Bicuspid aortic valve (BAV) is the most frequent congenital valvular abnormality, occurring in 0.5% to 2% of the population, with a male predominance. The bicuspid valve typically has two leaflets and is most frequently described using the Sievers classification scheme. Sievers type 0 valves have two, usually symmetrical leaflets, whereas Sievers type 1 valves have a raphe formed by the fusion of two underdeveloped cusps and Sievers type 2 valves have two raphes (Figure 1). Further subclassification is based on which cusps are fused and the functional status of the valve. The natural history of BAV disease is characterized by both valve-related complications and nonvalvular pathology, including aortopathy, with ascending thoracic aortic aneurysms in up to 50% of patients. Both aortic stenosis (AS) and aortic regurgitation are frequent manifestations of BAV disease and the mainstay of treatment remains surgical aortic valve replacement (SAVR). It has been shown that approximately 25% of patients with BAV will require aortic valve surgery and 5% will require ascending aorta surgery over a 20-year follow-up period. However, > 20% of patients with BAV requiring valve replacement are > 80 years old and some may also have medical comorbidities that increase their risk for surgical treatment. Given its proven safety and efficacy in patients with trileaflet AS who have elevated surgical risk, transcatheter aortic valve replacement (TAVR) has been investigated in higher-risk patients with BAV disease. The recent expansion of TAVR to younger and lower-risk populations has only intensified interest in its potential for treating patients with BAV. In this article, we review the available data on TAVR in BAV disease and describe some of the anatomic and technical considerations involved.

BICUSPID VALVE TAVR REGISTRIES

There are currently no randomized trials comparing SAVR and TAVR in patients with BAV. BAV patients were excluded from the pivotal TAVR trials due to the unique anatomic challenges that bicuspid valves present for TAVR, including frequent large size, elliptical shape, asymmetric cusps, and robust calcification. The early registries describing TAVR with first-generation transcatheter heart valves (THV) in BAV reported decreased device success with frequent incomplete THV expansion,
moderate or greater paravalvular leak, need for a second THV, annular rupture, and in some series, increased mortality. For example, Bauer et al described 38 patients with BAV stenosis in the German TAVR registry who were treated in 2009 and 2010 with either a Sapien (Edwards Lifesciences) or CoreValve (Medtronic) THV.\(^{12}\) When compared to patients with trileaflet AS undergoing TAVR, those with BAV had significantly more postprocedure grade II or higher aortic regurgitation (25% vs 15%), but no difference in mortality at 1 year.\(^{12}\) Costopoulos et al also used first-generation THVs in 21 patients with BAV and reported decreased device success (85.7% vs 94.4%) as well as a higher rate of mortality at 30 days (14.2% vs 3.6%)\(^ {13}\) when compared with TAVR for trileaflet AS. Similarly, among 139 BAV patients undergoing TAVR, Mylotte et al reported a device success of 89.9%, grade II or higher paravalvular leak in 28.4% of patients, and procedural mortality of 3.6%.\(^ {14}\) However, several other observational studies comparing TAVR outcomes in patients with BAV and trileaflet AS showed no difference in mortality, prompting continued exploration of TAVR as a treatment option for selected patients with bicuspid valves.\(^ {15-17}\)

With improved patient selection and advances in pre-procedural imaging, deployment technique, and device technology, more recent BAV TAVR registries have reported significantly improved procedural outcomes and mortality. Sannino et al used first- and second-generation THVs and compared TAVR outcomes in bicuspid and trileaflet valves; the results were not statistically significant, demonstrating similar procedural success (98.7% vs 99.1%), 30-day mortality (3.4% vs 3.1%), and 1-year mortality (8.5% vs 10.5%).\(^ {16}\) A recent propensity score–matched analysis of data from the Society of Thoracic Surgeons/ American College of Cardiology TAVR registry also demonstrated similar 30-day mortality (2.6% vs 2.5%; \(P = .82\)) and device success (96.5% vs 96.6%; \(P = .87\)) for TAVR in bicuspid and tricuspid AS, albeit with a slightly higher rate of moderate-to-severe AR in the bicuspid group (2.7% vs 2.1%; \(P < .001\)).\(^ {18}\) Finally, a recent meta-analysis of observational studies by Quintana et al also demonstrated no significant difference in mortality at 1 year between patients with trileaflet and bicuspid AS undergoing TAVR.\(^ {19}\) Other recent analyses that have compared the outcomes of TAVR and SAVR in BAV patients have also supported the finding of improved TAVR outcomes. For example, a recent propensity-matched analysis from the National Inpatient Sample database included 1,055 patients with BAV undergoing TAVR and showed similar in-hospital mortality (3.1% vs 3.1%) in a matched cohort of patients undergoing TAVR or SAVR.\(^ {19}\)

The more favorable results of the recent BAV TAVR registries may be due at least in part to the use of newer-generation THVs. In a propensity score–matched analysis of the Bicuspid AS TAVR registry, Yoon et al found that TAVR for bicuspid compared with trileaflet AS had a lower rate of device success (85.3% vs 91.4%; \(P = .002\)) and higher rates of moderate or severe paravalvular leak (PVL) (10.4 vs 6.8; \(P = .04\)), implantation of a second valve, root injury, and conversion to surgery.\(^ {17}\) However, additional analyses demonstrated that TAVR results in bicuspid AS were improved and not different from tricuspid AS with newer-generation THV devices, including the Sapien 3 (Edwards Lifesciences), Evolut R (Medtronic), and Lotus (Boston Scientific Corporation) valves.\(^ {16,17}\) Improvements in the newer devices that may have contributed to better outcomes in bicuspid valve TAVR include more stable, controlled deployments; the ability to recapture or reposition the THV (Evolut R, Lotus); and the addition of an external sealing skirt (Sapien 3, Lotus). Supporting the benefit of an external skirt in decreasing PVL in bicuspid TAVR, a recent case series of 50 BAV patients treated with TAVR with the Sapien 3 showed that only four patients required post-implantation balloon dilation and no patient had moderate or severe paravalvular leak.\(^ {20}\) Similarly, in an analysis of 31 BAV patients in the RESPOND registry, the repositioning feature of the Lotus valve was used in 10 patients and no patient had moderate or severe PVL.\(^ {21}\)

Despite the apparent improvement in results with new-generation THV systems, contemporary registries and meta-analyses continue to show that TAVR for bicuspid valve disease may be associated with higher rates of certain complications. For example, some studies have shown stroke risk to be higher with TAVR for BAV versus trileaflet AS (2.5% vs 1.6%), although the literature has been inconsistent.\(^ {22,23}\) It also remains unclear whether BAV may be associated with higher rates of permanent pacemaker insertion after TAVR, as it is with surgical aortic root replacement.\(^ {15,22,24}\) Finally, debate persists as to whether TAVR for BAV, as compared with trileaflet AS, remains associated with decreased device success and increased rates of moderate to severe PVL, requirement for a second THV, and conversion to conventional surgery.\(^ {15,25}\) Ultimately, additional research will be required to determine if TAVR outcomes in BAV can truly approach those in trileaflet AS and whether TAVR can be considered in lower-surgical-risk populations with BAV.

**PATIENT SELECTION AND PROCEDURAL CONSIDERATIONS**

The safety and efficacy of TAVR in BAV disease is likely to be highly dependent on careful patient selection and several important procedural considerations.\(^ {26}\) Recent improvements in cardiac multidetector CT (MDCT), in particular,
have greatly enhanced patient screening and procedural planning in challenging anatomic situations, including BAV. Transesophageal echocardiography also continues to play an important role, allowing detailed anatomic assessment even in patients with poor-quality MDCT imaging or prohibitive renal dysfunction. The preprocedural use of these three-dimensional imaging modalities specifically allows for delineation of the type of bicuspid valve (Sievers calcification), annulus size and ellipticity, calcium burden and location, and relationship of the coronary ostia. Preprocedural imaging also allows for evaluation for concomitant aortic aneurysm or other aortic pathology.

<table>
<thead>
<tr>
<th>Sievers type 0—Example 1.</th>
<th>Sievers type 0—Example 2.</th>
<th>Sievers type 1—Example 1.</th>
<th>Sievers type 1—Example 2.</th>
</tr>
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<tbody>
<tr>
<td>Annulus area, 398 mm</td>
<td>Annulus area, 539 mm</td>
<td>Annulus area, 478 mm</td>
<td>Annulus area, 508 mm</td>
</tr>
<tr>
<td>Perimeter, 72 mm</td>
<td>Perimeter, 84 mm</td>
<td>Perimeter, 78 mm</td>
<td>Perimeter, 81 mm</td>
</tr>
<tr>
<td>Morphology and calcification pattern at leaflet level</td>
<td>Degree of calcification will likely impact valve expansion</td>
<td>Fused RCC and LCC with heavily calcified NCC. Risk of contre-coup injury and root rupture</td>
<td>Fusion of LCC and RCC with mild calcification</td>
</tr>
<tr>
<td>Position of 23-mm Sapien 3 virtual valve, sinus unlikely to seal as good flow at other regions of STJ</td>
<td>Position of 26-mm Sapien 3 virtual valve</td>
<td>Position of 26-mm virtual valve</td>
<td>Position of 29-mm virtual valve</td>
</tr>
<tr>
<td>Intercommissural distance of 24 mm with likely good seal and low risk of PVL</td>
<td>Intercommissural distance of 26 mm with likely good seal if valve is allowed to expand considering calcification</td>
<td>Intercommissural distance of 29 mm with possible increased risk of PVL</td>
<td>Intercommissural distance of 28 mm with low likelihood of PVL at commissures</td>
</tr>
</tbody>
</table>

Figure 2. Two examples each of Sievers type 0 and 1 BAVs with anatomic and technical considerations. Abbreviations: LCC, left coronary cusp; NCC, noncoronary cusp; PVL, paravalvular leak; RCC, right coronary cusp; STJ, sinotubular junction.
The preprocedural imaging evaluation can be specifically tailored to focus on the risk of certain complications that may be more common in bicuspid valve anatomy, including paravalvular regurgitation, root injury, or coronary obstruction (Figure 2). Sievers type 0 and certain Sievers type 1 valves can exhibit an elliptical or "eye-shaped" distal landing zone for the THV. This elliptical nature may contribute to an increased risk of paravalvular regurgitation at the commissural regions, and there remains debate as to whether THVs similarly circularize the annulus in bicuspid and tricuspid anatomy. Multiple series have also demonstrated that THV underexpansion is a significant issue in BAV TAVR, raising theoretical concerns for leaflet thrombosis and long-term durability. The optimal THV sizing remains unclear because in some cases, the narrowest portion of the bicuspid valve anatomy may actually occur above the standard annulus plane as assessed by CTA. In this situation, the THV may anchor or seal above the annulus, leading to interest in so-called "supra-annular sizing." This may also have important implications for the target depth of implantation, which might be higher in bicuspid TAVR to achieve optimal sealing and minimize new pacemaker implantation.

Heavy, asymmetric calcification patterns are also a particular concern in bicuspid valve disease. Heavy calcification may result in incomplete or asymmetric valve expansion and root injury, which can occur due to a contrecoup injury with balloon inflation and THV expansion (Figure 3). Balloon aortic valvuloplasty may be useful in this setting to judge the response of the calcified BAV anatomy before THV implantation. Self-expanding or mechanically expandable THV designs may also be advantageous, although further research on optimal THV selection is required.

Unlike tricuspid aortic valves in which both coronary artery ostia are in the middle of the sinuses, in BAV anatomy, one or both ostia may be in proximity to the commissures (Figure 4). This, along with taller leaflet height and heavier calcification, may increase the risk of coronary obstruction, which also remains incompletely understood.

It is important to recognize that most patients with BAV treated with TAVR thus far have had stenotic valves. It remains unclear whether similar results will be achievable in patients with predominant or exclusive aortic regurgitation, particularly in the absence of significant calcification. Aortopathy also occurs in > 50% of patients with BAV disease and has a direct correlation with increasing patient age. However, predicting the rate of aneurysm progression and need for future root or aortic replacement can be difficult and may vary widely based on the underlying pathology. Although patients with BAV and aortic aneurysms meeting guideline indications are probably best suited for surgery, the optimal management of those with less severe aortic dilatation or other pathology remains unknown. It is also unknown whether aortopathy contributes to a risk of root injury with TAVR and if there is any impact of TAVR on the rate of aneurysm progression or associated outcomes. The use of an actively deflectable TAVR delivery system with active flexion may be theoretically advantageous in TAVR candidates with significant dilation of the ascending aorta in order to reduced stress on the outer curvature of the aorta. Additional research will be required to better delineate the impact of aortic regurgitation and aortopathy of TAVR candidacy and longer term clinical outcomes.

Given that patients with BAV disease are typically younger in age, THV durability is another particularly salient issue in this population. However, there are currently no available data on THV durability in BAV patients. In an all-comers population in the UK TAVI registry, 91% of patients remained free of structural valve deterioration between 5 to 10 years of implantation and < 1% had severe structural valve deterioration. In an analysis of 2,481 patients from the PARTNER I trial, which excluded BAV, with a median follow up of > 3 years, only five TAVR recipients received repeat intervention due to structural valve deterioration. In the NOTION trial, at more than 5-year follow-up, the rate of structural valve deterioration was higher for SAVR than TAVR (24% vs. 4.8%) and the rate of bioprosthetic valve failure (valve-related death, aortic valve reintervention, or severe hemodynamic structural valve deterioration) was similar between the two groups (6.7% vs. 7.5%). Although these data are encouraging, THV durability in BAV may not be equivalent and further dedicated studies in this population are needed.

Novel approaches to BAV TAVR have included both preprocedural and procedural innovations. Computer
simulations of TAVR in BAV have attempted to predict outcomes such as paravalvular regurgitation or conduction abnormalities.


CONCLUSION

BAV disease presents unique challenges for TAVR, but promising results are being reported with recent improvements in patient selection, procedural technique, and device technology. At present, TAVR should be reserved for higher-risk surgical candidates, and future research should focus on further refining patient selection and identifying the optimal devices and techniques in this population. Ultimately, randomized controlled clinical trials may be necessary to guide further expansion of TAVR to lower-risk patients with BAV. 

Hussein Rahim, MD Columbia University Irving Medical Center New York, New York Disclosures: None.

Mariusz Wolbinski, MD Columbia University Irving Medical Center New York, New York Disclosures: None.

Vinayak Bapat, MBBS Columbia University Irving Medical Center New York, New York Disclosures: None.

Tamin M. Nazif, MD Columbia University Irving Medical Center New York, New York tmn31@columbia.edu

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