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Transcatheter Aortic Valve Replacement in Low-risk Patients With Bicuspid Aortic Valve Stenosis

John K. Forrest, MD; Basel Ramlawi, MD; G. Michael Deeb, MD; Firas Zahr, MD; Howard K. Song, MD, PhD; Neal S. Kleiman, MD; Stanley J. Chetcuti, MD; Hector I. Michelena, MD; Abeel A. Mangi, MD; Jeffrey A. Skiles, MD; Jian Huang, MD, MS; Jeffrey J. Popma, MD; Michael J. Reardon, MD

➕ **Supplemental content**

IMPORTANCE The outcomes of transcatheter aortic valve replacement (TAVR) in low-risk patients with bicuspid aortic valve stenosis have not been studied in a large scale, multicentered, prospective fashion.

OBJECTIVE To evaluate the procedural safety, efficacy, and 30-day outcomes of TAVR in patients with bicuspid aortic stenosis at low surgical risk.

DESIGN, SETTING, AND PARTICIPANTS The Low Risk Bicuspid Study is a prospective, single-arm trial study with inclusion/exclusion criteria developed from the Evolut Low Risk Randomized Trial. Follow-up is planned for 10 years. Patients underwent TAVR at 25 centers in the United States who were also participating in the Evolut Low Risk Randomized Trial from December 2018 to October 2019. Eligible patients had severe bicuspid aortic valve stenosis and met American Heart Association/American College of Cardiology guideline indications for aortic valve replacement.

INTERVENTIONS Patients underwent attempted implant of an Evolut or Evolut PRO transcatheter aortic valve, with valve size based on annular measurements.

MAIN OUTCOMES AND MEASURES The prespecified primary end point was the incidence of all-cause mortality or disabling stroke at 30 days. The prespecified primary efficacy end point was device success defined as the absence of procedural mortality, the correct position of 1 bioprosthetic heart valve in the proper anatomical location, and the absence of more than mild aortic regurgitation postprocedure.

RESULTS A total of 150 patients underwent an attempted implant. Baseline characteristics include mean age of 70.3 (5.5) years, 48.0% female (n = 72), and a mean Society of Thoracic Surgeons score of 1.4 (0.6%). Most patients (136; 90.7%) had Sievers type I valve morphology. The incidence of all-cause mortality or disabling stroke was 1.3% (95% CI, 0.3%-5.3%) at 30 days. The device success rate was 95.3% (95% CI, 90.5%-98.1%). At 30 days, the mean (SD) AV gradient was 7.6 (3.7) mm Hg and effective orifice area was 2.3 (0.7) cm^2. A new permanent pacemaker was implanted in 22 patients (15.1%). No patients had greater than mild paravalvular leak.

CONCLUSIONS AND RELEVANCE Transcatheter aortic valve replacement in low–surgical risk patients with bicuspid aortic valve stenosis achieved favorable 30-day results, with low rates of death and stroke and high device success rate.

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Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: John K. Forrest, MD, Departments of Internal Medicine (Cardiology), Yale University School of Medicine, 789 Howard Ave, Dana 3 Cardiology Section, New Haven, CT 06519 (john.k.forrest@yale.edu).

Bicuspid aortic valve disease affects 1% to 2% of the US population[1,2] and is present in up to 40% of patients who undergo surgical aortic valve replacement.[3] While transcatheter aortic valve replacement (TAVR) has shown through rigorous clinical studies to be a viable treatment option for patients with trileaflet aortic valve stenosis regardless of surgical risk,[4-8] there have, to date, been limited prospective studies evaluating TAVR in low-risk surgical patients with bicuspid aortic valve disease. Data from the STS/TVT Registry have shown that intermediate-risk and high-risk patients with bicuspid aortic valve disease undergoing TAVR have outcomes similar to patients with tricuspid disease, although there remain concerns about stroke, paravalvular leak (PVL), and device success in this population.[9-12] A 2020 feasibility study[13] to evaluate the safety of TAVR in low-risk patients bicuspid aortic valve disease suggested that TAVR appears to be safe in these patients. The purpose of this study was to evaluate the procedural safety, efficacy, and 30-day outcomes of TAVR in low-risk patients with severe bicuspid aortic-valve stenosis using a self-expanding supra-annular valve and a standardized sizing strategy.

Methods

Study Design

The Low Risk Bicuspid Study is a multicenter, prospective, single-arm study that enrolled patients at 25 centers in the United States who were also participating in the Evolut Low Risk Randomized Trial (eTable 1 in the Supplement). The protocol was developed in collaboration with the study executive committee (J.K.F., B.R., M.J.R., and J.J.P.), the US Food and Drug Administration, and the study sponsor (Medtronic). The sponsor oversaw the collection and management of the data. Each institutional review board approved the study protocol, and each patient provided written informed consent. The trial was conducted in accordance with the International Conference on Harmonization, Good Clinical Practice Guidelines, and the Declaration of Helsinki. An independent clinical events committee adjudicated all deaths and end point–related adverse events. Patients were assessed at baseline, prior to hospital discharge, and at 30 days and will be followed up annually through 10 years.

Patients

Eligible patients had severe bicuspid aortic valve stenosis and an indication for surgical aortic valve replacement with a predicted risk of 30-day mortality less than 3.0% based on local Heart Team assessment. Bicuspid anatomy was confirmed using multislice computed tomography analysis (CTA). The screening committee (eTable 2 in the Supplement) confirmed bicuspid valve morphology and identified the Sievers classification.[14] Severe symptomatic aortic stenosis was defined as an aortic valve area of 1.0 cm² or less (or aortic-valve area index of ≤0.6 cm²/m²) or a mean gradient of at least 40 mm Hg or a maximum aortic valve velocity of at least 4.0 m/s by transthoracic echocardiography with exertional dyspnea, syncope/presyncope, or angina.[15] Patients who were

Key Points

Question What are the procedural and short-term outcomes of transcatheter aortic valve replacement (TAVR) in low-risk patients with bicuspid aortic valve stenosis?

Findings In this single-arm prospective study of 150 low-risk patients with bicuspid aortic valve stenosis undergoing TAVR using a self-expanding valve and a standardized sizing strategy, there was high device success with a low rate of death or disabling stroke at 30 days. Outcomes did not vary significantly by bicuspid type (Sievers classification), with excellent hemodynamics and low rates of significant paravalvular leak for both Sievers type 0 and type I bicuspid valves.

Meaning In this study, low-risk patients with bicuspid aortic valve stenosis undergoing TAVR had excellent procedural and 30-day outcomes, but longer-term outcomes are needed prior to widespread adoption of TAVR in low-risk patients with bicuspid severe aortic stenosis.

asymptomatic but met American Heart Association (AHA)/American College of Cardiology (ACC) class IIa criteria for AVR were also eligible.[15] Key exclusion criteria included an aortopathy for which surgery was indicated based on AHA/ACC guidelines (including ascending aorta >4.5 cm in diameter-Class IIa recommendation),[15] age younger than 60 years, and prohibitive left ventricular outflow tract (LVOT) calcification. All inclusion and exclusion criteria are listed in eTable 3 in the Supplement. The inclusion and exclusion criteria as well as the screening process were identical to the criteria used in the Evolut Low Risk randomized trial,[7] with the exceptions that patients had to have a bicuspid valve and with the added exclusion criteria of age younger than 60 years or an ascending aortic diameter greater than 4.5 cm.

Valve Sizing and Implant Technique

Patients underwent TAVR using the Evolut R or the Evolut PRO valve (Medtronic). Valve sizing was based on measurements performed at the level of the aortic annulus. The Evolut R valve could be implanted in aortic annuli 18 to 30 mm in diameter (perimeter-derived) and the Evolut PRO valve could be implanted in aortic annuli 18 to 26 mm in diameter (perimeter-derived). The Evolut R and Evolut PRO valves are similar, with the exception of a porcine pericardial outer wrap added to the first 1.5 cells (approximately 12 mm) of the Evolut PRO valve, designed to decrease PVL.[16] Predilation was strongly encouraged, and postdilation was recommended if there was greater than mild paravalvular leak following implant or a residual invasive hemodynamic gradient greater than 10 mm Hg. The use of conscious sedation, transesophageal echocardiography (TEE), and neuroprotection were left to the operators' discretion; however, TEE was encouraged if it was felt that transthoracic echocardiography (TTE) would be suboptimal owing to patient body habitus or other factors that would limit detailed evaluation of valve function including PVL.

End Points

The primary safety end point was the incidence of all-cause mortality or disabling stroke at 30 days. The primary efficacy

Figure 1. Patient Enrollment Flowchart
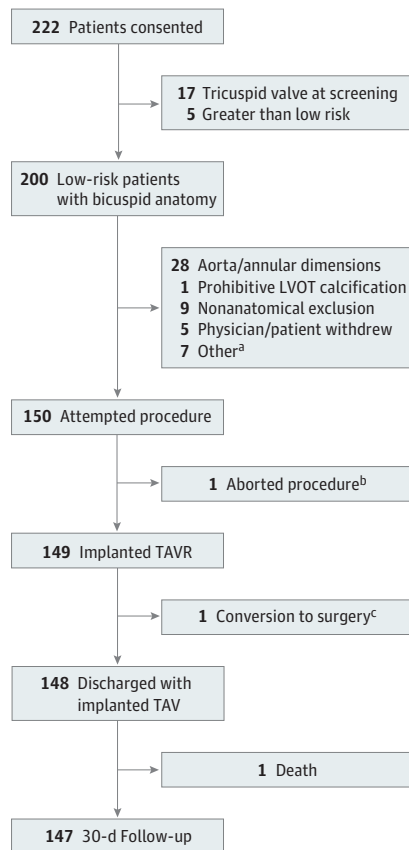
LVOT indicates left ventricular outflow tract.

a The 7 patients withdrawn for other reasons include 4 patients owing to insurance denial and 3 patients exited from the study due to completion of enrollment.

b During transthoracic echocardiographic imaging, a mass on the aortic valve was detected.

c Coronary obstruction requiring emergent surgery.

end point was a composite rate of device success comprising the absence of procedural mortality, the correct positioning of a single valve in the proper anatomical position, and the absence of more than mild aortic regurgitation (AR) prior to discharge. Additional outcome measures at 30 days included new permanent pacemaker implantation, bleeding, valve thrombosis, valve hemodynamics, and quality of life. Definitions are listed in eTable 4 in the Supplement. Quality of life was measured by the New York Heart Association symptom class and the Kansas City Cardiomyopathy Questionnaire. Prosthesis-patient mismatch was based on the Valve Academic Research Consortium 2 definition.[17]

Cardiac Imaging Analysis

An independent echocardiography core laboratory evaluated all echocardiograms (Mayo Clinic) as previously reported and consistent with the Evolut Low Risk Randomized Trial.[18] Postprocedural echocardiographic measures are reported for patients who had a successful transcatheter aortic valve implan-

tation. Computed tomographic angiography was performed by each site and by Medtronic clinical personnel using the 3mensio software system (Pie Medical). The screening committee adjudicated the CTA measurements.

Statistical Methods

The primary analysis cohort comprised patients who underwent an attempted implant, defined as when the patient is brought into the procedure room and any of the following have occurred: anesthesia administered, TEE probe, or any vascular catheter placed. Device success and echocardiographic outcomes are reported for patients with an implanted transcatheter valve. Continuous variables are reported as mean (standard deviation). Categorical variables are presented as frequencies and percentages. Adverse events at 30 days are reported using the Kaplan-Meier estimator. All statistical analyses were performed using SAS software, version 9.4 (SAS Institute Inc).

Results

Patients

A total of 222 patients consented at 25 centers in the United States. Of these, 72 were excluded; 60 did not meet the inclusion/exclusion criteria (eTable 5 in the Supplement), 2 patients withdrew themselves, 3 patients were withdrawn by their physician (1 for incidental CT findings, 1 owing to a stroke, and 1 in which the cardiologist recommended surgery), and 7 other patients exited the study (4 owing to insurance coverage and 3 who were enrolled but not approved because the study had reached maximum enrollment). This resulted in 150 patients undergoing attempted implant (Figure 1).

Baseline clinical, demographic, and valve morphology characteristics are shown in Table 1. The mean (SD) age was 70.3 (5.5) years, the mean Society of Thoracic Surgeons (STS) score was 1.4% (0.6%), and 72 were women (48.0%). A Sievers type I bicuspid valve was identified in 136 patients (90.7%), while the remaining 14 had Sievers type 0 (baseline characteristics by Sievers type are in the eTable 6 in the Supplement). Of the 136 patients with type I bicuspid valves, 107 (78.7%) were left-right cusp fusion, 27 (19.9%) were right nonfusion, and 2 (1.5%) were nonleft fusion. The baseline mean (SD) aortic valve area was 0.8 (0.2) cm² and the mean gradient was 49.9 (15.5) mm Hg.

Procedural Outcomes and Device Success

Table 2 shows the procedural outcomes. Of the 150 patients undergoing attempted implant, 149 underwent transcatheter aortic valve implantation (99.3%). In 1 patient after conscious sedation had been administered, TTE imaging identified a mobile echodensity on the noncoronary cusp of the aortic valve that had not been visualized on the preoperative echocardiogram. Given this finding, the implanting physician aborted the procedure and subsequently exited the patient from the study. General anesthesia was used in 95 patients (63.3%), and 147 patients (98.7%) were implanted via iliofemoral access (the remaining 2 patients via a subclavian approach). A cerebral embolic protection device was used in 45 patients (30.0%). Pre-

implant balloon valvuloplasty was performed in 137 patients (91.3%), and postimplant dilation was performed in 55 patients (36.9%). For the 14 patients with a Sievers type 0 bicuspid valve, all patients were predilated and postdilation was performed in 1 patient. Implanted valve type and size is shown in Table 2. No patients were implanted with a 23-mm valve. A second valve was implanted in 5 patients (3.3%). The primary efficacy end point of device success occurred in 141 of 148 patients (95.3%; 95% CI, 90.5%-98.1%) (eTable 7 in the Supplement).

Clinical Outcomes at 30 Days

The primary end point of the incidence of all-cause mortality or disabling stroke at 30 days was 1.3% (95% CI, 0.3%-5.3%) (Table 3). There was 1 death (0.7%), and 1 patient had a disabling stroke (0.7%). The major vascular complication rate was 1.3%, and life-threatening or disabling bleeding was 4.0%. In 1 patient, there was acute coronary obstruction following implant, which was successfully treated by conversion to open surgery. A new permanent pacemaker was implanted in 22 patients (15.1%) at 30 days. The cardiovascular-related rehospitalization rate at 30 days was 4.0%, including 1 patient with heart block.

Valve Performance

Baseline, discharge, and 30-day valve hemodynamics are shown in Figure 2. No patients had more than mild AR postprocedure or at 30 days. At 30 days, no or trace AR was seen in 11 of 13 patients (85%) with a Sievers type 0 bicuspid valve and 76 of 133 patients (57.1%) with a type I bicuspid valve. The mean (SD) gradient was 7.6 (3.7) mm Hg, and the effective orifice area was 2.3 (0.7) cm^2. Prosthesis-patient mismatch using Valve Academic Research Consortium 2[17] criteria was present in 17 of 132 patients (12.9%), with only 2 patients (1.4%) having a mean gradient greater than 20 mm Hg at 30 days (Table 3).

Quality of Life

At 30 days, 110 patients (75.3%) had New York Heart Association class I symptoms, 32 (21.9%) had class II, and 4 (2.7%) had class III. A total of 121 patients (82.3%) had improvement of at least 1 class. The mean (SD) Kansas City Cardiomyopathy Questionnaire overall summary score was 68.5 (19.6) at baseline and 90.3 (12.8) at 30 days.

Discussion

To our knowledge, this study represents the first prospective evaluation of low-risk patients with bicuspid aortic valve stenosis undergoing TAVR using a self-expanding supra-annular valve and a standardized sizing technique. In this 150-patient study, TAVR demonstrated excellent procedural safety and efficacy outcomes with low adverse event rates at 30 days (1.3% mortality or disabling stroke). A new permanent pacemaker was implanted in 15.1% of patients. Device success was very high, with excellent hemodynamics, and no patients had more than mild AR at 30 days.

Table 1. Baseline Characteristics

Characteristic	No. (%)
No.	150
Age, mean (SD), y	70.3 (5.5)
Body surface area, mean (SD), m^2	1.9 (0.2)
Female	72 (48.0)
STS score, mean (SD), %	1.4 (0.6)
New York Heart Association	
I	3 (2.0)
II	106 (70.7)
III	40 (26.7)
IV	1 (0.7)
Type 2 diabetes	37 (24.7)
Hypertension	112 (74.7)
Chronic lung disease/chronic obstructive pulmonary disease	26 (17.7)
Peripheral vascular disease	14 (9.3)
Cerebrovascular disease	10 (6.7)
SYNTAX I score, mean (SD)[a]	1.0 (2.8)
Previous coronary artery bypass grafting	2 (1.3)
Previous percutaneous coronary intervention	11 (7.3)
Myocardial infarction	5 (3.3)
Atrial fibrillation/atrial flutter	11 (7.3)
Preexisting permanent pacemaker or defibrillator	4 (2.7)
Left ventricular ejection fraction, mean (SD), %	63.4 (8.3)
Aortic valve area, mean (SD), cm^{2b}	0.8 (0.2)
Aortic valve gradient, mean (SD), mm Hg[b]	49.9 (15.5)
Native bicuspid aortic valve morphology	
Sievers	
Type 0	14 (9.3)
Type 1	136 (90.7)
Fusion, No./total No. (%)	
Left-right	107/136 (78.7)
Right-non	27/136 (19.9)
Nonleft	2/136 (1.5)
Sievers type 2	0
Raphe length, mean (SD), mm	11.1 (2.7)

Abbreviations: STS, Society of Thoracic Surgeons; SYNTAX, Synergy Between PCI With Taxus and Cardiac Surgery.

[a] The SYNTAX score is a measure of the severity and extent of coronary artery disease.

[b] Site reported.

Although TAVR has shown favorable results in the treatment of trileaflet aortic stenosis, there has been controversy regarding its role in bicuspid aortic valve disease, with early studies showing worse in-hospital outcomes including decreased device success and an increased incidence of paravalvular leak.[12,19] Using current-generation TAVR valves, data from 2019 and 2020 suggested similar outcomes of TAVR in bicuspid and tricuspid patients.[9-11,13] A particular issue which has arisen in TAVR for bicuspid valves is how to size the transcatheter valve. While TAVR sizing is routinely done at the level of the annulus for tricuspid valves, there has been significant debate regarding the optimal sizing strategy for TAVR in bicuspid aortic valves (annular vs supra-annular).[20] In this study, we implemented a

Table 2. Procedural Outcomes

Outcome	No. (%)		
	All patients (n = 150)	Type 0 (n = 14)	Type 1 (n = 136)
General anesthesia	95 (63.3)	9 (64.3)	86 (63.2)
Implanted valve size			
Evolut R, mm			
23	0	0	0
26	1 (0.7)	0	1 (0.7)
29	1 (0.7)	0	1 (0.7)
34	62 (41.6)	3 (21.4)	59 (43.7)
Evolut PRO, mm			
23	0	0	0
26	31 (20.8)	6 (42.9)	25 (18.5)
29	54 (36.2)	5 (35.7)	49 (36.3)
Preimplant balloon valvuloplasty	137 (91.3)	14 (100)	123 (90.4)
Postimplant balloon dilation	55 (36.9)	1 (7.1)	54 (40.0)
Iliofemoral access	147 (98.7)	14 (100)	133 (98.5)
Embolic protection device	45 (30.0)	5 (35.7)	40 (29.4)
Valve repositioned	49 (32.9)	4 (26.8)	45 (33.3)
Implant depth, mean (SD), mm[a]			
At NCS	2.8 (1.7)	2.0 (2.0)	2.9 (1.7)
At LCS	4.2 (2.0)	3.3 (1.7)	4.3 (2.0)
More than 1 valve implanted	5 (3.3)	0	5 (3.7)
Concomitant or staged PCI	4 (2.7)	0	4 (2.9)
Coronary artery obstruction	1 (0.7)	1 (7.1)	0
Conversion to open heart surgery	1 (0.7)	1 (7.1)	0

Abbreviations: LCS, left coronary sinus; NCS, noncoronary sinus; PCI, percutaneous coronary intervention.

[a] By aortography.

Figure 2. Valve Hemodynamics
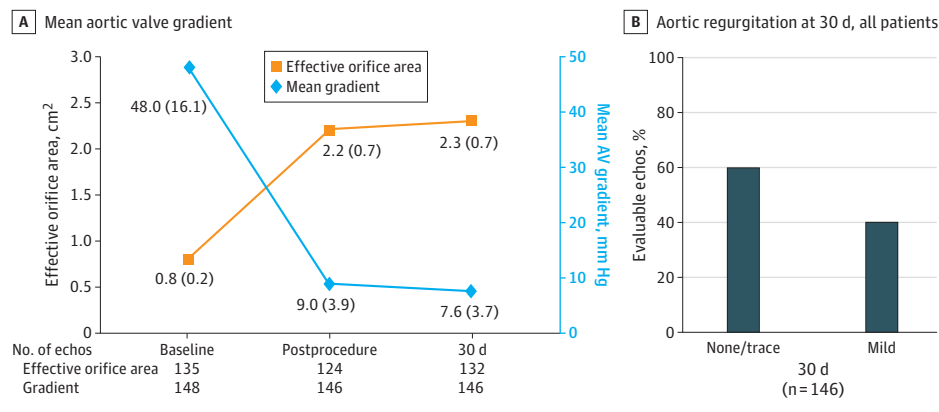
A, Mean aortic valve gradient and effective orifice area at baseline and 30 days. B, Aortic regurgitation at 30 days for all patients.

standardized sizing strategy adhering to the measurement obtained at the level of the aortic annulus to determine the valve size for implant. The decision to choose annular sizing was made by the study executive committee based on clinical experience and data showing that supra-annular sizing is less reproducible than annular sizing, with no difference in procedural complication rates.[21] Implementing this sizing method and using the latest generation valves, the procedural and 30-day results are similar to that seen for low-risk patients with trileaflet aortic valve stenosis undergoing TAVR.[7]

Other procedural techniques that were strongly encouraged, but not mandated, included routine use of predilation and liberal use of TEE if it was felt that TTE would result in suboptimal imaging. Predilation was recommended to facilitate complete valve expansion and potentially decrease PVL given the presence of heavy calcification along fused raphe often seen in bicuspid aortic stenosis. The importance of accurately assessing PVL in patients undergoing TAVR with a bicuspid aortic valve was a point of emphasis in this study. Because it has been shown that the use of TTE to evaluate PVL can be lacking in accuracy, especially in the setting of challenging body habitus or other factors resulting in poor echo windows,[22] sites were encouraged to use TEE when patients had poor transthoracic echo windows. This almost certainly resulted in an

increased use of general anesthesia in this study as compared with routine clinical practice. In clinical practice, the use of minimalist techniques that have been shown to decrease cost and improve efficiency[23] must be balanced with a potential for poorer imaging, especially in younger patients for whom the risks of general anesthesia are low and in whom unrecognized PVL owing to poor echo windows can result in worse long-term outcomes.[24]

Bicuspid aortic valve anatomy encompasses a variety of types[14] and other variations, including frequent atypical location of coronary-artery ostia, asymmetric leaflet calcification, and fused raphe.[20] Traditional thinking has been that this anatomy might adversely affect valve expansion, hemodynamics, and AR/PVL owing to the 2 commissures opening in a more elliptical fashion, especially in the setting of Sievers type 0 anatomy. Unfortunately, in contrast to the STS Surgical Database Form, which began collecting information on Sievers Classification in 2017 for patients with bicuspid valve disease undergoing SAVR, the ACC/STS TVT-Registry does not presently collect information on the type of bicuspid valve, and data on outcomes of TAVR in different bicuspid subtypes are limited. In this study, the results in patients with Sievers type 0 valves were excellent, with 11 of 13 patients having no/trace AR and the other 2 having mild AR at 30 days. All 5 patients who required a second valve had Sievers type I anatomy, although the 1 patient who had a coronary obstruction and subsequent conversion to surgery did have a Sievers type 0 valve (eTable 8 in the Supplement).

It should be noted that there was careful scrutiny of anatomy by the screening committee. Of the 72 patients who were excluded by the screening committee, the 2 most common reasons for exclusion were anatomic dimensions that fell outside the labeled sizing range (28 patients) and the presence of a trileaflet valve found on CTA (17 patients). While sites were encouraged to enroll all patients with bicuspid valve disease requiring AVR who met inclusion criteria regardless of valve calcification, only 1 patient (1.4% of all excluded patients) was excluded for prohibitive annular or leaflet calcification. This was likely owing to both the screening committee being liberal in allowing patients with heavy LVOT calcium to be included given the very low incidence of annular rupture and paravalvular leak using the Evolut PRO valve and the presence of selection bias by sites with regards to which bicuspid patients they chose to enroll. In comparison, in the Low Risk Placement of Aortic Transcatheter Valves (PARTNER) 3 trial,[6] approximately 38% of the patients who were excluded by the screening committee were excluded due to severe LVOT calcification (eAppendix in the Supplement of the PARTNER 3 trial).[6] These findings highlight that optimal results for low-risk patients undergoing TAVR (regardless of valve anatomy) are best achieved with careful screening by the multidisciplinary heart team, with particular focus on anatomic suitability based on CTA.

The incidence of new permanent pacemaker in this study (15.1%) was slightly lower than seen for low-risk patients with trileaflet aortic valve stenosis undergoing TAVR with a self-expanding, supra-annular valve (17.8%), although higher than seen for low-risk patients undergoing TAVR with a balloon-

Table 3. Outcomes at 30 Days

Outcome	No. of patients (%)[a]
No.	50
All cause	
Mortality or disabling stroke	2 (1.3)
Mortality	1 (0.7)
Any stroke	6 (4.0)
Disabling	1 (0.7)
Nondisabling	5 (3.3)
Myocardial infarction	1 (0.7)
Life threatening or disabling bleeding	6 (4.0)
Major vascular complication	2 (1.3)
Acute kidney injury: stage 2 or 3	0
Valve	
Thrombosis	1 (0.7)
Embolization	2 (1.3)
Migration	0
Related dysfunction requiring repeat procedure	0
New permanent pacemaker[b]	22 (15.1)
Aortic valve-related rehospitalization	6 (4.0)
Mean AV gradient >20 mm Hg[c]	2 (1.4)
Prosthesis-patient mismatch, No.[c,d]	132
None	115 (87.1)
Moderate	10 (7.6)
Severe	7 (5.3)

Abbreviation: AV, aortic valve.

[a] Data presented as number of patients with events (Kaplan-Meier estimate) except for the valve gradient and prosthesis-patient mismatch data, which are presented as number of patients (%).

[b] Excluding patients with a pacemaker at baseline.

[c] Echocardiographic data provided for patients with a successful implant.

[d] Per Valve Academic Research Consortium 2 definition (indexed effective orifice area ≤0.85 cm²/m² for patients with body mass index 30 [calculated as weight in kilograms divided by height in meters squared], or <0.7 cm²/m² for patients with body mass index ≥30 kg/cm²).[17]

expandable valve (6.6%)[6] and similarly higher than SAVR in either of the large low-risk randomized studies (4.1% and 6.2%). The frequency of new pacemakers with self-expanding and mechanically expanding valves[25,26] is an area of continued clinical investigation, with modified implant techniques showing the potential to reduce this incidence.[27] Compared with balloon-expandable annular valves, where the incidence of prosthesis-patient mismatch in low-risk patients is up to 62.1%,[6] TAVR using supra-annular self-expanding valves has been associated with significantly better hemodynamics.[7,28] Similarly, in low-risk patients undergoing SAVR, prosthesis-patient mismatch is reported to occur in more than 50% of patients.[6] Given the association between prosthesis-patient mismatch and longer-term outcomes,[29] the consistent hemodynamic performance across bicuspid patient populations may be an important consideration when planning AVR, especially in patients with smaller annuli.

To date, the data available for patients with bicuspid-valve disease undergoing TAVR have been generated primarily from large retrospective registries and smaller feasibility

studies using a variety of valve types and without a standardized sizing approach.[9-13] Outcomes from these studies have showed potentially positive results in patients with bicuspid aortic-valve disease undergoing TAVR but have provided very limited or no details describing the bicuspid anatomy or implant and sizing techniques used. Therefore, this study was developed to evaluate the Evolut System in low-risk patients with CTA-confirmed bicuspid anatomy using annular sizing with inclusion/exclusion and screening criteria based on the Evolut Low Risk Trial. Although there was no control group for this study, when compared with the 2 large-scale and similarly constructed randomized studies of low-risk patients with trileaflet aortic-valve stenosis,[6,7] the 30-day incidence of mortality or disabling stroke observed in this study (1.3%) was similar to low-risk patients with trileaflet aortic-valve stenosis undergoing TAVR (0.8%[7] and 1.0%[6]) or SAVR (2.6%[7] and 3.3%[6]). While these procedural and 30-day results are promising, longer-term outcomes will be important in this low-risk population, and patients within this study will be followed up for 10 years.

Limitations

The Low Risk Bicuspid Study was a nonrandomized study performed at 25 sites who were also participating in the Evolut Low Risk Randomized Trial and thus had significant experience with TAVR. Data have shown that TAVR outcomes are related to procedural volume[30] and as such these data cannot necessarily be extrapolated to all TAVR centers.

In addition to a comprehensive heart team evaluation by each site, there was strict adherence to anatomical measurements to determine patient eligibility. The inclusion/exclusion criteria as well as screening process were based off the Evolut Low Risk trial, with the added exclusion criteria of an ascending aorta greater than 4.5 cm and patients younger than 60 years. As noted previously, while sites were encouraged to enroll all patients with bicuspid valve disease requiring AVR who met inclusion criteria, the potential for selection bias by sites and their multidisciplinary heart teams has long been a challenge in TAVR studies, particularly the low-risk studies. It will be important that the role of the heart team and the potential for selection bias be accounted for in both the design of future studies and in the development of guidelines for patients with bicuspid aortic valve disease undergoing TAVR.

Conclusions

Transcatheter aortic valve replacement in low-risk patients with bicuspid aortic valve stenosis achieved favorable early results, with high device success and low rates of death or disabling stroke. Longer-term outcomes are needed, and carefully constructed randomized clinical trials comparing TAVR with surgery in this patient population should be considered prior to any changes in clinical guidelines for patients with bicuspid aortic valve disease undergoing AVR.

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