Imaging techniques in aortic valve and root surgery

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PART II

Postoperative evaluation of patients after aortic valve and root surgery

Effects of aortic valve and root surgery on aortic dilation

Chapter 11:

Effect of aortic valve replacement on aortic root dilation rate in patients with bicuspid and tricuspid aortic valves

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Abstract

Background: It remains unclear whether aortic valve replacement (AVR) has an effect on the aortic root dilation rate in patients with bicuspid (BAV) and tricuspid aortic valves (TAV). The present study evaluated the pre- and postoperative annual aortic root dilation rate in BAV and TAV.

Methods: A total of 93 patients (67 ± 11 years, 71% male) who underwent AVR between 2003 and 2013 and had at least 2 pre- and post-operative echocardiographic studies 1 year or more apart were included in this retrospective observational study. The sinus of Valsalva (SOV), sinotubular junction (STJ) and ascending aorta (AAo) were measured in the parasternal long-axis view.

Results: Patients with BAV (n=22) were significantly younger and had less coronary artery disease than patients with TAV (n=71). At all points in time, the aortic root diameters were larger in BAV compared with TAV. Preoperatively, the STJ and AAo grew significantly faster in BAV compared with TAV (STJ: 0.27 vs. 0.04 mm/year; p=0.021 and AAo: 0.42 vs. 0.15 mm/year; p=0.019). After surgery, there were no significant differences in aortic root dilation rates between BAV and TAV (SOV: -0.01 vs. 0.15 mm/year; p=0.096, STJ: 0.08 vs. 0.05 mm/year; p=0.676 and AAo 0.28 vs. 0.35 mm/year; p=0.745).

Conclusion: The annual aortic root dilation rates were significantly higher in BAV compared with TAV before AVR. However, after AVR, aortic root dilation rates were similar in BAV and TAV, suggesting an important role of hemodynamics on aortic root dilation in BAV.

Introduction

Bicuspid aortic valve (BAV) anatomy is associated with increased dilation rate of the aortic root compared to tricuspid aortic valve (TAV) anatomy.[1] Although intrinsic differences in the aortic wall structure due to an underlying genetic substrate may explain the differences in aortic root dilatation over time between patients with BAV and those with TAV,[2] abnormal aortic wall stress distribution in patients with BAV is also an important pathophysiologic mechanism explaining faster aortic root dilation compared with patients with TAV.[3]
Surgical aortic valve replacement (AVR) changes valvular hemodynamics and their impact on aortic wall stress distribution, and therefore, we could hypothesize that after AVR, differences in aortic root dilation rate between patients with TAV and those with BAV would be secondary to the underlying genetic substrate. To date, the evidence characterizing aortic root dilation rate after AVR in patients with TAV and those with BAV is controversial.[4-9] The aim of the present study was to assess the differences in patients with TAV and those with BAVundergoing AVR regarding aortic root diameters and dilation rate before and after AVR.

Methods

Patients

Adult patients with symptomatic moderate and severe aortic valve dysfunction and an aortic root and ascending thoracic aorta of less than 45 mm who underwent AVR between 2003 and 2013 at the Leiden University Medical Center, The Netherlands were considered eligible for the present observational study. Patients should have had 2 preoperative and 2 postoperative transthoracic echocardiograms (TTEs) performed with at least 1 year between each. The last TTE was included as the follow-up TTE. In case of repeated aortic root operations during follow-up, the last TTE before the repeated operation was evaluated. Of 656 patients who underwent AVR and who had a preoperative TTE, 123 patients had 4 echocardiograms (2 preoperative and 2 postoperative) meeting the inclusion criteria. Thirty patients were excluded because of aortic coarctation, connective tissue disease, an aortic root diameter of 45 mm or greater at time of AVR and/or concomitant aortic root or ascending aorta replacement during initial surgery. Patients with aortic root or ascending thoracic aorta 45 mm or greater were excluded because contemporary guidelines consider it reasonable to perform aortic root/ascending aorta replacement in patients with dysfunctional bicuspid aortic valves and an indication for AVR (Class IIaC). [9,10] Patients who underwent other concomitant surgical procedures (coronary artery bypass grafting, mitral valve or tricuspid valve surgery) were not excluded. Clinical and echocardiographic characteristics were prospectively collected in the departmental Cardiology Information System (EPD-Vision®, Leiden University Medical Center, Leiden, The Netherlands) and the echocardiographic database (ImageVault General Electric Healthcare) and retrospectively analyzed. The institutional review board approved this retrospective study of clinically acquired data and waived the need for patient written informed consent.

Two-dimensional transthoracic echocardiography

TTE was performed using commercially available ultrasound systems (System Five, Vivid 7, and E9, General Electric Healthcare, Vingmed, Horten, Norway) equipped with 3.5-MHz or M5S transducers. Two-dimensional, M-mode and Doppler data were acquired according to current recommendations.[11] The echocardiographic data were digitally stored in cine-loop format and data were retrospectively analyzed using commercially available software (EchoPac 112.0.1, GE Medical Systems, Horten, Norway).

Left ventricular (LV) end-diastolic and end-systolic diameters were measured in the M-mode parasternal long-axis view. LV end-diastolic and end-systolic volumes were measured and LV ejection fraction was calculated in the apical 2- and 4-chamber views according to the Simpson's biplane method.[11]

Preoperative aortic valve function was evaluated using color, continuous and pulsed-wave Doppler. Aortic regurgitation (AR) grade was assessed using a multiparametric approach including the measurement of the jet width relative to the LV outflow tract width and the vena contracta in parasternal and apical views and the pressure half time of the regurgitant flow (if feasible). AR was graded as 0 (absent), 1 (mild), 2 (mild-moderate), 3 (moderate-severe) or 4 (severe).[12] Aortic stenosis (AS) grade was assessed measuring the aortic jet velocity and transaortic mean pressure gradient and calculating the aortic valve area using the continuity equation.[13] Pre- and postoperative aortic root dimensions were measured at and end-diastolic frame in the parasternal long-axis view at 3 predefined levels: (1) the sinuses of Valsalva (SOV), (2) the sinotubular junction (STJ) and (3) the ascending aorta (AAo) 4 cm distal from the aortic valve.[14]

Surgery

After median sternotomy, arterial cannulation of the AAo was performed. Blood cardioplegia was delivered antegrade first into the aortic root and later selectively into the coronary ostia. The AAo was incised and the aortic valve was inspected. The presence of BAV or TAV anatomy was noted in the surgical report. The aortic valve was excised and replaced by mechanical or biological aortic valve prosthesis.

Statistical analysis

Continuous variables were reported as mean ± standard deviation or median and interquartile range (IQR) when appropriate. Categorical variables were reported as numbers and percentages. Continuous and categorical variables were compared with the Student's t-test (or

Mann Whitney U test in non-normally distributed variables) and the chi-square test, respectively.
Repeated-measurement analysis of variance was performed to assess the impact of BAV on the aortic root diameters at each point in time. BAV was incorporated in the model as factor. Estimated marginal means ± standard error of the mean for the aortic root diameters were reported.
The aortic root dilation was assumed to be linear and, therefore linear regression analysis without including an intercept was performed separately in BAV and TAV to assess aortic root dilation in millimeters per year in both groups before and after operation. We included BAV multiplied by follow-up duration in years to assess the difference in dilation of the aortic root between BAV and TAV.[15] All statistical tests were two-sided. A p-value <0.05 was considered statistically significant. Data analyses were performed using IBM SPSS Statistics version 20.0 (SPSS Inc, Chicago, IL).

Results

Ninety-three patients (mean age 67 ± 11 years, 71% men) were included. There were 22 (24%) patients with BAV and 71 (76%) patients with TAV. Of the patients with BAV, 19 patients had fusion of the right and left coronary cusps and 3 patients had fusion of the right and noncoronary cusps. Clinical and echocardiographic characteristics at baseline are presented in Table 1.

Preoperative aortic root dilation rate

The estimated mean duration between baseline and preoperative echocardiographic measurements was 5.5 years. The aortic root diameters at baseline and before operation are displayed in Figure 1 and Table 2. The diameters of the aortic root were significantly larger in patients with BAV compared with patients with TAV at baseline and directly preoperatively. In the entire cohort, the average annual dilation rate of the aortic root was 0.13 mm/year at the SOV level, 0.07 mm/year at the STJ and 0.19 mm/year at the AAo. The preoperative aortic root dilation rate for BAV and TAV patients is displayed in Table 3. The dilation of the STJ and AAo was significantly faster in patients with BAV compared with patients with TAV.

Postoperative aortic root dilation rate

The estimated mean duration between postoperative and late follow-up echocardiographic measurements was 4.1 years. The aortic root diameters after surgery are presented in Figure 2 and Table 2. The diameter of the aortic root remained significantly larger in patients with BAV compared with patients with TAV directly postoperatively and during follow-up. In the entire cohort, the average annual dilation rate of the aortic root was 0.11 mm/year at the SOV level,

Table 1. Baseline clinical, echocardiographic and surgical characteristics.

	BAV (n=22)	**TAV (n=71)**	**p-value**
Age (years)	60±10	69±10	0.001
Male	18 (82%)	48 (68%)	0.310
Body surface area (m^2)	2.01±0.20	1.96±0.21	0.287
Smoking	4 (18%)	12 (17%)	1
Diabetes mellitus	1 (5%)	18 (25%)	0.070
Hypertension	9 (41%)	44 (62%)	0.134
Dyslipidemia	9 (41%)	58 (82%)	0.001
NYHA functional class III/IV	6 (27%)	30 (42%)	0.313
Previous cardiac surgery	1 (5%)	11 (15%)	0.330
Coronary artery disease	7 (32%)	46 (65%)	0.013
LV end-diastolic diameter (mm)	52±9	49±8	0.160
LV end-systolic diameter (mm)	34±10	31±8	0.280
LV end-diastolic volume (ml)	149±70	135±48	0.300
LV end-systolic volume (ml)	69±46	63±36	0.522
LV ejection fraction (%)	56±8	55±9	0.637
Aortic regurgitation			0.677
grade 0	7 (32%)	32 (45%)	
grade 1	4 (18%)	13 (18%)	
grade 2	10 (45%)	21 (30%)	
grade 3	1 (5%)	4 (6%)	
grade 4	0 (0%)	1 (1%)	
Aortic stenosis			0.121
mild	3 (14%)	11 (15%)	
moderate	6 (27%)	35 (49%)	
severe	13 (59%)	25 (35%)	
EuroSCORE II (%)	1.0 (0.8-2.0)	2.3 (1.5-5.5)	<0.001
AVR type			0.195
Biological	14 (64%)	55 (77%)	
Mechanical	8 (36%)	16 (23%)	
AVR size	25.3±2.3	23.9±2.1	0.012
Cardio-pulmonary bypass time (min)	140±58	161±62	0.207
Aortic cross clamp time (min)	112±43	117±48	0.638
Mitral valve surgery	3 (14%)	8 (11%)	1
Tricuspid valve surgery	2 (9%)	5 (7%)	1
CABG	6 (27%)	37 (52%)	0.072

Continuous data are presented as mean ± SD or median (interquartile range). Categorical data are presented as number (percentage). AVR: aortic valve replacement; CABG: coronary artery bypass grafting; LV: left ventricular; NYHA: New York Heart Association.

0.06 mm/year at the STJ and 0.33 mm/year at the AAo. Table 3 shows the postoperative aortic root dilation rate for patients with BAV and TAV, which was not significantly different at all levels.

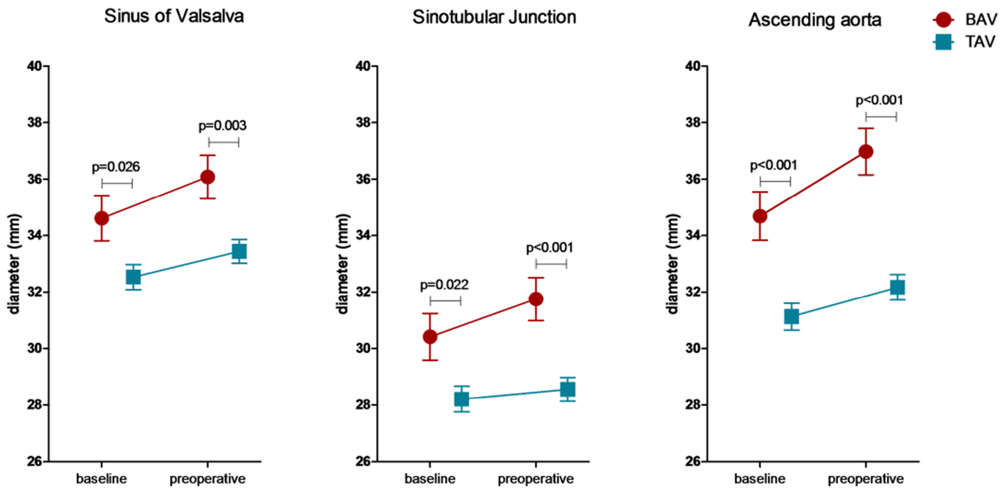

Figure 1. Preoperative change in aortic diameters over time.
Data are presented as estimated marginal mean ± SEM. AAo: ascending aorta, BAV: bicuspid aortic valve, SOV: sinus of Valsalva, STJ: sinotubular junction, TAV: tricuspid aortic valve. Estimation at mean follow-up duration between baseline and preoperative of 5.5 years.

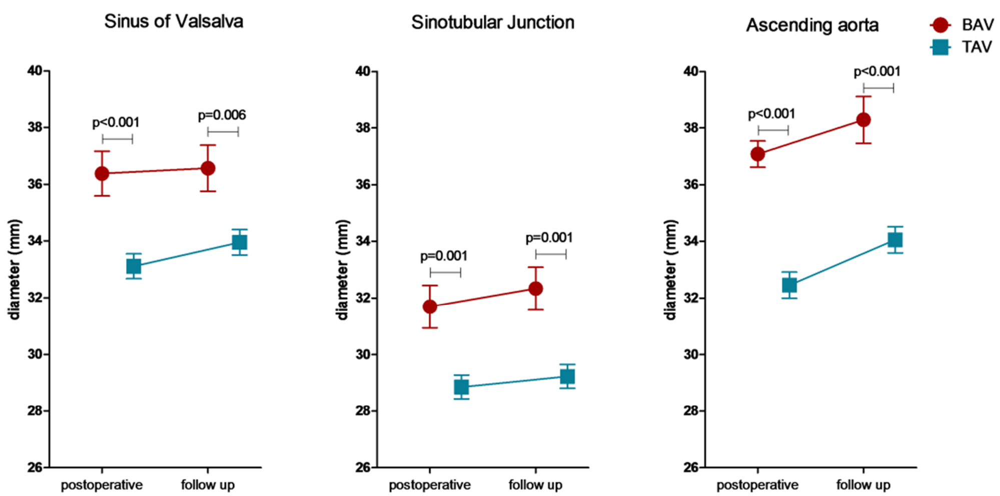

Figure 2. Postoperative change in aortic diameters over time.
Data are presented as estimated marginal mean ± SEM. AAo: ascending aorta, BAV: bicuspid aortic valve, SOV: sinus of Valsalva, STJ: sinotubular junction, TAV: tricuspid aortic valve. Estimation at mean follow-up duration between postoperative and follow-up of 4.1 years.

Table 2. Aortic diameters at baseline, preoperative, postoperative and follow-up.

	BAV (n=22)	TAV (n=71)	p-value
Sinus of Valsalva (mm)			
Baseline	34.6±0.8	32.5±0.4	0.026
Preoperative	36.1±0.8	33.4±0.4	0.003
Postoperative	36.4±0.8	33.1±0.4	<0.001
Follow-up	36.6±0.8	34.0±0.5	0.006
Sinotubular junction (mm)			
Baseline	30.4±0.8	28.2±0.5	0.022
Preoperative	31.7±0.8	28.6±0.4	<0.001
Postoperative	31.7±0.8	28.9±0.4	0.001
Follow-up	32.3±0.8	29.2±0.4	0.001
Ascending aorta (mm)			
Baseline	34.7±0.9	31.1±0.5	<0.001
Preoperative	37.0±0.8	32.2±0.5	<0.001
Postoperative	37.1±0.5	32.5±0.5	<0.001
Follow-up	38.3±0.8	34.1±0.5	<0.001

Data are presented as estimated marginal means and standard error of the mean. BAV: bicuspid aortic valve, TAV: tricuspid aortic valve. Average time between baseline and preoperative TTE is 5.5 years. Average time between postoperative and follow-up TTE is 4.1 years.

Table 3. Average preoperative and postoperative annual dilation rates in mm/year per aortic segment in BAV and TAV.

	BAV B (95% CI)	p-value	TAV B (95% CI)	p-value	BAV vs. TAV p-value
Preoperative					
SOV	0.24 (0.02-0.46)	0.034	0.11 (0.04-0.19)	0.003	0.207
STJ	0.27 (0.07-0.46)	0.010	0.04 (-0.04-0.11)	0.295	0.021
AAo	0.42 (0.21-0.63)	<0.001	0.15 (0.07-0.24)	0.001	0.019
Postoperative					
SOV	-0.01 (-0.22-0.19)	0.884	0.15 (0.03-0.27)	0.015	0.170
STJ	0.08 (-0.08-0.24)	0.321	0.05 (-0.05-0.15)	0.307	0.790
AAo	0.28 (0.15-0.42)	<0.001	0.35 (0.24-0.46)	<0.001	0.546

Data are presented as regression coefficient (B) and 95% confidence interval (95% CI) indicating annual dilation rates in mm/year. AAo: ascending aorta, BAV: bicuspid aortic valve, SOV: sinus of Valsalva, STJ: sinotubular junction, TAV: tricuspid aortic valve.

Aortic valve hemodynamics

In patients who underwent AVR for severe aortic stenosis, the transaortic mean pressure gradient was 26.7±2.9 mmHg and 22.8±2.0 mmHg at baseline in BAV and TAV, respectively (p=0.273). The transaortic mean pressure gradient was 49.8±3.3 mmHg in patients with BAV and 53.1±2.3 mmHg in patients with TAV at the preoperative TTE (p=0.420). After AVR, in the overall population, the transaortic mean pressure gradient was comparable immediate after AVR (BAV vs. TAV: 12.5±1.1 vs. 13.0±0.6 mmHg, p=0.702) and during follow-up (BAV vs. TAV: 10.1±1.4 vs. 12.6±0.8 mmHg, p=0.115).

Discussion

The present study shows that patients with BAV had larger aortic roots and significantly faster dilation before surgical AVR compared with patients with TAV. However, in this particular group of patients with BAV, with baseline aortic root diameters <45 mm and who underwent AVR mainly because of severe AS, the aortic root diameters remained relatively stable after AVR and similar to that of patients with TAV.

Aortic root dilation rate before AVR

Before AVR, the dilation rate of the AAo in patients with BAV described in the present study was comparable to previously reported rates. In a study including 353 patients with BAV, Detaint et al showed a dilation rate of the SOV and AAo of 0.21 mm/year and 0.42 mm/year, respectively.[1] In the control group with 51 patients with TAV, these dilation rates were significantly lower (0.09 mm/year and 0.20 mm/year, respectively).[1] In addition, Etz and associates showed an AAo dilation rate of 0.77 mm/year in 116 patients with BAV, which was approximately 5 times higher than age-related AAo dilation for the normal population (0.16 mm/year).[16,17]

Currently there are 2 main hypotheses explaining the relation between BAV and aortic root dilation (aortopathy).[2,3] The first factor which might explain the difference in aortic dilation between BAV and TAV is an underlying genetic substrate. The autosomal dominant inheritance of BAV with reduced penetrance is well documented.[18] In relatives of patients with BAV, 14% had BAV, and of these individuals 67% had associated thoracic aortic aneurysm. Interestingly, 30% of relatives of patients with BAV with normal functioning TAV anatomy also had thoracic aortic aneurysm.[19] Histopathologic studies showed increased smooth muscle cell apoptosis, increased matrix metalloproteinase-9 and lower expression of α smooth muscle actin, smooth muscle 22α, calponin, smoothelin and lamin A/C in aortic wall of patients with BAV.[20,21] Although collagen orientation is almost identical in BAV and TAV, there are some differences in biomechanical properties of the aortic wall that may explain the differences in dilation rate such as decreased wall thickness, lowered aortic distensibility and increased aortic stiffness in patients with BAV.[21-23]

The second hypothesis on the association between BAV and aortic root dilatation is the hemodynamics theory. Recent studies using 4-dimensional flow magnetic resonance imaging have provided more insight into the different hemodynamic burden on the aortic wall caused by flow disturbances.[3,24] In TAV, the flow is directed along the curvature of the aorta. In BAV,

the flow angle is disturbed resulting in different increased wall shear stress, depending on the orientation of the cusps.[3,24] In BAV with fusion of the right and left coronary cusps the flow is directed toward the right anterior, with increased wall shear stress in this region, resulting in aortic root dilation. In BAV, with fusion of the right and noncoronary cusps, the flow is directed higher into the AAo toward the posterior aortic wall resulting in AAo dilation.[3,24]
In addition, these two theories may overlap because increased wall shear stress influences gene expression in the aortic wall.[25] Preliminary clinical data comparing regions with increased and normal wall shear stress in BAV aortas showed increased collagen stiffness and increased transforming growth factor-β_1 and matrix metalloproteinases in regions with increased wall shear stress.[26]

Aortic root dilation rate after AVR
In patients with BAV with an indication for AVR, it is debatable whether concomitant aortic root or AAo replacement, or both, should be performed if the aortic dimensions do not exceed specific cutoff values.[27-29] Current guidelines advise aortic root operations in BAV with aortic root dilation 55 mm or more or 50 mm or more in the presence of additional risk factors (family history, systemic hypertension, coarctation of the aorta or aortic dilation >3mm/year).[30] For patients with an indication for AVR, lower thresholds (>45 mm) can be used for concomitant aortic root and AAo replacement.[30]
If the genetics hypothesis is the only factor determining aortic dilation in BAV, the aortic root dilation rate after AVR would be as high as is was preoperatively. This may result in higher rates of AAo-related complications in operated patients with BAV compared with patients with TAV. However, if the hemodynamics theory were the only factor explaining the different aortic dilation rate between BAV and TAV, once the dysfunctional aortic valve has been replaced, the aortic dilation rate and the risk of adverse aortic events at follow-up would be similar between BAV and TAV. There is conflicting evidence regarding aortic root dilation after AVR. Dayan and colleagues reported that after AVR, the aortic root dimensions remained stable in patients with BAV.[4] Similarly, in a study comparing 143 patients with BAV and 129 patients with TAV undergoing isolated AVR, the aortic dimensions remained stable.[5] Furthermore, Charitos and coworkers compared the aortic dilation rate after AVR in 361 patients with BAV and 87 patients with TAV and observed no significant difference in SOV diameter directly postoperative (difference 0.6±0.5 mm, p=0.2) between BAV and TAV, with comparable postoperative SOV dilation rate (0.13±0.04 mm/year in the entire cohort; difference between BAV and TAV 0.08±0.05 mm/year, p=0.12).[8] Furthermore, the AAo dimensions were slightly larger in patients with BAV compared to those with TAV directly after AVR (difference: 1.2±0.7 mm, p=0.09) whereas the postoperative AAo dilation rate was 0.25±0.05 mm/year in their entire cohort with no significant difference in dilation rate between BAV and TAV.[8] Similar to

the present study, these studies would confirm the role of hemodynamics on the dilation rate of the aortic root and AAo. In contrast, Yasuda and associates showed increased ascending aortic dilation in BAV (0.18 mm/m2/year) compared with regression in aortic size in TAV (-0.08 mm/m2/year; p=0.03) [6], which would confirm the genetics theory.

Study limitations

Several limitations should be acknowledged. This was a small retrospective, single center study in which patients were included when at least 2 preoperative and 2 postoperative TTEs were available. Two-dimensional TTE may underestimate aortic root diameters and is prone for off-axis measurements. In addition, TTE measurements of the aortic diameters, especially at the level of the distal ascending aorta, are challenging and the spatial resolution of TTE is inferior to that of computed tomography or magnetic resonance imaging which may influence on the reproducibility of the measurements.[30] We previously reported the inter-observer and intra-observer variability in aortic root diameter measurements by two-dimensional TTE.[31] Patients with aortic aneurysms 45mm or larger at the time of surgery were excluded; therefore the results of the study cannot be extrapolated to patients with aortic dimensions beyond this cutoff value. Patients with coarctation of the aorta were also excluded since their aortopathy might be of different genesis. Patients with BAV and TAV were different in clinical characteristics such as age and the presence of coronary artery disease which may hamper the comparison between the two groups. The patients included in the BAV group were relatively old (mean age 60 years) and underwent AVR predominantly because of AS. The conclusions drawn from the present study may therefore not be applicable to a younger BAV patient cohort with predominantly AR. Moreover, subanalysis comparing different morphologic types of BAV (fusion of the right and left coronary cusps versus fusion of the right and noncoronary cusps) or different types of valve dysfunction (AR versus AS) was not possible because of the small cohort of patients.

Conclusion

The annual aortic root dilation rates of patients with BAV was significantly higher compared with patients with TAV before AVR. After AVR, there was no significant difference in aortic root dilation rates, indicating that hemodynamics seem to play an important role in aortic dilation. BAV patients who undergo operation in whom the aortic root is not yet dilated should not be treated differently from TAV patients, and regular surveillance after AVR should be similar in both groups of patients.

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