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Aortic valve anatomy and outcomes after transcatheter aortic valve implantation in bicuspid aortic valves

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ABSTRACT

Purpose: Aortic stenosis (AS) in bicuspid aortic valve (BAV) remains a challenge for transcatheter aortic valve implantation (TAVI). BAV is a condition encountered in young adults as well as elderly patients. Frequently we face in clinical practice elderly patients with BAV and severe AS, but there is little evidence concerning TAVI in this population. The aim of our study was to compare anatomic features and outcomes of bicuspid and tricuspid patients with AS undergoing TAVI.

Methods: 83 consecutive BAV patients undergoing TAVI were matched, in a 1:2 ratio, to 166 tricuspid patients. Multi-detector computed tomography (MDCT) and transthoracic echocardiogram (TTE) were assessed at baseline. Primary endpoint was all-cause mortality and early safety at 30 days according to Valve Academic Research Consortium criteria 2 (VARC-2). Secondary endpoint included device success.

Results: BAV patients presented more aortic root calcifications, smaller diameter of left ventricular outflow tract (LVOT) and dilated aorta. We did not observe any statistically significant difference concerning all-cause mortality and early safety at 30 days. However higher intra-procedural TAV-in-TAV bailout procedure was observed in the BAV cohort, with consequent reduction of device success rate.

Conclusions: Patients with BAV present more complex anatomy at baseline as compared to tricuspid AS patients. These anatomical features lead to more frequent TAV-in-TAV bailout procedure and lower device success rate, but are not associated with higher mortality rate at 30 days. Our findings support the feasibility of TAVI in BAV, but larger studies with longer follow-up and a focus on sizing are required.

1. Introduction

Transcatheter aortic valve implantation (TAVI) for severe aortic stenosis (AS) is a robust alternative to surgery in intermediate to high-risk patients [1–5]. In contemporary TAVI practice AS in bicuspid aortic valve (BAV) represents a challenge for percutaneous treatment due to anatomical specificities.

BAV can be distinguished in two basic categories, congenital and functional when the native aortic valve 'functions' as a bicuspid. Therefore it is a condition encountered in young adults as well as elderly patients. It can be associated with aortic regurgitation or stenosis and is often correlated with dilation of the ascending aorta [6]. BAV patients represent 0.5% to 2% of the general population, and 2% to 6% of patients with severe AS. When compared to patients with tricuspid aortic valve, BAV patients are younger with a male predominance of 3:1 [6, 7]. These patients present with more aortic valve calcifications, larger annulus dimensions, asymmetric cusps and ascending aorta dilation [8].

These features, together with the altered aortic geometry, can lead to procedural complications as for example device mal-positioning, high-residual gradient or significant residual aortic regurgitation (AR) [9]. These potential suboptimal procedural outcomes translate into worse long-term outcomes [10]. Thus BAV has been regarded as a relative contraindication to TAVI and has been excluded from major randomized clinical trials. However, recent registries demonstrated the feasibility of TAVI in this specific anatomical subset [11–14].

We aimed at comparing the anatomical characteristics and clinical outcomes of patients with bicuspid or tricuspid aortic valves undergoing TAVI for severe AS in our centre.

2. Methods

From January to December 2016, 460 patients with tricuspid aortic valve underwent TAVI procedure in our institution for symptomatic severe AS. Risk evaluation and decision-making were performed by a dedicated heart team (interventional cardiologist,

Abbreviations: AR, aortic regurgitation; AS, aortic stenosis; BAV, bicuspid aortic valve(s); CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; ER, Medtronic Evolut R; LVOT, left ventricular outflow tract; MI, myocardial infarction; MDCT, multi-detector computed tomography; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; PPM, prosthesis-patient mismatch; PVL, para-valvular leak; S3, Edwards Sapien 3; STS, Society of Thoracic Surgery; TAVI, transcatheter aortic valve implantation; TAV-in-TAV, transcatheter aortic valve in transcatheter aortic valve; TTE, transthoracic echocardiogram; VARC 2, Valve Academic Research Consortium criteria 2.

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cardiac surgeon, anaesthesiologist, echo-cardiographer, and geriatrician). From January 2015 to April 2017, 83 consecutive patients with BAV had TAVI at our institution. Patients undergoing TAVI due to bio-prosthesis degeneration were not included.

BAV were classified following the Sievers classification, according to the number of leaflets and presence/number of raphes: type 0-valve with no raphe and symmetric leaflets (purely BAV), type 1-valve with one raphe between two leaflets (right-left, non-coronary-left, non-coronary-right), type 2-valve with two raphes [15]. Multi-detector computed tomography (MDCT) and transthoracic echocardiogram (TTE) were assessed at baseline. BAV anatomy was identified by baseline MDCT after analysis using the 3mensio Structural Heart software version 8.0 (Pie Medical Imaging, Maastricht, the Netherlands) Workstation software. MDCT was the method of choice for sizing using the perimeter-derived diameter of the aortic annulus. In the BAV group, we used as additional measurement for sizing the inter-commissural distance 4 mm above the annulus.

Continuous variables are presented as mean ± standard deviation. Categorical variables are presented as count and percentages. Continue variables were compared using a Student's t-test and categorical variables with a chi-square test. A propensity-score matching was applied to account for differences in baseline characteristics of both groups.

A 1:2 propensity-score matching was performed on the basis of clinical risk factors for cardiovascular mortality and was developed by a multivariate logistic regression according to a non-parsimonious approach. A total amount of 249 patients, 83 with bicuspid and 166 with tricuspid aortic valve, were included in the final analysis.

After matching was completed clinical characteristics were re-evaluated for any potential significant difference at baseline.

The Valve Academic Research Consortium-2 definitions (VARC)-2 were used. The considered VARC-2 endpoints were: all-cause mortality, disabling and not disabling stroke, prosthesis-patient mismatch (PPM) and composite endpoints of in-hospital device success and early safety. PPM values were classified into mild (PPM >0.85 cm^2/m^2), moderate (0.65 > PPM <0.85 cm^2/m^2), and severe (PPM <0.65 cm^2/m^2) and were analyzed at both in-hospital and 30 days follow-up [16–19].

Device success was defined as 'absence of procedural mortality, correct positioning of a single prosthetic heart valve into the proper anatomical position and intended performance of the prosthetic heart valve (no prosthesis-patient mismatch, mean aortic valve gradient <20 mm Hg or peak velocity <3 m/s and no moderate or severe prosthetic valve regurgitation)'.

Early safety was evaluated at 30 days as composite of 'all-cause mortality, all stroke (disabling and non-disabling), life-threating bleeding, stage II or III of acute kidney injury (including renal replacement therapy), coronary artery obstruction requiring intervention, major vascular complication and valve-related dysfunction requiring repeat procedure (percutaneous or surgical)' [20].

The primary endpoint was all-cause mortality and early safety at 30 days. Secondary endpoint included device success.

Pacemaker implantation rate, para-valvular leak (PVL) and mean aortic gradient at in-hospital and 30 days follow-up together with hospital stay and mean time to follow-up were compared between the two groups.

Statistical significance was considered as p value ≤.05. All results were obtained using the Statistical Package for the Social Sciences version 21.0 (SPSS v21.0, *SPSS Inc.*, *Chicago*, *IL*).

3. Results

We originally screened a population of 543 patients undergoing TAVI procedure, of whom 83 had a BAV: type 0 (7%), type 1 L-R (75%), type 1 R-N (12%), type 1 L-N (6%). No patients had type 2 BAV.

Baseline clinical characteristics of the study population showed a statistically significant difference for mean age (83.1 ± 5.5 vs 81.3 ± 7.6; p < .01), male gender (242/460 (50%) vs 58/83 (69%); p < .01), smoking (41/460 (8%) vs 13/83 (15%); p = .04), previous myocardial infarction (MI) (5/460 (1%) vs 2/83 (2%); p < .01) and mean LVEF (57.1 ± 12.2 vs 52.4 ± 15.6; p < .01). BAV patients were younger, predominantly male, with a moderate decrease of baseline LVEF. After a 1:2 propensity-score matching we obtained a final population of 249 patients with similar baseline characteristics (Table 1). In this matched population mean age was 82.2 ± 6.4 years, 67% were male, NYHA III class was observed in 50% and mean baseline LVEF (%) was 54.2 ± 14.4. Mean Society for Thoracic Surgery (STS) predicted risk for mortality was 5.1 ± 2.9%. In both groups indication to TAVI was mainly represented by pure AS (97%) while three patients presented pure aortic regurgitation (AR) (2%) and two patients had a combined disease (AS + AR) (1%).

Baseline TTE identified thicker inter-ventricular septum in the BAV group (13.9 ± 3 vs 15 ± 2.9; p = .03), without any difference for left ventricular end-diastolic diameter (LVEDd), aortic-valve-area (AVA), indexed-AVA or mean aortic gradient (Table 3).

Baseline MDCT revealed several differences between the two groups: the BAV group presented a greater volume of calcium in the aortic root (1694.3 ± 1695.2 vs 2798.3 ± 2606.6; p < .01), a smaller perimeter-derived LVOT diameter (24.5 ± 3 vs 28.7 ± 2.1; p < .01) and a larger ascending aorta diameter (32.3 ± 2.8 vs 36 ± 4.4; p < .01). No statistical significant difference was observed concerning femoral arteries diameter (Table 2).

Procedural characteristics are reported in Table 3. Access site choice was determined according to MDCT analysis. The transfemoral approach was selected in 99% (246/249) of the population. In 3 patients the femoral arteries were of unsuitable anatomy and the transaortic access route was preferred.

The choice of valvuloplasty rested upon operator choice but was more frequently performed in the BAV group (7/166 (4%) vs 20/83 (23%); p < .01). New-generation devices Evolut R (ER), Sapien 3 (S3)

Table 1
Baseline characteristics of matched population.

	N	Tricuspid (*N* = 166)	Bicuspid (*N* = 83)	*P*
Age (year)	249	82.9 ± 5.7	81.4 ± 7.6	0.07
Male n. (%)	249	108/166 (66)	57/83 (69)	0.57
Hypertension n. (%)	249	119/166 (73)	60/83 (71)	0.92
Dyslipidaemia n. (%)	249	47/166 (28)	28/83 (33)	0.37
Diabetes n. (%)	249	26/166 (15)	16/83 (19)	0.47
Dialysis n. (%)	249	3/166 (2)	1/83 (1)	0.72
Prior/Current smoker n. (%)	249	19/166 (11)	12/83 (15)	0.49
Coronary artery disease n. (%)	249	81/166 (49)	39/83 (47)	0.78
Previous MI n. (%)	249	2/166 (2)	2/83 (2)	0.46
Previous PCI n. (%)	249	66/166 (38)	30/83 (36)	0.55
Previous CABG n. (%)	249	8/166 (6)	4/83 (5)	1
Dialysis n. (%)	249	3/166 (2)	1/83 (1)	0.72
Atrial fibrillation n. (%)	249	33/166 (20)	14/83 (17)	0.56
Cerebrovascular disease n. (%)	249	11/166 (8)	5/83 (6)	0.85
Porcelain aorta n (%)	249	4/166 (2)	3/83 (3)	0.58
BPCO n. (%)	249	39/166 (21)	24/83 (28)	0.6
BMI (kg/m^2)	249	33.8 ± 54.9	33.9 ± 54.3	0.99
BSA (m^2)	249	1.7 ± 0.2	1.7 ± 0.2	0.31
LVEF (%)	249	55.3 ± 13.9	52.5 ± 15.6	0.15
NYHA class III n. (%)	249	84/166 (49)	43/83 (52)	0.85
NYHA class IV n. (%)	249	6/166 (4)	5/83 (6)	0.38
STS score (%)	249	5.1 ± 2.9	5.1 ± 3.3	0.99

BMI: body mass index; BSA: body surface area; CABG: coronary artery by-pass grafting; COPD: chronic obstructive pulmonary disease; LVEF: left ventricular ejection fraction; MI: myocardial infarction; NYHA: New York Heart Association; PCI: percutaneous coronary intervention; STS: Society for Thoracic Surgery.

Table 2
TTE and MDCT baseline characteristics of matched population.

	N	Tricuspid (*N* = 166)	Bicuspid (*N* = 83)	*P*
Echo				
Septum (mm)	249	13.9 ± 3	15 ± 2.9	0.03
EDLVd (mm)	249	52 ± 7.9	52.5 ± 7.9	0.68
AVA (cm^2)	249	0.7 ± 0.3	0.6 ± 0.2	0.29
Indexed AVA (cm^2/m^2)	249	0.4 ± 0.1	0.3 ± 0.1	0.5
Mean aortic gradient (mm Hg)	249	46.4 ± 14.7	47.8 ± 15.5	0.18
Vmax (m/s)	249	3.5 ± 1.6	4 ± 0	0.66
SPAP (mm Hg)	249	43.9 ± 12.5	45.1 ± 12.4	0.52
MDCT				
Calcium scoring (mm^3)	249	1694.3 ± 1695.	2798.3 ± 2606.6	<0.01
Perimeter derived annulus diameter (mm)	249	25.5 ± 2.2	27 ± 1.4	0.07
Perimeter derived LVOT diameter (mm)	249	24.5 ± 3	28.7 ± 2.1	<0.01
Sinus of valsalva diameter (mm)	249	34.5 ± 3.9	35.7 ± 5	0.16
Ascending aorta diameter (mm)	249	32.3 ± 2.8	36 ± 4.4	<0.01
Right femoral diameter (mm)	249	8.3 ± 2.1	8.4 ± 2	0.94
Left femoral diameter (mm)	249	8.4 ± 2.1	8.2 ± 1.9	0.64

AVA: aortic valve area; EDLV: end-diastolic left ventricular diameter; LVOT: left ventricular outflow tract; MDCT: multi-detector computed tomography; SPAP: systolic pulmonary artery pressure; TTE: transthoracic echocardiogram; Vmax: velocity max.