Aortic Stenosis Severity is not a Risk Factor for Poststenotic Dilatation of the Ascending Aorta

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Background Dilatation of the ascending aorta in aortic stenosis may be partly explained by intrinsic wall structure changes, but the relative contribution of altered hemodynamics is unclear. The aim of this study was to assess the association between ascending aortic dimensions and valve stenosis severity.

Methods and Results An analysis of echocardiographic examinations was conducted in 296 patients with aortic stenosis (179 males, mean age 71 years), 57 with bicuspid and 239 with tricuspid aortic valve, mean transaortic gradient 43 ± 20 mmHg, and not more than moderate aortic regurgitation. Aortic dimensions at the level of annulus, sinuses of Valsalva, sinotubular junction and proximal ascending aorta were measured. Only height ($p < 0.001$), degree of aortic regurgitation ($p < 0.01$) and presence of bicuspid aortic valve ($p < 0.001$) were independent predictors of ascending aortic dimensions.

Conclusions An independent association between aortic pressure gradients and proximal ascending aortic dimensions was not observed in patients with bicuspid or tricuspid aortic valve stenosis. Therefore, the post-stenotic dilatation of the ascending aorta is not explained by aortic stenosis severity itself. Possible nonhemodynamic causes deserve detailed study at the time of diagnosis. (Circ J 2007; 71: 84–88)

Key Words: Aortic stenosis; Ascending aorta; Echocardiography

Poststenotic dilatation of the ascending aorta may accompany aortic stenosis, requiring treatment decision making at the time of valve surgery.^{1,2} Intrinsic aortic wall structure abnormalities, and the effect of altered hemodynamics, are hypothesized to be the main risk factors for aortic dilatation.

Wider aortic root dimensions have been found in patients with a functionally normal bicuspid aortic valve (BAV) than with tricuspid aortic valve (TAV), and irrespective of stenosis or regurgitation severity.^{3,4} Reduced fibrillin-1 content and increased matrix-metalloproteinase production, contributing to derangement of wall structure and aortic dilatation, have been identified in the vasculature of patients with BAV.^{5–7}

With regard to hemodynamics, a positive association between the degree of aortic regurgitation and proximal ascending aortic dimensions has been found in patients with BAV and TAV.^{3,8} However, the effect of the high velocity stenotic jet on the aortic dimensions is unclear. In patients without valvular dysfunction, Nkomo et al found a wider ascending aorta and higher transaortic flow velocity in patients with BAV than with TAV.⁴ In patients with BAV stenosis, no or even inverse association between ascending aortic dimensions and severity of stenosis was found.^{8,9} In

patients with TAV, this issue has not yet been specifically addressed.

Therefore, the aim of our study was to assess the relationship between ascending aortic dimensions and aortic jet velocity in patients with dominant aortic stenosis and identifiable TAV or BAV morphology.

Methods

We performed a retrospective analysis of prospectively collected data from the Department of Medicine, Charles University of Prague, School of Medicine Hospital in Pilsen, where 15,789 echocardiographic examinations were performed between January 2002 to June 2004. From this database we identified 598 patients with dominant aortic stenosis with peak velocity ≥ 2.5 m/s. Cases with more than moderate aortic regurgitation, Marfan syndrome, aortic dissection, congenital heart disease except for BAV, infective endocarditis, severe left ventricular dysfunction (ejection fraction $< 30\%$), unstable hemodynamics (systolic blood pressure < 100 mmHg) were not included. A total of 323 patients were initially selected. Excluding patients with an incomplete study or with unidentifiable valve morphology, 296 patients were enrolled for the final data analysis. We performed a standard transthoracic echocardiographic examination of all patients, and transesophageal echocardiography (TEE) of 118 (40%) of them (GE Vingmed System Five or Vivid Five, Horten, Norway, TU4 multiplane TEE probe). Blood pressure and anthropometric data were obtained at the time of the examination. The study followed the principles established in the Declaration of Helsinki.

Echocardiographic Analysis

Videotapes of all examinations were analyzed. All dimensions were measured offline by one echocardiographer.

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Table 1 Baseline Characteristics of 296 Patients With Dominant Aortic Stenosis and Comparison Between Patients With Bicuspid and Tricuspid Aortic Valve Stenosis

	All (n=296)	BAV (n=57)	TAV (n=239)	p value*
Gender, males (%)	179 (60)	39 (68)	140 (59)	NS
Age (years)	71 (62, 76)	62 (52, 69)	71 (66, 76)	<0.001
Height (cm)	170 (162, 175)	170 (164, 175)	170 (162, 175)	NS
Weight (kg)	80 (70, 91)	83 (70, 91)	80 (70, 92)	NS
Body surface area (m ²)	1.9 (1.8, 2.1)	1.9 (1.8, 2.0)	1.9 (1.8, 2.0)	NS
Body mass index (kg/m ²)	28 (25, 31)	29 (24, 32)	28 (25, 31)	NS
Systolic blood pressure (mmHg)	140 (120, 150)	140 (125, 150)	140 (120, 150)	NS
Diastolic blood pressure (mmHg)	80 (70, 90)	80 (80, 90)	80 (70, 85)	NS
Maximal aortic valve gradient (mmHg)	65 (40, 87)	79 (60, 92)	63 (39, 86)	<0.01
Mean aortic valve gradient (mmHg)	42 (25, 56)	50 (36, 61)	40 (25, 55)	NS
Aortic regurgitation severity				
No regurgitation n (%)	99 (34)	18 (31)	81 (34)	NS
1+/4 n (%)	163 (55)	34 (60)	128 (54)	NS
2+/4 n (%)	34 (11)	5 (9)	30 (12)	NS

Values are presented as median (25th, 75th percentile).

Data on gender and aortic regurgitation severity are presented as numbers and percentages.

*Bicuspid vs tricuspid aortic valve patients, Mann-Whitney U-test.

BAV, bicuspid aortic valve; TAV, tricuspid aortic valve.

Data from 3 beats were measured and averaged. The aorta was measured from the 2-dimensional (D) parasternal long-axis view by the leading edge-to-leading edge method according to standard criteria,¹⁰ at the level of the aortic annulus, sinuses of Valsalva, sinotubular junction and proximal ascending aorta, 1–1.5 cm from the sinotubular junction. The ejection fraction was assessed from the M mode, using the Teichholz formula or from the 2-D 4 chamber view using the Simpson's formula.

BAV was defined by the presence of 2 commissures and 2 aortic cusps¹¹ on the parasternal or mid-esophageal short-axis view. BAV was assessed by 2 echocardiographers from our team, whose consensus regarding valve morphology was reached in all patients included in the present study. At the time of examination, peak and mean aortic velocities were measured by continuous wave Doppler, and the gradients counted using the modified Bernoulli equation; the aortic valve area was measured by the continuity equation.¹² The degree of regurgitation was assessed semi-quantitatively from the regurgitation jet area and width, according to the American Society of Echocardiography guidelines,¹³ converting the terms none, mild, and moderate into numbers 0, 1 and 2.

Statistical Analysis

Continuous measurements are presented as median and interquartile range, as some of the variables (proximal ascending aortic dimensions and aortic valve gradients) were not normally distributed. Categorical measurements are presented as numbers and percentages. First, continuous and categorical variables were compared between patients with BAV and TAV, using the Mann-Whitney U-test and the Kruskal-Wallis test. A Box-Cox transformation of aortic dimensions was performed to achieve normal distribution. The correlation between aortic dimensions and the hemodynamic and anthropometric parameters was then studied. We performed separate sets of calculations at each of the 4 aortic levels. Aortic dimensions, first unadjusted, and then indexed by height, were used as dependent variables. Age, anthropometric parameters (height, weight, body surface area (BSA)), and valve disease severity parameters (maximal and mean gradients, severity of regurgitation)

were independent variables. Spearman rank correlation coefficients were counted in the univariate analysis. Further, independent predictors of aortic dimensions were evaluated by linear step-wise regression. A p-value <0.05 was considered statistically significant.

Results

Baseline characteristics of the 296 patients included in the study and comparisons between patients with BAV and TAV are shown in Table 1. The distribution of transaortic velocities in the whole study group is shown in Fig 1. Severe aortic stenosis with mean aortic gradient >50 mmHg was present in 34% of patients, and peak aortic gradient >50 mmHg in 66% of patients. The stenosis was pure in one-third of the study group, and accompanied by mild regurgitation in 56%. Moderate regurgitation was present in 11% of patients, all of whom had severe stenosis with orifice area <1 cm². The patients with BAV were 9 years younger, on average, than those with TAV and had higher transaortic jet velocity, but did not differ in the severity of regurgitation.

Using univariate analysis for the whole study group, we found a positive association of aortic dimensions with severity of regurgitation (p<0.01) (Fig 2), and a weak but significant association with severity of stenosis (p<0.05) (Fig 3). The correlations between aortic dimensions at each of the 4 measured levels and the anthropometric and valve disease parameters are listed in Table 2.

The ascending aorta at all 4 measured levels was significantly wider in patients with BAV than with TAV (Table 3).

Significant univariate correlates were entered into the multivariate model and the results are shown in Table 4. The aortic diameters had an independent positive association with the degree of aortic regurgitation (p<0.01) and the presence of BAV (p<0.001). Of the anthropometric parameters, only height had an independent correlation with the aortic diameters (p<0.001) at all 4 levels, therefore we considered indexing the aortic dimensions by height appropriate for our study group.

Presence of BAV and severity of regurgitation remained the only positive independent predictors of aortic dimen-

Fig 1. Distribution of peak aortic velocities in the 296 patients with dominant aortic stenosis.

sions indexed by height at the same levels of significance (data not shown).

Discussion

We did not observe an independent association between transaortic pressure gradients and any diameter of the aortic root and proximal ascending aorta, despite evaluating a large group of patients with a wide range of stenosis severi-

Fig 3. Association of mean transaortic jet velocity with the dimension of proximal ascending aorta. The association with the dimensions of the annulus, Valsalva sinuses and sinotubular junction was not significant. r , Spearman rank correlation coefficient; p , p value.

Fig 2. Association between aortic dimensions from the annulus to the proximal ascending aorta and severity of aortic regurgitation (AR). *Spearman rank correlation.

Table 2 Correlation of Aortic Dimensions With Anthropometric and Aortic Valve Disease Parameters (Univariate Analysis*)

	Annulus		Valsalva sinuses		Sinotubular junction		Proximal ascending aorta	
	r	p value	r	p value	r	p value	r	p value
Height	0.39	<0.001	0.40	<0.001	0.33	<0.001	0.25	<0.001
Weight	0.28	<0.001	0.15	<0.01	0.14	<0.05	0.14	<0.05
Body surface area	0.35	<0.001	0.23	<0.001	0.20	<0.01	0.18	<0.01
Age	-0.19	<0.01	-0.13	<0.05	-0.09	NS	-0.17	<0.01
Maximal aortic valve gradient	0.01	NS	0.09	NS	0.02	NS	0.15	<0.05
Mean aortic valve gradient	0.06	NS	0.10	NS	0.00	NS	0.13	<0.05
Maximal aortic jet velocity	0.01	NS	0.09	NS	0.02	NS	0.15	<0.05
Mean aortic jet velocity	0.06	NS	0.10	NS	0.00	NS	0.13	<0.05
Aortic regurgitation severity	0.08	NS	0.17	<0.01	0.15	<0.05	0.1	NS

*r values are Spearman rank correlation coefficients.

Table 3 Comparison of Ascending Aortic Dimensions in Patients With Bicuspid vs Tricuspid Aortic Valve Stenosis

	All (n=296)	BAV (n=57)	TAV (n=239)	p value*
Aortic annulus (cm)	2.6 (2.3, 2.8)	2.7 (2.4, 3.0)	2.5 (2.3, 2.8)	<0.01
Valsalva sinuses (cm)	3.5 (3.2, 3.8)	3.8 (3.4, 4.1)	3.4 (3.2, 3.7)	<0.001
Sinotubular junction (cm)	3.2 (2.9, 3.6)	3.5 (3.2, 3.9)	3.2 (2.9, 3.5)	<0.001
Proximal ascending aorta (cm)	3.6 (3.2, 4.0)	4.0 (3.5, 4.3)	3.5 (3.1, 3.8)	<0.001

Values are presented as median (25th, 75th percentile).

Abbreviations see in Table 1.

*Bicuspid vs tricuspid aortic valve patients, Mann-Whitney U-test.

Table 4 Correlation of Aortic Dimensions With Anthropometric and Aortic Valve Disease Parameters (Multivariate Analysis*)

Aortic dimensions	Value (cm)	Height		BAV		Aortic regurgitation	
	Mean $\pm$ SD	Partial correlation	p value	Partial correlation	p value	Partial correlation	p value
Annulus	2.6 $\pm$ 0.4	0.40	<0.001	0.23	<0.001		NS
Valsalva sinuses	3.3 $\pm$ 0.5	0.36	<0.001	0.34	<0.001	0.22	<0.01
Sinotubular junction	3.5 $\pm$ 0.5	0.34	<0.001	0.30	<0.001	0.16	<0.05
Proximal ascending aorta	3.6 $\pm$ 0.7	0.26	<0.001	0.411	<0.001		NS

*Partial correlation coefficients using linear step-wise regression.

Abbreviation see in Table 1.

ty. To our knowledge this is the first echocardiographic study addressing this association in patients mainly with stenosis of the TAV. We identified severity of aortic regurgitation and number of aortic valve cusps as independent predictors of aortic dimensions indexed by height.

We believe that our data are important for the following reasons. First, we studied the hemodynamic concept of a relationship between the high velocity jet in aortic stenosis and aortic dimensions, and second, we extended our attention beyond the aortic root to the proximal ascending aortic diameter. The new finding of a positive correlation of this dimension with the aortic gradient from the univariate analysis was not significant in the multivariate model, with valve morphology as an independent variable. Thus, it may be explained by the presence of more severe stenosis in the patients with BAV in our study group.

The velocity, however, is one important aspect of the stenotic jet, while other fluid dynamic factors (eg, the shape of the jet) may influence the aortic dimensions. The shape of the stenotic orifice may affect the spatial orientation of the aortic jet and the distribution of the induced vortices. Thus, the irregular orifice in BAV may result in a more

eccentric jet contributing to remodelling of the proximal aorta. As shown by Robicsek et al, the degree of turbulence may not be proportional to the degree of stenosis.¹⁴ The influence of flow distribution deserves detailed attention also in TAV stenosis with its complex stellate orifice, which was beyond the scope of our clinical study.

The independent positive association between regurgitation severity and aortic dimensions suggests the importance of the hemodynamic burden of higher stroke volume for the aortic dimensions. In BAV, manifestation of intrinsic wall pathology⁵⁻⁷ may be initiated or aggravated by altered hemodynamics. Our data suggest that in TAV stenosis if it is accompanied by aortic dilatation the possibility of significant aortic wall tissue abnormalities should also, be investigated.

As specifically height and not BSA were entered in the multivariate analysis in our obese population, we considered indexing by height more appropriate than by BSA; however, the indexing did not change the outcome of our study.

Study Limitations

These originate mainly from retrospective study group selection in a tertiary care centre with cardiac surgery. First, the assessment of valve morphology was based more often on a transthoracic examination, which is less accurate than TEE;¹⁵ however, such inaccuracy would not alter the relationship between dimensions and hemodynamics. Second, selection was biased towards patients with more severe valve disease, including those evaluated for valve surgery, in whom the heavily calcified valves may be less amenable to reliable morphology assessment. Significant correlation of aortic dimensions with aortic regurgitation, although graded as mostly mild in our study, may also reflect limitations in regurgitation evaluation. Finally, this was a cross-sectional study and the impact of valve disease progression rate on aortic dimensions is of further interest.

Conclusion

We did not observe any independent association between aortic jet velocity and the dimensions of the ascending aorta in patients with aortic stenosis. We confirmed a positive independent association between aortic dimensions and the presence of BAV, height and regurgitation severity. Therefore, post stenotic dilatation of the ascending aorta is not explained by the stenosis itself in patients with BAV, but also with TAV stenosis. It may be a marker of intrinsic aortic wall structure pathology and thus deserves detailed study at the time of diagnosis.

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