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Dilatation of the initially non-aneurysmal ascending aorta after replacement of a bicuspid versus tricuspid aortic valve

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Abstract

Objective: To compare the aortic diameter after isolated aortic valve replacement (AVR) in patients with a bicuspid (BAV) or tricuspid aortic valve (TAV) and an initially normal ascending aorta.

Methods: Patients with an ascending aortic diameter of < 45 mm who had undergone isolated AVR were studied. Ultrasonic cardiographic measurements of the ascending aortic diameter made pre- and postoperatively and follow-up data concerning adverse aortic events and death were analyzed.

Results: A total of 613 patients were included in this retrospective study; of these, 211 had a BAV and 402 had a TAV. In both groups, the ascending aorta significantly expanded but was non-aneurysmal during follow-up; however, the difference between the two groups was not significant. Cox regression analysis showed no significant effect associated with the presence of a BAV on adverse aortic events or death.

Conclusion: Dilatation of the ascending aorta was observed after AVR in both groups, but was not more pronounced in patients with a BAV. Long-term follow-up for ascending aortic aneurysm is necessary after AVR in both patients with a BAV and those with a TAV.

Keywords

Aortic root, aortic valve, valve replacement, congenital heart disease, heart valve prosthesis

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Introduction

A bicuspid aortic valve (BAV) is the most common congenital cardiac anomaly and has a prevalence of 1–2% in the general population.[1] The clinical presentation of BAV disease is heterogeneous but it predominantly manifests as aortic stenosis, aortic insufficiency or mixed lesions of valvular dysfunction, and approximately 50% of patients with a BAV require aortic valve replacement (AVR).[2]

In addition to valvular dysfunction, BAV is associated with a variety of vascular abnormalities, such as aortic dilatation, coarctation of the aorta, interrupted aortic arch, anomalous coronary ostium and patent ductus arteriosus, with enlargement of the ascending aorta being the most common anomaly.[3–5] The aortic root diameter is significantly greater in children and adults with a functionally normal BAV compared with those with a tricuspid aortic valve (TAV), independent of the effect of haemodynamic disturbances caused by aortic stenosis or aortic regurgitation,[6] and progressive enlargement or dilatation of the aorta has been documented, even after AVR.[7,8] However, it is not clear whether dilatation of the remaining aorta after AVR is related to the presence of a BAV, as several institutions have reported analogous dimensions in the remaining aorta of patients with a BAV compared with patients with a TAV.[9–11]

It is therefore important to compare dilatation of the ascending aorta after AVR in patients with a BAV and those with a TAV. In the present retrospective study, the diameter of the ascending aorta and adverse aortic events were studied in patients with either a BAV or a TAV who had undergone AVR without aortic intervention.

Patients and methods

Patients

The records of consecutive patients ≥ 18 years old with an initially normal diameter aorta (< 45 mm) who had undergone isolated AVR in Fu Wai Hospital, Peking Union Medical College and Chinese Academy of Medical Sciences, Beijing, China, between January 2002 and December 2008 were studied. Patients with Marfan's syndrome or other known connective tissue diseases, those with a TAV functioning as a BAV or a valve with four or more cuspids, patients with acute or chronic dissection, those undergoing a repeat procedure and patients requiring replacement of the arch and descending thoracic aorta were excluded from the study. The study protocol was approved by the institutional review board at Fu Wai Hospital and Cardiovascular Institute, Peking Union Medical College and Chinese Academy of Medical Sciences, Beijing, China. The requirement for patient consent was waived due to the retrospective nature of the study.

Surgical procedure and perioperative assessment

All patients underwent preoperative examination of the entire heart and ascending aorta using ultrasonic cardiography (UCG). The AVR was performed according to the standard surgical procedure used in our institution. The involved valve was replaced with either a mechanical or biological valve prosthesis under the support of full cardiopulmonary bypass, leaving the non-dilated ascending aorta untreated. The indication for AVR was based on the current surgical guidelines but was ultimately at the surgeon's discretion.

The valve phenotype (BAV or TAV) was determined intraoperatively and confirmed by UCG and pathological examination. The pattern of the valve and the ascending aorta were assessed using UCG during the operation. The diameter of the proximal ascending aorta was obtained from the parasternal long-axis view using two-dimensional mode, as this depicts the maximum aortic diameter perpendicular to the long axis of the aorta.

All aortic diameters were measured at end-diastole using the leading edge-to-leading edge convention. When the AVR has been completed, transoesophageal echocardiography was used to evaluate the function of the valve prosthesis and the ascending aorta. UCG was performed by two cardiac surgeons and two cardiologists specializing in echocardiography. Postoperative complications were documented.

Follow up

Follow-up information was obtained from annual outpatient reviews or telephone follow up (which was offered to those unable to attend an outpatient review). All postoperative imaging data and echocardiography reports obtained from our institution or from hospitals with comparable techniques and standards were analyzed. Adverse aortic events, defined as an enlarged ascending aorta requiring medical treatment, aortic dissection or aneurysm, and all causes of death were recorded. For all out-of-hospital deaths, sudden cardiac death was confirmed or excluded. Aortic aneurysm was defined as dilatation of the aorta to greater than 1.5 times the normal size.

Statistical analyses

Categorical variables were expressed as percentages, and continuous variables were expressed as the mean ± SD (range). Analysis of freedom from events was performed according to the methods of Kaplan–Meier, and significant differences were analyzed using the log-rank test. A multivariable analysis (Cox regression) of the risk factors for total aortic events and death was performed. A number of variables (presence of BAV, baseline characteristics, ascending aorta data, valve dysfunction, intraoperative variables, in-hospital outcomes and the need for coronary artery intervention) were initially screened using a univariate model and were considered for clinical relevance before being included in the multivariate model. A P-value < 0.05 was considered to be statistically significant. All statistical analyses were performed using SPSS software version 18.0 (SPSS Inc., Chicago, IL, USA).

Results

A total of 613 patients were included in the study. Of these, 211 had a BAV and 402 had a TAV.

Baseline characteristics

Baseline patient characteristics are summarized in Table 1. There were no significant differences between the TAV and BAV groups in terms of age, gender, body surface area, compromised heart function (grade III/IV based on the New York Heart Association functional classification[12] or the presence of peripheral arterial disease. The proportion with arterial hypertension (systemic blood pressure > 140/90 mmHg recorded at multiple measurements) was significantly different in the two groups ($P = 0.033$).

The diameter of the ascending aorta before AVR was not significantly different between the two groups (Table 1). However, when divided according to the diameter of the ascending aorta into a normal subgroup (<40 mm) and a relatively normal subgroup (≥ 40 mm but < 45 mm), the BAV group had a significantly larger proportion of patients in the relatively normal subgroup compared with the TAV group ($P = 0.04$).

Most patients had a dysfunctional aortic valve, which manifested as aortic valve stenosis ($n = 115$), aortic valve regurgitation ($n = 138$) or combined dysfunction ($n = 355$); four patients with infective endocarditis with vegetation had normal valve function (Table 1). Patients with stenosis were divided into mild (>1.5 cm^2), moderate (1.0–1.5 cm^2) or severe (< 1.0 cm^2) subgroups based on the

Table 1. Baseline characteristics of patients with either a bicuspid aortic valve (BAV group) or a tricuspid aortic valve (TAV group) undergoing aortic valve replacement.

Variable	BAV group $n = 211$	TAV group $n = 402$	Statistical significance
Age, years	48.5 ± 13.1 (18–73)	52.1 ± 13.1 (19–87)	NS
Gender			NS
Male	149 (70.6)	281 (69.9)	
Female	62 (29.4)	121 (30.1)	
Body surface area, m^2	1.73 ± 0.17 (1.31–2.24)	1.72 ± 0.18 (1.17–2.47)	NS
NYHA class III/IV	44 (20.9)	92 (22.9)	NS
Arterial hypertension	80 (37.9)	189 (47.0)	$P = 0.033$
Peripheral arterial disease	37 (17.5)	81 (20.1)	NS
Diameter of ascending aorta, mm	34.4 ± 5.2 (23–45)	33.3 ± 4.9 (19–45)	NS
Diameter of ascending aorta			$P = 0.004$
< 40 mm	179 (84.8)	371 (92.3)	
≥ 40 mm but < 45 mm	32 (15.2)	31 (7.7)	
Valve function			$P < 0.001$
Normal	3 (1.4)	1 (0.2)	
Mild stenosis	4 (1.9)	2 (0.5)	
Moderate stenosis	16 (7.6)	13 (3.5)	
Severe stenosis	43 (20.4)	37 (9.2)	
Moderate regurgitation	21 (10.0)	88 (21.9)	
Severe regurgitation	15 (7.1)	14 (3.5)	
Mixed dysfunction	109 (51.7)	246 (61.2)	

Data presented as mean ± SD (range) or number of patients (%).
NS, no statistically significant between-group differences ($P \geq 0.05$) using χ^2-test and Student's *t*-test for categorical and non-categorical data, respectively.
NYHA, New York Heart Association.

Table 2. Intraoperative variables and in-hospital outcomes in patients with either a bicuspid aortic valve (BAV group) or a tricuspid aortic valve (TAV group) undergoing aortic valve replacement.

Variable	BAV group $n = 211$	TAV group $n = 402$
Clamp time, min	70.7 ± 28.4 (10–185)	69.3 ± 30.8 (25–215)
CPB time, min	97.5 ± 38.3 (38–295)	95.6 ± 40.0 (42–282)
Operation time, min	213.6 ± 58.7 (100–520)	209.9 ± 62.2 (115–615)
Mechanical prosthesis	179 (84.8)	322 (80.1)
Prosthesis size, mm	22.7 ± 2.4 (17–29)	23.0 ± 2.2 (17–29)
ICU stay, days	2.2 ± 1.4 (1–11)	2.3 ± 1.9 (1–19)
Hospital stay, days	9.6 ± 5.2 (6–48)	9.9 ± 4.6 (6–40)
Reoperation for bleeding	3 (1.4)	14 (3.5)
Hospital mortality	0 (0)	0 (0)

Data presented as mean ± SD (range) or number of patients (%).
No statistically significant between-group differences ($P \geq 0.05$) using χ^2-test and Student's *t*-test for categorical and non-categorical data, respectively.
CPB, cardiopulmonary bypass; ICU, intensive care unit.

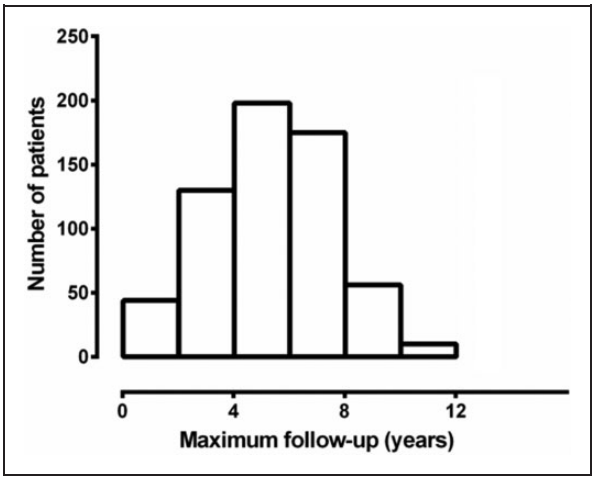

Figure 1. Distribution of the maximum follow-up time in patients with either a bicuspid or tricuspid aortic valve who had undergone aortic valve replacement.

preoperative stenotic area on UCG. In both the BAV and the TAV group, severe stenosis of the aortic valve accounted for a higher proportion of those with stenosis compared with the other subgroups. A combination of stenosis and regurgitation was seen in more than half of the patients in both groups (Table 1).

Perioperative data

Procedural, intraoperative and in-hospital outcome data are presented in Table 2. There were no significant differences in cardiopulmonary bypass time or operation time between the two groups. Mechanical prostheses were used as replacement valves in the majority of patients.

There were no in-hospital deaths in either group. The major complication was postoperative bleeding requiring surgical intervention, which occurred in three patients in the BAV group and 14 patients in the TAV group; however, this difference was not statistically significant. Most of the patients had a smooth, quick recovery, with a short and similar length of stay in the intensive care unit. However, some patients ($n < 10$) remained in hospital for > 1 month due to infection or delayed healing.

Follow-up data

Follow-up data were obtained in all 613 patients. The distribution of the maximum follow-up times is given in Figure 1. The mean follow-up time was comparable in the two groups (5.6 ± 2.2 years in the BAV group versus 5.3 ± 2.2 years in TAV group). The overall mean follow-up time was 5.4 ± 2.2 years.

Significant dilatation of the ascending aorta was observed during follow-up in both groups, with pre- and postoperative diameters of 34.4 ± 5.2 mm and 37.1 ± 6.4 m, respectively ($P < 0.001$) in the BAV group and 33.3 ± 4.9 mm and 35.4 ± 5.9 mm, respectively ($P < 0.001$) in the TAV group. The individual diameters of the ascending aorta in all patients are shown in Figure 2; there was no significant difference in the level of increase in ascending aortic diameter between the two groups. Additionally, a significant reduction in left ventricular volume and improved heart ejection fraction were observed postoperatively in both groups

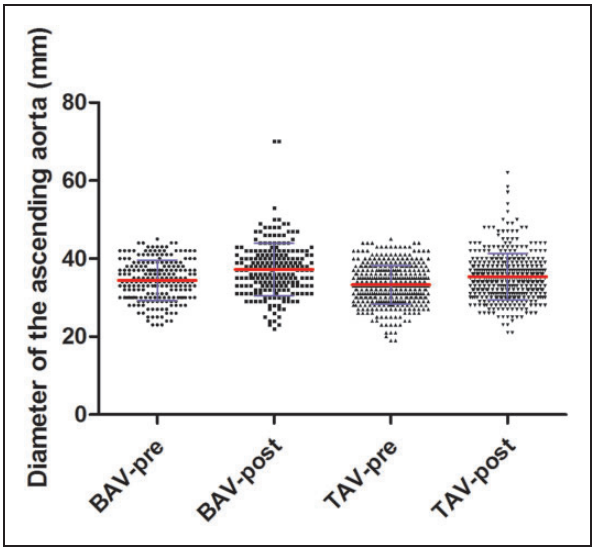

Figure 2. Diameter of the ascending aorta pre- and postoperatively in patients with either a bicuspid aortic valve (BAV-pre and BAV-post, respectively) or a tricuspid aortic valve (TAV-pre and TAV-post, respectively) undergoing aortic valve replacement.

(Figure 3); again, there were no significant differences between the two groups.

Follow-up data concerning aortic dilatation and cardiac function are given in Table 3. Adverse aortic events and deaths were mostly related to the cardiovascular system in both the BAV and the TAV group, with the proportion of cardiac and non-cardiac causes being similar in both groups.

One patient in the BAV group underwent replacement of the ascending aorta because of progression of aortic dissection, while two patients in the TAV group suffered an aortic dissection and underwent further surgery. One patient in the BAV group experienced sudden death during UCG evaluation due to rupture of an aortic dissection.

Data concerning freedom from aortic events and death are given in Figure 4. There were no significant differences between the endpoint values for the BAV group (64.0%) and the TAV group (45.7%).

All variables were screened using univariate analysis. Cox regression analysis was performed on four of these variables to identify independent risk factors for aortic events and death. Of these, preoperative mixed dysfunction of the valve and preoperative diameter of the ascending aorta were shown to be significant predictors of adverse aortic events and death (Table 4).

Discussion

In the present study of 613 patients who had undergone isolated AVR surgery, postoperative dilatation of the ascending aorta was compared in those with a BAV and those with a TAV after a mean follow-up time of 5.4 ± 2.2 years.

Since a link between BAVs and ascending aortic aneurysms was first suggested by Abbott in 1928,[13] the optimal management of patients with BAV disease, especially when combined with ascending aortic aneurysm, has been the focus of numerous studies. An AVR is often considered to be a necessary intervention, and an aortoplasty or aortic root replacement is often also performed when the BAV is associated

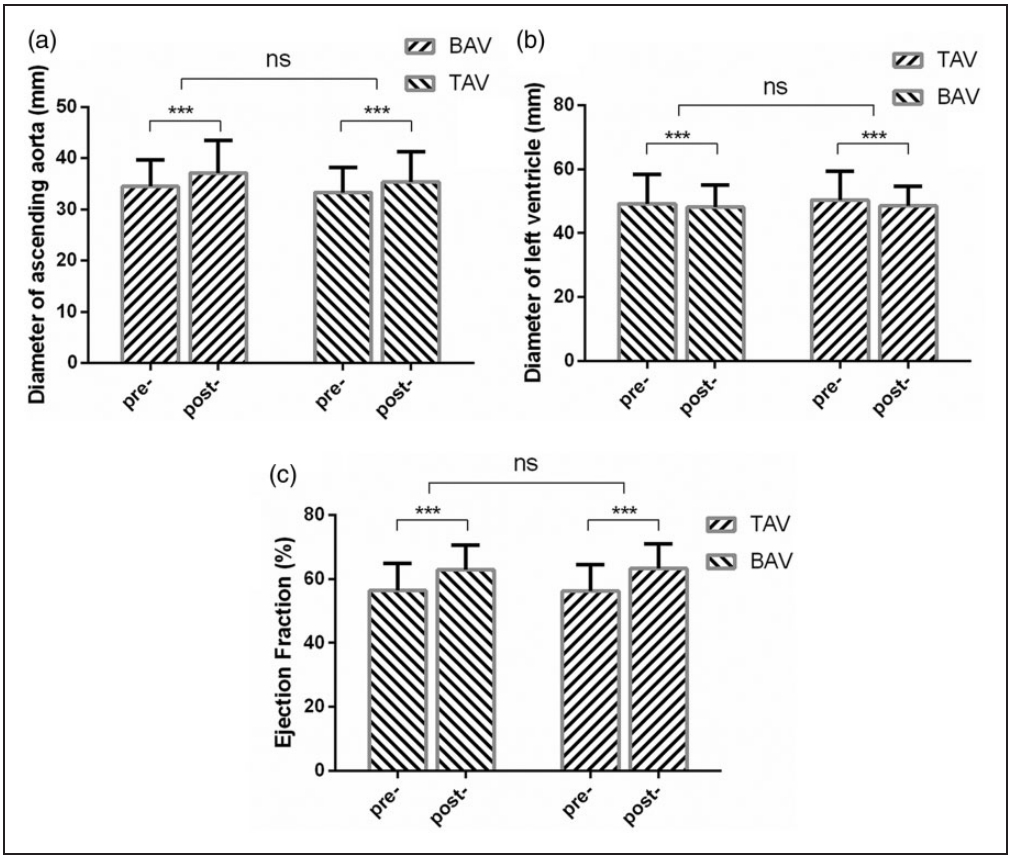

Figure 3. Ultrasonic cardiographic parameters preoperatively (pre-) and postoperatively (post-) in patients with either a bicuspid (BAV) or a tricuspid (TAV) aortic valve undergoing aortic valve replacement: (a) diameter of the ascending aorta; (b) diameter of the left ventricle; (c) ejection fraction. ns, no statistically significant between-group differences ($P \geq 0.05$). ***, $P < 0.001$ using Student's *t*-test.

with dilatation of the ascending aorta. Updated practice guidelines and several studies[14–17] support the generally accepted practice that an aorta dilated to a diameter ≥ 45 mm should be considered for concomitant replacement. However, it is controversial whether normal or mildly dilated ascending aortas should be treated at the initial time of AVR.

Several studies have demonstrated progressive enlargement of the aorta after AVR in patients with a BAV. Yasuda et al.[8] reported progressive dilatation of the aorta in BAV patients both with and without AVR; the results of this small study suggested that AVR could not prevent progressive aortic dilatation in BAV. Russo et al.[18] reported on 100 patients with a BAV or a TAV followed up after AVR for 234 ±47 months; patients with hypertension or Marfan's syndrome were excluded. At the final time point, the mean diameter of the ascending aorta in the BAV group (48.4 mm) was significantly larger than in the TAV group (36.8 mm). They therefore recommended prophylactic replacement of even a seemingly normal or mildly enlarged ascending aorta during AVR in patients

Table 3. Follow-up data in patients with either a bicuspid aortic valve (BAV group) or a tricuspid aortic valve (TAV group) who had undergone aortic valve replacement.

Variable	BAV group $n = 211$	TAV group $n = 402$	Statistical significance
Diameter of ascending aorta, mm[a]	37.1 ± 6.4 (22–70)	35.4 ± 5.9 (21–62)	NS
Dilated ascending aorta (>45 mm)	22 (10.4)	20 (5.0)	$P = 0.017$
Valve dysfunction[a]	8 (3.8)	13 (3.2)	NS
Coronary artery intervention required[a]	19 (9.0)	61 (15.2)	$P = 0.032$
CABG	18 (8.5)	61 (15.2)	
PCI	1 (0.5)	0 (0)	
Aortic events and deaths	23 (10.9)	34 (8.5)	NS
Cardiovascular event	21 (10.0)	26 (6.5)	
Cerebrovascular accident	1 (0.5)	3 (0.7)	
Death from other reasons	1 (0.5)	5 (1.2)	

Data presented as mean ± SD (range) or number of patients (%).
NS, no statistically significant between-group differences ($P \geq 0.05$) using χ^2-test and Student's *t*-test for categorical and non-categorical data, respectively.
CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention.
[a]Data for one patient was not available due to an aortic dissection that suddenly ruptured during ultrasonic cardiographic evaluation.

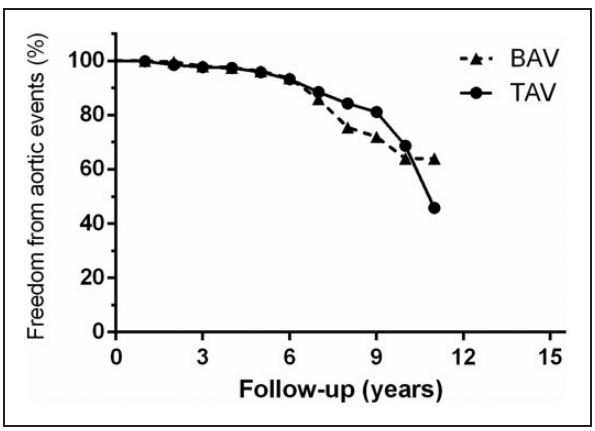

Figure 4. Freedom from aortic events and death in patients with either a bicuspid aortic valve (BAV) or a tricuspid aortic valve (TAV) who had undergone aortic valve replacement ($n = 613$).

with a BAV; they also recommended considering a similar approach for any other cardiac surgical procedures in patients with a BAV.[18]

In the study of Borger et al.,[17] patients with a BAV who had undergone AVR without aortic replacement were divided into three groups based on the size of the ascending aorta at the initial operation. The 15-year freedom from ascending aorta-related complications was 86% and 81% in patients with an aortic diameter of < 40 mm and 40–44 mm, respectively, which was significantly higher than in those with an aortic diameter of 45–49 mm (43%). However, these authors did not further analyze

Table 4. Risk factors for complex aortic events and death calculated using Cox regression in patients with either a bicuspid or a tricuspid aortic valve who had undergone aortic valve replacement.

Variable	Hazard ratio	95% confidence intervals	Statistical significance
Bicuspid aortic valve	0.93	0.53–1.64	NS
Preoperative mixed dysfunction of valve	2.21	1.02–4.81	$P = 0.045$
Preoperative diameter of ascending aorta	1.13	1.06–1.20	$P < 0.001$
Coronary artery intervention	0.52	0.22–1.25	NS

NS, no statistically significant between-group differences ($P \geq 0.05$) using χ^2-test and Student's *t*-test for categorical and non-categorical data, respectively.

the differences between the < 40 mm and 40–44 mm groups.

Abdulkareem et al.[9] also reported that only BAV patients with an aortic diameter of ≥ 45 mm required aortic replacement surgery. Patients with mild aortic dilatation (40–45 mm) had good outcomes that were comparable to those with non-dilated aortas (< 40 mm); therefore, these authors did not see the need for aortic replacement for smaller diameters.[9]

In the present study, adult patients with a BAV or a TAV with an ascending aorta with a normal or relatively normal diameter showed a significant increase in aortic diameter after AVR; however, no significant difference was found between the two groups. This suggests that a BAV may not be a risk factor for dilatation of the ascending aorta post-AVR. Additionally, despite the presence of dilatation, the diameter of the ascending aorta did not increase to the point of aneurysm and did not require further surgical intervention. Improved ventricular function and ejection fraction were seen in both groups after surgery.

That a BAV is not a risk factor for dilatation of the ascending aorta post-AVR was supported by multivariable Cox regression analysis of the risk factors for total aortic events and death in the present study. In most published articles, the presence or severity of aortic valve dysfunction has been considered to be a risk factor for aortic dilatation or even dissection.[19–21] In the present study, the presence of a mixed aortic valve lesion was a risk factor for dilatation of the remaining ascending aorta ($P = 0.045$). However, the presence of a BAV alone did not have a significant influence. This finding may be explained by the distribution of the UCG results, which differs a little from the results of other researchers who reported valve stenosis in the majority of patients due to valve morphology.[22,23] The other risk factor identified in the present study was the preoperative diameter of the ascending aorta ($P < 0.001$). This result is in accordance with Laplace's Law, which states that for a given pressure the wall tension in a vessel is proportional to the radius, and is supported by other studies.[9,24]

Although a significantly faster aortic dilatation rate has been reported in patients with a BAV compared with patients with a TAV,[25] in the present study there was no significant difference in aortic dilatation between the BAV and TAV groups during the follow-up period. In addition, the presence of a BAV was not a significant predictor of later aortic events or death. This observation is consistent with the results of a study in which cross-sectional analysis of echocardiographic data was performed in 595 patients undergoing isolated AVR.[26] In a further longitudinal follow-up

study aimed at evaluating aortic expansion rates, no difference between the BAV and TAV groups was reported.[27]

In the present study, coronary artery intervention did not significantly increase the risk of total aortic events or death. This finding is in agreement with the results of Girdauskas et al.,[28] who studied a total of 325 consecutive patients with aortic valve stenosis and concomitant ascending aortic dilatation (diameter of 40–50 mm) who underwent isolated AVR; they found that mildly to moderately dilated ascending aortas in patients with BAV or TAV stenosis behaved similarly during 15 years of follow-up. As surgical techniques develop and improve, the incidence of such adverse aortic events should decrease.

The present study was a retrospective analysis, with all the known limitations of this type of study design. In addition, a limitation of the present study was that BAV subtypes were not identified, as information concerning subtypes or the echocardiographic parameters necessary for identification were not consistently available.

A further limitation was that the size of the ascending aorta during the initial aortic valve operation was only assessed by UCG, which is not as precise as computed tomography, magnetic resonance imaging or other imaging modalities; it has been reported that the diameter of the ascending aorta is underestimated by UCG.[29,30] UCG is still a well-proven modality for accurately measuring the size of the ascending aorta during routine outpatient examinations without the accompanying radiation hazards of other methods, and it is also acceptable in assessment of the ascending aorta during follow-up.[31] However, we believe a more accurate method of measurement should be used in further studies.

In conclusion, the present study demonstrated that in adult patients with a BAV or a TAV with an initially non-dilated ascending aorta (< 45 mm), the remaining aorta expanded after AVR but did not require additional intervention. The presence of a BAV did not significantly contribute to the extent of dilatation of the ascending aorta postoperatively. However, the preoperative diameter of the ascending aorta was a significant predictor of adverse aortic events and death.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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