were treated

Table 2
Multislice computed tomography assessment

Variable	Total BAV cohort(n = 187)	Device failure(n = 37)	Device success(n = 150)	p value
BAV classification				0.10
Type 0	10 (5.4%)	3 (8.1%)	7 (4.7%)	
Type 1	176 (94.1%)	33 (89.2%)	143 (95.3%)	
Type 2	1 (0.5%)	1 (2.7%)	0 (0%)	
Severe leaflet calcification	150 (80.2%)	33 (89.2%)	117 (78.0%)	0.13
Calcified raphe	118 (63.1%)	31 (83.8%)	87 (58%)	0.004
EC-BAV*	87 (46.5%)	30 (81.1%)	57 (38.0%)	<0.001
Moderate to severe LVOT calcification	32 (17.1%)	11 (29.7%)	21 (14.0%)	0.023
Annulus area (mm^2)	549.4 ± 100.7	539.7 ± 119.4	551.8 ± 95.6	0.51
Annulus area according to THV sizing (mm^2)				0.58
≤430	30 (16.0%)	8 (21.6%)	22 (14.7%)	
>430, ≤550	52 (27.8%)	10 (27.0%)	42 (28.0%)	
>550	105 (56.2%)	19 (51.4%)	86 (57.3%)	
Annulus area derived diameter (mm)	26.3 ± 2.5	26.1 ± 2.9	26.4 ± 2.3	0.43
Annulus perimeter (mm)	84.9 ± 7.8	83.8 ± 1.2	85.2 ± 0.64	0.33
Annulus perimeter derived diameter (mm)	27.0 ± 2.5	26.7 ± 0.41	27.1 ± 0.20	0.33
Annulus mean diameter (mm)	26.4 ± 2.6	26.0 ± 3.0	26.5 ± 2.4	0.24
Ellipticity index	1.30 ± 0.11	1.30 ± 0.12	1.29 ± 0.11	0.65
Annulus perimeter (mm)	84.9 ± 7.8	83.8 ± 9.2	85.2 ± 7.5	0.33
Annulus perimeter derived diameter (mm)	27.0 ± 2.5	26.7 ± 3.0	27.1 ± 2.4	0.33
ICD at 4 mm above annulus (mm)	28.1 ± 2.8	27.7 ± 3.2	28.3 ± 2.7	0.32
Perimeter derived diameter/ICD at 4 mm	0.97 ± 0.07	0.96 ± 0.07	0.97 ± 0.07	0.77
Configuration of LDZ type				0.49
Tube	76 (40.6%)	12 (32.4%)	64 (42.7%)	
Flare	105 (56.2%)	24 (64.9%)	81 (54.0%)	
Taper	6 (3.2%)	1 (2.7%)	5 (3.3%)	

* EC-BAV (excessively calcified bicuspid aortic valve) = calcified raphe plus severe leaflet calcification.

Values are n (%) or mean ± SD.

Ellipticity index = annulus diameter max/annulus diameter minimum; ICD = intercommissure distance; LDZ = landing zone; LVOT = left ventricular outflow tract; THV = transcatheter heart valve.

Table 3
Procedural characteristics

Variable	Total BAV cohort(n = 187)	Device failure(n = 37)	Device success(n = 150)	p value
TF-approach	174 (93.1%)	33 (89.2%)	141 (94.0%)	0.72
SAPIEN3 ultra THV	50 (26.7%)	10 (27.0%)	40 (26.7%)	0.97
Labeled THV size (mm)				0.08
20	0 (0%)	0 (0%)	0 (0%)	
23	37 (19.8%)	12 (32.4%)	25 (16.7%)	
26	58 (31.0%)	8 (21.6%)	50 (33.3%)	
29	92 (49.2%)	17 (46.0%)	75 (50.0%)	
MDCT % area oversizing (%)	3.0 ± 10.9	2.0 ± 13.4	3.2 ± 10.3	0.56
THV labeled diameter/perimeter derived diameter ratio	0.99 ± 0.05	0.99 ± 0.07	0.99 ± 0.01	0.65
THV labeled diameter/ICD at 4-mm ratio	0.96 ± 0.09	0.96 ± 0.10	0.96 ± 0.08	0.88
ID below NCC (mm)	3.9 ± 2.2	4.0 ± 2.3	3.9 ± 2.1	0.75
ID below LCC (mm)	3.5 ± 2.2	3.2 ± 2.2	3.5 ± 2.2	0.45
Mean ID (mm)	3.6 ± 1.9	3.6 ± 1.7	3.6 ± 1.9	0.91
Pre-dilation	114 (61.0%)	22 (59.5%)	92 (61.3%)	0.83
Post-dilation	3 (1.6%)	0 (0%)	3 (2.0%)	0.39
Second valve implantation	0 (0%)	0 (0%)	0 (0%)	
Coronary obstruction	0 (0%)	0 (0%)	0 (0%)	
Annulus rupture	1 (0.5%)	1 (2.7%)	0 (0%)	0.58
Cardiac tamponade	4 (2.1%)	2 (5.4%)	2 (1.3%)	0.13
Intraprocedural death	0 (0%)	0 (0%)	0 (0%)	

Values are n (%) or mean ± SD.

BAV = bicuspid aortic valve; ID = implantation depth; LCC = left coronary cusp; MDCT = multislice detector computed tomography; NCC = noncoronary cusp; TF = transfemoral; THV = transcatheter heart valve.

Table 4
In-hospital and 30-day outcomes

Variable	Total BAV cohort(n = 187)	Device failure(n = 37)	Device Success(n = 150)	p value
Predischarge echocardiogram				
Peak aortic velocity (m/s)	2.2 ± 0.43	2.5 ± 0.65	2.1 ± 0.36	<0.001
Mean aortic gradient (mm Hg)	11.3 ± 4.9	15.3 ± 8.4	10.3 ± 3.5	<0.001
PVL				<0.001
None to mild	160 (85.5%)	10 (27.0%)	150 (100%)	
Moderate or severe	27 (14.5%)	27 (73.0%)	0 (0%)	
In-hospital and 30-day clinical outcomes				
All-cause mortality	2 (1.1%)	1 (2.7%)	1 (0.7%)	0.28
Stroke or TIA	4 (2.1%)	1 (2.7%)	3 (2.0%)	0.79
Bleeding complication				
Life-threatening or disabling	5 (2.7%)	2 (5.4%)	3 (2.0%)	0.25
Major	14 (7.5%)	7 (18.9%)	7 (4.7%)	0.003
Major vascular complication	14 (7.5%)	7 (18.9%)	7 (4.7%)	0.003
AKI	4 (2.1%)	2 (5.4%)	2 (1.3%)	0.13
PMI	14 (7.5%)	3 (8.1%)	11 (7.3%)	0.87

Values are n (%) or mean ± SD.
AKI = acute kidney injury; BAV = bicuspid aortic valve; PMI = pacemaker implantation; PVL = paravalvular leakage; TIA = transient ischemic attack.

with 23-mm THV, unacceptable aortic velocity or gradient after TAVI was a major cause of device failure.

The current generation of THV showed superior outcomes compared with the precedent THV in patients with tricuspid AS.[3,14,15] With an expanding indication of TAVI in younger populations, these technological advancements have been applied to patients with BAV. The first multicenter study including 51 patients with BAV treated by SAPIEN 3 showed favorable outcomes without PVL ≥moderate.[16] As with TAVI in tricuspid AS, the larger BAV registry demonstrated superiority of current generation THV in comparison to early-generation in terms of device success and PVL ≥moderate (92.2% vs 80.9%, p = 0.01; 0.0% vs 8.5%, p = 0.002, respectively).[17] Recently, TVT Registry reported the comparable 1-year mortality between patients with BAV and tricuspid AS after TAVI in 81,822 patients with AS.[4] In contrast, a significantly higher incidence of PVL ≥moderate in patients with BAV was observed (15.9% vs 10.3%) leading to lower device success (85.3% vs 91.4%).[18] In the present study, a further lower incidence of device success (80.2%) with 14.5% of PVL ≥moderate was observed. To make an overall consideration, TAVI in patients with BAV seems to be feasible using current-generation THV in terms of mortality. However, the incidence of PVL ≥moderate leading to device failure considerably varies between studies. Therefore, early hemodynamics in patients with BAV is now open to debate. Because of its heterogeneous and asymmetric anatomy, the interaction between BAV morphology and specific THV should be considered for outcomes after TAVI.

Although the Sievers' classification has been applied to understand the various BAV morphology,[9] TAVI outcomes may be more dependent on factors such as presence of calcified raphe limiting device expansion. Recently, Yoon et al[5]

Table 5
Factors associated with device failure

Model 1. Preprocedural variables						
	Univariate			Multivariate		
Variable	OR	(95% CI)	p value	OR	(95% CI)	p value
Preprocedural mean aortic gradient	1.03	(1.01, 1.07)	0.018	1.03	(1.02, 1.06)	0.014
Calcified raphe	3.74	(1.47, 9.50)	0.002	2.1	(0.30, 38.4)	0.50
EC-BAV	7.00	(2.88, 17.0)	<0.001	16.7	(2.87, 79.1)	<0.01
Moderate to severe LVOT calcification	2.60	(1.12, 5.03)	0.026	1.90	(0.71, 4.94)	0.20
Annulus area according to THV sizing (≤430 vs >550 mm^2)	2.02	(1.05, 8.82)	0.090	3.87	(1.29, 12.2)	0.04
Model 2. Preprocedural and intraprocedural variables						
	Univariate			Multivariate		
Variable	OR	(95% CI)	p value	OR	(95% CI)	p value
Preprocedural mean aortic gradient	1.03	(1.01, 1.07)	0.018	1.01	(0.98, 1.07)	0.24
Calcified raphe	3.74	(1.47, 9.50)	0.002	2.20	(0.24, 20.3)	0.49
EC-BAV	7.00	(2.88, 17.0)	<0.001	16.7	(1.99, 39.6)	0.01
Moderate to severe LVOT calcification	2.60	(1.12, 5.03)	0.026	2.02	(0.76, 5.43)	0.16
Implanted THV size (23 vs 29 mm)	2.12	(0.89, 5.04)	0.090	4.41	(1.43, 13.6)	0.02

CI = confidence interval; EC-BAV = excessively calcified bicuspid aortic valve (calcified raphe plus severe leaflet calcification); LVOT = left ventricular outflow tract; OR = odds ratio; THV = transcatheter heart valve.

Table 6
The impact of THV size on outcomes in patients with or without EC-BAV

	EC-BAV (+)(n = 87)				EC-BAV (−)(n = 100)			
Variable	23-mm (n = 12)	26-mm (n = 19)	29-mm (n = 56)	p value	23-mm (n = 25)	26-mm (n = 39)	29-mm (n = 36)	p value
Device failure	11 (91.7%)	6 (31.6%)	13 (23.2%)	<0.001	1 (4.0%)	2 (5.1%)	4 (11.1%)	0.47
Mean PG (mm Hg)	17.7 ± 10.1	13.1 ± 6.1	9.4 ± 2.9	<0.001	13.7 ± 5.1	10.6 ± 3.6	10.2 ± 4.6	0.005
≥ Moderate PVL	4 (33.3%)	4 (21.1%)	13 (23.2%)	0.71	0 (0%)	2 (5.1%)	4 (11.1%)	0.19

EC-BAV = excessively calcified bicuspid aortic valve (calcified raphe plus severe leaflet calcification); PG = pressure gradient; PVL = paravalvular leakage; THV = transcatheter heart valve.

reported that EC-BAV is associated with an increased risk of mid-term mortality. Moreover, a higher incidence of PVL ≥moderate was observed in patients with calcified raphe and excess leaflet calcification compared with those without. In our cohort, EC-BAV is associated with device failure as with the report by Yoon et al. Although the presence of calcified raphe itself was not independently associated with increased device failure, the association of calcified raphe and significant leaflet calcification was a major determinant of early device performance after TAVI with SAPIEN 3. Indeed, our cohort included 46.5% of EC-BAV, and approximately more than one-half of patients showed calcified raphe. In contrast, the report by Yoon et al included 26.0% of EC-BAV.[5] These facts could explain the highest incidence of device failure in the present study among recent studies in patients with BAV.[4,5,16–18] In our cohort, most device failures were caused by PVL ≥moderate, especially in patients with EC-BAV. It might indicate that EC-BAV with asymmetric supra-annulus geometry may hinder the expansion and sealing of THV within the aortic annulus, leading to significant PVL. Attempts to decrease the PVL by selecting larger THV or performing postdilation may also have resulted in aortic root injury.[5,19] In the case of TAVI with self-expanding THV for BAV, although the aortic injury may be less frequent, the incidence of PVL may be higher than that with SAPIEN 3.[20] Therefore, EC-BAV could be challenging and might be unsuitable anatomy to treat with TAVI.

Moreover, device size seems to be one of the considerable issues in terms of early device performance after intra-annular leaflet SAPIEN 3 THV. Our data suggested that patients who underwent TAVI with smaller THV have a higher aortic gradient according to the THV sizes. Smaller SAPIEN 3 was independently associated with device failure as with EC-BAV morphology. Although 4% of patients who underwent TAVI with SAPIEN3 23-mm have device failure in the non−EC-BAV group, 91.7% of those with SAPIEN3 23-mm in the EC-BAV group experienced device failure mainly because of the high aortic gradient association with significant PVL. Small prosthesis size leading to abnormal residual gradient may contribute to an increased incidence of structural valve deterioration.[21,22] From the viewpoint of valve durability, TAVI using intra-annular designed THV for EC-BAV with small annulus should be avoided, especially for patients with long life expectancy. For this hostile anatomy, TAVI with supra-annular designed self-expanding THV might be beneficial in terms of the aortic gradient. However, it may be a trade-off relation with significant PVL, as discussed previously.[20] The decision whether to treat BAV with TAVI or surgery has been generally made through multiple factors.[19,23–25] This study highlights the importance of meticulous CT assessment of BAV morphology. Moreover, it suggests that TAVI would be the acceptable treatment for patients with favorable BAV anatomy. In contrast, EC-BAV with small annulus should be treated with surgery unless the surgical risk is high or inhibitive.

Our study has limitations typical of those with a retrospective design. First, this was an observational study, and the results should be hypothesis-generating. Second, there were no patients who met the indication of SAPIEN 3 20 mm. Therefore, our data do not support the performance of the 20-mm device. Third, outcomes were self-reported by participating centers. Moreover, there was no core

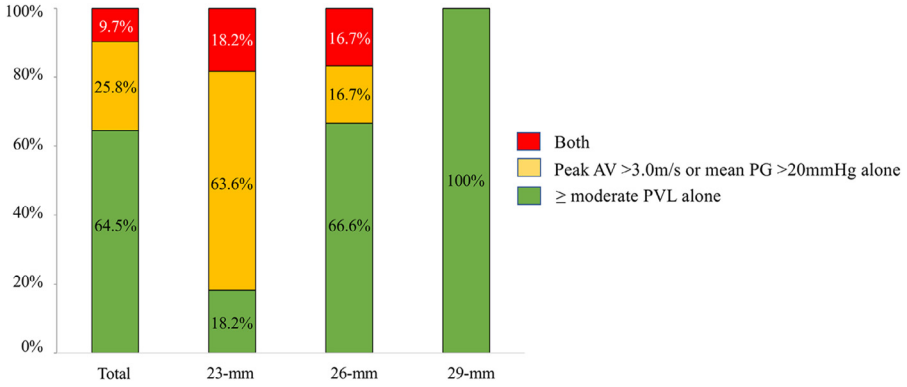


Figure 4. Details of device failure in patients with EC-BAV according to the THV sizes. Both = high peak velocity, high aortic gradient, and/or moderate or severe PVL. AV = aortic velocity; PG = pressure gradient.

laboratory evaluation of MDCT and echocardiographic results. The external validity of these results should be evaluated in larger populations. Fourth, the degree of leaflet calcification was assessed in a semiquantitative fashion. There might be a difference in assessment of its severity between each MDCT analyst. In future studies, EC-BAV should be defined in a quantitative fashion using the calcium scoring method. Finally, patient selection for treatment using SAPIEN 3 was at the discretion of the heart team at each participating center. Therefore, it may affect the results reported in this study.

In conclusion, EC-BAV is a significant determinant of device failure after TAVI with SAPIEN 3. Especially, EC-BAV requiring small SAPIEN 3 seems to be a considerable issue. Further data on device and treatment selection for patients with specific BAV morphology are warranted.

Disclosures

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Supplementary materials

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