

# Ascending aortic dilatation rate after transcatheter aortic valve replacement in patients with bicuspid and tricuspid aortic stenosis: A multidetector computed tomography follow-up study

Yu-xin He<sup>1</sup>, Jia-qi Fan<sup>1</sup>, Qi-feng Zhu<sup>1</sup>, Qi-jing Zhou<sup>2</sup>, Ju-bo Jiang<sup>1</sup>, Li-han Wang<sup>1</sup>, Stella Ng<sup>1</sup>, Xian-bao Liu<sup>1</sup>, Jian-an Wang<sup>1</sup>

<sup>1</sup> Department of Cardiology, the Second Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou 310009, China

<sup>2</sup> Department of Radiology, the Second Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou 310009, China

**Corresponding Author:** Jian-an Wang, Email: wangjianan111@zju.edu.cn; Xian-bao Liu, Email: liuxb@zju.edu.cn

**BACKGROUND:** Current data is lacking about the progression of ascending aortic dilatation after transcatheter aortic valve replacement (TAVR) in aortic stenosis (AS) patients with bicuspid aortic valve (BAV) and tricuspid aortic valve (TAV). This study aims to assess the ascending aortic dilatation rate (mm/year) after TAVR in patients with BAV versus TAV using a multidetector computed tomography (MDCT) follow-up and to determine the predictors of ascending aortic dilatation rate.

**METHODS:** Severe AS patients undergoing TAVR from March 2013 to March 2018 at our center with MDCT follow-ups were included. BAV and TAV were identified using baseline MDCT. Baseline and follow-up MDCT images were analyzed, and the diameters of ascending aorta were measured. Study end point is ascending aortic dilatation rate (mm/year). Furthermore, factors predicting ascending aortic dilatation rate were also investigated.

**RESULTS:** Two hundred and eight patients were included, comprised of 86 BAV and 122 TAV patients. Five, 4, 3, 2, and 1-year MDCT follow-ups were achieved in 7, 9, 30, 46, and 116 patients. The ascending aortic diameter was significantly increased after TAVR in both BAV group (43.7±4.4 mm vs. 44.0±4.5 mm;  $P<0.001$ ) and TAV group (39.1±4.8 mm vs. 39.7±5.1 mm;  $P<0.001$ ). However, no difference of ascending aortic dilatation rate was found between BAV and TAV groups (0.2±0.8 mm/year vs. 0.3±0.8 mm/year,  $P=0.592$ ). Multivariate linear regression revealed paravalvular leakage (PVL) grade was independently associated with ascending aortic dilatation rate in the whole population and BAV group, but not TAV group. No aortic events occurred during follow-ups.

**CONCLUSION:** Ascending aortic size continues to grow after TAVR in BAV patients, but the dilatation rate is mild and comparable to that of TAV patients. PVL grade is associated with ascending aortic dilatation rate in BAV patients post-TAVR.

**KEY WORDS:** Transcatheter aortic valve replacement; Aortic dilatation; Bicuspid aortic valve

World J Emerg Med 2019;10(4):197–204  
DOI: 10.5847/wjem.j.1920–8642.2019.04.001

## INTRODUCTION

After a fast development, transcatheter aortic valve replacement (TAVR) has become a safe and effective alternative to surgical aortic valve replacement (SAVR) for symptomatic severe aortic stenosis (AS) patients with increased surgical risks.<sup>[1,2]</sup> However, the indication

of TAVR for bicuspid AS is still controversial.<sup>[2,3]</sup> Nevertheless, satisfactory results are accumulating regarding patients with bicuspid aortic valve (BAV) undergoing TAVR.<sup>[4,5]</sup> Comparable outcomes have been achieved in BAV patients versus tricuspid aortic valve (TAV) patients, especially with new-generation devices.<sup>[5,6]</sup>

Given the fact that aortic dilatation is seen more commonly in patients with bicuspid AS,<sup>[7]</sup> and as TAVR does not provide simultaneous ascending aortic intervention, a concern arises about progressive aortic dilatation in patients with bicuspid AS after TAVR. A series of studies about aortic dilatation after SAVR were reported, but the results were conflicting.<sup>[8-10]</sup> Limited data suggested that ascending aortic size remained stable after TAVR in TAV patients with mild and moderate dilatation.<sup>[11]</sup> Data regarding aortic dilatation in BAV patients after TAVR are scarce, especially with midterm to long-term follow-ups. Currently, the development and progression of aortic dilatation in bicuspid patients are believed to be affected by both genetic and hemodynamic factors.<sup>[12-16]</sup> With abnormal hemodynamics being corrected by TAVR in bicuspid AS patients, whether the progression of aortic dilatation will be decelerated or not is unclear.

This study aims to assess the ascending aortic dilatation rate (mm/year) after TAVR in patients with BAV versus TAV using a multidetector computed tomography (MDCT) follow-up and to determine the predictors of ascending aortic dilatation rate.

## METHODS

### Study population

Patients undergoing TAVR for symptomatic severe AS were all prospectively included in our single-center TAVR cohort. Those undergoing TAVR from March 2013 to March 2018 were included in this study. Those without MDCT follow-ups or with poor MDCT image quality were excluded. The decision for the TAVR procedure for each patient was carefully evaluated by the dedicated heart team of our hospital. The ethics committee of our center approved the study protocol and written informed consents were obtained in all patients. Patient characteristics, clinical data, transthoracic echocardiography (TTE) measurements, procedural variables, and regular follow-up data were prospectively collected in our TAVR database. Aortic dissection post-TAVR and reoperation for aortopathy were also recorded, as well as TTE measurements. Baseline grade of aortic regurgitation (AR), and follow-up paravalvular leakage (PVL) were graded as none/trace (0), mild (1), moderate or more (2).

### MDCT images acquisition and measurements

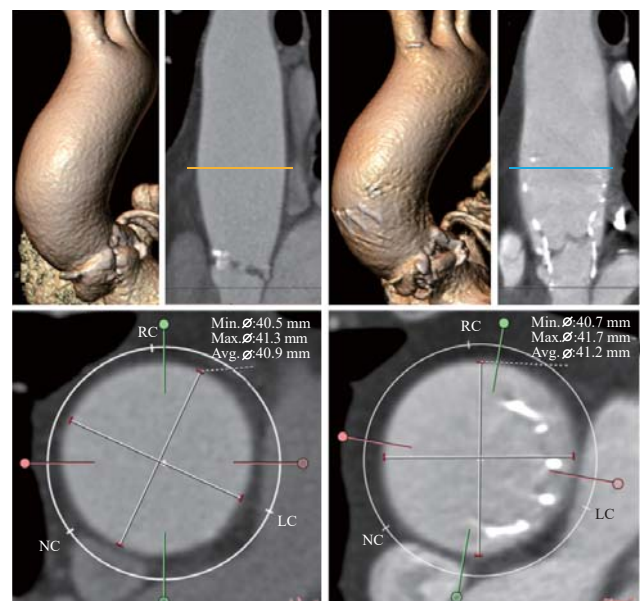
Echocardiography is the primary imaging modality used to evaluate aortic valve and aortopathy. However, MDCT can obtain an excellent image of the full length

of the aorta with the feature of 3D reconstruction, which makes MDCT a better method to identify ascending aorta diameter than echocardiography. No data were reported before about the ascending aorta diameter after TAVR using midterm to long-term MDCT follow-ups.

All MDCT examinations were performed with the second generation dual-source CT (SOMATOM Definition Flash, Siemens Medical Solutions, Germany) as previously reported.<sup>[17]</sup> End-systolic images of baseline and follow-up MDCT were analyzed using 3mensio 8.0 (3mensio Medical Imaging BV, the Netherlands)<sup>[18]</sup> as presented in Figure 1. Both maximal and minimal diameters were obtained at the broadest level of ascending aorta. The diameter of the ascending aorta was calculated as: (maximal diameter + minimal diameter)/2. BAV was classified into three types by the number of raphe (type 0, type 1, and type 2) based on pre-TAVR MDCT analysis.<sup>[19]</sup> Patients with ascending aorta diameter >45 mm were identified. Changes of ascending aorta diameter were defined as the differences between follow-up and baseline measurements. Ascending aortic dilatation rates were calculated by dividing the change of ascending aorta diameter by the time interval in years for each patient.

### Procedure

Detailed procedures of TAVR were previously reported.<sup>[17,20]</sup> A large proportion of patients were implanted with self-expanding valves, such as:



**Figure 1.** Diagram of ascending aortic diameter measurements of baseline and follow-up. The diameter of ascending aorta was measured at the broadest level of ascending aorta using baseline (left side) and follow-up (right side) multidetector computed tomography images.

CoreValve (Medtronic Inc., Minnesota, USA), VenusA-Valve (Venus Medtech, Hangzhou, China), VitaFlow (Microport, Shanghai, China) and Taurus One-Valve (Peijia Medical, Suzhou, China). The rest of the patients were implanted with the Lotus valve (Boston Scientific, Marlborough, MA) or Edwards SAPIEN XT valve (Edwards Lifesciences, Irvine, California).

### Statistical analysis

The data were analyzed using SPSS Statistics 22.0 (SPSS, Inc., Chicago, IL). Continuous variables were described by mean±standard deviation (SD), and means were compared using *t*-test for normally distributed variables, or Mann-Whitney *U* test for skewed distributed variables. Categorical variables were expressed by frequencies and percentages, and they were compared using Chi-square test or Fisher exact test between two groups. Univariate linear regression models were constructed to identify significant associations. If any univariate associations were identified with *P* value<0.20, they would be included in the multivariate linear regression to identify independent predictors. Age, sex, body surface area (BSA), history of hypertension, history of diabetes mellitus, BAV, types of prosthesis (self-expanding or others), years of follow-up, baseline and follow-up TTE parameters (mean gradient, Max velocity, aortic valve area [AVA], left ventricular ejection fraction [LVEF], and grade of AR and PVL) were evaluated as predictors of ascending aortic dilatation rate. Statistical significance was defined as *P*<0.05.

## RESULTS

### Patient characteristics and procedural data

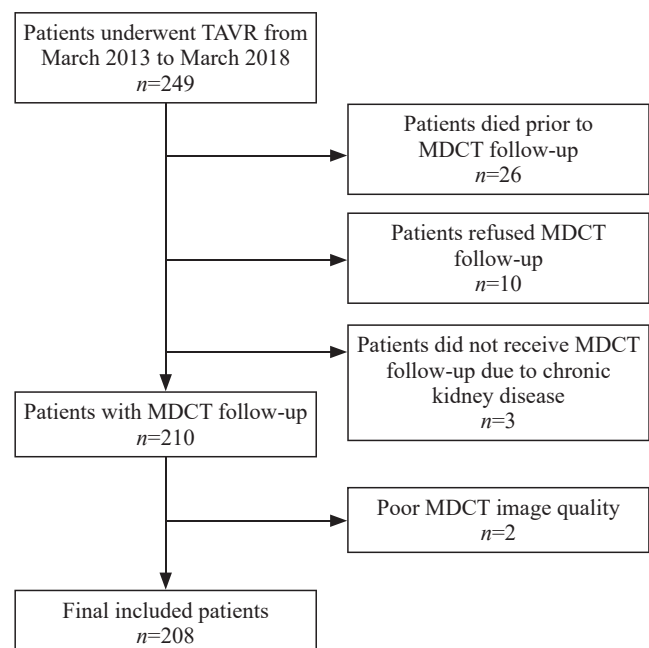
The flowchart of patient inclusion was shown in Figure 2. Two hundred and forty-nine consecutive patients underwent TAVR through transarterial approach for symptomatic severe AS from March 2013 to March 2018 at our center. Twenty-six patients died prior to MDCT follow-ups, 3 patients did not receive MDCT follow-ups due to chronic kidney disease, 10 patients refused MDCT follow-ups, and 2 patients had poor MDCT image quality. Thus, 208 patients with MDCT follow-ups constituted our study population. Baseline patient characteristics are listed in Table 1. The mean age was 76±6 years, the mean BMI was 22.78±3.41 kg/m<sup>2</sup>, and the mean BSA was 1.63±0.16 m<sup>2</sup>. Sixty-two percent of the patients were male. Baseline MDCT classified 86 patients as BAV out of 208 patients (60 patients with no raphe, 26 patients with one raphe).

The male and peripheral vascular disease were more common in tricuspid patients than in bicuspid patients. Bicuspid patients were complicated by more severe AS, but more severe AR was found in tricuspid patients. Ascending aorta diameters were significantly enlarged in bicuspid patients than tricuspid patients (43.7±4.4 mm vs. 39.1±4.8 mm, *P*<0.001). Meanwhile, more patients were found with ascending aortic diameter >4.5 cm in the bicuspid group than in the tricuspid group (36.0% vs. 10.7%, *P*<0.001).

Transfemoral access was selected in 205 (98.6%) patients, with 170 patients were implanted with self-expanding valves. All procedural data were comparable between the bicuspid and the tricuspid groups.

### Ascending aortic diameter after TAVR

Table 2 summarizes the ascending aortic diameters and TTE measurements after TAVR. Five, 4, 3, 2, and 1-year MDCT follow-ups were achieved in 7, 9, 30, 46, and 116 patients. Follow-up MDCTs showed that ascending aortic diameters were significantly increased in all patients (40.0±5.1 mm vs. 41.5±5.3 mm; *P*<0.001), in BAV group (43.7±4.4 mm vs. 44.0±4.5 mm; *P*<0.001) and in TAV group (39.1±4.8 mm vs. 39.7±5.1 mm; *P*<0.001). Mean change of ascending aortic diameter was 0.5±1.0 mm, and the mean dilatation rate was 0.3±0.8 mm/year in all patients. Diameters of ascending aorta were still larger in BAV group compared with TAV group (44.0±4.5 mm vs. 39.7±5.1 mm, *P*<0.001) after



**Figure 2.** Flow diagram of patients' inclusion. MDCT: multidetector computed tomography; TAVR: transcatheter aortic valve replacement.

TAVR, but both change ( $0.4\pm 0.9$  mm/year vs.  $0.6\pm 1.1$  mm/year,  $P=0.238$ ) and dilatation rate of ascending aorta ( $0.2\pm 0.8$  mm/year vs.  $0.3\pm 0.8$  mm/year,  $P=0.592$ ) were similar between two groups. The frequency distribution of aortic dilatation rates is shown in Figure 3, and no rapid progressions (defined as  $\geq 5$  mm/year)<sup>[21]</sup> were found. No significant differences of ascending aortic dilatation rate

were found between patients with or without baseline ascending aortic diameter  $\geq 45$  mm in BAV group ( $0.4\pm 0.7$  mm/year vs.  $0.1\pm 0.8$  mm/year,  $P=0.105$ ), but a tendency was observed in TAV group ( $0.8\pm 1.1$  mm/year vs.  $0.3\pm 0.8$  mm/year,  $P=0.052$ ).

TTE measurements showed that valve performances were comparable between two groups, except greater

**Table 1.** Baseline characteristics and procedural data

Parameters	All (n=208)	BAV (n=86)	TAV (n=122)	P value <sup>a</sup>
<b>Patient characteristics</b>				
Mean age (years)	76±6	76±5	77±6	0.070
Male, n (%)	129 (62.0)	44 (51.2)	85 (69.7)	0.007
BMI (kg/m <sup>2</sup> )	22.78±3.41	22.80±3.13	22.75±3.61	0.918
BSA (m <sup>2</sup> )	1.63±0.16	1.62±0.16	1.64±0.16	0.286
<b>Bicuspid aortic valve type, n (%)</b>				
Type 0		60 (69.8)		
Type 1		26 (30.2)		
Type 2		0 (0.0)		
Hypertension, n (%)	120 (57.7)	46 (53.5)	74 (60.7)	0.321
Diabetes mellitus, n (%)	46 (22.1)	20 (23.3)	26 (21.3)	0.865
COPD, n (%)	42 (20.2)	20 (23.3)	22 (18.0)	0.384
Atrial fibrillation, n (%)	38 (18.3)	19 (22.1)	19 (15.6)	0.275
Prior PCI, n (%)	27 (13.0)	13 (15.1)	14 (11.5)	0.531
Peripheral vascular disease, n (%)	54 (26.0)	15 (17.4)	39 (32.0)	0.024
NYHA class III or IV, n (%)	187 (89.9)	77 (89.5)	110 (90.2)	1.000
STS score (%)	6.45±4.24	5.99±3.62	6.78±4.62	0.222
<b>Baseline TTE measurements</b>				
Aortic valve area (cm <sup>2</sup> )	0.58±0.18	0.54±0.17	0.62±0.19	0.003
Mean gradient (mmHg)	56±17	60±19	53±14	0.028
Maximal velocity (m/s)	4.83±0.72	4.97±0.78	4.73±0.66	0.021
LVEF (%)	53.8±13.0	54.4±13.6	53.4±12.6	0.418
<b>AR, n (%)</b>				
None or trace	37 (17.8)	27 (31.4)	10 (8.2)	
Mild	95 (45.7)	48 (55.8)	47 (38.5)	<0.001
Moderate or more	76 (36.5)	11 (12.8)	65 (53.3)	
Ascending aorta diameter (mm)	41.0±5.1	43.7±4.4	39.1±4.8	<0.001
Ascending aorta diameter $\geq 45$ mm, n (%)	44 (54.8)	31 (36.0)	13 (10.7)	<0.001
<b>Procedural data, n (%)</b>				
<b>Transfemoral access</b>				
Device	205 (98.6)	85 (98.8)	120 (98.4)	
Self-expanding	170 (81.7)	75 (87.2)	95 (77.9)	0.102
Others	38 (18.3)	11 (12.8)	27 (22.1)	
Pre-dilation	200 (96.2)	83 (96.5)	117 (95.9)	1.000
Post-dilation	85 (40.9)	42 (48.8)	43 (35.2)	0.063
Need for second valve implantation	17 (8.2)	6 (7.0)	11 (9.0)	0.621

<sup>a</sup>: BAV vs. TAV; AR: aortic regurgitation; BAV: bicuspid aortic valve; BMI: body mass index; BSA: body surface area; COPD: chronic obstructive pulmonary disease; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association; PCI: percutaneous coronary intervention; TAV: tricuspid aortic valve; TAVR: transcatheter aortic valve replacement; TTE: transthoracic echocardiography.

**Table 2.** Ascending aorta diameters and TTE measurements at follow-ups

Parameters	All (n=208)	BAV (n=86)	TAV (n=122)	P value <sup>a</sup>
<b>Follow-up period (years)</b>				
5-year follow-up, n (%)	7 (3.4)	3 (3.5)	4 (3.3)	0.182
4-year follow-up, n (%)	9 (4.3)	4 (4.6)	5 (4.1)	
3-year follow-up, n (%)	30 (14.4)	9 (10.5)	21 (17.2)	0.317
2-year follow-up, n (%)	46 (22.1)	17 (19.8)	29 (23.8)	
1-year follow-up, n (%)	116 (55.8)	53 (61.6)	63 (51.6)	
<b>Ascending aorta diameter at follow-ups (mm)</b>				
Change of ascending aorta diameter at follow-ups (mm)	0.5±1.0	0.4±0.9	0.6±1.1	0.238
Ascending aortic dilatation rate (mm/year)	0.3±0.8	0.2±0.8	0.3±0.8	0.592
<b>TTE measurements at follow-ups</b>				
Aortic valve area (cm <sup>2</sup> )	1.57±0.35	1.51±0.33	1.61±0.36	0.115
Mean gradient (mmHg)	11±6	10±4.5	11±7	0.635
Maximal velocity (m/s)	2.25±0.55	2.27±0.46	2.24±0.61	0.650
LVEF (%)	62.5±8.7	64.5±5.9	61.0±10.0	0.028
<b>PVL, n (%)</b>				
None or trace	105 (50.5)	43 (50.0)	62 (50.8)	
Mild	84 (40.4)	36 (41.9)	48 (39.3)	0.924
Moderate or more	19 (9.1)	7 (8.1)	12 (9.8)	

<sup>a</sup>: BAV vs. TAV; BAV: bicuspid aortic valve; LVEF: left ventricular ejection fraction; PVL: paravalvular leakage; TAV: tricuspid aortic valve; TTE: transthoracic echocardiography.

LVEF in the BAV group. BAV was not associated with more PVL. No aortic dissections or reoperations for aortic dilatation were observed post-TAVR during follow-ups.

### Predictors of ascending aorta dilatation rate after TAVR

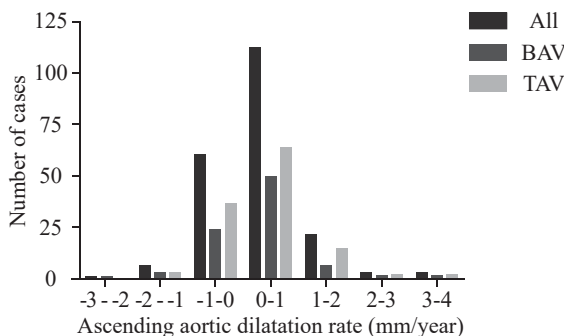
In the whole population, univariate linear regression revealed that age, sex, BMI, BSA, history of hypertension, history of diabetes mellitus, BAV, baseline ascending aortic diameter, implantation of self-expanding valves, years of follow-up, baseline TTE parameters (mean gradient, Max velocity, AVA, LVEF, and grade of AR) and follow-up TTE parameters (mean gradient, Max velocity, AVA and LVEF) were not associated with ascending aortic dilatation rate, except grade of PVL (Coefficient=0.240, standard error=0.082,  $P=0.004$ ) (Figure 4A). Baseline ascending aorta diameter, baseline AVA, and PVL were included in the multivariate linear regression model, and PVL was revealed as the only independent predictor (Coefficient=0.247, standard error=0.083,  $P=0.003$ ). Subgroup analysis showed that PVL grade was significantly associated

with the ascending aortic dilatation rate in the BAV group (Coefficient=0.482, standard error=0.115,  $P<0.001$ ) (Figure 4B, Table 3) but not in the TAV group (Coefficient=0.081, standard error=0.112,  $P=0.470$ ) (Figure 4C). PVL grade was still independently associated with ascending aortic dilatation rate in the multivariate regression model in the BAV group (Coefficient=0.495, standard error=0.117,  $P<0.001$ ) (Table 3). A weak correlation was found between the ascending aortic dilatation rate at baseline and the ascending aortic diameter in the tricuspid group (Coefficient=0.031, standard error=0.015,  $P=0.049$ ).

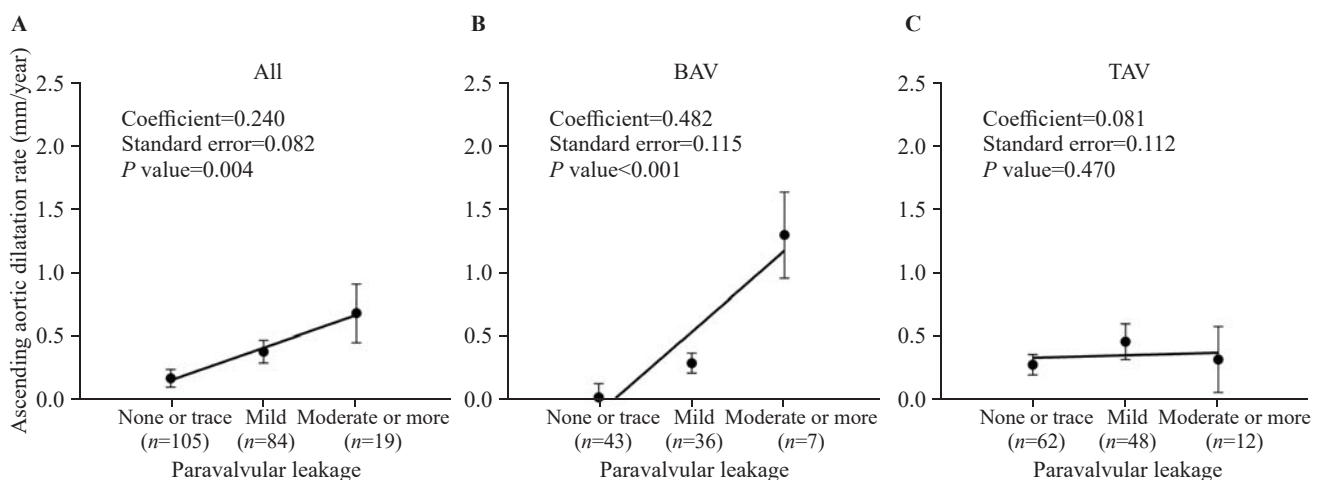
### DISCUSSION

This present study reveals for the first time that ascending aorta continued to dilate after TAVR in both bicuspid and tricuspid AS patients after a midterm to a long-term MDCT follow-up. However, ascending aortic dilatation rate is similar between two groups. Multivariate regression analysis demonstrates that PVL after TAVR is independently associated with ascending aortic dilatation rate in BAV patients, but not in TAV patients.

The size of the ascending aorta is changing throughout the lifetime. The average growth rate of ascending aorta in the population with TAV is found to be 0.15 to 0.20 mm/year.<sup>[22-24]</sup> In the setting of bicuspid patients, the growth rate of ascending aorta is altered by different phases of bicuspid natural history. In “normally functioning” BAV, the growth rate of ascending aorta is reported to be 0.39 to 0.77 mm/year, which is 2–4 times faster than that in the healthy tricuspid population.<sup>[25,26]</sup> The faster growth rate may be related to the genetically impaired aortic wall in patients with BAV and altered



**Figure 3.** Frequency distribution of ascending aortic dilatation rate after transcatheter aortic valve replacement of the whole population, bicuspid group, and tricuspid group.



**Figure 4.** Correlation between paravalvular leakage grade and ascending aortic dilatation rate in the whole population (A), bicuspid group (B) and tricuspid group (C). Data are presented as mean ± standard error. BAV: bicuspid aortic valve; TAV: tricuspid aortic valve.

blood flow generated by normal functioning BAV.<sup>[7,15,27]</sup> When BAV becomes dysfunctional, ascending aorta seems to dilate faster with a growth rate of 0.6 to 0.9 mm/year.<sup>[23,28]</sup> As a result, aortic dilatation and aneurysm are more commonly seen in bicuspid AS than tricuspid AS patients,<sup>[29]</sup> which is consistent with this study. After BAV is removed by SAVR, the growth rate of ascending aorta was reduced to 0.18–0.28 mm/year,<sup>[8,30]</sup> which appears to be close to that in TAV population. In this study, after TAVR, the mean ascending aortic dilatation rate of BAV group was 0.2 mm/year, which was comparable to that of the TAV group after TAVR, as well as the previously reported average growth rate in normal TAV population (0.15 to 0.20 mm/year).<sup>[22-24]</sup> These results indicate that after hemodynamic abnormality is corrected, growth rate returns to be normal range, which supports the hemodynamic theory of bicuspid AS related aortic dilatation.

Despite advanced age, there are several reported predictors of ascending aortic dilatation, such as sex, BSA, hypertension, and hemodynamic parameters.<sup>[16,31,32]</sup> In our study, no correlation is found between ascending aortic dilatation rate and demographic variables or hemodynamic measurements at baseline. Interestingly, more serious PVL grades are strongly associated with faster ascending aortic dilatation. Thanassoulis et al<sup>[32]</sup> and Keane et al<sup>[33]</sup> reported AR as a predictor of aortic dilatation. Kinoshita et al<sup>[34]</sup> found that AR at the time of surgery was a significant predictor of dilatation of the aorta after SAVR. However, to the best of our knowledge, no study has reported before about the relationship between PVL and ascending aortic dilatation

rate after SAVR or TAVR, probably due to the low incidences of PVL after SAVR and limited studies about aortic dilatation after TAVR. Theoretically, PVL might result in altered hemodynamics and increased stroke volume that places increased wall stress on the aorta and leads to faster aortic dilatation. This result, again, indicates the hemodynamic impact on aortic dilatation.

Furthermore, subgroup analysis shows that PVL grade is associated with ascending aortic dilatation rate in BAV group, but not in the TAV group. The aortic wall of BAV patients seemed more vulnerable to PVL regardless of similar PVL grades between BAV and TAV groups. These results imply that genetically triggered aortic wall abnormality of BAV patients still plays a role in progressive aortic dilatation after TAVR. Therefore, it is reasonable to assume that the interactions of both hemodynamics and genetics lead to aortic dilatation in bicuspid AS patients but not merely due to any single factor. Unfortunately, this study was unable to fully explain the mechanism of the relationship between PVL and progressive aortic dilatation after TAVR. With newer generation devices<sup>[35]</sup> available in the Chinese mainland shortly, which can significantly decrease the severity of PVL, it is worth finding out whether newer generation devices affect slowing down the aortic dilatation rate in BAV patients by minimizing PVL grade.

The risks of aortic dissection in bicuspid patients with aortic dilatation are well established.<sup>[7,36]</sup> For patients with BAV undergoing SAVR, maximal ascending aorta  $\geq 45$  mm is indicated for concomitant surgery for aortic dilatation.<sup>[2,37]</sup> However, these suggestions are mainly experience-based, and the reported incidences of aortic

**Table 3.** Predictors of ascending aortic dilatation rate after TAVR in bicuspid group

Predictors	Univariate regression			Multivariate regression		
	Coefficients ( $\beta$ )	Standard error of $\beta$	P value	Coefficients ( $\beta$ )	Standard error of $\beta$	P value
Age, years	-0.022	0.015	0.136	-0.018	0.014	0.211
Male	0.130	0.161	0.419			
BMI (kg/m <sup>2</sup> )	0.014	0.026	0.599			
BSA (m <sup>2</sup> )	0.296	0.501	0.557			
Hypertension	0.219	0.160	0.174	0.278	0.148	0.065
Diabetes	-0.011	0.191	0.955			
Baseline ascending aortic diameter (mm)	0.020	0.018	0.279			
Self-expanding valve	0.124	0.241	0.607			
Years of follow-up (years)	-0.019	0.076	0.799			
Baseline TTE measurements						
Mean gradient (mmHg)	-0.008	0.004	0.042	-0.007	0.014	0.614
Maximal velocity (m/s)	-0.206	0.101	0.045	0.019	0.342	0.956
Aortic valve area (cm <sup>2</sup> )	0.637	0.471	0.180	-0.195	0.513	0.705
LVEF (%)	-0.006	0.006	0.336			
AR 0–2	0.014	0.126	0.911			
Follow-up TTE measurements						
Mean gradient (mmHg)	0.004	0.018	0.802			
Maximal velocity (m/s)	-0.036	0.178	0.840			
Aortic valve area (cm <sup>2</sup> )	0.176	0.250	0.482			
LVEF (%)	-0.019	0.014	0.164	-0.011	0.013	0.399
PVL 0–2	0.482	0.115	<0.001	0.495	0.117	<0.001

AR: aortic regurgitation; BMI: body mass index; BSA: body surface area; LVEF: left ventricular ejection fraction; TTE: transthoracic echocardiography; PVL: paravalvular leakage.

dissection are rare (0.1%–0.45% per patient-year).<sup>[25,38]</sup> Ascending aortic diameter  $\geq 45$  mm was found in 36.0% BAV patients in the present study, but no faster aortic dilatation was observed in patients with larger ascending aortic diameter prior to TAVR. Moreover, no aortic events were observed post-TAVR in our current study, which suggest that a conservative approach to mild-to-moderate ascending aortic dilatation is reasonable in bicuspid AS patients such as isolated SAVR or TAVR. However, a larger cohort and more extended follow-up period are needed to fully answer this question.

### Limitations

Our study is limited by the fact that it was a single-center study with a limited number of cases and selection bias. MDCT follow-ups were obtained in 83.5% (208/249) patients, which was incomplete. Different types of THVs were used in this study, which was a confounding factor when interpreting the results. Furthermore, PVL has been identified as an independent predictor of aortic dilatation rate in BAV patients who underwent TAVR, but our study failed to explain or verify this finding. Considering the slow rate of aortic dilatation progression after TAVR and low incidence of aortic events in the real-world practice, studies with a more significant number of cases and a longer follow-up are needed.

### CONCLUSIONS

The current study demonstrates that ascending aorta continues to dilate after TAVR in both bicuspid and tricuspid AS patients after TAVR based on MDCT follow-up. However, aortic dilatation rate is similar between two groups. Aortic events are rare in real-world practice post-TAVR. PVL grade is associated with ascending aortic dilatation rate after TAVR.

### ACKNOWLEDGMENTS

The authors thank all the members of the heart team of the Second Affiliated Hospital, School of Medicine, Zhejiang University, for their persevering work.

**Funding:** This study was supported by the Advanced Technique Research of Valvular Heart Disease Treatment Project (2015C03028); Role of TPP1 in anti-senescence and functional optimization of aged mesenchymal stem cells (81570233); Zhejiang Clinical Research Center for Cardiovascular and Cerebrovascular Disease (2018E50002); Role of FAIM in survival and functional improvement for aged mesenchymal stem cells

(81770253); Zhejiang Clinical Research Center for Cardiovascular and Cerebrovascular Disease (2018E50002).

**Ethical approval:** The ethics committee of our center approved the study protocol and written informed consents were obtained in all patients.

**Conflicts of interests:** The authors declare that they have no competing interests. The funders had no role in the design, conduct, analysis, or interpretation of data or in writing the manuscript.

**Contributors:** All authors of this paper have read and approved the final version of the submitted manuscript.

### REFERENCES

- 1 Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP, 3rd, Fleisher LA, et al. 2017 AHA/ACC Focused Update of the 2014 AHA/ACC Guideline for the Management of Patients with Valvular Heart Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol.* 2017;70(2):252-89.
- 2 Baumgartner H, Falk V, Bax JJ, De Bonis M, Hamm C, Holm PJ, et al. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. *Eur Heart J.* 2017;38(36):2739-91.
- 3 Vahanian A, Alfieri O, Andreotti F, Antunes MJ, Baron-Esquivias G, Baumgartner H, et al. Guidelines on the management of valvular heart disease (version 2012): the Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). *Eur J Cardiothorac Surg.* 2012;42(4):S1-44.
- 4 Bauer T, Linke A, Sievert H, Kahlert P, Hambrecht R, Nickenig G, et al. Comparison of the effectiveness of transcatheter aortic valve implantation in patients with stenotic bicuspid versus tricuspid aortic valves (from the German TAVI Registry). *Am J Cardiol.* 2014;113(3):518-21.
- 5 Yoon SH, Bleiziffer S, De Backer O, Delgado V, Arai T, Ziegelmueller J, et al. Outcomes in transcatheter aortic valve replacement for bicuspid versus tricuspid aortic valve stenosis. *J Am Coll Cardiol.* 2017;69(21):2579-89.
- 6 Makkar RR, Yoon SH, Leon MB, Chakravarty T, Rinaldi M, Shah PB, et al. Association between transcatheter aortic valve replacement for bicuspid vs tricuspid aortic stenosis and mortality or stroke. *JAMA.* 2019;321(22):2193-202.
- 7 Verma S, Siu SC. Aortic dilatation in patients with bicuspid aortic valve. *N Engl J Med.* 2014;370(20):1920-9.
- 8 Yasuda H, Nakatani S, Stugaard M, Tsujita-Kuroda Y, Bando K, Kobayashi J, et al. Failure to prevent progressive dilation of ascending aorta by aortic valve replacement in patients with bicuspid aortic valve: comparison with tricuspid aortic valve. *Circulation.* 2003;108 Suppl 1(10 SUPPL.):II291-4.
- 9 Girdauskas E, Rouman M, Disha K, Dubsclaff G, Fey B, Misfeld M, et al. The fate of mild-to-moderate proximal aortic dilatation after isolated aortic valve replacement for bicuspid aortic valve stenosis: a magnetic resonance imaging follow-up study. *Eur J Cardiothorac Surg.* 2016;49(4):e80-6; discussion e86-7.
- 10 Charitos EI, Stierle U, Petersen M, Mohamed SA, Hanke T, Schmidt C, et al. The fate of the bicuspid valve aortopathy after aortic valve replacement. *Eur J Cardiothorac Surg.* 2014;45(5):e128-35.
- 11 Rylski B, Szeto WY, Bavaria JE, Walsh E, Anwaruddin S, Desai ND, et al. Transcatheter aortic valve implantation in patients with ascending aortic dilatation: safety of the procedure and mid-

- term follow-up-dagger. *Eur J Cardiothorac Surg.* 2014;46(2):228-33; discussion 233.
- 12 Kong WKF, Regeer MV, Poh KK, Yip JW, van Rosendael PJ, Yeo TC, et al. Inter-ethnic differences in valve morphology, valvular dysfunction, and aortopathy between Asian and European patients with bicuspid aortic valve. *Eur Heart J.* 2018;39(15):1308-13.
  - 13 Tsamis A, Phillippi JA, Koch RG, Chan PG, Krawiec JT, D'Amore A, et al. Extracellular matrix fiber microarchitecture is region-specific in bicuspid aortic valve-associated ascending aortopathy. *J Thorac Cardiovasc Surg.* 2016;151(6):1718-28 e5.
  - 14 Wu J, Song HF, Li SH, Guo J, Tsang K, Tumiaty L, et al. Progressive aortic dilation is regulated by miR-17-associated miRNAs. *J Am Coll Cardiol.* 2016;67(25):2965-77.
  - 15 Barker AJ, Markl M, Burk J, Lorenz R, Bock J, Bauer S, et al. Bicuspid aortic valve is associated with altered wall shear stress in the ascending aorta. *Circ Cardiovasc Imaging.* 2012;5(4):457-66.
  - 16 Roman MJ, Pugh NL, Devereux RB, Eagle KA, Holmes K, LeMaire SA, et al. Aortic dilatation associated with bicuspid aortic valve: relation to sex, hemodynamics, and valve morphology (the National Heart Lung and Blood Institute-Sponsored National Registry of Genetically Triggered Thoracic Aortic Aneurysms and Cardiovascular Conditions). *Am J Cardiol.* 2017;120(7):1171-5.
  - 17 Liu X, He Y, Zhu Q, Gao F, He W, Yu L, et al. Supra-annular structure assessment for self-expanding transcatheter heart valve size selection in patients with bicuspid aortic valve. *Catheter Cardiovasc Interv.* 2018;91(5):986-94.
  - 18 Watanabe Y, Morice MC, Bouvier E, Leong T, Hayashida K, Lefevre T, et al. Automated 3-dimensional aortic annular assessment by multidetector computed tomography in transcatheter aortic valve implantation. *JACC Cardiovasc Interv.* 2013;6(9):955-64.
  - 19 Sievers HH, Schmidtke C. A classification system for the bicuspid aortic valve from 304 surgical specimens. *J Thorac Cardiovasc Surg.* 2007;133(5):1226-33.
  - 20 Liu XB, Jiang JB, Zhou QJ, Pu ZX, He W, Dong AQ, et al. Evaluation of the safety and efficacy of transcatheter aortic valve implantation in patients with a severe stenotic bicuspid aortic valve in a Chinese population. *J Zhejiang Univ Sci B.* 2015;16(3):208-14.
  - 21 Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP, 3rd, Guyton RA, et al. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol.* 2014;63(22):e57-185.
  - 22 Hager A, Kaemmerer H, Rapp-Bernhardt U, Blücher S, Rapp K, Bernhardt TM, et al. Diameters of the thoracic aorta throughout life as measured with helical computed tomography. *J Thorac Cardiovasc Surg.* 2002;123(6):1060-6.
  - 23 Wolak A, Gransar H, Thomson LE, Friedman JD, Hachamovitch R, Gutstein A, et al. Aortic size assessment by noncontrast cardiac computed tomography: normal limits by age, gender, and body surface area. *JACC Cardiovasc Imaging.* 2008;1(2):200-9.
  - 24 Hannuksela M, Lundqvist S, Carlberg B. Thoracic aorta--dilated or not? *Scand Cardiovasc J.* 2006;40(3):175-8.
  - 25 Michelena HI, Khanna AD, Mahoney D, Margaryan E, Topilsky Y, Suri RM, et al. Incidence of aortic complications in patients with bicuspid aortic valves. *JAMA.* 2011;306(10):1104-12.
  - 26 Etz CD, Zoli S, Brenner R, Roder F, Bischoff M, Bodian CA, et al. When to operate on the bicuspid valve patient with a modestly dilated ascending aorta. *Ann Thorac Surg.* 2010;90(6):1884-90; discussion 1891-2.
  - 27 Hope MD, Hope TA, Meadows AK, Ordovas KG, Urbana TH, Alley MT, et al. Bicuspid aortic valve: four-dimensional MR evaluation of ascending aortic systolic flow patterns. *Radiology.* 2010;255(1):53-61.
  - 28 Ferencik M, Pape LA. Changes in size of ascending aorta and aortic valve function with time in patients with congenitally bicuspid aortic valves. *Am J Cardiol.* 2003;92(1):43-6.
  - 29 Kerneis C, Pasi N, Arangalage D, Nguyen V, Mathieu T, Verdonk C, et al. Ascending aorta dilatation rates in patients with tricuspid and bicuspid aortic stenosis: the COFRASA/GENERAC study. *Eur Heart J Cardiovasc Imaging.* 2018;19(7):792-9.
  - 30 Regeer MV, Versteegh MI, Klautz RJ, Schaliij MJ, Bax JJ, Marsan NA, et al. Effect of aortic valve replacement on aortic root dilatation rate in patients with bicuspid and tricuspid aortic valves. *Ann Thorac Surg.* 2016;102(6):1981-7.
  - 31 Della Corte A, Bancone C, Quarto C, Dialetto G, Covino FE, Scardone M, et al. Predictors of ascending aortic dilatation with bicuspid aortic valve: a wide spectrum of disease expression. *Eur J Cardiothorac Surg.* 2007;31(3):397-404; discussion 404-5.
  - 32 Thanassoulis G, Yip JW, Filion K, Jamorski M, Webb G, Siu SC, et al. Retrospective study to identify predictors of the presence and rapid progression of aortic dilatation in patients with bicuspid aortic valves. *Nat Clin Pract Cardiovasc Med.* 2008;5(12):821-8.
  - 33 Keane MG, Wieggers SE, Plappert T, Pochettino A, Bavaria JE, Sutton MG. Bicuspid aortic valves are associated with aortic dilatation out of proportion to coexistent valvular lesions. *Circulation.* 2000;102(19 Suppl 3):III35-9.
  - 34 Kinoshita T, Naito S, Suzuki T, Asai T. Valve phenotype and risk factors of aortic dilatation after aortic valve replacement in Japanese patients with bicuspid aortic valve. *Circ J.* 2016;80(6):1356-61.
  - 35 Liu XB, He YX, Liu CH, Wang LH, Gao F, Yu L, et al. First-in-man implantation of the retrievable and repositionable Venus-A-Plus valve. *World J Emerg Med.* 2018;9(1):64-6.
  - 36 Edwards WD, Leaf DS, Edwards JE. Dissecting aortic aneurysm associated with congenital bicuspid aortic valve. *Circulation.* 1978;57(5):1022-5.
  - 37 Hiratzka LF, Creager MA, Isselbacher EM, Svensson LG, Nishimura RA, Bonow RO, et al. Surgery for aortic dilatation in patients with bicuspid aortic valves: A Statement of Clarification from the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol.* 2016;67(6):724-31.
  - 38 Tzemos N, Therrien J, Yip J, Thanassoulis G, Tremblay S, Jamorski MT, et al. Outcomes in adults with bicuspid aortic valves. *JAMA.* 2008;300(11):1317-25.

Received August 1, 2018

Accepted after revision April 8, 2019