JAMA Cardiology | Original Investigation

Prognostic Implications of Raphe in Bicuspid Aortic Valve Anatomy

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IMPORTANCE Little is known about the association between bicuspid aortic valve (BAV) morphologic findings and the degree of valvular dysfunction, presence of aortopathy, and complications, including aortic valve surgery, aortic dissection, and all-cause mortality.

OBJECTIVE To investigate the association between BAV morphologic findings (raphe vs nonraphe) and the degree of valve dysfunction, presence of aortopathy, and prognosis (including need for aortic valve surgery, aortic dissection, and all-cause mortality).

DESIGN, SETTING, AND PARTICIPANTS In this large international multicenter registry of patients with BAV treated at tertiary referral centers, 2118 patients with BAV were evaluated. Patients referred for echocardiography from June 1, 1991, through November 31, 2015, were included in the study.

EXPOSURES Clinical and echocardiographic data were analyzed retrospectively. The morphologic BAV findings were categorized according to the Sievers and Schmidtke classification. Aortic valve function was divided into normal, regurgitation, or stenosis. Patterns of BAV aortopathy included the following: type 1, dilation of the ascending aorta and aortic root; type 2, isolated dilation of the ascending aorta; and type 3, isolated dilation of the sinus of Valsalva and/or sinotubular junction.

MAIN OUTCOMES AND MEASURES Association between the presence and location of raphe and the risk of significant (moderate and severe) aortic valve dysfunction and aortic dilation and/or dissection.

RESULTS Of the 2118 patients (mean [SD] age, 47 [18] years; 1525 [72.0%] male), 1881 (88.8%) had BAV with fusion raphe, whereas 237 (11.2%) had BAV without raphe. Bicuspid aortic valves with raphe had a significantly higher prevalence of valve dysfunction, with a significantly higher frequency of aortic regurgitation (622 [33.1%] vs 57 [24.1%], $P < .001$) and aortic stenosis (728 [38.7%] vs 51 [21.5%], $P < .001$). Furthermore, aortic valve replacement event rates were significantly higher among patients with BAV with raphe (364 [19.9%] at 1 year, 393 [21.4%] at 2 years, and 447 [24.4%] at 5 years) vs patients without raphe (30 [14.0%] at 1 year, 32 [15.0%] at 2 years, and 40 [18.0%] at 5 years) ($P = .02$). In addition, the all-cause mortality event rates were significantly higher among patients with BAV with raphe (77 [5.1%] at 1 year, 87 [6.2%] at 2 years, and 110 [9.5%] at 5 years) vs patients without raphe (2 [1.8%] at 1 year, 3 [3.0%] at 2 years, and 5 [4.4%] at 5 years) ($P = .03$). However, on multivariable analysis, the presence of raphe was not significantly associated with all-cause mortality.

CONCLUSIONS AND RELEVANCE In this large multicenter, international BAV registry, the presence of raphe was associated with a higher prevalence of significant aortic stenosis and regurgitation. The presence of raphe was also associated with increased rates of aortic valve and aortic surgery. Although patients with BAV and raphe had higher mortality rates than patients without, the presence of a raphe was not independently associated with increased all-cause mortality.

JAMA Cardiol. 2017;2(3):285-292. doi:10.1001/jamacardio.2016.5228
Published online January 4, 2017.

Supplemental content

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Bicuspid aortic valve (BAV) encompasses a broad spectrum of diseases that present most frequently in isolation but are also associated with several congenital, aortic, and genetic disorders.[1] The morphologic findings of BAV are also variable and have been classified according to the number of cusps, commissures, and raphes.[1,2] The clinical implications of each BAV configuration remain controversial, and although some studies[3,4] in adult cohorts have suggested the association between specific BAV phenotypes with aortic stenosis (right and noncoronary cusp fusion) or regurgitation (left and right coronary cusp fusion), to our knowledge, these findings have not been found in other studies. Furthermore, it remains elusive whether the presence of a raphe determines an early degeneration and dysfunction of the aortic valve, leading to earlier aortic valve surgery and higher risk of aortic dilation and dissection compared with BAV without raphe. Accordingly, the present study evaluated whether the presence and location of raphe would be associated with increased risk of significant (moderate and severe) aortic valve dysfunction and aortic dilation and/or dissection in a large multicenter registry. In addition, the prognostic implications of the presence of raphe in terms of aortic valve surgery and all-cause mortality were investigated.

Key Points

Question Is there any association between bicuspid aortic valve morphologic findings (with or without raphe) and degree of valve dysfunction, presence of aortopathy, and prognosis (including need for aortic valve surgery and all-cause mortality)?

Findings In this large international registry of 2118 patients with bicuspid aortic valves, the presence of raphe was associated with a higher prevalence of significant aortic stenosis and regurgitation and increased rates of aortic valve and aorta surgery. Although patients with bicuspid aortic valve and raphe had higher mortality rates than patients without raphe, the presence of raphe was not independently associated with increased all-cause mortality.

Meaning The presence of raphe in bicuspid aortic valve is associated with a higher prevalence of significant valvular dysfunction and increased rates of aortic valve surgery.

Methods

Patient Population

Patients with BAV were included in this large international, multicenter registry. Patients referred for echocardiography from June 1, 1991, through November 31, 2015, were included in the study. Five centers were involved. The distribution of patients across the centers was as follows: Leiden, the Netherlands, 789 patients (37.3%); Singapore, 625 (29.5%); Brisbane, Australia, 508 (24.0%); Edmonton, Alberta, Canada, 98 (4.6%); and Bucharest, Romania, 98 (4.6%). Baseline demographics and cardiovascular risk factors were collected from medical records at the time of transthoracic echocardiography. Demographic data included age, sex, height, weight, and body surface area according to the Mosteller method.[5] Clinical data included cardiovascular risk factors (hypertension, dyslipidemia, diabetes, and smoking history).[6-8] Analysis of aortic valve morphologic findings and function as well as aortic dimensions was performed at the first echocardiogram diagnosing BAV, or in case of inadequate image to define the valve anatomy, the diagnosis was based on first cardiac magnetic resonance imaging or computed tomography. Patients were excluded if they had previous aortic valve surgery. Data were collected in accordance with regulations approved by institutional review boards of each research center and retrospectively analyzed (Commissie Medische Ethiek LUMC, Leiden; National Healthcare Group Domain Specific Review Board, Singapore; Research Ethics Board from University of Alberta, Edmonton; and Hospital and Health Boards of the Princess Alexandra Hospital, Brisbane). Because of the retrospective nature of the study, ethics committees of participating centers waived the need for written informed consent. All data were deidentified.

Echocardiography

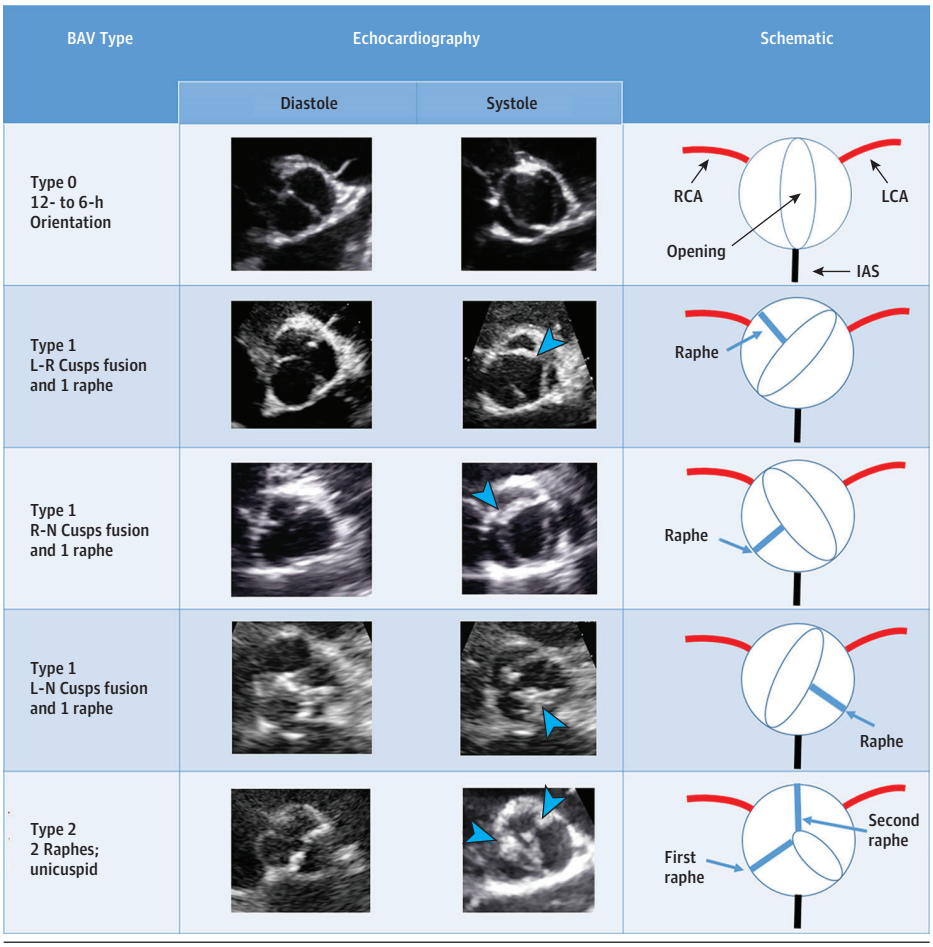
All echocardiographic studies were performed using commercially available ultrasound systems with standard views from the parasternal, apical, subcostal, and suprasternal windows to visualize the aortic valve. Images were retrospectively analyzed by experienced investigators in each center. The first transthoracic echocardiographic study with the diagnosis of BAV was considered as the index study for this analysis. Bicuspid aortic valve was defined by the presence of 2 commissures in systole delimiting 2 aortic valve leaflets in the parasternal short-axis view (**Figure 1**).[2] The presence of a raphe, defined as the conjoined area of the 2 underdeveloped leaflets turning into a malformed commissure between both leaflets, was noted.[2] In addition, the function of the aortic valve was recorded as normal function, stenosis, and regurgitation. Aortic stenosis and aortic regurgitation were graded as none, mild, moderate, and severe based on current recommendations.[10,11]

The diameters of various segments of the aortic root (sinus of Valsalva and sinotubular junction) and ascending aorta were measured on 2-dimensional echocardiography from leading edge to leading edge in the parasternal long-axis view perpendicular to the centerline of the aorta in end diastole.[12] The presence and severity of aortic root dilation were based on the nomogram by Roman et al,[13] whereas aortopathy was defined by an ascending aorta diameter of 40 mm or larger. Aortic dilation configurations were grouped according to currently proposed classification: type 1, dilation of the ascending aorta and aortic root; type 2, isolated dilation of the ascending aorta; and type 3, isolated dilation of the sinus of Valsalva and/or sinotubular junction.[14] Left ventricular ejection fraction (LVEF) was calculated using the biplane method.[12]

Follow-up

The occurrence of surgical aortic valve repair or replacement and/or aortic replacement was recorded during follow-up. Indications for aortic valve surgery were based on contemporary guidelines.[9,15,16] Patients with symptomatic severe aortic valve dysfunction (stenosis or regurgitation) or asymptomatic severe aortic valve dysfunction but with signs of left

Figure 1. Schematic Overview of Bicuspid Aortic Valve (BAV) Morphologic Findings and 2-Dimensional Echocardiographic Views of BAV



Aortic valves are visualized from the short-axis views from a left ventricular view. Blue bands and arrows represent the raphe (commissural fusion). Type 0 denotes BAV with 2 cusps and 2 commissures but no raphe; type 1, BAV with 1 fusion raphe; and type 2, BAV with 2 fusion raphes. Based on Sievers and Schmidtke classification.[9] IAS indicates interatrial septum; LCA, left coronary artery; L-N, left and noncoronary; L-R, left and right; RCA, right coronary artery; and R-N, right and noncoronary. Blue arrowheads in the echocardiographic images indicate the position of the raphe.

ventricular systolic dysfunction (LVEF ≤50%) were referred for aortic valve surgery. Regardless of the grade of aortic valve dysfunction, patients with aortic dilation of 50 mm or greater or 45 mm or greater in patients with Marfan syndrome and associated risk factors were referred for aortic surgery. In addition, all-cause mortality was recorded. Follow-up started from the date of the first echocardiogram diagnosing BAV, and censoring was applied at the time of all-cause mortality or aortic valve replacement.

Statistical Analysis

Continuous variables are expressed as mean (SD) after assessment of a normal distribution and categorical variables as number (percentage). The unpaired 2-tailed *t* test was used to compare continuous variables between the groups and the χ^2 test for the comparison of categorical variables. The independent association between the presence of a raphe and significant aortic valve dysfunction (defined as moderate and severe stenosis or regurgitation) was evaluated using binary logistic regression analysis introducing significant aortic stenosis and aortic regurgitation as dependent variables and age, sex, and cardiovascular risk factors as independent variables. Furthermore, the association between the location of a raphe and the type of valve dysfunction (stenosis or regurgitation), aortic dilation, and aortic dissection was assessed using the χ^2 test. Event-free survival curves were generated using the Kaplan-Meier method, and differences between groups (raphe vs nonraphe) were analyzed using the log-rank test. The independent association between the presence of a raphe and all-cause mortality was investigated with Cox proportional hazards regression models correcting for demographic, clinical, and echocardiographic variables. A 2-sided $P < .05$ was considered to indicate statistical significance. SPSS statistical software, version 20.0 (IBM Corp), was used for statistical analysis.

Results

Patient Population

Of 2118 patients with BAV (mean [SD] age, 47 [18] years; 1525 male [72.0%]), 1881 (88.8%) had fusion raphe, whereas the remaining 237 (11.2%) had BAV morphologic findings without raphe. The most frequent form was the presence of a raphe between the left and right coronary cusp in 1435 (76.3%) followed by the right and noncoronary cusp configuration in 343 (18.2%).

Table 1. Baseline and Echocardiographic Characteristics of Patients With BAV (With or Without Raphe)[a]

Characteristic	With Raphe (n = 1881)	Without Raphe (n = 237)	*P* Value
Age, mean (SD), y	47.8 (17.8)	39.7 (17.3)	<.001
Male	1362 (72.4)	163 (68.8)	.25
Body surface area, mean (SD), m^2	1.9 (0.3)	1.9 (0.2)	.66
Height, mean (SD), cm	171.5 (10.9)	172.4 (11.5)	.25
Weight, mean (SD), kg	75.7 (17.9)	75.2 (18.6)	.67
Hypertension	647 (35.9)	58 (26.9)	.008
Dyslipidemia	522 (27.8)	46 (19.4)	.006
Diabetes	213 (11.3)	11 (4.6)	.001
Smoking	291 (15.6)	44 (18.6)	.27
Aortic stenosis			
None	808 (43.7)	136 (58.1)	<.001
Mild	312 (16.9)	47 (20.1)	
Moderate	340 (18.4)	23 (9.8)	
Severe	388 (21.0)	28 (12.0)	
Aortic regurgitation			
None	701 (37.3)	122 (51.5)	<.001
Mild	557 (29.6)	58 (24.5)	
Moderate	391 (20.8)	33 (13.9)	
Severe	231 (12.3)	24 (10.1)	
Normal aortic valve function	250 (13.3)	69 (29.1)	<.001
Diameter, mean (SD), mm			
SOV	34.8 (6.2)	34.2 (7.3)	.20
STJ	29.6 (6.3)	29.7 (6.6)	.86
AA	36.8 (7.4)	36.2 (7.5)	.23
BAV aortopathy			
Normal	1204 (64.0)	155 (65.4)	.39
Type 1	261 (13.9)	34 (14.3)	
Type 2	190 (10.1)	28 (11.8)	
Type 3	226 (12.0)	20 (8.4)	
LVEF, mean (SD), %	60.7 (11.9)	60.6 (11.7)	.84

Abbreviations: AA, ascending aorta; BAV, bicuspid aortic valve; LVEF, left ventricular ejection fraction; SOV, sinus of Valsalva; STJ, sinotubular junction.

[a] Data are presented as number (percentage) of patients unless otherwise indicated.

Table 2. Univariable and Multivariable Regression Analyses to Evaluate the Association Between Raphe and Valve Dysfunction

	Significant Aortic Stenosis				Significant Aortic Regurgitation			
	Univariable		Multivariable		Univariable		Multivariable	
Characteristic	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value
Age	1.04 (1.03-1.04)	<.001	1.04 (1.03-1.04)	<.001	0.99 (0.98-0.99)	<.001	0.99 (0.98-0.99)	<.001
Male	0.63 (0.52-0.77)	<.001	0.62 (0.49-0.77)	<.001	1.74 (1.40-2.16)	<.001	1.57 (1.25-1.98)	<.001
Hypertension	1.60 (1.32-1.93)	<.001	0.93 (0.74-1.17)	.54	0.72 (0.58-0.88)	.001	0.95 (0.75-1.20)	.66
Dyslipidemia	1.85 (1.52-2.25)	<.001	1.10 (0.87-1.39)	.44	0.61 (0.49-0.75)	<.001	0.76 (0.59-0.98)	.04
Diabetes	2.35 (1.78-3.12)	<.001	1.45 (1.05-1.99)	.02	0.43 (0.30-0.61)	<.001	0.54 (0.36-0.79)	.002
Aortopathy	0.83 (0.69-0.99)	.049	0.62 (0.50-.77)	<.001	1.81 (1.50-2.18)	<.001	2.10 (1.70-2.60)	<.001
Presence of a raphe	2.33 (1.69-3.23)	<.001	1.88 (1.32-2.68)	<.001	1.56 (1.14-2.13)	.005	1.78 (1.28-2.50)	.001

Abbreviation: HR, hazard ratio.

Differences Between Patients With BAV With vs Without Raphe

Table 1 outlines the demographic, clinical, and echocardiographic characteristics of patients with BAV with vs without raphe. Patients without raphe had their conditions diagnosed at a younger age compared with patients with raphe (mean [SD], 39.7 [17.3] vs 47.8 [17.8] years; $P < .001$). Normal functioning aortic valves were more common in the patients with BAV without raphe (69 [29.1%] vs 250 [13.3%], $P < .001$). In terms of aortic valve dysfunction, patients with BAV with raphe presented more frequently with significant aortic regurgitation (622 [33.1%] vs 57 [24.1%], $P < .001$) and significant aortic stenosis (728 [38.7%] vs 51 [21.5%], $P < .001$) than patients with BAV without raphe. The differences in sinus of Valsalva, sinotubular junction, and ascending aorta diameters were not statistically significant

between patients with BAV with raphe and patients with BAV without raphe (Table 1).

Association Between Raphe and Significant Valve Dysfunction

Significant aortic stenosis (moderate and severe) was present in 779 patients (728 patients with raphe and 51 patients without raphe). At multivariable analysis, older age, female sex, diabetes, aortopathy, and presence of raphe remained independently associated with significant aortic stenosis (**Table 2**).

Moderate and severe aortic regurgitation was diagnosed in 679 patients (622 patients with raphe and 57 without raphe). On multivariable analysis, age, male sex, dyslipidemia, diabetes, aortopathy, and presence of raphe remained independently associated with significant aortic regurgitation (Table 2).

When assessing the association between the location of the raphe and the type of significant valve dysfunction, the frequency of significant aortic stenosis was significantly higher among patients with BAV with 2 raphes (11 patients [100%]) followed by patients with right and noncoronary cusp fusion (154 patients [45.0%]) (**Figure 2**). The frequency of significant aortic regurgitation was slightly higher among patients with BAV with 2 raphes (4 patients [36.4%]) but evenly distributed among patients with BAV with 1 raphe (regardless of the location) (Figure 2).

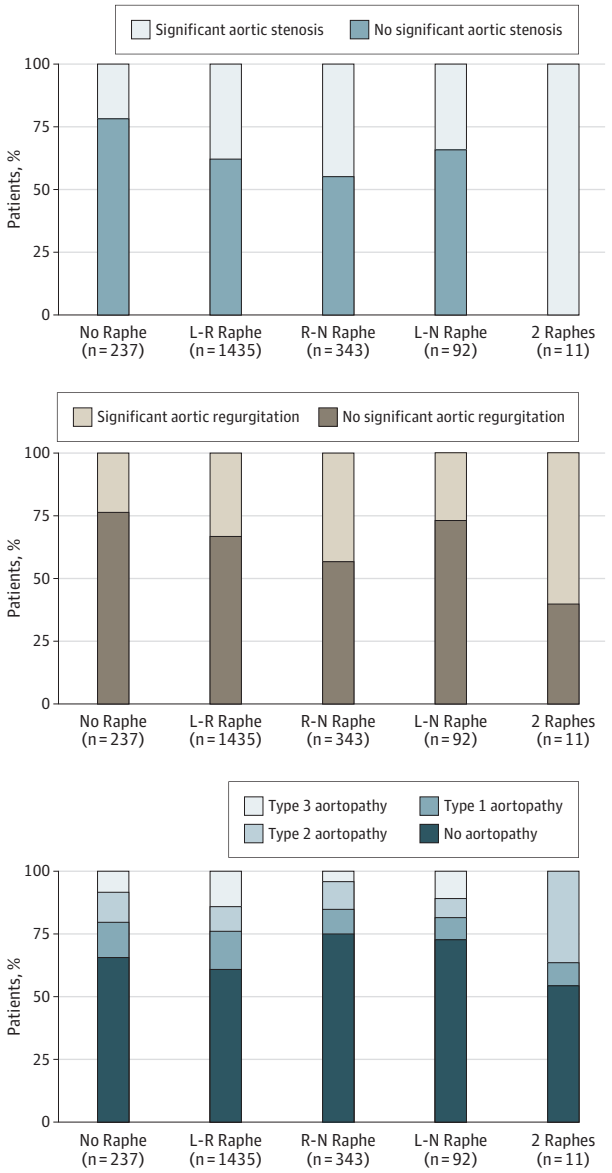
Association Between Raphe and Aortic Dilation and Dissection

Aortic dilation was observed in 759 patients (35.8%). The most frequent pattern of aortic dilation was type 1 aortopathy (295 patients [38.9%]) followed by type 3 (246 patients [32.4%]) and type 2 (218 patients [28.7%]). The presence of a raphe was not associated with the pattern of aortic dilation (Table 1). The distribution of types of aortopathy and type of BAV is presented in Figure 2. All configurations of aortic dilation were more prevalent among patients with BAV and raphe fusion between the left and right coronary cusp (Figure 2). However, isolated dilation of the ascending aorta or dilation of the root and ascending aorta were more frequent in patients with BAV without raphe (Figure 2). Patients with aortic dissections most often had fusion raphe between the left and right coronary cusps (5 patients [62.5%]), followed by fusion raphe between the right and the noncoronary cusps (2 patients [25.0%]) and no raphe (1 patient [12.5%]).

Long-term Outcomes in Patients With BAV With vs Without Raphe

The total follow-up time for the entire study sample was 7169 patient-years. Median follow-up duration was 2 years (interquartile range, 0-6 years). During the follow-up, 591 patients underwent aortic valve repair or replacement, and surgical aortic replacement was performed in 307 patients. The aortic valve replacement event rates were significantly higher among patients with BAV with raphe (364 [19.9%] at 1 year, 393 [21.4%] at 2 years, and 447 [24.4%] at 5 years) vs patients without raphe (30 [14.0%] at 1 year, 32 [15.0%] at 2 years, and 40 [18.0%] at 5 years) (P = .02) (**Figure 3**).

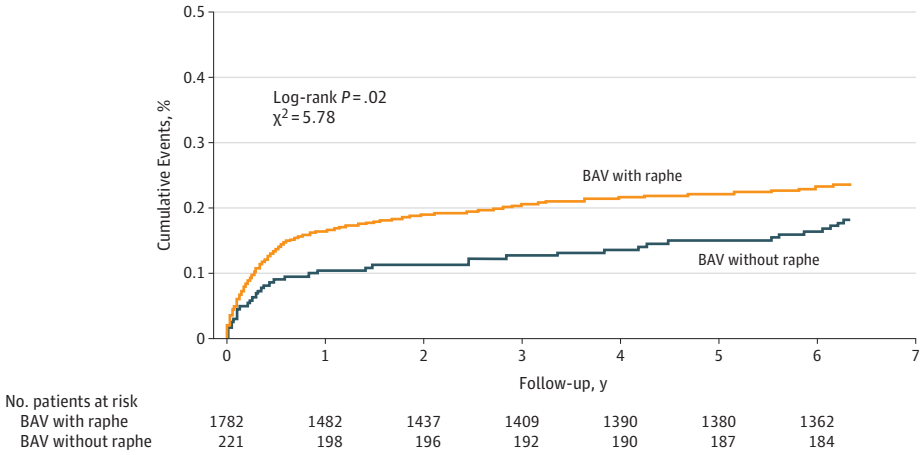
Figure 2. Association Between Location of the Raphe and Significant Valve Dysfunction and Aortic Dilation Pattern



L-N indicates left and noncoronary; L-R, left and right; and R-N, right and noncoronary.

During a median follow-up of 2 years, 144 patients died. The clinical status (alive or dead) was not available for 15 patients (0.7%). The number of outcomes is presented in eTable 1 of the Supplement. The all-cause mortality event rates at 1, 2, and 5 years of follow-up were significantly higher among patients with BAV with raphe (77 [5.1%] at 1 year, 87 [6.2%] at 2 years, and 110 [9.5%] at 5 years) vs patients without raphe (2 [1.8%], 3 [3.0%], and 5 [4.4%]) (P = .03) (eTable 1 in the Supplement). Univariable and multivariable Cox proportional hazards regression analyses were performed to investigate the association between the presence of a raphe and survival (eTable 2 in the Supplement). On univariable regression analysis, the

Figure 3. Cumulative Event Rates for Aortic Valve Repair or Replacement and/or Aorta Replacement in Patients With Bicuspid Aortic Valve (BAV) Divided According to the Presence of Raphe



No. patients at risk							
BAV with raphe	1782	1482	1437	1409	1390	1380	1362
BAV without raphe	221	198	196	192	190	187	184

presence of a raphe was significantly associated with increased risk of all-cause mortality (hazard ratio, 2.11; 95% CI, 1.03-4.30; *P* = .04). On multivariable analysis, age, diabetes and LVEF were independently associated with all-cause mortality, whereas the presence of a raphe was not associated with all-cause mortality, suggesting that the prognosis of patients with BAV is determined by factors that also affect the prognosis of the general population.

Discussion

This large multicenter, international BAV registry found that the presence of a raphe is the most frequent phenotype of BAV, particularly with fusion of the left and right coronary cusps, and is associated with increased risk of significant aortic valve dysfunction (stenosis and regurgitation). Although patients with BAV with raphe had more frequent aortic dilation, the presence of a raphe was not associated with the pattern of aortic dilation. Furthermore, patients with BAV with raphe had higher rates of aortic valve replacement compared with patients without raphe. Presence of a raphe was associated with an increased risk of all-cause mortality. However, after correcting for age, diabetes, and LVEF, the presence of a raphe was not associated with increased risk of all-cause mortality.

Prevalence of BAV Phenotypes and Association With Valve Dysfunction

The morphologic BAV findings are diverse in terms of the number of raphes, spatial orientation of cusp fusion, and functional status of the valve.[2] Interest in the differences in BAV morphologic findings has increased gradually because of its association with valvulopathy and aortopathy. The presence of a raphe is common, and it has been described in almost 90% of patients with BAV.[17] Of 1362 patients with BAV undergoing cardiac surgery, 1078 (79.1%) had 1 raphe, involving the left and right coronary cusps most frequently, 169 (12.4%) had 2 raphes, and the remaining 115 patients did have 2 aortic cusps without raphe.[17] Similarly, the present multicenter registry of patients with BAV revealed a prevalence of BAV with raphe of 89%.

Clinically more relevant is the association of the presence of a raphe with the occurrence of aortic valve dysfunction. So far, few studies[4,17-19] have evaluated this question, and the results may be influenced by the type of patients included in the study. In the series by Sievers et al,[17] in which all patients underwent aortic valve surgery, a similar prevalence of aortic stenosis and aortic regurgitation was noted among patients with BAV with raphe (aortic stenosis, 44%; aortic regurgitation, 19%) and among patients without raphe (aortic stenosis, 56%; aortic regurgitation, 21%). In the present study, the prevalence of significant aortic stenosis and significant aortic regurgitation was significantly higher among patients with raphe compared with patients without raphe. Furthermore, the present study extends previous results by associating the location of the raphe (and configuration of the BAV) with the predominant valvular lesion. The presence of 2 raphes was associated with higher prevalence of significant aortic stenosis and regurgitation compared with the presence of 1 raphe; however, among patients with 1 raphe (the largest group), the fusion between the right and noncoronary cusps more frequently had significant aortic stenosis compared with the other configurations, whereas no association between the location of raphe and significant aortic regurgitation was observed. This finding is in contrast to the results reported by a smaller study[4] of a heterogeneous population of 255 patients with BAV that evaluated the association between completeness of the raphe and the prevalence of aortic valve dysfunction. Aortic regurgitation was more frequently observed among patients with fusion of the left and right coronary cusps and complete raphe compared with the remaining population (57% vs 42%, *P* = .02), whereas no differences were observed in the prevalence of aortic stenosis. The subdivision in smaller groups (type of BAV and complete vs incomplete raphe) may have accounted for the discrepant results.[4]

Association Between BAV Morphologic Findings (Raphe vs Nonraphe) and Aortopathy

Dilation of the thoracic aorta is frequently present in patients with BAV, leading to the concept of valvuloaortopathy.[1,20,21] Genetic and hemodynamic factors have been proposed as underlying mechanisms of aortopathy in patients with BAV.[20,22,23] On the basis of preoperative aortographies of 828 patients with BAV undergoing cardiac surgery, Sievers et al[24] found that isolated dilation of the tubular ascending aorta was the most frequent form of aortopathy and was particularly more frequent in stenotic BAV compared with regurgitant BAV. Stenotic type 2 BAV (2 raphes) (71%) followed by type 0 BAV (without raphe) (70%) and BAV with fusion between the left and the right coronary cusps (60%) were the most frequent BAV configurations associated with this type of aortic dilation. In contrast, isolated dilation of the aortic root was more frequently observed in patients with significant aortic regurgitation who had type 0 BAV (without raphe) (31%) followed by type 1 BAV with fusion between the right and the noncoronary cusps (24%) compared with other BAV phenotypes.[24] In young patients (age range, 4 months to 40 years) with BAV and aortic dilation, Ruzmetov and coworkers[25] found that the BAV with fusion between the right and noncoronary cusps (88%) was more frequently associated with dilation of the tubular ascending aorta compared with left and right coronary cusps' fusion (68%) (P = .004), whereas isolated dilation of the aortic root was more frequently observed in patients with left and right coronary cusps' fusion (46%) than patients with right and noncoronary cusps' fusion (20%) (P = .001). In the present study, which included a large number of patients with BAV, the presence of a raphe was not associated with higher prevalence of aortopathy compared with BAV without raphe.

Presence and Location of Raphe vs Outcome

To our knowledge, the association between the presence of raphe and its location in BAV disease and clinical outcomes has not been studied. The raphe of a BAV and higher tendency for calcium deposition are important causes of significant valve dysfunction.[26] Therefore, patients with BAV with raphe tend to develop significant valvular dysfunction at a younger age, predisposing them to higher cumulative event rates of aortic valve surgery and aortic surgery than those without raphe. Yotsumoto et al[19] found that patients with BAV with raphe were significantly younger than those without raphe at the time of surgery (mean [SD], 50 [15] vs 57 [11 years]; P = .02). This was also found in the present study, with patients with BAV with raphe having higher event rates for aortic valve surgery and aortic surgery compared with patients with BAV without raphe. The presence of a raphe was associated with increased all-cause mortality on univariate analysis but not on multivariable analysis, reflecting the fact that BAV is usually diagnosed at a young age and the risks associated with contemporary surgery are low. However, the present study included asymptomatic and symptomatic patients. Symptomatic patients may be referred relatively late for surgery, increasing the operative risk, which may result in higher mortality.

Limitations

Several study limitations should be acknowledged. First, the present study is retrospective, and although it concerns a large registry of patients with BAV, there may be a selection bias because the participating centers are all referral centers for cardiac surgery. Second, aortic dimensions were measured on transthoracic echocardiography, which is the imaging technique of first choice to evaluate the presence of aortopathy in these patients.[27] However, the reproducibility of this technique to measure certain segments of the aorta (aortic arch) is limited.[28] Most patients had normal aortic dimensions. Therefore, the study may be underpowered to assess the influence of type of BAV on the presence and type of aortopathy.

Conclusions

This large multicenter, collaborative BAV registry reveals that the presence or absence of raphe is of clinical and prognostic importance. Raphe was more frequently associated with significant valve dysfunction and aortic dilation. The location of the raphe influenced the type of valve dysfunction but was not associated with the type of aortic dilation. Finally, the presence of a raphe was associated with increased rates of aortic valve and aortic surgery or all-cause mortality. However, the presence of a raphe was not independently associated with all-cause mortality.

ARTICLE INFORMATION

Accepted for Publication: November 9, 2016.

Published Online: January 4, 2017. doi:10.1001/jamacardio.2016.5228

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Conflict of Interest Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.

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