Comparison of Efficacy and Safety of Transcatheter Aortic Valve Implantation in Patients With Bicuspid Versus Tricuspid Aortic Valves

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Bicuspid aortic valve (BAV) stenosis has been considered a contraindication to transcatheter aortic valve implantation (TAVI). The aim of this study is to compare the efficacy and safety of TAVI in patients with BAV with those with tricuspid aortic valve (TAV) using balloon-expandable and self-expanding transcatheter heart valves. This retrospective study included 823 consecutive patients with severe, symptomatic aortic valve stenosis undergoing TAVI in 2 institutions, Baylor Heart and Vascular Hospital (Dallas, TX) and The Heart Hospital Baylor Plano (Plano, TX), from January 2012 to February 2016. Efficacy was evaluated by postprocedural valve function as mean gradient, peak velocity, effective orifice area, and ≥moderate paravalvular leak. Safety end points included all-cause 30-day and 1-year mortality, immediate postprocedural mortality and 30-day cardiovascular mortality, procedural success, pacemaker implantation, and procedural complications. Of the 823 included patients, 735 had TAV and 77 had BAV. Baseline characteristics were similar between the 2 groups. Procedural success was high in both BAV and TAV (98.7% vs 99.1%, p = ns). There were no significant differences between groups in valve hemodynamics after TAVI, pacemaker implantation rate, or procedural complications. There were no differences regarding immediate postprocedural mortality (BAV vs TAV, 1.1% vs 0.8%, p = ns), nor 30-day cardiovascular mortality (3.4% vs 2.3%, p = ns). All-cause mortality at 30 days (3.4% vs 3.1%, p = ns) and 1-year (8.5% vs 10.5%) were similar. Patients with BAV showed similar procedural and clinical outcomes to patients with TAV. Therefore, TAVI appears to be a safe and effective procedure for patients with BAVs as well as those with TAVs. **(Am J Cardiol 2017;■■:■■–■■)**

Bicuspid aortic valve (BAV) is one of the most common congenital heart disorders, occurring in 1% to 2% of the general population, with a male preponderance ratio of 2:1.[1,2] It occurs either in isolation or in association with complex congenital heart defects. BAV is associated with increased mechanical stress, which predisposes to calcification and development of aortic stenosis (AS) and/or aortic regurgitation.[3] Aortopathy may accompany BAV, leading to ascending aortic enlargement, aneurysm formation, and aortic dissection.[4] Transcatheter aortic valve implantation (TAVI) is currently approved for the treatment of intermediate- to high-risk patients with severe AS. Despite previous assumptions, BAV is common even in octogenarians with symptomatic AS.[5] However, BAV has been considered a relative contraindication to TAVI. Therefore, data on the role of TAVI in the treatment of severe AS in patients with BAV are limited because such patients were excluded from most clinical trials because of concerns regarding uneven valve expansion, bioprosthesis malposition or malfunction, paravalvular leak, annular rupture, or aortic dissection.[6] However, case reports and small case series have suggested that TAVI can be successfully performed with acceptable clinical outcomes in high-risk patients with BAV.[7–10] Some reports have suggested higher success rate with new-generation devices than earlier devices.[11,12] Recently, results from a multicenter registry reported a higher procedural complication rate and incidence of paravalvular leak in patients with BAV.[13] In light of this discordant evidence, we report the efficacy and safety of TAVI in a large series of patients with BAV in comparison with patients with tricuspid aortic valve (TAV).

Methods

Data were collected on consecutive patients with severe, symptomatic AS undergoing TAVI at Baylor Heart and Vascular Hospital (Dallas, TX) and The Heart Hospital Baylor Plano (Plano, TX) from January 2012 to February 2016. Baseline demographics, procedural data, and clinical outcomes were retrospectively collected and analyzed. For the purpose of the current analysis, data from both medical centers were pooled, and a joint database was created. The study was approved by the Baylor Institutional Review Board.

Patients were stratified into 2 groups according to aortic valve morphology as detected at intra-procedural transesophageal echocardiography and preprocedural computed tomography (CT) scans. BAV morphology was classified as previously described by Sievers and Schmidtke[14] according

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to the number of cusps and the presence of raphes, as well as spatial position and symmetry of raphes and cusps: (1) type 0 in the presence of 2 symmetric leaflets or cusps and 1 commissure without evidence of a raphe; (2) type 1, presence of 1 raphe; (3) and type 2, presence of 2 raphes. The imaging studies were reviewed by 2 experts (PAG and AS). Patients were excluded if the diagnosis of BAV was not consistent or remained uncertain after both transesophageal echocardiography and CT evaluation. Follow-up was obtained by clinical visits and clinical charts revision.

Primary efficacy end points included measures of prosthetic valve function, defined according to the Valve Academic Research Consortium criteria as mean gradient, peak velocity, effective orifice area, and ≥moderate paravalvular leak.[15] Safety end points included all-cause 30-day and 1-year mortality, immediate postprocedural mortality and 30-day cardiovascular mortality, pacemaker implantation, and the incidence of procedural complications (acute kidney injury, vascular complication, minor, major, and life-threatening bleedings, stroke or transient ischemic attack, valve-in-valve intervention, procedural success), defined in accordance to the Valve Academic Research Consortium criteria.[15] Procedural success was defined as deployment of the valve as intended, without need for conversion to immediate surgery. The degree of postprocedural PVL was evaluated by both angiography and transesophageal echocardiography at the end of the TAVI procedure after final device deployment.

Continuous variables are summarized as mean ± standard deviation (SD) or as medians and interquartile range as appropriate, and were compared using Student *t* test or Mann-Whitney rank sum test. Categorical variables were compared using chi-square or the Fisher's exact test. Survival curves were constructed using Kaplan-Meier estimates, whereas comparisons relied on the log-rank test. A 2-sided alpha level of 0.05 was used for all superiority testing. All statistical analyses were performed using SPSS Statistics version 19 (SPSS Inc., Chicago, IL).[16,17]

Results

Between January 2012 and February 2016, 829 patients underwent TAVI in the included institutions. Of those, 88 were classified as BAV, 735 as TAV, and 6 were excluded because valve morphology could not be clearly established. Baseline characteristics are summarized in Table 1. Patients with BAV displayed a higher prevalence of peripheral arterial disease (70.9% vs 67.1%, p = 0.033); moreover, the BAV group had a slightly smaller calculated aortic valve area at baseline (0.65 ± 0.17 vs 0.69 ± 0.19, p = 0.049). The 2 groups were otherwise similar in baseline characteristics, as well as baseline echocardiographic features. The most common morphology in BAVs was type 1 (85.2%), followed by type 0 (13.6%) and type 2 (1.1%). No differences emerged in the type valve and approach used. Of the total study population, 616 were treated with older devices (Sapien-XT: n = 384, CoreValve: n = 232), and 204 were treated with newer generation devices (Sapien 3: n = 99, Evolut: n = 83, Lotus: n = 22). One-year follow-up was completed by 92% of the initial population.

Postprocedural echocardiographic findings are described in Table 2. After TAVI, both patients with BAV and patients with TAV had similar values for mean aortic gradient (7.96 ± 4.15 vs 8.5 ± 4.2, p = 0.268, Figure 1) and peak aortic velocity (1.9 ± 0.4 vs 2.02 ± 0.51, p = 0.265). Postprocedural aortic valve area was slightly larger in the BAV group than in the TAV group (2.15 ± 0.55 vs 1.90 ± 0.54, p = 0.007). The incidence of ≥moderate PVL was low in our population, with no differences in patients with BAV or TAV (5.3% vs 5.0%, p = 0.903, respectively; Figure 2). Table 3 describes procedural and follow-up clinical outcomes of the study population. Patients with BAV and those with TAV showed similar incidence of acute kidney injury (3.4% vs 2.3%, p = 0.528), vascular complications (4.5% vs 4.8%, p = 0.928), life-threatening, major, and minor bleeding (0.4% vs 0%, p = 0.792; 3.4% vs 2.0%, p = 0.792 and 9.1% vs 9.1%, p = 792), stroke (2.3% vs 3.7%, p = 0.499), and valve-in-valve intervention (3.4% vs 1.6%, p = 0.240). Procedural success was high in the whole population and not different between the 2 groups (98.7% vs 99.1%, p = ns). Rate of pacemaker implantation was similar between the 2 groups (22.7% vs 18.2%, p = 0.303). Similarly, immediate postprocedural mortality (1.1% vs 0.8%, p = 0.757), 30-day cardiovascular (3.4% vs 2.3%, p = 0.528) and all-cause mortality (3.4% vs 3.1%, p = 0.887), as well as 1-year all-cause mortality (8.5% vs 10.5%, p = 0.579) did not differ between groups. Even after stratifying the population according to newer versus older generation device, no differences in 1-year mortality were observed (Figure 3).

Discussion

In this large patient cohort, no significant differences were found in clinical outcomes of patients undergoing TAVI with BAV. Although the use of TAVI in patients with BAV is increasing, TAVI is not currently approved for use in patients with BAV in the United States. The reasons for this lie in theoretical concerns regarding the elliptical shape of leaflet opening in BAV together with a possible asymmetric distribution of calcification. Accordingly, patients with known BAV have been excluded from TAVI clinical trials, or are younger patients with low surgical risk for whom TAVI is not currently approved. As a result, the available evidence regarding TAVI in BAV (Table 4) comes mostly from case reports or small series and few registries.[7–10,13,18] One large registry has been recently published on this topic, showing overall good result of TAVI in patients with BAV especially with newer generation devices.[11] However, the majority of the studies have been performed with first-generation transcatheter heart valve (THV). In our population, BAV and TAV showed similar hemodynamic results after TAVI. Moreover, the incidence of significant paravalvular leak was not different between groups. Previous reports have shown conflicting evidence regarding the risk of significant paravalvular leak in patients with BAV compared with those with TAV.[7–9] The German TAVI Registry described a higher frequency of residual paravalvular leak in patients with BAV.[7] A recent report from the Bicuspid TAVI Registry, including 301 patients with BAV, reported a significantly lower rate of paravalvular leak in patients being treated with new-generation (Sapien 3 and Lotus) compared with first-generation THV (Sapien XT and CoreValve).[11] The findings were recently confirmed a propensity matched comparison of patients with BAV and those with TAV.[13]

Table 1
Characteristics of the study population

Variables	Aortic Valve Structure		p value
	Bicuspid (n = 88)	Tricuspid (n = 735)	
Baseline characteristics			
Age, mean ± SD (years)	80.2 ± 8.4	81.8 ± 7.9	0.081
Men	53 (60.2%)	389 (52.9%)	0.194
Body Mass Index, mean ± SD (kg/m^2)	27.0 ± 6.8	27.6 ± 6.6	NS
Society of Thoracic Surgery risk of mortality, mean ± SD	7.4 ± 3.9%	7.6 ± 3.9%	NS
Hypertension	71 (81.6%)	612 (84.3%)	0.518
Hyperlipidemia	62 (72.1%)	516 (71.7%)	0.934
Diabetes mellitus	29 (37.7%)	283 (40.4%)	0.645
Chronic kidney disease	45 (52.3%)	330 (45.5%)	0.227
End stage renal disease	4 (5.3%)	21 (3.1%)	0.315
Coronary artery disease	61 (70.9%)	487 (67.1%)	0.471
Peripheral arterial disease	35 (43.2%)	219 (31.5%)	**0.033**
Chronic obstructive pulmonary disease	15 (19.5%)	149 (22.1%)	0.602
Atrial Fibrillation	15 (17.9%)	142 (19.6%)	0.789
Previous bypass surgery/percutaneous coronary intervention	40 (49.4%)	322 (46.1%)	0.571
Previous stroke	17 (22.4%)	132 (19.5%)	0.556
Echocardiographic findings			
Left ventricle ejection fraction <50%	28 (31.8%)	197 (27.1%)	0.354
Aortic valve mean gradient, mean ± SD (mmHg)	46.9 ± 16.9	44.3 ± 13.6	0.102
Aortic valve area, mean ± SD (cm^2)	0.65 ± 0.17	0.69 ± 0.19	**0.049**
Aortic regurgitation ≥moderate	8 (9.1%)	76 (10.4%)	0.700
Mitral regurgitation ≥moderate	14 (15.9%)	140 (19.1%)	0.472
Mitral annular calcium ≥moderate	55 (62.5%)	388 (53.1%)	0.094
Pulmonary Hypertension	49 (71.0%)	410 (75.6%)	0.402
Bicuspid Morphology Type			
0	12 (13.6%)		
1	75 (85.2%)		
2	1 (1.1%)		
Procedural characteristics			
Type of Valve			0.174
Balloon-expandable	46 (52.3%)	439 (59.8%)	
1st generation	*36 (40.9%)*	*348 (47.3%)*	
new generation	*10 (11.4%)*	*89 (12.1%)*	
Self-expandable	42 (47.7%)	295 (40.2%)	
1st generation	*30 (34.1%)*	*202 (27.5%)*	
new generation	*12 (13.6%)*	*93 (12.6%)*	
Approach			**0.622**
Trans-femoral		640 (89.1%)	
Trans-apical	8 (9.1%)	61 (8.3%)	
Trans-aortic	1 (1.1%)	28 (3.8%)	
Subclavian	1 (1.1%)	6 (0.8%)	
Valve Size (mm)			
Balloon-expandable			0.556
20	1 (2.2%)	4 (0.9%)	
21	-	1 (0.2%)	
23	11 (24.4%)	94 (22.0%)	
25	-	5 (1.2%)	
26	12 (34.5%)	159 (46.2%)	
27	-	7 (1.6%)	
29	18 (40.0%)	118 (27.6%)	
31	3 (6.7%)	40 (9.3%)	
Self-Expandable			0.500
20	1 (2.4%)	3 (1.0%)	
23	7 (16.7%)	62 (21.4%)	
25	-	5 (1.7%)	
26	16 (38.1%)	95 (32.8%)	
27	-	3 (1.0%)	
29	17 (40.5%)	94 (32.4%)	
31	1 (2.4%)	28 (9.7%)	

SD = standard deviation.

Table 2
Efficacy end points

	Aortic Valve Structure		
	Bicuspid (n = 88)	Tricuspid (n = 735)	p value
Prosthetic Valve function			
Mean Gradient (mmHg)	7.96 ± 4.15	8.5 ± 4.2	0.268
Peak Velocity, mean ± SD (m/s)	1.9 ± 0.40	2.02 ± 0.0.51	0.265
Effective Orifice Area, mean ± SD (cm^2)	2.15 ± 0.55	1.90 ± 0.54	**0.007**
Paravalvular leak ≥ moderate	4/75 (5.3%)	32/639 (5.0%)	0.903

LVEF = left ventricle ejection fraction.

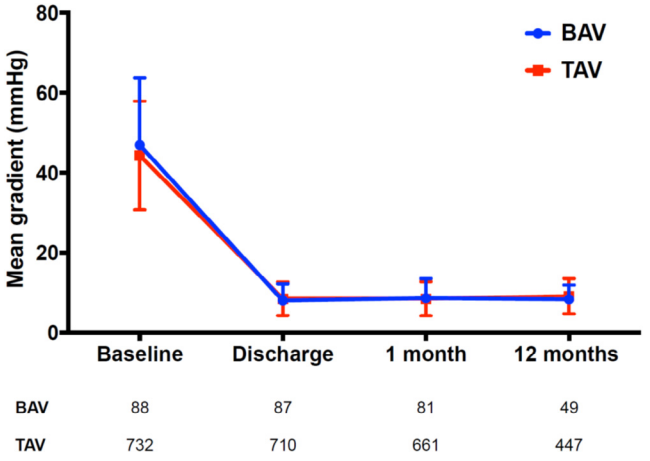

Figure 1. Aortic mean gradient over time. Evolution of mean aortic gradient in patients with BAV and those with TAV at baseline and at different time points after TAVI. BAV = bicuspid aortic valve; TAV = tricuspid aortic valve; TAVI = transcatheter aortic valve implantation.

Table 3
Safety end points

	Aortic Valve Structure		
	Bicuspid (n = 88)	Tricuspid (n = 735)	p value
Acute Kidney Injury	3 (3.4%)	17 (2.3%)	0.528
Vascular complication	4 (4.5%)	35 (4.8%)	0.928
Minor Bleeding	8 (9.1%)	67 (9.1%)	0.792
Major Bleeding	3 (3.4%)	15 (2.0%)	0.792
Life-threatening bleeding	-	3 (0.4%)	0.792
Stroke	2 (2.3%)	27 (3.7%)	0.499
Valve-in-Valve	3 (3.4%)	12 (1.6%)	0.240
Procedural success	76 (98.7%)	646 (99.1%)	0.556
Pacemaker Implantation	20 (22.7%)	133 (18.2%)	0.303
Immediate post-procedural Mortality	1 (1.1%)	6 (0.8%)	0.757
30-day Cardiovascular Mortality	3 (3.4%)	17 (2.3%)	0.528
30-day All-cause Mortality	3 (3.4%)	23 (3.1%)	0.887
1-year All-cause Mortality	7 (8.5%)	68 (10.5%)	0.579

BAV was found in 10.7% of all patients undergoing TAVI in this series. This may partly reflect selection bias in that younger patients with known BAV tend to undergo surgical aortic valve replacement in our institution. Many of the patients in this study were not known to have BAV preoperatively, but were discovered during TAVI by transesophageal echocardiography. As more and more patients are undergoing TAVI using moderate sedation without transesophageal echocardiography, it is likely that BAV will not be recognized in many patients with calcified aortic valves. The ability of transthoracic echocardiography to accurately classify aortic valve morphology is only around 70%.[19] Three-dimensional transesophageal echocardiogram and 4-dimensional CT allow superior detection of the number of commissures and raphes, thus allowing classification of BAV versus TAV more

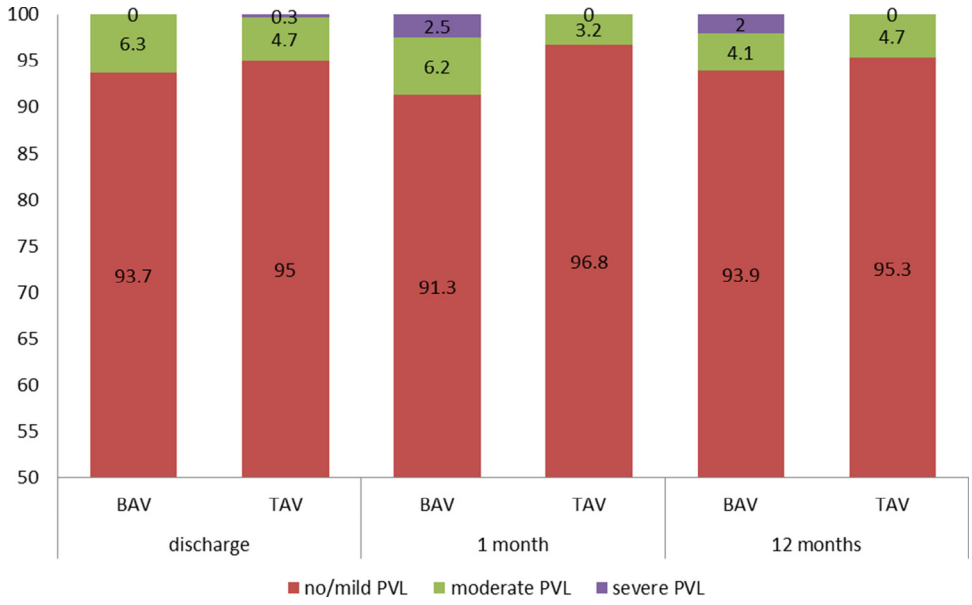

Figure 2. Paravalvular leak (PVL). Incidence of PVL over time in patients with BAV and those with TAV. BAV = bicuspid aortic valve; TAV = tricuspid aortic valve.

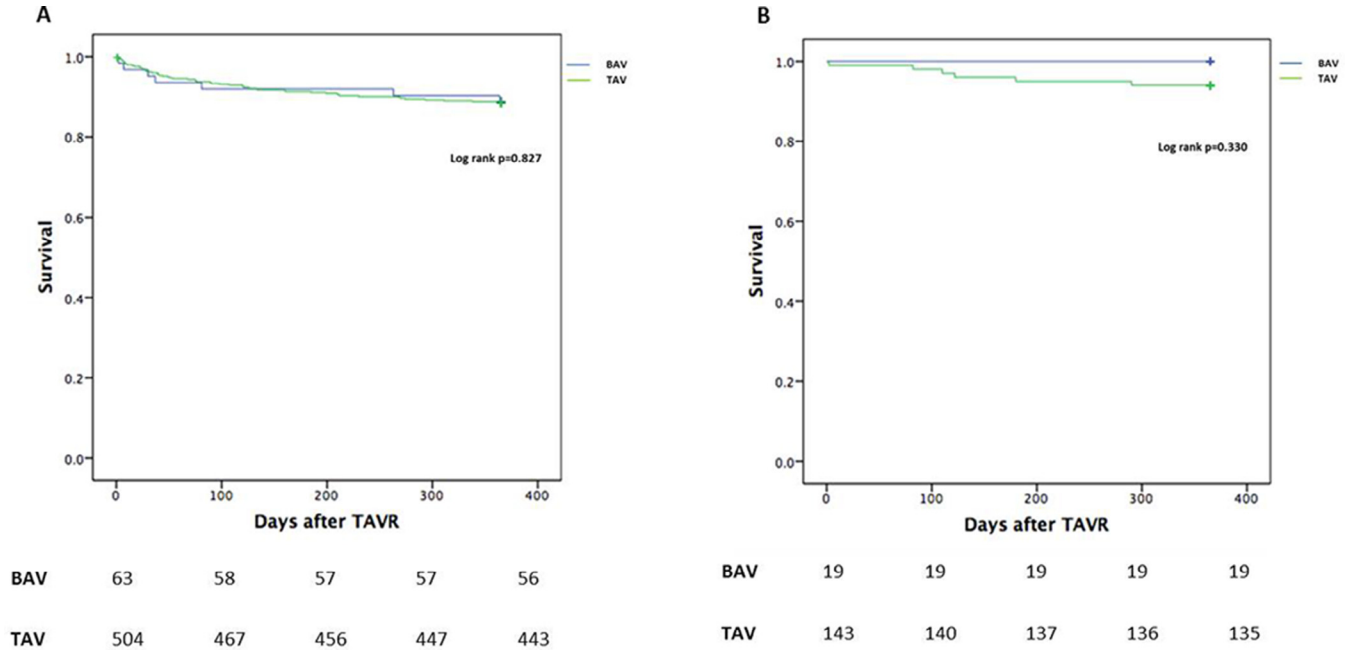

Figure 3. Kaplan-Meier survival curves. *(A)* One-year survival in patients with BAV and those with TAV treated with first-generation THV. *(B)* One-year survival in patients with BAV and those with TAV treated with new-generation THV. BAV = bicuspid aortic valve; TAV = tricuspid aortic valve; THV = transcatheter heart valve.

Table 4
Studies comparing BAV and TAV outcomes with TAVI

Study Design	Authors	Year	Number of Patients	Number of BAV	Type of THV used	THV generation
Case-Control	Liu XB. et al	2015	40	15	CoreValve and Venus A-valve	First generation
Case-Control	Bauer T. et al	2014	1395	38	CoreValve and Edwards SAPIEN	First generation
Case-Control	Costopopulos et al	2014	468	21	CoreValve and Edwards SAPIEN	First generation
Case-Control	Hayashida et al	2013	229	21	CoreValve and Edwards SAPIEN	First generation
Case-Control with matching (3:1)	Kockman et al	2014	112	28	CoreValve and Edwards SAPIEN	First generation
Case-series	Yoon et al	2016	301	301	CoreValve, Edwards SAPIEN, Sapien 3 and Lotus	First and Second generation
Case-series	Mylotte et al	2014	139	139	CoreValve and Edwards SAPIEN	First generation
Case-series	Yousef et al	2015	108	108	nr	nr
Case-series	Perlman et al	2016	51	51	Sapien 3	Second generation
Case-series	Wijesihghe et al	2010	11	11	Edwards SAPIEN	First generation

BAV = bicuspid aortic valve; TAV = tricuspid aortic valve; THV = transcatheter heart valve.

precisely.[20] It also helps avoid the common mistake of classifying patients as "functionally bicuspid" when a raphe is mistaken for fusion of 2 of 3 leaflet edges.

Our study suffers from the known limitation intrinsic to retrospective, observational study design. Although the decision to refer a patient to TAVI or surgery was not randomized, it was made by a Heart Valve Team with patients in the same setting by a group of experienced cardiologists and heart surgeons. A prospective randomized trial of TAVI versus surgical aortic valve replacement in patients with BAV is needed to confirm that TAVI is an effective treatment for BAV.

Disclosures

The authors have no conflicts of interest to disclose.

1. Michelena HI, Desjardins VA, Avierinos JF, Russo A, Nkomo VT, Sundt TM, Pellikka PA, Tajik AJ, Enriquez-Sarano M. Natural history of asymptomatic patients with normally functioning or minimally dysfunctional bicuspid aortic valve in the community. *Circulation* 2008;117:2776–2784.
2. Michelena HI, Khanna AD, Mahoney D, Margaryan E, Topilsky Y, Suri RM, Eidem B, Edwards WD, Sundt TM 3rd, Enriquez-Sarano M. Incidence of aortic complications in patients with bicuspid aortic valves. *JAMA* 2011;306:1104–1112.
3. Song ZZ. Valve calcification and patients with bicuspid aortic valves. *JAMA* 2009;301:935–936. author reply 936.
4. Verma S, Siu SC. Aortic dilatation in patients with bicuspid aortic valve. *N Engl J Med* 2014;370:1920–1929.
5. Roberts WC, Janning KG, Ko JM, Filardo G, Matter GJ. Frequency of congenitally bicuspid aortic valves in patients >/=80 years of age undergoing aortic valve replacement for aortic stenosis (with or without aortic regurgitation) and implications for transcatheter aortic valve implantation. *Am J Cardiol* 2012;109:1632–1636.

6. Tarantini G, Gasparetto V, Napodano M, Fraccaro C, Gerosa G, Isabella G. Valvular leak after transcatheter aortic valve implantation: a clinician update on epidemiology, pathophysiology and clinical implications. *Am J Cardiovasc Dis* 2011;1:312–320.
7. Bauer T, Linke A, Sievert H, Kahlert P, Hambrecht R, Nickenig G, Hauptmann KE, Sack S, Gerckens U, Schneider S, Zeymer U, Zahn R. 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;113:518–521.
8. Costopoulos C, Latib A, Maisano F, Testa L, Bedogni F, Buchanan L, Naganuma T, Sticchi A, Sato K, Miyazaki T, Figini F, Giannini F, Taramasso M, Naim C, Carlino M, Chieffo A, Montorfano M, Alfieri O, Colombo A. Comparison of results of transcatheter aortic valve implantation in patients with severely stenotic bicuspid versus tricuspid or nonbicuspid valves. *Am J Cardiol* 2014;113:1390–1393.
9. Hayashida K, Bouvier E, Lefevre T, Chevalier B, Hovasse T, Romano M, Garot P, Watanabe Y, Farge A, Donzeau-Gouge P, Cormier B, Morice MC. Transcatheter aortic valve implantation for patients with severe bicuspid aortic valve stenosis. *Circ Cardiovasc Interv* 2013;6:284–291.
10. Liu XB, Jiang JB, Zhou QJ, Pu ZX, He W, Dong AQ, Feng Y, Jiang J, Sun Y, Xiang MX, He YX, Fan YQ, Dong L, Wang JA. 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;16:208–214.
11. Yoon SH, Lefevre T, Ahn JM, Perlman GY, Dvir D, Latib A, Barbanti M, Deuschl F, De Backer O, Blanke P, Modine T, Pache G, Neumann FJ, Ruile P, Arai T, Ohno Y, Kaneko H, Tay E, Schofer N, Holy EW, Luk NH, Yong G, Lu Q, Kong WK, Hon J, Kao HL, Lee M, Yin WH, Park DW, Kang SJ, Lee SW, Kim YH, Lee CW, Park SW, Kim HS, Butter C, Khalique OK, Schaefer U, Nietlispach F, Kodali SK, Leon MB, Ye J, Chevalier B, Leipsic J, Delgado V, Bax JJ, Tamburino C, Colombo A, Sondergaard L, Webb JG, Park SJ. Transcatheter aortic valve replacement with early- and new-generation devices in bicuspid aortic valve stenosis. *J Am Coll Cardiol* 2016;68:1195–1205.
12. Perlman GY, Blanke P, Dvir D, Pache G, Modine T, Barbanti M, Holy EW, Treede H, Ruile P, Neumann FJ, Gandolfo C, Saia F, Tamburino C, Mak G, Thompson C, Wood D, Leipsic J, Webb JG. Bicuspid aortic valve stenosis: favorable early outcomes with a next-generation transcatheter heart valve in a multicenter study. *JACC Cardiovasc Interv* 2016;9:817–824.
13. Yoon SH, Bleiziffer S, De Backer O, Delgado V, Arai T, Ziegelmueller J, Barbanti M, Sharma R, Perlman GY, Khalique OK, Holy EW, Saraf S, Deuschl F, Fujita B, Ruile P, Neumann FJ, Pache G, Takahashi M, Kaneko H, Schmidt T, Ohno Y, Schofer N, Kong WK, Tay E, Sugiyama D, Kawamori H, Maeno Y, Abramowitz Y, Chakravarty T, Nakamura M, Kuwata S, Yong G, Kao HL, Lee M, Kim HS, Modine T, Wong SC, Bedgoni F, Testa L, Teiger E, Butter C, Ensminger SM, Schaefer U, Dvir D, Blanke P, Leipsic J, Nietlispach F, Abdel-Wahab M, Chevalier B, Tamburino C, Hildick-Smith D, Whisenant BK, Park SJ, Colombo A, Latib A, Kodali SK, Bax JJ, Sondergaard L, Webb JG, Lefevre T, Leon MB, Makkar R. Procedural and clinical outcomes in transcatheter aortic valve replacement for bicuspid versus tricuspid aortic valve stenosis. *J Am Coll Cardiol* 2017;69:2579–2589.
14. Sievers HH, Schmidtke C. A classification system for the bicuspid aortic valve from 304 surgical specimens. *J Thorac Cardiovasc Surg* 2007;133:1226–1233.
15. Kappetein AP, Head SJ, Genereux P, Piazza N, van Mieghem NM, Blackstone EH, Brott TG, Cohen DJ, Cutlip DE, van Es GA, Hahn RT, Kirtane AJ, Krucoff MW, Kodali S, Mack MJ, Mehran R, Rodes-Cabau J, Vranckx P, Webb JG, Windecker S, Serruys PW, Leon MB, Valve Academic Research Consortium (VARC)-2. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document (VARC-2). *Eur J Cardiothorac Surg* 2012;42:S45–S60.
16. Sannino A, Stoler RC, Lima B, Szerlip M, Henry AC, Vallabhan R, Kowal RC, Brown DL, Mack MJ, Grayburn PA. Frequency of and prognostic significance of atrial fibrillation in patients undergoing transcatheter aortic valve implantation. *Am J Cardiol* 2016;118:1527–1532.
17. Sannino A, Losi MA, Giugliano G, Canciello G, Toscano E, Giamundo A, Scudiero F, Brevetti L, Scudiero L, Prastaro M, Perrino C, Perrone-Filardi P, Galderisi M, Trimarco B, Esposito G. Aortic and mitral calcification is marker of significant carotid and limb atherosclerosis in patients with first acute coronary syndrome. *Echocardiography* 2015;32:1771–1777.
18. Kochman J, Huczek Z, Scislo P, Dabrowski M, Chmielak Z, Szymanski P, Witkowski A, Parma R, Ochala A, Chodor P, Wilczek K, Reczuch KW, Kubler P, Rymuza B, Koltowski L, Scibisz A, Wilimski R, Grube E, Opolski G. Comparison of one- and 12-month outcomes of transcatheter aortic valve replacement in patients with severely stenotic bicuspid versus tricuspid aortic valves (results from a multicenter registry). *Am J Cardiol* 2014;114:757–762.
19. Ayad RF, Grayburn PA, Ko JM, Filardo G, Roberts WC. Accuracy of two-dimensional echocardiography in determining aortic valve structure in patients >50 years of age having aortic valve replacement for aortic stenosis. *Am J Cardiol* 2011;108:1589–1599.
20. Jilaihawi H, Chen M, Webb J, Himbert D, Ruiz CE, Rodes-Cabau J, Pache G, Colombo A, Nickenig G, Lee M, Tamburino C, Sievert H, Abramowitz Y, Tarantini G, Alqoofi F, Chakravarty T, Kashif M, Takahashi N, Kazuno Y, Maeno Y, Kawamori H, Chieffo A, Blanke P, Dvir D, Ribeiro HB, Feng Y, Zhao ZG, Sinning JM, Kliger C, Giustino G, Pajerski B, Imme S, Grube E, Leipsic J, Vahanian A, Michev I, Jelnin V, Latib A, Cheng W, Makkar R. A bicuspid aortic valve imaging classification for the TAVI era. *JACC Cardiovasc Imaging* 2016;9:1145–1158.