

Research Article

Transcatheter Aortic Valve Implantation in a Patient with Severe Aortic Stenosis with Bicuspid Aortic Valve

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Case Report

Bicuspid aortic valve

bicuspid aortic valve is defined as a spectrum of abnormal aortic valve morphology which consists of two functional cusps with <3 zones of parallel apposition between cusps. BICUSPID AORTIC VALVE is a common congenital disorder found in adults at a rate of 0.5–2% with a predilection towards males, with a demonstrated association with mutations in the NOTCH1 gene. Interestingly, its heritability is as high as 89%, suggesting an autosomal dominant pattern of inheritance.

Individuals with BICUSPID AORTIC VALVE are prone to develop Aortic Stenosis (AS) at an earlier age. In fact, it is observed that its frequency is as high as 6% of the population over 85 years of age.

Approximately 20–50% of the patients with a BICUSPID AORTIC VALVE require aortic valve replacement in their lifetime. BAS is generally treated with surgical aortic valve replacement (SAVR) in patients <70 years of age. 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 percutaneous balloon valvuloplasty can be an option in this population, AS reoccurs in the majority of the patients in the long-term [1].

Transcatheter aortic valve implantation (TAVI)

TAVI is a minimally invasive procedure in which a new biopro-

thetic valve is inserted through catheter delivery system and implanted into aortic valve position without removing the old and diseased valve. 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. 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.

Bicuspid aortic valve anomaly, Associated complications

BICUSPID AORTIC VALVE anomaly has several variants. BICUSPID AORTIC VALVE without any unwanted tissue generally develops stenosis, whereas valves with unwanted tissue usually tend to develop valvular incompetence.

AS is one of the most important complications of BICUSPID AORTIC VALVE and its incidence on autopsy ranges from 15% to 75%. Stenosis in BICUSPID AORTIC VALVE 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 BICUSPID AORTIC VALVE [2].

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

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

They further subdivided these types into two subcategories based on:

Spatial arrangements of the cusp free edges (for example, BICUS-

PID AORTIC VALVE type 1 L/R means one raphe positioned between the left and right coronary sinuses) Type 0 – lateral and antero-posterior Type 1- L-R, R-N, and N-L Type 2 – L-R/R-N. (L = left coronary cusp, R = Right coronary cusp, and N = Non coronary cusp) 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 BICUSPID AORTIC VALVE Type 1 (88%) predominantly L-R, S category.

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.

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. 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 BICUSPID AORTIC VALVE and may signify the use of surgical intervention.

Current management scenario

Tanaka *et al.* reported a sensitivity of 94% and specificity of 100% for ECG gated MDCT in detecting BICUSPID AORTIC VALVE. 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 [3].

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 BICUSPID AORTIC VALVE and aortic aneurysm. Moreover, beta-blocker treatment now has been recommended as a Class IIa for BICUSPID AORTIC VALVE patients with an enlarged aorta. Angiotensin receptor blockade is also a Class IIa recommendation to reduce the dilatation of the aorta.

However, SAVR currently remains the gold standard of treatment for patients with BAS <70 years of age. 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 BICUSPID AORTIC VALVE, at aortic diameters from 4 to 5 cm. 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. Percutaneous aortic balloon valvotomy is of limited use due to high recurrence rates.

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 BICUSPID AORTIC VALVE?

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

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. The elliptical annular anatomy of a BICUSPID AORTIC VALVE may lead to valve malpositioning. There is a risk of severe aortic regurgitation due to the disruption of the fused commissures. The concomitant aortic disease increases the chances of rupture or dissection during the procedure. 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 BICUSPID AORTIC VALVE leaflets is different as compared to that of tricuspid AS (TAS). As mentioned above, the extensive calcium deposition in the body of BICUSPID AORTIC VALVE leaflets

and asymmetrical nature of the bicuspid aortic root could impair TAVI outcomes.

In a retrospective study conducted by Mylotte *et al.* [4] 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. 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 BICUSPID AORTIC VALVE 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 ± 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 BICUSPID AORTIC VALVE is feasible in a selected group of patients.

Himbert *et al.* [5] conducted a study to assess the results of TAVI in BICUSPID AORTIC VALVE with self-expandable valve Medtronic CoreValve system (MCS; Medtronic, Inc., Minneapolis, Minnesota) in which 15 patients with a mean age of 80 ± 10 and high mortality risk (Society of Thoracic Surgeons score 8 ± 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 ± 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 BICUSPID AORTIC VALVE can be also safely treated with a self-expandable prosthesis. However, a major disadvantage an absence of a control group (patients with tricuspid anatomy) and population size.

The above issue was addressed in the next studies. Hayashida *et al.* compared the results of TAVI obtained in 21 BICUSPID AORTIC VALVE 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).

In a similar study by Costopoulos *et al.*, comparing BICUSPID AORTIC VALVE ($n = 21$) 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 [6]. The researchers concluded that even though TAVI in BICUSPID AORTIC VALVE patients with high surgical risk is feasible with acceptable mid-term outcomes, a careful selection of patients is necessary as patients with BICUSPID AORTIC VALVE showed lower early survival rates and device success. The reasons are mainly anatomic challenges posed by BICUSPID AORTIC VALVE 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 BICUSPID AORTIC VALVE group (52.4% vs. 23.5%, $P < 0.01$). This could be due to the asymmetric calcification seen BICUSPID AORTIC VALVE patients. This study is limited by its small sample size to draw any real-world long-term conclusions.

Subsequently, in a sub-analysis of the German Aortic Valve Registry (GARY), a higher rate of PVL was reported amongst 38 BICUSPID AORTIC VALVE 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 BICUSPID AORTIC VALVE.

In 2014–15, two relatively large, multicenter studies were carried out on TAVI in BICUSPID AORTIC VALVE. One of them was conducted by Mylotte *et al.* [7] in which 139 BICUSPID AORTIC VALVE patients were included, and the procedural outcomes were evaluated for both self- and balloon-expandable bioprostheses. The mean age of the patients enrolled was 78.0 ± 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 BICUSPID AORTIC VALVE.

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

Presentation

A 60-year-old male patient with cardiovascular risk factors like hypertension and hyperlipidemia presented with a 6-month history of progressive dyspnea class II that worsened over the last few weeks. He also experienced exertional chest pain intermittently. His medications included ramipril 5 mg OD and rosuvastatin 40 mg OD. He did not describe any palpitations, syncope, or inter-

mittent claudication.

Examination

On physical examination at admission, the patient's temperature was 36.3°C, pulse 85 bpm, respiration rate 19/min, and blood pressure (BP) 110/80 mmHg without orthostatic changes. On chest examination bilateral clear vesicular breath sounds. There was a slow rising peripheral pulse associated with a delayed sustained peak. Auscultation revealed a grade 4/6 crescendo-decrescendo midsystolic ejection murmur heard best at the right upper sternal border radiating to the neck and carotid arteries with an associated systolic thrill in the corresponding ICS. No diastolic murmur was heard. The apex beat was slightly displaced laterally at the left side, which suggests the evidence of left ventricular hypertrophy (LVH). No lower-extremity edema was detected.

Investigations

The initial hematologic and biochemical investigations were within normal with a haemoglobin of 15.9 gm/dl, white blood cells 5,000/ μ l, creatinine 1.0 mg/dl, potassium 4.7 mg/L, sodium 146 mg/L, and alanine aminotransferase 25 U/L. The chest x-ray demonstrated a prominent right mediastinal border occupied by

the ascending aorta. There was an enlarged aortic knob. An echocardiogram revealed a Bicuspid Aortic Valve (AV) that was severely stenotic and calcified with a maximum gradient of 100 mmHg, a mean gradient of 60 mmHg, an AV annulus diameter of 19 mm, an impaired left ventricular systolic function with an ejection fraction (EF) of 38%, and with mild LVH. The trans-mitral spectral Doppler flow pattern is suggestive of impaired LV relaxation without regional wall motion abnormalities noted.

Cardiac CT confirmed severe as the right coronary artery was dominant with diffuse irregularities, especially distally. The AV annulus to the left main height was 0.98 cm, and the AV annulus area is 3.98 cm².

Management (Medical/Interventional)

The heart team-meeting consensus was to proceed with TAVR using an Myval THV valve with high implant as the patient was not willing for AVR. The procedure was successfully done as follows: Through the left common femoral vein sheath, a temporary balloon tipped pacing catheter (cordis) was inserted. Through the left femoral arterial sheath, a pigtail was advanced. Through the right arterial sheath, a Myval THV delivery sheath was advanced over a

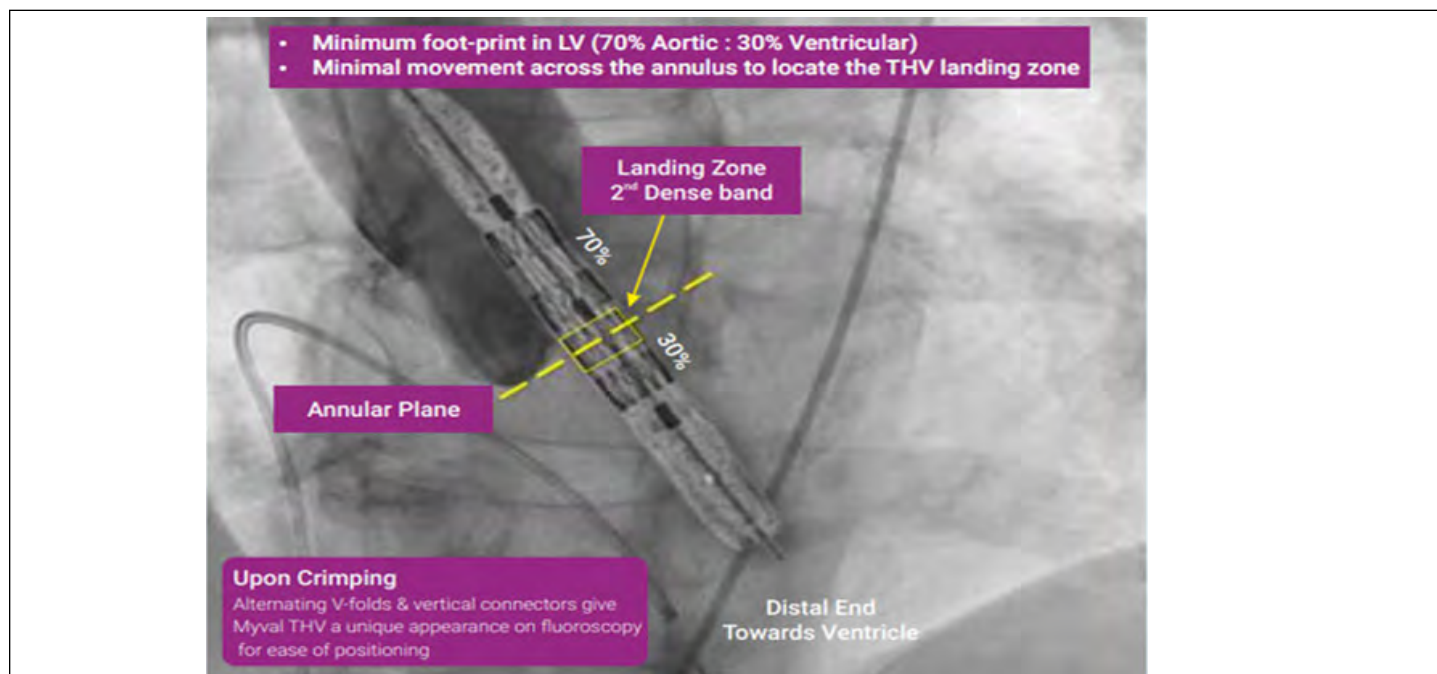


Figure 1: Showing aortic valve prosthesis placement and measurements

Sapphire wire that had been placed in the LV through the standard method. The valve was predilated using rapid pacing, and an angiogram through the pigtail catheter demonstrated a patent RCA, LCX, and LM artery ostium.

Landing of MyVal THV

The implant was performed with rapid ventricular pacing. Angiography using a power injector confirmed appropriate expansion of the valve and no paravalvular regurgitation. The echocardiogram further confirmed the angiographic findings. Post procedure, the gradient by echocardiography was 7 mmHg, and the EF had improved to 44.5%. It may indicate timely replacement with improvement in the left ventricular systolic and diastolic functions. The postoperative course was uneventful, and he was discharged on day 3 in stable condition without a need for a pacemaker on dual antiplatelet therapy (aspirin 75 mg and clopidogrel 75 mg daily). He was evaluated after 1 month at an outpatient clinic, where she was completely asymptomatic. A repeat Cardiac CT demonstrated thin leaflets with normal mobility.

Discussion

The role of CCT has conventionally been limited to the pre-procedure planning of TAVR. Finally, we selected a balloon-expandable valve which has a more controlled and predictable deployment. The Boston Scientific ACURATE neo valve has an open-cell design and a lower metal-to-artery ratio than the Medtronic CoreValve. Both valves permit reasonable coronary access with commissural alignment; however, studies including that published by Tang et al. demonstrated a rate of right coronary artery overlap of 7.1% for both the CoreValve and ACURATE neo and no difference for the Edwards SAPIEN [8]. As such, we opted for the balloon-expandable MyVal THV valve.

It is important to recognize that the role of CCT was not restricted to the pre-procedure workup, but in the follow-up as well [9]. We were able to non-invasively evaluate the valve position, leaflet thickness, and mobility and reassess the LCX patency in the follow-up Cardiac CT [10,11].

Conclusions

TAVR is considered a minimally invasive interventional procedure with a high success rate largely due to meticulous pre-procedure planning and patient selection. It also underscores the importance



Figure 2: showing the procedure of TAVI placement

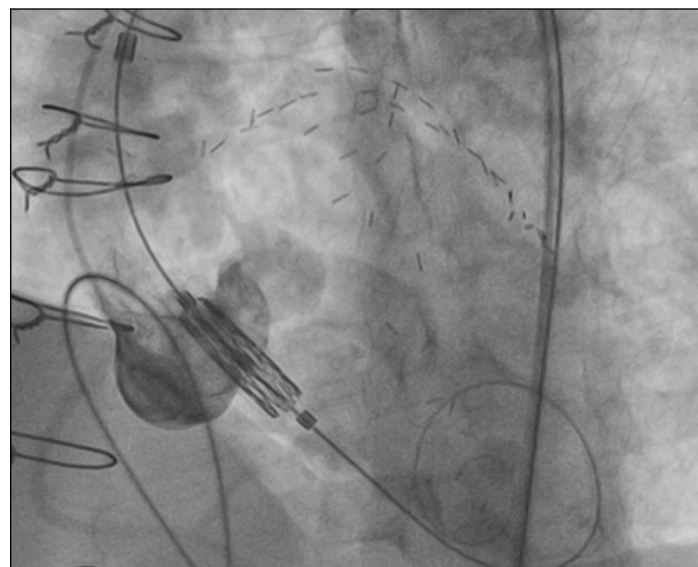


Figure 3: Showing the balloon inflation

of CCT in the post-procedure evaluation of the valve itself and its relationship to the anomalous vessel.

Ethics statement

Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

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