

# Transcatheter Aortic Valve Replacement in Bicuspid Aortic Valve Disease: An Insight

Varshil Mehta<sup>1†</sup>, Nikhil Nalluri<sup>2†</sup>, Varun Kumar<sup>3</sup>, Nileshkumar Patel<sup>4</sup>,  
Varunsiri Atti<sup>5</sup>, Arvin Narula<sup>4</sup>, Mauricio Cohen<sup>4</sup>

<sup>1</sup>Icahn School of Medicine at Mount Sinai, New York, <sup>2</sup>Staten Island University Hospital, New York, <sup>3</sup>Mt. Sinai St. Luke's Roosevelt Hospital Center, New York, <sup>4</sup>University of Miami/Miller School of Medicine, Miami, Florida, <sup>5</sup>Michigan State University, Michigan, USA

†Authors share equal contribution to this manuscript.

Address for correspondence: Varshil Mehta, Icahn School of Medicine at Mount Sinai, New York, USA.  
E-mail: varshilmehta@gmail.com



## Abstract

As per the current scenario, the role of transcatheter aortic valve implantation (TAVI) is controversial in bicuspid aortic valve (BAV) stenosis. All the randomized clinical trials comparing outcomes of TAVI with surgery, till date, have excluded patients with the BAV. Some of the observational studies have reported outcomes of TAVI in BAV stenosis patients who are not a surgical candidate. The recent advances in TAVI and its expansion into intermediate groups, which includes younger age groups sparks a debate on the efficacy and safety of TAVI in BAV. The purpose of the present article is to review the available literature regarding the feasibility, safety, and outcomes of TAVI in BAV stenosis.

**Keywords:** Aortic stenosis, bicuspid aortic valve disease, transcatheter aortic valve implantation

## Case Report

Eighty-five year-old female patient with the medical history of diabetes, hyperlipidemia on statins, and chronic atrial fibrillation on Coumadin was referred to our institute for severe symptomatic aortic stenosis. She endorses that her condition has deteriorated over past year. She started noticing lower extremity swelling, two pillow orthopnea and fatigue on exertion. Echocardiogram at our institute showed severe aortic stenosis with a peak velocity of 4.1 m/sec, peak gradient 67, mean gradient 39 mmHg, and AVA 0.8 cm<sup>2</sup>. It was not clear that the patient has bicuspid or tricuspid aortic valve from the echocardiogram. After heart team discussion, it was decided that the patient is not a candidate for open surgical valve replacement because of her age and frailty. CT scan showed done as a part of TAVI work up showed: Bicuspid aortic valve.

## Introduction

### Bicuspid aortic valve (BAV)

BAV is defined as a spectrum of abnormal aortic valve morphology which consists of two functional

cusps with <3 zones of parallel apposition between cusps.<sup>[1]</sup> BAV is a common congenital disorder found in adults at a rate of 0.5–2% with a predilection towards males,<sup>[2-4]</sup> with a demonstrated association with mutations in the NOTCH1 gene.<sup>[5]</sup> Interestingly, its heritability is as high as 89%, suggesting an autosomal dominant pattern of inheritance.<sup>[6-8]</sup> Individuals with BAV are prone to develop aortic stenosis (AS) at an earlier age when compared to people with tricuspid aortic valve (TAV). Nonetheless, bicuspid valves also pose a risk of developing symptomatic AS in elderly patients.<sup>[9]</sup> In fact, it is observed that its frequency is as high as 6% of the population over 85 years of age.<sup>[10]</sup> Approximately 20–50% of the patients with a BAV require aortic valve replacement in their lifetime.<sup>[11]</sup> BAS is generally treated with surgical aortic valve replacement (SAVR) in patients <70 years of age.<sup>[9]</sup> However, SAVR may not be a treatment option for patients with high surgical risk due to comorbidities or in the presence of absolute contraindications such as porcelain aorta (extensively calcified ascending aorta and/or aortic arch). Even though

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percutaneous balloon valvuloplasty can be an option in this population, AS reoccurs in the majority of the patients in the long-term.<sup>[12,13]</sup>

### Transcatheter aortic valve implantation (TAVI)

TAVI is a minimally invasive procedure in which a new bioprosthetic (self-expandable or balloon-expandable) valve is inserted through catheter delivery system and implanted into aortic valve position without removing the old and diseased valve.<sup>[14]</sup> Once the new valve is placed and expanded, it pushes the old valve leaflets from the site, and the tissue in the replacement valve takes over the job of regulating blood flow.

TAVI is performed through different approaches: Transfemoral, transapical, subclavian, direct aortic, and transcaval.<sup>[14]</sup> Current ACC/AHA guidelines recommend TAVI as Class I for patients with prohibitive and high surgical risk (with a post-TAVR survival greater than 12 months), whereas Class II for patients with intermediate surgical risk.

The recent advances with the valve design, TAVI is being studied in lower-risk populations as well as to treat other disease states such as BAS, native aortic valve regurgitation, and failed bioprosthetic aortic valve stenosis.<sup>[15]</sup>

### BAV Anomaly, Associated Complications

BAV anomaly has several variants. BAV without any unwanted tissue generally develops stenosis, whereas valves with unwanted tissue usually tend to develop valvular incompetence.<sup>[16]</sup>

AS is one of the most important complications of BAV and its incidence on autopsy ranges from 15% to 75%.<sup>[17]</sup> Stenosis in BAV progresses with age, with fibrosis beginning in the second decade and calcification after the fourth decade. Among octogenarians and nonagenarians, who underwent SAVR, 22% and 18%, respectively, were observed to have BAV.<sup>[9]</sup>

The most popular BAV classification was described by Sievers *et al.* in 2007. They identified three major types of BAV based on the number of raphe:

1. Type 0 – No raphe
2. Type 1 – One raphe
3. Type 2 – Two raphe.

They further subdivided these types into two subcategories based on:

1. Spatial arrangements of the cusp free edges (for example, BAV type 1 L/R means one raphe positioned between the left and right coronary sinuses)

- a. Type 0 – lateral and antero-posterior
- b. Type 1- L-R, R-N, and N-L
- c. Type 2 – L-R/R-N.

(L = left coronary cusp, R = Right coronary cusp, and N = Non coronary cusp)

2. Functional status – predominant insufficiency (I), predominant stenosis (S), balanced insufficiency and stenosis (B), and no insufficiency and stenosis (No)

Most patients in the study had BAV Type 1 (88%) predominantly L-R, S category.<sup>[1]</sup>

Bicuspid aortopathy (i.e., dilation of any part or all segments of the proximal aorta from the aortic root to the aortic arch) is the most common non-valvular finding found in approximately 50% of the affected patients.<sup>[3,18]</sup> Abnormal dilation of the ascending aorta is generally found secondary to the abnormalities of the aortic media and becomes of significant surgical interest when the diameter of the aorta exceeds 4.5 cm.<sup>[18]</sup> Aortic media changes are present independent of the valve functionality (normal, stenotic, or incompetent). The pathology of ascending aorta is considered to be an expression of the genetic basis of BAV and may signify the use of surgical intervention.<sup>[4]</sup>

### Current Management Scenario

At present, echocardiography is the most important and common imaging modality used with regard to diagnosis and surveillance. Transthoracic echocardiography (TTE), when compared to surgical operative records or surgical pathology, demonstrated a specificity of 96% and sensitivity of 78% for the diagnosis.<sup>[19]</sup> One study with multiplane transesophageal echocardiogram (TEE) and operative records observed a sensitivity of 87% and a specificity of 91%.<sup>[20]</sup> Furthermore, pre-operative echocardiography and intraoperative TEE are crucial not only for planning the surgical approach but also, assessing repair status, respectively, when valve repair is considered for BAV regurgitation.<sup>[21]</sup>

Because echocardiography is generally diagnostic, but it is limited by patient and operator related factors. Especially in the setting of heavy calcification, echocardiography can be challenging due to artifacts. Multidetector CT (MDCT) and magnetic resonance imaging (MRI) are emerging as alternatives for the diagnosis of the BAV.

Tanaka *et al.* reported a sensitivity of 94% and specificity of 100% for ECG gated MDCT in detecting BAV.<sup>[22]</sup> Cardiac MRI could also play an important role. A recent article reported a specificity of



95% and sensitivity of 100% with steady-state free-precession cine MRI in the correct classification of a valve as bicuspid.<sup>[23]</sup>

With regard to treatment options, there is a recent emergence of new data suggesting that medical therapy may help in slowing down the progression of expansion and dissection in patients with BAV and aortic aneurysm.<sup>[21]</sup> Moreover, beta-blocker treatment now has been recommended as a Class IIa for BAV patients with an enlarged aorta.<sup>[24]</sup> Angiotensin receptor blockade is also a Class IIa recommendation to reduce the dilatation of the aorta.<sup>[25]</sup>

However, SAVR currently remains the gold standard of treatment for patients with BAS <70 years of age.<sup>[9]</sup> 2010 Guidelines for the Diagnosis and Management of Patients with Thoracic Aortic Disease suggested surgery as a Class I recommendation in patients with genetic syndromes which could possibly lead to aortic dissection and BAV, at aortic diameters from 4 to 5 cm.<sup>[25]</sup> However, surgical method has its own limitations where it cannot be done, for example, porcelain aorta (extensively calcified ascending aorta and/or aortic arch), hostile chest (patients with a history of sternotomy or radiation) or in patients who are suffering from comorbidities.<sup>[12,13]</sup> Percutaneous aortic balloon valvotomy is of limited use due to high recurrence rates.<sup>[12]</sup>

The latest method, which is in growing in popularity for its ability to treat patients who are at high or prohibitive risk for surgery is TAVI.

### **Should TAVI be used in BAV?**

Treatment of BAV disease with TAVI is yet considered as an off-label indication. Most randomized clinical trials have excluded patients with BAV stenosis. The specific concerns regarding TAVI for BAV include:

1. The asymmetry and heavy calcification involving the leaflets can prevent the valve from expanding properly, which might result in a para-valvular leak and high transvalvular gradients.
2. The elliptical annular anatomy of a BAV may lead to valve malpositioning.<sup>[26]</sup>
3. There is a risk of severe aortic regurgitation due to the disruption of the fused commissures.
4. The concomitant aortic disease increases the chances of rupture or dissection during the procedure.
5. Finally, if a valve is malpositioned or under expanded due to the above-mentioned challenges, it affects its long-term durability.

The bicuspid valves which are surgically excised typically demonstrate leaflet fusion (raphe) and extensive nodular calcification. The morphological distribution of calcific deposits in BAV leaflets is different as compared to that of tricuspid AS (TAS).<sup>[27]</sup> As mentioned above, the extensive calcium deposition in the body of BAV leaflets and asymmetrical nature of the bicuspid aortic root could impair TAVI outcomes.<sup>[1,28]</sup>

In a retrospective study conducted by Mylotte *et al.*,<sup>[29]</sup> they have noticed that Guidewire crossing and transcatheter heart valve (THV) positioning were more difficult with bicuspid than TAV stenosis. However, the procedural results were acceptable and comparable to those reported in TAVI with TAS.<sup>[30-35]</sup> The acute valve embolization occurred in 2.2% and conversion to SAVR occurred in 2.2%, whereas the 30-day rates of VARC-defined device safety (79.1%), efficacy (84.9%), and success (89.9%) were encouraging as well.

However, there are very few studies done in the past which support the use of TAVI in BAS. The first description of TAVI procedure in the BAV population was done and published by Wijesinghe *et al.*, and it included 11 high-risk patients who were treated with a balloon-expandable prosthesis (Edwards-SAPIEN [Edwards Lifesciences, Irvine, California]). The mean age was  $73.2 \pm 12.5$  and predicted the risk of mortality (PROM) was  $4.4 \pm 2.6\%$  according to the Society of Thoracic Surgeons score. TAVI was performed through the transfemoral (63.4%) or transapical route (36.4%) under general anesthesia. After the implantation, 18% of the patients had a moderate perivalvular leak (PVL), and the 30 days mortality was 18%. At follow-up (median time: 208 days) mortality rate was found out to be 36.4%, which was mainly driven by deaths occurring in the transapical group in which all four patients died. At follow up, all survivors at follow-up were either in Class I or Class II of New York Heart Association (NYHA). Limited by only one type of bioprosthesis, this study for the first time showed that TAVI in BAV is feasible in a selected group of patients.<sup>[36]</sup>

Yoon *et al.* in 2016 reported clinical outcomes of TAVI in BAS with regard to early and new-generation devices in the multicenter bicuspid TAVI registry. This registry enrolled 301 consecutive patients undergoing TAVI for BAS which included 199 patients (71.1%) receiving early-generation devices (Sapien XT [Edwards Lifesciences, Irvine, California]:  $n = 87$ ; and CoreValve [Medtronic, Minneapolis, Minnesota]: ( $n = 112$ ) and 102 patients (29.9%) receiving new-generation devices (Sapien 3



[Edwards Lifesciences]:  $n = 91$ ; and Lotus [Boston Scientific, Marlborough, Massachusetts]: ( $n = 11$ ). Mean age in the studied group was  $77.0 \pm 9.2$  years, and the Society of Thoracic Surgeons score was  $4.7 \pm 5.2$ , which classified the population as intermediate surgical risk group.<sup>[37]</sup> They also provided a comparison between the old and new generation devices, showing the superiority of new-generation over old-generation devices for the treatment of BAS (device success 92.2% vs. 80.9%;  $P = 0.01$ , and second valve implantation 1% vs. 6.5%;  $P = 0.04$ ). All-cause mortality rates were 4.3% at 30 days and 14.4% at 1 year, which was comparable to that of TAVI for TAS in the general population. Moreover, there were no reported cases of moderate-to-severe paravalvular regurgitation with new-generation devices (Sapien 3 [Edwards Lifesciences] and Lotus [Boston Scientific, Marlborough, Massachusetts]) while the old generation devices had an incidence rate of 8.5% (Sapien XT [Edwards Lifesciences, Irvine, California]:  $n = 5$  (5.7%); and CoreValve [Medtronic, Minneapolis, Minnesota]:  $n = 12$  (1)). These results from Yoon *et al.* offered a reassurance that TAVI may indeed be a reasonable treatment option for such patients.<sup>[37]</sup>

Himbert *et al.* conducted a study to assess the results of TAVI in BAV with self-expandable valve Medtronic CoreValve system (MCS; Medtronic, Inc., Minneapolis, Minnesota) in which 15 patients with a mean age of  $80 \pm 10$  and high mortality risk (Society of Thoracic Surgeons score  $8 \pm 5$ ) were evaluated. The transfemoral approach was used in all except for one patient, and three procedures were performed under general anesthesia, which gave access for periprocedural trans-esophageal guidance. Although six patients required permanent pacemaker implantation (40%), moderate PVL was seen only in one patient (6.7%) and 30 days survival rate was 93%. After a mean follow-up of  $8 \pm 7$  months, two patients were dead (13%), and the survivors (78.6%) achieved an improvement in their functional status according to NYHA I or II. The results of this observation suggest that BAV can be also safely treated with a self-expandable prosthesis. However, a major disadvantage is an absence of a control group (patients with tricuspid anatomy) and population size.<sup>[38]</sup>

The above issue was addressed in the next studies. Hayashida *et al.* compared the results of TAVI obtained in 21 BAV cases with the results achieved in 208 patients with a normal tricuspid valve. They only included patients who also underwent MDCT

before TAVI along with other imaging modalities (TTE and TEE). However, no statistically significant differences were found between the groups in age, sex, and mortality risk. Similar results were observed in terms of 30 days mortality and moderate/severe PVL (4.8% vs. 8.2%;  $P = 1.00$ , and 19.0% vs. 14.9%;  $P = 0.54$ , respectively).<sup>[39]</sup>

In a similar study by Costopoulos *et al.*, comparing BAV ( $n = 21$ ) and TAV patients ( $n = 447$ ) treated with Edwards or CoreValve bioprosthesis from November 2007 to December 2012, a difference in 30 days mortality and 1-year mortality (14.2% vs. 3.6%,  $P = 0.02$ ) and 10.5% vs. 7.4%,  $P = 0.62$ , respectively) was observed. The researchers concluded that even though TAVI in BAV patients with high surgical risk is feasible with acceptable mid-term outcomes, a careful selection of patients is necessary as patients with BAV showed lower early survival rates and device success. The reasons are mainly anatomic challenges posed by BAV patients. They have encountered one case of dissection, one case of valve migration, but the most common problem they encountered was a need for frequent post-dilatation in BAV group (52.4% vs. 23.5%,  $P < 0.01$ ). This could be due to the asymmetric calcification seen in BAV patients. This study is limited by its small sample size to draw any real-world long-term conclusions.<sup>[40]</sup>

Subsequently, in a sub-analysis of the German Aortic Valve Registry (GARY), a higher rate of PVL was reported amongst 38 BAV patients when compared with a large control group of 1357 TAV patients (25% vs. 15%;  $P = 0.05$ ) which they attributed to the anatomic features of a BAV.<sup>[41]</sup>

In 2014–15, two relatively large, multicenter studies were carried out on TAVI in BAV. One of them was conducted by Mylotte *et al.*, in which 139 BAV patients were included, and the procedural outcomes were evaluated for both self- and balloon-expandable bioprosthesis. The mean age of the patients enrolled was  $78.0 \pm 8.9$  years, and the mean Society of Thoracic Surgeons (STS) PROM score was  $4.9 \pm 3.4$ . A balloon-expandable THV (Sapien XT, Edwards Lifesciences, Inc., Irvine, California) and self-expandable THV (CoreValve, Medtronic, Inc., Minneapolis, Minnesota) were used in 48 patients (34.5%) and 91 patients (65.5%), respectively. Interestingly, the rate of moderate/severe PVL in the studied group was 28.4% but was 17.4% in the subgroup in which valve size was based on MDCT. A trend toward a higher rate of relevant PVL in patients treated with a self-expandable valve (19.6 vs. 32.2;  $P = 0.11$ ) was observed, but as per the





authors, it could be because of lower use of MDCT for valve sizing in this group. This study emphasizes on patient selection and pre-procedural imaging for better outcomes, especially in BAV.<sup>[29]</sup>

The other study was by Yousef *et al.*, which looked into the outcomes of TAVI in 108 BAV patients. This study also confirmed the general feasibility and acceptable clinical outcomes of TAVI in BAV, in spite of the fact that a relatively high rate of re-intervention was seen (9.3%) because of either valve embolization or migration.<sup>[42]</sup>

The study conducted by Perlman *et al.*, in 2016, it was concluded that TAVI in BAS using a new-generation device (SAPIEN 3) was feasible and effective. Furthermore, valve performance was favorable, and no cases of moderate or severe AR were observed. This again was attributed to pre-procedural CT annular sizing which was used to select an appropriately sized implant. The lack of significant PVL (>mild) could also be attributed to the improved sealing properties of the external sealing layer of the inflow portion of the SAPIEN 3 valve and improvements in the accuracy of valve positioning with an improved valve delivery system. In the study, 51 patients underwent TAVI using the SAPIEN 3 valve. The mean age in the patient group was  $76.2 \pm 9.3$  years, and the predicted risk of mortality scores was  $5.2 \pm 3.7\%$  according to the Society of Thoracic Surgeons. The most common bicuspid valve type was type 1 (82.3%) followed by type 0 (11.8%) and type 2 (1.9%). Post-dilation was performed in 7.8% of the cases. There were no cases of valve embolization or need for a second valve. The mean aortic gradient decreased from  $49.4 \pm 16.0$  mm Hg to  $11.2 \pm 4.7$  mm Hg. Post-implantation AR was mild in 37% and none/trivial in 63%. There were no cases of moderate or severe AR. At 30 days follow-up, 2 deaths (3.9%), two major vascular complications were observed with 12 patients (23.5%) requiring pacemaker implantation.<sup>[43]</sup>

The results of a recent international multicenter, observational study comparing outcomes of TAVI in bicuspid versus TAV were presented at the American college of cardiology conference. Here researchers compared outcomes of 561 patients with bicuspid AS and 4546 patients with TAS after propensity-score matching; assembling 546 pairs of patients with similar baseline characteristics. The study found that when compared to patients with TAS, patients with BAS had more frequent conversion to surgery (2.0% vs. 0.2%;  $P = 0.006$ ) and significantly lower device success rate (85.3% vs. 91.4%;  $P = 0.002$ ). Interestingly in these study

early-generation devices (Sapien XT, CoreValve) were implanted in 320 patients with bicuspid and 321 patients with TAS, whereas new-generation devices (Sapien 3, Lotus, Evolut R) were implanted in 226 and 225 patients with bicuspid and TAS, respectively.

The early generation devices had a high incidence of moderate to severe PVL (15.4%), whereas the incidence was low and comparable to TAS with newer generation devices (2.7%). Among the early generation devices, the CoreValve had more moderate-to-severe PVL (19.4% vs. 10.5%,  $P = 0.02$ ). Among the BAS patients receiving early-generation devices, Sapien XT had more frequent aortic root injury (4.5% vs. 0.0%,  $P = 0.015$ ). They concluded that TAVI in BAS was associated with similar prognosis but higher adverse procedural events compared to TAS. However, there were no differences with the new generation devices. The patients with newer-generation devices had acceptable and comparable procedural results to tricuspid TAVI and this was similar across different prostheses. The cumulative all-cause mortality rates at 2 years were comparable between bicuspid and TAS (17.2% vs. 19.4%,  $P = 0.28$ ). The important finding of the study is that TAVI is feasible with certain BAS patients with newer generation valves (Sapien 3, Lotus, Evolut R).<sup>[44]</sup>

These studies are compared in Table 1. With the advancement of technology, it seems that TAVI can indeed be technically feasible in selected BAV patients, especially with the newer generation valves. However, a meticulous preprocedural assessment and planning are needed for better outcomes.

### **Role of Pre-procedural Imaging in BAV TAVI**

In this new era of TAVI, there is a large role played by preprocedural assessment and imaging. The goals of preprocedural imaging are as follows:

1. Identify the patients with AS and confirm the severity.
2. Identifying patients suitable for TAVI.
3. Help in device selection (type and size) by defining the anatomic characteristics.
4. To develop a procedural plan (Vascular access/ fluoroscopic angulation).

The imaging methods vary among institution and individuals. ACC recently released expert consensus decision pathway for TAVI. The most commonly used imaging modalities are TTE, TEE, and CT scan.





Table 1: Comparison of studies

Author	Year of publication	N	Mean age	BAV $\mu$ Type (Sievers)	Valve used	Access	Mortality	Device success in BAV pts (%)	Paravalvular leak % (mod-severe)	Other Complications in BAV pts (%)
Wijesinghe et al. <sup>[36]</sup>	2010	11	73.2±12.5	-	Edwards-SAPIEN valve (26-mm): 90.90% Edwards-SAPIEN valve (23-mm): 9.10%	Transfemoral (63.4%) Transapical (36.4%)	30 days: 18% 208 days: 36.4%	-	30 days: 18%	Major Vascular complication: 4.0% New Pacemaker: 14.3% Coronary occlusion: 1.0% AKI <sup>+</sup> : 2.7% Stroke 7% Annulus rupture: 1.7% Second valve implantation: 4.7% Major Bleeding: 4.7%
Yoon et al. <sup>[37]</sup>	2016	301	77.0±9.2	Type 0: 0.29% Type 1: 74.41% Type 2: 1.66% Undetermined: 13.64%	Early Generation Devices in 199 (71.1%) patients: Sapien XT (87); CoreValve (102) New Generation Devices in 102 (29.9%) patients: Sapien 3 (91); Lotus (11)	Transfemoral: 84% Transapical: 6.31% Transsubclavian: 3.32% Transaortic: 5.64% Transcarotid: 0.66%	30 days: 4.3% 365 days: 14.4%	Overall 84.7% early generation-80.9% newgeneration-92.2%	Early Generation Devices: 8.5% New Generation Devices: NIL	Major Vascular complication: 4.0% New Pacemaker: 14.3% Coronary occlusion: 1.0% AKI <sup>+</sup> : 2.7% Stroke 7% Annulus rupture: 1.7% Second valve implantation: 4.7% Major Bleeding: 4.7%
Himbert et al. <sup>[38]</sup>	2012	15	80.0±10.0	Type 0: 13.33% Type 1: 66.67%	-	Transfemoral: 93.33% Transsubclavian: 6.67%	30 days: 7% 240 ± 210 days: 13%	-	6.70%	-
Hayashida et al. <sup>[39]</sup>	2013	229	82.0±7.0	-	Edwards: 52.4% Core Valve: 47.6%	Transfemoral (61.9%) Transaortic (23.8%) Transapical (14.3%)	30 days: 4.8%	100%	19%	Major Vascular complication: 4.8% New Pacemaker: 14.3% Coronary occlusion: 4.8% AKI <sup>+</sup> : 4.8% Stroke 0% Annulus rupture: 0% Valve migration: 0% Major Bleeding: 4.8%

(contd...)

Table 1: (Continued)

Author	Year of publication	N	Mean age	BAV/L Type (Sievers)	Valve used	Access	Mortality	Device success in BAV pts (%)	Paravalvular leak % (mod-severe)	Other Complications in BAV pts (%)
Costopoulos et al. <sup>[40]</sup>	2014	21	76.7 ± 7.1	-	-	-	30 days: 14.2% 365 days: 10.5%	86%	-	Major Vascular complication: 10% New Pacemaker: 14% Coronary occlusion: 0% AKI: 19% Stroke 0%
Bauer et al. <sup>[41]</sup>	2014	38	-	-	-	-	30 days: 11%	-	25%	New Pacemaker: 17% Stroke: 0% Reoperation: 3%
Mylotte et al. <sup>[29]</sup>	2014	139	78.0 ± 8.9	Type 0 (26.7%) Type 1 (68.3%) Type 2 (5.0%)	Balloon-expandable THVβ (SapienXT, Edwards Lifesciences, Inc., Irvine, California) used in 34.5% Self-expandable THVβ (CoreValve, Medtronic, Inc., Minneapolis, Minnesota) used in 65.5%	Transfemoral : 78.5% Subclavina: 3.6% Carotid: 0.7% Apical: 8.6% Aortic: 8.6%	30 days: 5% 365 days: 17.5%	89.9%	30 days: 28.4%	Major Vascular complication: 6.5% New Pacemaker: 23.2% Stroke: 2.2% AKI: 2.2%
Yousef et al. <sup>[42]</sup>	2015	108	75.5 ± 14.4	Type 0 (16.7%) Type 1 (73.0%) Type 2 (10.3%)	Balloon expandable valves	Femoral: 83% Subclavian: 5.6% Transaortic: 5.6% Transapical: 8.7%	30 days: 8.3% 365 days: 16.9%	85.2%	30 days: 30.8% 365 days: 27.7%	Major Vascular complication: 6.5% Coronary artery obstruction requiring intervention: 4.6% New Pacemaker: 19.4% Stroke: 2.8% AKI: 6.5% 1 annular rupture

(contd...)





Table 1: (Continued)

Author	Year of publication	N	Mean age	BAV,μ Type (Sievers)	Valve used	Access	Mortality	Device success in BAV pts (%)	Paravalvular leak % (mod-severe)	Other Complications in BAV pts (%)
Perlman et al. <sup>[43]</sup>	2016	51	76.2 ± 9.3	Type 0 (11.8%) Type 1 (82.3%) Type 2 (1.9%)	SAPIEN 3 valve	-	30 days: 3.9%	98%	NIL	Major Vascular complication: 3.9% Annular rupture/ Aortic root injury: New Pacemaker: 23.5% Stroke: 1.9% AKI <sup>ε</sup> : 1.9%
Sung-Han Yoon <sup>[44]</sup>	2017	546	BAV-77 ± 8 TAV 77 ± 8	Type 1-86%	Early generation devices BAVμ: 59% TAVΣ: 59% (Sapient XT, 28% versus 28% CoreValve, 30% versus 31%) Newer generation Devices BAVβ: 41% TAVΣ: 41% (Sapient 3, 29% versus 30% Lotus, 8% vs. 9%, Evolut R, 4% versus 3%)	Transfemoral (86%)	30 days: 3.7% 1 year: 11.4% 2 years: 17.2%	85% Newer generation: 95%	Total: 10.4% early generation 15.4% newer generation 2.7%	Major Vascular complication: 2.9% Annular rupture/Aortic root injury: 1.6% New Pacemaker: 15.4% Stroke: 2.9%

ε: AKI = Acute Kidney Injury, μ: BAV = Bicuspid aortic valve, β: THV = Transcatheter heart valve, Σ: TAV = Transcatheter aortic valve



TTE is routinely used for initial assessment of aortic valve type, AS severity, and left ventricular function. TTE or TEE imaging can sometimes be limited in detection of BAV by factors such as patient body habitus and excessive calcification. Although a 3D TEE can improve the detection of BAV, it is not always feasible in seriously ill patients. Hayasida *et al.* reported disparity regarding the diagnosis of BAV between MDCT and TTE/TEE. In their study, MDCT detected BAV in 21 patients (9.2%), but TTE/TEE was able to pick only nine out of the 21 cases.<sup>[39]</sup>

Given the favorable data coming out for TAVI in high-risk population,<sup>[45]</sup> TAVI is being evaluated in the intermediate risk group. This risk group includes younger patients, whose frequency of BAV is higher than the elderly.<sup>[46]</sup> With more BAV patients undergoing TAVI, there is a larger role for pre-procedural imaging to identify various anatomic as well as high-risk properties. This is achieved by a three-dimensional assessment of annular dimensions, which is commonly obtained by MDCT.<sup>[47,48]</sup>

MDCT helps in precise characterization of leaflet morphology, assessment of the symmetry of the aortic valve leaflets, and distribution of valvular calcification. All these mentioned factors are useful in selecting the type and size of the THV. MDCT also provides other anatomic information such as assessment of the left ventricular outflow tract, aortic root ("sinus of Valsalva"), determination of coronary heights, and identification of concomitant ascending aortopathy.

There are several classifications for BAV proposed earlier based on the pathological findings and echocardiography of which Sievers being the most popular one (e.g., Sievers *et al.* and Michelena *et al.*) [Table 2]. Most of the studies showed a high incidence of Sievers type 1 BAV.<sup>[1,44]</sup> Each type of BAV has unique anatomic features which may affect the outcomes of TAVI. Mylotte *et al.* described higher rates of post-implantation aortic regurgitation in Sievers type 1 (34.2%) compared to Sievers type 0 (13.3%).<sup>[29]</sup> In the advent of TAVI becoming more popular and widely used, there is a need for an alternative classification which can predict TAVI outcomes in BAV population. In the process, Jilaihawi *et al.* proposed a the TAVI-Specific BAV classification using cardiac computed tomography analyzed by corelab (cedars-Sinai heart institute) to aid in pre-procedural planning in patients with BAV who are being evaluated for TAVI.<sup>[49]</sup> The MDCT images in 91 of 130 patients

were reviewed and a novel classification was proposed in an effort to predict procedural outcomes after TAVI. The classification is depicted in Figure 1.

Here, they came up with a simplified TAVI directed classification based on the leaflet morphologies and orientation.

The specified three morphologies of BAV

1. Tricommissural (23.3%) – here one commissure is completely fused between two cusps, also known as functional or acquired type)
2. Bicommissural raphe type(55.6%) – here two cusps are fused (usually a or proximal to the basal third of the sinus) by a fibrous or calcified ridge of various heights, does not reach the height of the commissure
3. Bicommissural non-raphe type (21.1%) – the two cusps are completely fused from their basal origin by no visible seam here you see, only two commissures with no raphe or third commissure.

The leaflet orientation was divided based on the cusp fusion into:

1. Coronary cusp fusion – comparable to Sievers left-right for raphe type or anteroposterior for non-raphe type
2. Mixed noncoronary – coronary cusp fusion – comparable with Sievers right-non or non- Left for raphe type or lateral for non-raphe type (1).

They found no difference in overall rates of 30-day mortality (3.8%), rates of moderate to severe AR (19% vs. 19.5% vs. 15%), the rate for new pacemakers and cerebrovascular events (3.2%) among anatomical subsets. The lack of outcomes correlation compared to Sievers classification (1), calls for an expansion of Jilaihawi *et al.*'s morphological classification. Assessment of the length of the raphe, the extent of calcification along the raphe could be important in predicting the outcomes of BAV TAVI.

One more important finding of Jilaihawi *et al.* was that the incidence of perivalvular aortic regurgitation (PAR) > moderate was 18.1% overall, but it was lower in patients who got a pre-procedural CT (11.5%). Predictors of post-procedural aortic regurgitation included intercommissural distance for bicommissural BAV and lack of baseline CT sizing before the procedure. This further emphasized the need for pre-procedural imaging for better sizing and anatomic definition of the valve, which further helps in better outcomes.<sup>[49]</sup>



**Table 2: Different classifications of BAV**

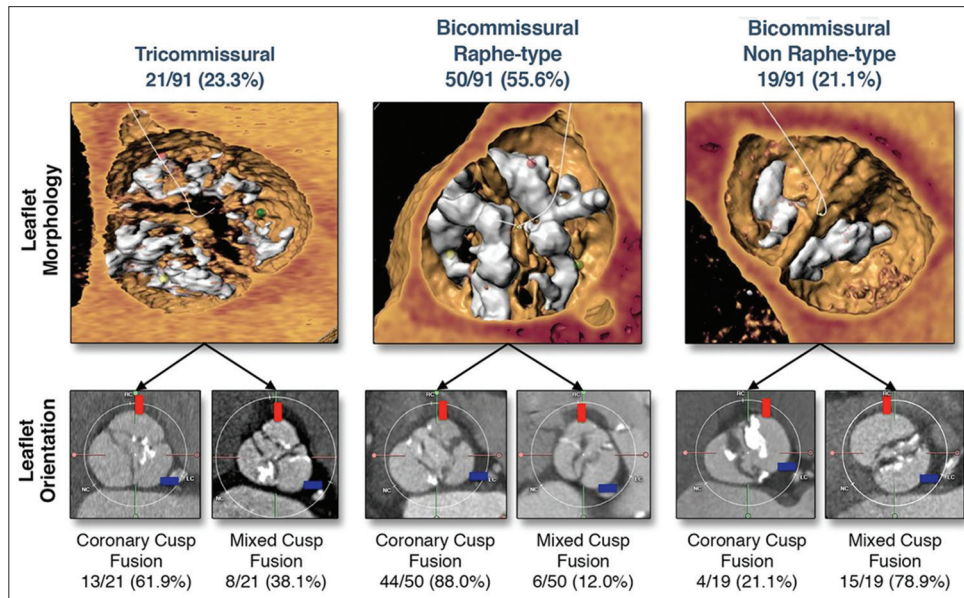
Author (Ref. #)	Specimens/Imaging test	Number of Cases	Criteria	Types			
Roberts <i>et al.</i> <sup>[17]</sup>	Surgical specimens	59	Cusp orientation	Anterior-posterior cusps			
				Left-right cusps			
Sabet <i>et al.</i> <sup>[3]</sup>	Pathology	534	Raphe orientation	RCC and LCC Fusion			
				RCC and NCC fusion			
				LCC and RCC fusion			
			Relative cusp size/ volume	Equal cusps			
				Unequal cusps			
				Thirds			
Sievers <i>et al.</i> <sup>[1]</sup>	Pathology	304	Number of rapheae	Type 0 (none)			
				Type 1 (one)			
				Type 2 (two)			
			Spatial position of raphe/cusp	Anterior-posterior cusps			
				Lateral cusps			
				RCC and LCC fusion			
				RCC and NCC fusion			
				LCC and NCC fusion			
			Functional status of the valve	Stenosis			
				Insufficiency			
				Both			
				None			
			Michelena <i>et al.</i> <sup>[11]</sup>	Echocardiogram	—	Location of the commissures	Type 1: LCC and RCC fusion
							Type 2: RCC and NCC fusion
Type 3: LCC and NCC fusion							
Cusp symmetry	Symmetric						
	Nonsymmetrical						
Jilaihawi <i>et al.</i> <sup>[49]</sup>	MDCT	91	Leaflet morphology	Tricommissural			
				Bicommissural non-raphe type			
				Bicommissural raphe type			
			Leaflet orientation	Coronary cusp fusion			
				Coronary/noncoronary cusp fusion			

**Back to the Case**

Based on CT scan finding, we decided to use 26 mm Evolut R valve for our patient. We accessed the common femoral artery with the help of fluoroscopy and ultrasound guidance. 26 mm

Evolut R valve was advanced into the LV. We noticed complete heart block, so we decided to pace at 80 bpm. We attempted two deployments, but the valve would dive in at the level of the left coronary into the LVOT. We decided to attempt





**Figure 1: Transcatheter aortic valve replacement-specific bicuspid aortic valve classification**

a third time with similar results. Even though we were not completely satisfied with the position of the valve; we had to deploy the valve as the patient became hemodynamically unstable. TEE revealed moderate PVL. The valve was post dilated the valve with a 20 mm true balloon. The BAV improved the expansion of the valve; however, there was still significant PVL. We decided to obtain right ulnar access (the radial artery had a loop and was occluded from a previous cath). We advanced a JR4 catheter an using a 10 mm Cook GooseNeck snare; we were able to snare one of the plates of the valve and slowly pulled back to a position where we achieved trivial PVL. We then noticed contrast stagnation and a contrast stain in the non-coronary cusp. We suspected a localized dissection of the non-coronary cusp. The patient became hypotensive and repeat CINE showed double contrast of the cardiac border. We confirmed this finding with TEE and performed pericardiocentesis with the removal of approximately 400 cc of blood. The patient also received permanent pacemaker for complete heart block.

The patient was transferred to CCU in a hemodynamically stable condition. The patient became anuric and developed acute tubular necrosis from hypotension during the procedure. She initially required CVVHD for acute renal failure. Hospital course was further complicated by pneumonia and septic shock. The patient briefly required

vasopressors for sepsis, but her pneumonia and sepsis improved with broad-spectrum antibiotics. Her renal function recovered completely and she no longer required CVVHD. She was transferred to the floor after 4 days in CCU. The patient improved dramatically and eventually discharged to inpatient rehab at a facility near her house. With subsequent follow-up, she is doing well and her symptoms of AS improved significantly.

### Conclusion

With the available observational data, it seems that TAVI is indeed technically feasible in selected BAV patients with acceptable results, especially with new-generation devices. Most of the current data studies highlight the importance of preprocedural imaging (esp. MDCT) determining the outcome of TAVI in BAV patients. To further evaluate the role of TAVI in the BAV patients, we would need to follow the standards set by the PARTNER trial, which suggested the role of TAVI in the treatment of high risk and inoperable patients with TAS. More research into the subject involving more clinical trials should be done to compare the success rate and efficiency between TAVI and SAVR.

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