

Original Article



Clinical Characteristics of Korean Patients with Bicuspid Aortic Valve Who Underwent Aortic Valve Surgery

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Received: Jun 12, 2017

Revised: Sep 13, 2017

Accepted: Sep 19, 2017

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ABSTRACT

Background and Objectives: Clinical data for Korean patients with bicuspid aortic valve (BAV) that underwent aortic valve (AV) surgery are currently limited.

Methods: Data for 1,160 consecutive adult BAV patients who underwent AV surgery from 2000 to 2014 in 4 tertiary referral centers were retrospectively analyzed. A standard case report form was used for clinical and echocardiographic parameters.


Results: Mean age at the time of AV surgery was 59±13 years. The most common cause of AV surgery was aortic stenosis (AS, 892 [77%]), followed by aortic regurgitation (AR, 199 [17%]), and infective endocarditis (69 [6%]). AS showed a skewed peak in the aged population and was the predominant cause of AV surgery (87%) in patients ≥50 years of age, whereas AR (46%) and active infective endocarditis (19%) were more common in younger patients (p<0.001). Echocardiographic determination of the BAV phenotype revealed that fusion of the right coronary cusp (RCC) and left coronary cusp (LCC) was most common (622 [53%]), followed by fusion of RCC and non-coronary cusp (NCC) (313 [27%]), and fusion of LCC and NCC (42 [4%]); the BAV phenotype could not be determined in the remaining 183 patients (16%). Fusion of RCC and LCC was more commonly observed in patients with AR than in those with AS (74% vs. 49%; p<0.001).

Conclusion: BAV patients were characterized by distinct surgical indications according to their age. Possible associations between BAV phenotypes and surgical indications with potential impacts of ethnicity need to be tested in further studies.


Keywords: Bicuspid aortic valve; Heart valve diseases; Phenotype; Cardiac surgical procedures

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Funding

This work was supported in part by the Korean Society of Cardiology (grant number 201303-5, 2013) and the KoBAV Research Group of the Korean Society of Echocardiography.

Conflict of Interest

The authors have no financial conflicts of interest.

Author Contributions

Conceptualization: Song JK; Data curation: Jin X, Lee S, Lee JH, Park JB, Lee SP, Kim DH, Park SJ, Kim YJ, Cho GY, Song JM, Kang DH, Sohn DW; Formal analysis: Sun BJ, Jin X; Funding acquisition: Song JK; Writing - original draft: Sun BJ, Jin X; Writing - review & editing: Sun BJ, Song JK.

INTRODUCTION

Bicuspid aortic valve (BAV) is one of the most common congenital cardiac anomalies that affects 1–2% of the global population.^{1,2)} BAV is defined as the morphological features of an aortic valve (AV) with “two cusps”, and is associated with a variety of clinical manifestations that include hemodynamic alteration, premature valvular failure, aortic pathologies such as aneurysm or dissection, and association with other complex congenital disorders.^{3–5)} Little is known about the genetic components of BAV, as they range from single nucleotide polymorphisms to complex mutations, such as Notch homolog 1, translocation-associated (NOTCH1).⁶⁾ Several clinical studies on overall survival, incidence of adverse cardiac events, and aortic complications have been published recently.^{7–9)} Nevertheless, the current volume of evidence is insufficient, considering the many unanswered questions and clinical needs. A leading BAV research group recently suggested that current knowledge gaps need to be more clearly defined.¹⁰⁾

To-date, most large-sized clinical studies are from western countries;^{7–9)} therefore, the possibility that ethnicity can be a potential disease modifier in BAV¹¹⁾ needs to be examined. Specifically, there is a need for large-scale clinical evidence for Asian subjects. The Korean Bicuspid Aortic Valve (KoBAV) registry was launched in 2014 with 2 study arms. The prospective arm was designed to construct a cohort of newly diagnosed BAV patients for observation of long-term clinical consequences, and the retrospective arm included patients with full-blown BAV disease, with particular focus on their clinical presentations and morphological features. In the present report, we describe a large-sized patient group with BAV in Korea in terms of clinical features, patterns of practice, and morphological phenotypes.

METHODS

Study outline

At a preliminary meeting of nationwide KoBAV researchers in April 2014, we proposed the outline of the present study. The enrollment criteria were: 1) adult patients aged ≥ 19 , 2) AV surgery during 2000–2014, and 3) BAV confirmed in an operative or pathology report. We shared a standard case record form in which all the clinical and echocardiographic parameters were predefined. The definition of terminology, criteria for defining groups and protocols for image reviewing were fully explained before data collection. Finally, 4 tertiary referral centers (anonymized as center A to D) collaborated to construct a clinical and echocardiographic database of 1,160 patients (739 from center A, 223 from center B, 81 from center C, and 117 from center D; **Figure 1**). The study protocol was approved by the ethics committee of each center, and informed consent was waived due to the retrospective nature of the study.

Clinical parameters

The baseline clinical and echocardiographic data immediately before surgery (median interval of 7 days; interquartile range, 3–22) were obtained. All patients were categorized by dominant valvular pathologies for corrective surgery, which included aortic stenosis (AS, group I), aortic regurgitation (AR, group II), and active infective endocarditis (group III). Endocarditis was considered to be a prior criterion, regardless of dominant valvular dysfunction type, in patients that presented with typical clinical features of infective endocarditis. In other patients without infective endocarditis, more dominant moderate to

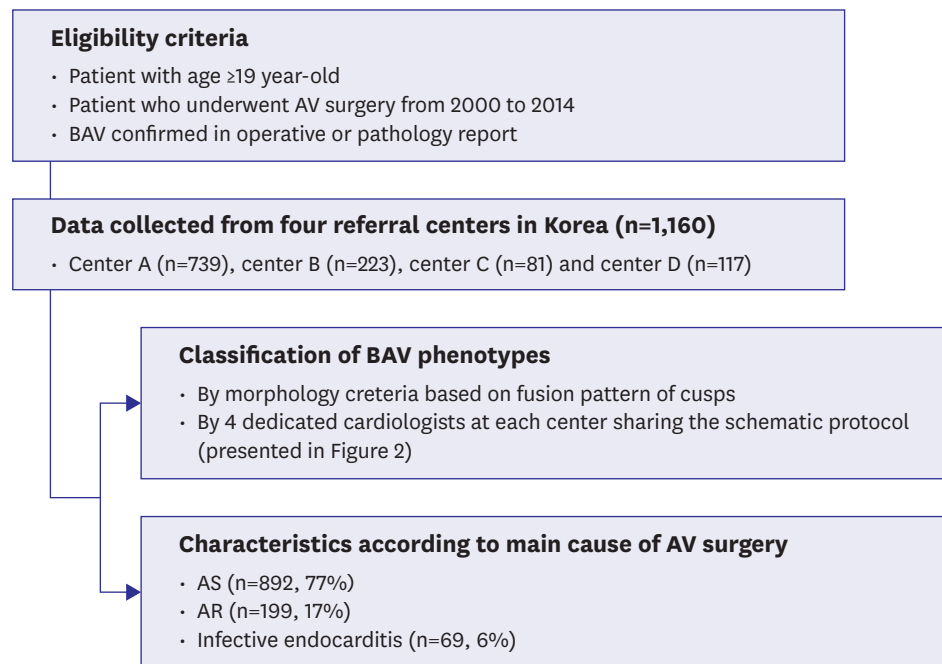


Figure 1. Study outline for subject enrollment and analysis.

AR = aortic regurgitation; AS = aortic stenosis; AV = aortic valve; BAV = bicuspid aortic valve.

severe valvular dysfunction was selected as an underlying valvular lesion for AV surgery. In rare cases with moderate to severe AS and AR, priority was given to AS. Demonstration of a ‘typical double channel aorta with both the true and false lumen’ on echocardiography or computed tomography (CT), which was confirmed during surgery, was required to define aortic dissection. Echocardiographic or CT demonstration of abnormal tissue thickening or cyst-like structures around the infected AV, which was confirmed during surgery, was used to define abscess. Aortic diameter greater than 45 mm on any imaging study was used as the definition of an aneurysm.⁹⁾

BAV phenotype classification

We reviewed articles that discussed BAV phenotypes,¹²⁾¹³⁾ and categorized BAVs using morphological criteria based on cusp fusion patterns. One dedicated cardiologist was responsible for classifying the BAV phenotypes at each center, using the common protocol (Figure 2). The examiner reviewed all echocardiographic images, including a transesophageal study that assessed 561 patients (48%). The practical steps for phenotype classification were

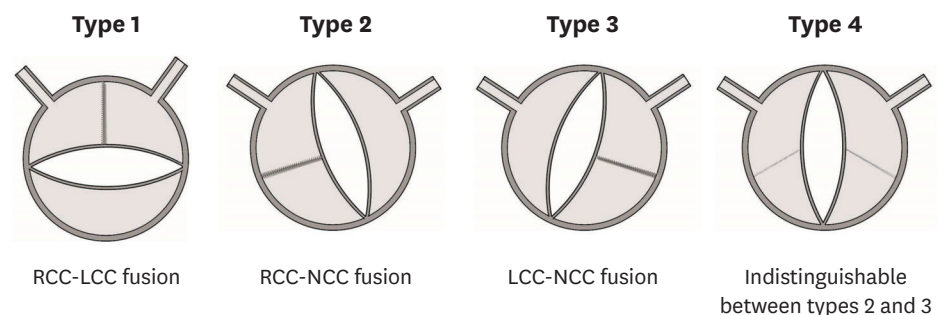


Figure 2. Morphological criteria for BAV phenotype classification.

BAV = bicuspid aortic valve; LCC = left coronary cusp; NCC = non-coronary cusp; RCC = right coronary cusp.

also shared: 1) Define right coronary cusp (RCC) or left coronary cusp (LCC) as a reference on short axis image, considering the relationship with the coronary ostium and adjacent structures, such as right and left atria, right ventricular outflow tract and main pulmonary artery; 2) estimate other cusps based on the spatial relationship to the reference cusp, and because of possible image deviation, this was not based on apparent directions; and 3) determine the cusp fusion pattern by examining the conjoined motion during opening. Finally, the BAV morphological phenotypes were classified into 4 types: type 1, fusion between RCC and LCC; type 2, fusion between RCC and non-coronary cusp (NCC); type 3, fusion between LCC and NCC. We defined type 4 as those that were difficult to discriminate between type 2 or 3, while type 1 was clearly rejected due to the separation between RCC and LCC.

Data analysis

We presented categorical variables as numbers with percentages and continuous variables as mean±standard deviation. For comparison among the three groups, we used a χ^2 test and 1-way analysis of variance (ANOVA) with the Bonferroni correction for categorical and continuous variables. All reported p values were 2-tailed and a p value of <0.05 was considered statistically significant. SPSS software, version 22 (SPSS Inc., Chicago, IL, USA) was used for statistical analyses.

RESULTS

Baseline characteristics

The baseline clinical and echocardiographic characteristics are presented in **Table 1**. The mean age was 59±13 years and 763 patients (66%) were male. Prevalence of hypertension, diabetes and atrial fibrillation were 37%, 13%, and 8%, respectively. About 65% of patients presented with dyspnea of New York Heart Association (NYHA) functional class ≥2. Evaluation of echocardiographic parameters demonstrated that the mean left ventricular

Table 1. Baseline clinical and echocardiographic characteristics

Variables	Total patients (n=1,160)
Age (years)	59±13
Male gender	763 (66)
Body surface area (m ²)	1.69±0.18
Hypertension	429 (37)
Diabetes	145 (13)
Coronary artery disease	162 (14)
Smoking	500 (43)
Atrial fibrillation	92 (8)
NYHA class	
0	234 (20)
1	178 (15)
2	568 (49)
3	161 (14)
4	19 (2)
LV mass index (g/m ²)	171±63
LV ejection fraction (%)	57±12
Transesophageal echocardiography	561 (48)
Dominant lesion for surgery	
AS	892 (77)
AR	199 (17)
Infective endocarditis	69 (6)

Values are presented as mean±standard deviation or number of patients (%).

AR = aortic regurgitation; AS = aortic stenosis; LV = left ventricle; NYHA = New York Heart Association.

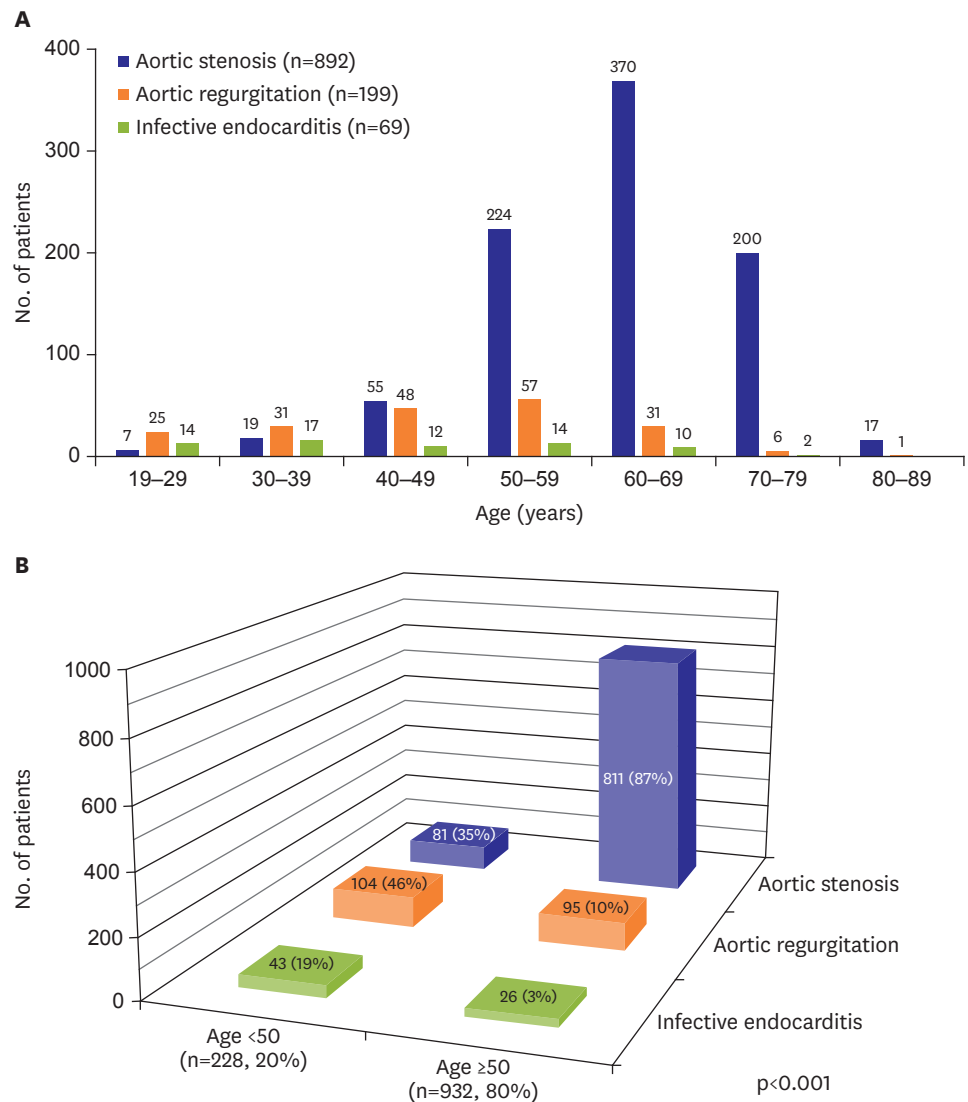


Figure 3. Dominant valvular lesion for AV surgery according to the age groups by decades (A) and cut-off value of 50 years (B).

AR = aortic regurgitation; AS = aortic stenosis; AV = aortic valve.

*Comparison between groups by age cut-off of 50 years.

(LV) mass index was increased to 171 ± 63 g/m² with LV ejection fraction being preserved at $57 \pm 12\%$. The most common valvular pathology for surgery (number of patients [%]) was AS (892 [77%]), followed by AR (199 [17%]) and infective endocarditis (69 [6%]). **Figure 3** shows the relationship between age and the dominant valvular lesion for AV surgery in patients with BAV. AS showed a skewed peak in the aged population and infective endocarditis occurred more frequently in young patients. AR showed a relatively symmetric distribution with a smooth peak in middle-aged patients (**Figure 3A**). AS was the predominant valvular lesion (87%) in patients aged ≥ 50 , whereas AR (46%) was predominant in those aged < 50 years ($p < 0.001$, **Figure 3B**).

Clinical features based on main valvular pathology

Table 2 shows clinical and surgical characteristics of patient groups, according to dominant valvular pathology. Group I (AS) was characterized by a higher mean age with higher

Table 2. Characteristics according to primary cause of AV surgery

Variables	AS (group I)	AR (group II)	Infective endocarditis (group III)	p value*
Number of patients	892 (77)	199 (17)	69 (6)	-
Age (years)	62±10 [†]	47±14	44±15	<0.001
Male gender	531 (60) [†]	173 (87)	59 (86)	<0.001
Hypertension	352 (40)	65 (33)	12 (17)	<0.001
Diabetes	133 (15) [†]	6 (3)	6 (9)	<0.001
Coronary artery disease	142 (16) [†]	16 (8)	4 (6)	0.002
LV mass index (g/m ²)	160±56 [†]	217±72	180±65	<0.001
LV ejection fraction (%)	58±12 [†]	52±10	57±9	<0.001
LV diastolic diameter (mm)	51±7 [†]	69±9	62±10	<0.001
LV systolic diameter (mm)	33±9 [†]	48±10	40±9	<0.001
Aortic diameters (mm)				
LV outflow tract	22±2 [†]	26±4	24±3	<0.001
Valsalva sinus	33±5 [†]	40±8	36±5	<0.001
Sinotubular junction	30±5 [†]	34±7	30±5	<0.001
Ascending aorta	42±7	42±8	39±7	0.018
Types of AV surgery				<0.001
Replacement	879 (99) [†]	160 (80)	66 (96)	
Valvuloplasty	13 (1) [†]	39 (20)	3 (4)	
Types of prosthetic valve				<0.001
Mechanical valve	550 (63) [†]	138 (86)	57 (86)	
Tissue valve	329 (37) [†]	20 (14)	9 (14)	
Prosthetic valve size (mm)	22±2 [†]	25±3	24±2	<0.001
Coronary artery bypass	103 (12) [†]	5 (3)	3 (4)	<0.001
Combined aortic surgery	383 (43)	86 (43)	19 (28)	0.042
Cause of aortic surgery				<0.001
Aortic dissection	6 (2)	1 (1)	0 (0)	
Aortic aneurysm	377 (98)	83 (97)	2 (11)	
Aortic root abscess	0 (0)	0 (0)	17 (89)	
Coarctation of aorta	0 (0)	2 (2)	0 (0)	

Values are presented as mean±standard deviation or number of patients (%).

AR = aortic regurgitation; AS = aortic stenosis; AV = aortic valve; LV = left ventricle.

*p value among 3 groups; [†]Significant difference presented between groups with aortic stenosis and regurgitation.

prevalence of hypertension, diabetes, and coronary artery disease. Almost all of these patients (879 [99%]) underwent AV replacement with relatively frequent use of tissue valve (329 [37%]). The proportion of combined aortic surgery in group I (383 [43%]) was similar to that of group II (86 [43%]). Aortic aneurysm was the most common cause of aortic surgery, and aortic dissection was rarely observed in either group I (6 [2%]) or group II (1 [1%]). Group II was characterized by younger age (47±14 years) and a higher proportion of males (173 [87%]) compared to group I. Group II also presented with more cases of increased LV mass and cavity size, as well as more dilated aortic root at the Valsalva sinus and sinotubular junction levels. Thirty-nine (20%) patients in group II underwent AV repair, which was significantly more frequent than in group I (13 [1%]). Only 2 patients (2%) in group II presented with coarctation of aorta, while this was not observed in other groups. Patients in group III with infective endocarditis were younger on average (44±15 years). Although 54 patients (78%) in this group had moderate or severe AR, only 3 patients (4%) were feasible candidates for AV repair. Aortic root abscess (17 [89%]) was the main pathology in 19 cases (28%) with combined aortic surgery in group III.

BAV morphological phenotypes

Figure 4 shows the distribution of BAV morphological phenotypes overall and at individual centers. Type 1 was the most frequent (622 [53%]), followed by type 2 (313 [27%]), type 4 (183 [16%]) and type 3 (42 [4%]). This trend was similar in each center but significant variability in proportions was observed by center (p<0.001). The most frequent phenotype was type 1

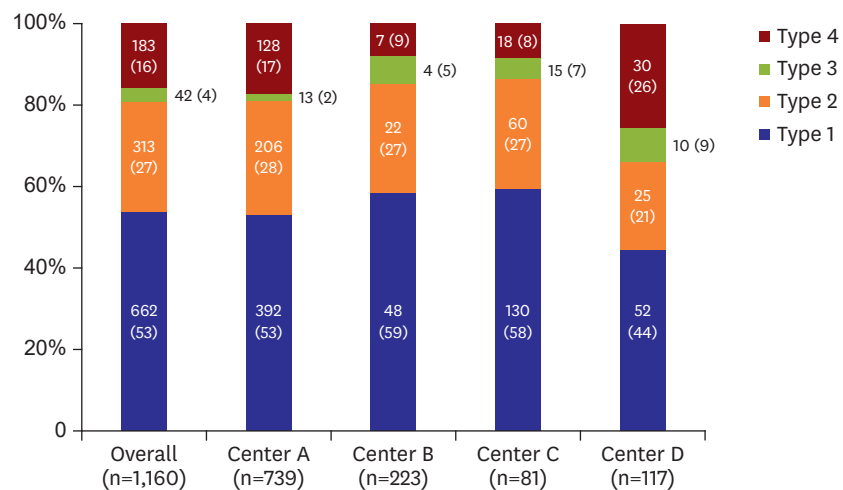


Figure 4. BAV phenotypes in overall and individual centers. BAV morphological phenotypes were classified into 4 type: type 1, RCC-LCC fusion; type 2, RCC-NCC fusion; type 3, LCC-NCC fusion; and type 4, indistinguishable between type 2 and 3.

BAV = bicuspid aortic valve; LCC = left coronary cusp; NCC = non-coronary cusp; RCC = right coronary cusp.

which ranged from 44% to 59%. The frequency of type 1 was significantly higher in AR than in AS (74% vs. 49%; $p < 0.001$).

DISCUSSION

We described the clinical features, current practice patterns, and morphological phenotypes in a large patient group with BAV, which is the first report of this kind in Korea. BAV has historically been considered an ominous disease, which is likely due to sporadic reports on fatal infective endocarditis¹⁴⁾ and aortic dissection or histologic similarity to Marfan's disease, based on an excised aorta.¹⁰⁾ Recent representative clinical studies revealed that perceptions about the fatality of BAV have been biased or exaggerated, resulting from a lack of clinical evidence. Patients with BAV actually have similar overall survival rates compared to the general population.^{7,8)} Moreover, the risk of aortic dissection was found to be as low as 0.5% in a 25-year follow-up.⁹⁾ Nevertheless, these clinical studies also provided information about the risk for aortic aneurysm, which was 26% in a 25-year follow-up,⁹⁾ and approximately 27% of the patients underwent AV or aortic surgery during a 20-year follow-up.⁷⁾ These findings are a reminder that development of valvular disease and aortic aneurysm that require surgery is an actual lifetime health risk. In this context, data focused on indications for AV surgery and clinical features in Korean patients with BAV are beneficial for improving patient care.

We have shown that development of valvular dysfunction (AS or AR) and infective endocarditis was the main cause of AV surgery, and AS was the predominant lesion for AV surgery (77% [892/1,160]). Interestingly, there was a unique relationship between age and predominant valvular lesions that required AV surgery. Surgery for AS before 60 years of age was reported to represent premature degeneration of BAV,¹⁵⁾ and BAV is more frequent than tricuspid AV in younger ages based on data for AV replacement.¹⁶⁾ However, in our study, surgery for AS due to BAV was mainly performed in the aged population and more than 90% (811/892) of patients who underwent surgery were older than 50 years. The second common cause of AV surgery in patients with BAV was development of AR and the mean age was significantly lower for those with AR than AS (47 ± 14 vs. 62 ± 10 years; $p < 0.001$). More than 50% (104/199) underwent AV

surgery due to AR before age 50. Infective endocarditis was the primary lesion for AV surgery in 6% of cases, comprising the smallest proportion. However, this number is not negligible, considering the prevalence of BAV in the general population and the volume of AV surgery. Infective endocarditis developed in relatively young patients and more than 60% of patients (43/69) underwent surgery before 50 years of age. Aortic root abscess was observed in 25% of patients with infective endocarditis, which is comparable with the previously reported frequency (22%) in patients with AV endocarditis¹⁷⁾ but lower than that (50%) in specified BAV endocarditis groups.¹⁸⁾ The relationship between age and predominant valvular lesions that required AV surgery in our patients with BAV is similar to that reported previously: In a surgical pathology study of 542 cases, the authors confirmed that AS surgery was predominantly performed in the aged population with the peak in the 60s.¹⁹⁾

Although BAV has unique morphological features with recognizable patterns, its clinical impact or significance has remained elusive. Different classification systems for BAV phenotypes have been reported since the 1970s.¹⁹⁻²¹⁾ The current representative classification was proposed by Sievers and Schmidtke,¹²⁾ who applied a sophisticated method to 304 surgical reports and derived 3 main and 6 subcategories. This system was utilized by other researchers who demonstrated the feasibility of AV repair based on detailed anatomic features.²²⁾ However, such a classification process is difficult to reproduce in routine practice using non-invasive imaging studies alone, which are limited in their ability to document fused individual cusps; moreover, its benefit is doubtful as 95% of patients undergo AV replacement rather than repair surgery. Conversely, the influence of BAV phenotype on hemodynamics has been highlighted recently.²³⁻²⁵⁾ Most of these studies, however, used magnetic resonance images for better spatial resolution, which is inconsistent with real clinical practice, in which echocardiography remains the mainstay of diagnosis. Therefore, we investigated the classification system presented by Schaefer et al.,¹³⁾ in which echocardiographic images were used to derive 3 main patterns. In this study, due to the potential ambiguity of real images, we added a type 4 that represented indeterminate patterns between types 2 and 3.

We confirmed that type 1 (fusion between right and left coronary cusp) was the most frequent phenotype despite some variations in the frequency between the 4 institutions. Notably, the relative frequency of the type 1 phenotype in our study was lower compared to that reported in western countries, suggesting the possibility of ethnic differences in the frequency of different BAV phenotypes. The prevalence of the type 1 phenotype in western countries was over 70% (up to 86%), whereas that reported in Japan and Korea was less than 60% (**Table 3** and **Figure 5**).⁷⁾⁸⁾¹²⁾¹³⁾²⁶⁻²⁸⁾ One potential explanation for this difference is different study cohorts: our study included BAV patients with significant valvular dysfunction that needed AV surgery, whereas western reports based on imaging studies included variable degrees of valve dysfunction. Currently, the clinical impact of ethnic differences on the frequency of specific BAV phenotypes is unclear; however, considering the different embryologic pathogenesis of different BAV phenotypes,²⁹⁾ these could manifest in ethnically-based differences in clinical features or outcomes in patients with BAV. This hypothesis requires additional testing in future investigations.

This study is limited in that we only included patients who underwent AV surgery in tertiary referral hospitals, and thus, the actual incidence of valvular dysfunction or aortic dissection/aneurysm in the general population cannot be accurately estimated based on these results. This selection bias may have also affected the frequency of BAV phenotypes in real clinical

Table 3. BAV phenotypes described in previous research

Authors (reference)	Number of patients	Age	Valve functions	Modality	Nation	Phenotype distribution
Fernandes et al. ²⁷⁾	1,135	Median 3 (range, 0–18)	Subgroup analysis (n=864); moderate/severe AS (14%), moderate/severe AR (4.5%)	TTE	US	RL (70%), RN (28%), LN (1%)
Sievers and Schmidtke ¹²⁾	304	53±15	All surgically corrected lesions; AS (51%), AR (38%), ASR (9%), normal (1%)	Operative report	Germany	RL (73%), RN (15%), LN (3%), Lat* (4%), Unicuspid (5%)
Schaefer et al. ¹³⁾	192	45±14	Moderate/severe ASR (5.8%), normal (11%)	TTE	US	RL (79%), RN (20%), LN (1%)
Michelena et al. ⁷⁾	212	32±20	Normal or minimal dysfunction	TTE	US	RL (typical, 86%), other types (atypical, 14%)
Tzemos et al. ⁸⁾	510	35±16	Moderate/severe AS/AR (37%)	TTE	Canada	RL (anterior-posterior orientation, 75%), other types (right-left orientation, 25%)
Kinoshita et al. ²⁸⁾	135	64±12	All surgically corrected lesions; AS (42%), AR (31%), ASR (27%)	Operative report	Japan	RL (53%), other types (Non RL, 47%)

AR = aortic regurgitation; AS = aortic stenosis; ASR = both aortic stenosis and regurgitation; BAV = bicuspid aortic valve; CT = computed tomography; Lat = lateral; LN = fusion between left and non-coronary cusps; RL = fusion between right and left coronary cusps; RN = fusion between right and non-coronary cusps; TTE = transthoracic echocardiography.

*Lat, BAV presenting with 2 even cusps, no raphe and right-left orientation.

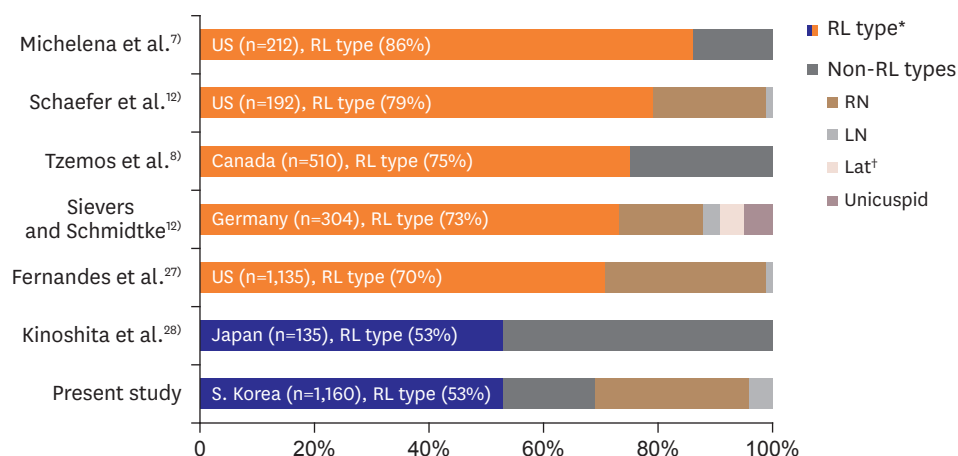


Figure 5. BAV phenotypes described in previous research.

BAV = bicuspid aortic valve; Lat = lateral; LN = fusion between left and non-coronary cusps; RL = fusion between right and left coronary cusps; RN = fusion between right and non-coronary cusps.

*Orange and blue bars present data from western and Asian countries, respectively; †Lat, BAV presenting with 2 even cusps, no raphe and right-left orientation.

practice, which includes patients with mild or no valvular dysfunction. Moreover, although aortic complication is common in patients with BAV, our retrospective study was not ideal for adequately evaluating this important clinical outcome. Patients who underwent primary aortic surgery without AV surgery were not included in this study.

In summary, clinical characteristics of patients with BAV who underwent AV surgery were studied according to the 3 different valvular lesions for surgery (AS, AR, and infective endocarditis). We observed a possible ethnic difference in a specific BAV phenotype and a potential association with types of valvular dysfunction. Further investigations are necessary to evaluate whether these observations may be applied in daily clinical practice for the general population.

REFERENCES

1. Hoffman JJ, Kaplan S. The incidence of congenital heart disease. *J Am Coll Cardiol* 2002;39:1890-900.
[PUBMED](#) | [CROSSREF](#)
2. Roger VL, Go AS, Lloyd-Jones DM, et al. Heart disease and stroke statistics--2011 update: a report from the American Heart Association. *Circulation* 2011;123:e18-209.
[PUBMED](#) | [CROSSREF](#)
3. Fedak PW, Verma S, David TE, Leask RL, Weisel RD, Butany J. Clinical and pathophysiological implications of a bicuspid aortic valve. *Circulation* 2002;106:900-4.
[PUBMED](#) | [CROSSREF](#)
4. Prakash SK, Bossé Y, Muehlschlegel JD, et al. A roadmap to investigate the genetic basis of bicuspid aortic valve and its complications: insights from the International BAVCon (Bicuspid Aortic Valve Consortium). *J Am Coll Cardiol* 2014;64:832-9.
[PUBMED](#) | [CROSSREF](#)
5. Verma S, Siu SC. Aortic dilatation in patients with bicuspid aortic valve. *N Engl J Med* 2014;370:1920-9.
[PUBMED](#) | [CROSSREF](#)
6. Garg V, Muth AN, Ransom JF, et al. Mutations in NOTCH1 cause aortic valve disease. *Nature* 2005;437:270-4.
[PUBMED](#) | [CROSSREF](#)
7. Michelena HI, Desjardins VA, Avierinos JF, et al. Natural history of asymptomatic patients with normally functioning or minimally dysfunctional bicuspid aortic valve in the community. *Circulation* 2008;117:2776-84.
[PUBMED](#) | [CROSSREF](#)
8. Tzemos N, Therrien J, Yip J, et al. Outcomes in adults with bicuspid aortic valves. *JAMA* 2008;300:1317-25.
[PUBMED](#) | [CROSSREF](#)
9. Michelena HI, Khanna AD, Mahoney D, et al. Incidence of aortic complications in patients with bicuspid aortic valves. *JAMA* 2011;306:1104-12.
[PUBMED](#) | [CROSSREF](#)
10. Michelena HI, Prakash SK, Della Corte A, et al. Bicuspid aortic valve: identifying knowledge gaps and rising to the challenge from the International Bicuspid Aortic Valve Consortium (BAVCon). *Circulation* 2014;129:2691-704.
[PUBMED](#) | [CROSSREF](#)
11. Chandra S, Lang RM, Nicolarsen J, et al. Bicuspid aortic valve: inter-racial difference in frequency and aortic dimensions. *JACC Cardiovasc Imaging* 2012;5:981-9.
[PUBMED](#) | [CROSSREF](#)
12. Sievers HH, Schmidtke C. A classification system for the bicuspid aortic valve from 304 surgical specimens. *J Thorac Cardiovasc Surg* 2007;133:1226-33.
[PUBMED](#) | [CROSSREF](#)
13. Schaefer BM, Lewin MB, Stout KK, et al. The bicuspid aortic valve: an integrated phenotypic classification of leaflet morphology and aortic root shape. *Heart* 2008;94:1634-8.
[PUBMED](#) | [CROSSREF](#)
14. Cedars A, Braverman AC. The many faces of bicuspid aortic valve disease. *Prog Pediatr Cardiol* 2012;34:91-6.
[CROSSREF](#)
15. Otto CM, Prendergast B. Aortic-valve stenosis--from patients at risk to severe valve obstruction. *N Engl J Med* 2014;371:744-56.
[PUBMED](#) | [CROSSREF](#)
16. Roberts WC, Ko JM. Frequency by decades of unicuspid, bicuspid, and tricuspid aortic valves in adults having isolated aortic valve replacement for aortic stenosis, with or without associated aortic regurgitation. *Circulation* 2005;111:920-5.
[PUBMED](#) | [CROSSREF](#)
17. Anguera I, Miro JM, Cabell CH, et al. Clinical characteristics and outcome of aortic endocarditis with periannular abscess in the International Collaboration on Endocarditis Merged Database. *Am J Cardiol* 2005;96:976-81.
[PUBMED](#) | [CROSSREF](#)
18. Tribouilloy C, Rusinaru D, Sorel C, et al. Clinical characteristics and outcome of infective endocarditis in adults with bicuspid aortic valves: a multicentre observational study. *Heart* 2010;96:1723-9.
[PUBMED](#) | [CROSSREF](#)
19. Sabet HY, Edwards WD, Tazelaar HD, Daly RC. Congenitally bicuspid aortic valves: a surgical pathology study of 542 cases (1991 through 1996) and a literature review of 2,715 additional cases. *Mayo Clin Proc* 1999;74:14-26.
[PUBMED](#) | [CROSSREF](#)

20. Roberts WC. The congenitally bicuspid aortic valve. A study of 85 autopsy cases. *Am J Cardiol* 1970;26:72-83.
[PUBMED](#) | [CROSSREF](#)
21. Angelini A, Ho SY, Anderson RH, et al. The morphology of the normal aortic valve as compared with the aortic valve having two leaflets. *J Thorac Cardiovasc Surg* 1989;98:362-7.
[PUBMED](#)
22. Boodhwani M, de Kerchove L, Glineur D, et al. Repair of regurgitant bicuspid aortic valves: a systematic approach. *J Thorac Cardiovasc Surg* 2010;140:276-284.e1.
[PUBMED](#) | [CROSSREF](#)
23. Bissell MM, Hess AT, Biasioli L, et al. Aortic dilation in bicuspid aortic valve disease: flow pattern is a major contributor and differs with valve fusion type. *Circ Cardiovasc Imaging* 2013;6:499-507.
[PUBMED](#) | [CROSSREF](#)
24. Mahadevia R, Barker AJ, Schnell S, et al. Bicuspid aortic cusp fusion morphology alters aortic three-dimensional outflow patterns, wall shear stress, and expression of aortopathy. *Circulation* 2014;129:673-82.
[PUBMED](#) | [CROSSREF](#)
25. Guzzardi DG, Barker AJ, van Ooij P, et al. Valve-related hemodynamics mediate human bicuspid aortopathy: insights from wall shear stress mapping. *J Am Coll Cardiol* 2015;66:892-900.
[PUBMED](#) | [CROSSREF](#)
26. Kang JW, Song HG, Yang DH, et al. Association between bicuspid aortic valve phenotype and patterns of valvular dysfunction and bicuspid aortopathy: comprehensive evaluation using MDCT and echocardiography. *JACC Cardiovasc Imaging* 2013;6:150-61.
[PUBMED](#) | [CROSSREF](#)
27. Fernandes SM, Sanders SP, Khairy P, et al. Morphology of bicuspid aortic valve in children and adolescents. *J Am Coll Cardiol* 2004;44:1648-51.
[PUBMED](#) | [CROSSREF](#)
28. 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;80:1356-61.
[PUBMED](#) | [CROSSREF](#)
29. Fernández B, Durán AC, Fernández-Gallego T, et al. Bicuspid aortic valves with different spatial orientations of the leaflets are distinct etiological entities. *J Am Coll Cardiol* 2009;54:2312-8.
[PUBMED](#) | [CROSSREF](#)