BRIEF REPORT

Effect of Age on Valvular Dysfunction and Aortic Dilatation in Patients With a Bicuspid Aortic Valve

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Aortic regurgitation was the commonest functional anomaly among younger patients in a group of 63 individuals with a diagnosis of bicuspid aortic valve. With increasing age, a rise in the number with combined aortic valve disease and aortic stenosis was observed. Aortic dilatation was found in 65% of cases. Dilatation was independently associated with age and transvalvular aortic gradient.

Key words: *Bicuspid aortic valve. Valvular dysfunction. Aortic dilatation.*

Efecto de la edad en la disfunción valvular y la dilatación aórtica en pacientes con válvula aórtica bicúspide

En 63 pacientes diagnosticados de válvula aórtica bicúspide, la insuficiencia aórtica fue la alteración funcional más frecuente en los pacientes más jóvenes, mientras que con el envejecimiento se observó un aumento de casos con doble lesión y estenosis aórtica. Se detectó una dilatación aórtica en el 65% de los casos. La edad y el gradiente transvalvular aórtico eran factores independientes relacionados con la dilatación.

Palabras clave: *Válvula aórtica bicúspide. Disfunción valvular. Dilatación aórtica.*

INTRODUCTION

Although ageing among the general population is known to be related to aortic dilation[1] and degenerative aortic valve disease,[2] there is little information on these effects in patients with a bicuspid aortic valve (BAV).

The purposes of the present study were to define the functional alterations of the aortic valve and the presence of aortic dilation in patients diagnosed with BAV at a general hospital, as well as to describe the variables related to aortic dilation in these patients. In particular, the effect of age was studied.

METHODS

We studied patients over 14 years of age diagnosed with BAV by echocardiography between January 1999 and December 2003.

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Received February 23, 2005.
Accepted for publication November 3, 2005.

An Acuson Aspen Advanced ultrasound system was used, with BAV defined by transthoracic echocardiography findings of 2 clear cusps on the short-axis parasternal view, with or without a raphe.[3] The diagnosis required agreement between 2 observers. In the cases in which the transthoracic echocardiogram was indicative of BAV, but not definitive, transesophageal echocardiography was required to establish the diagnosis.

The variables analyzed were age, sex, height, body surface area, hypertension, vascular disease (myocardial infarction, stroke, or peripheral vascular disease), aortic root diameter measured at the aortic sinuses (in mm and mm/m^2), maximum diameter of the ascending aorta (in mm and mm/m^2), and presence and severity of stenosis and aortic regurgitation. Aortic stenosis was established at a mean gradient of ≥10 mm Hg. Stenosis was classified as severe at a mean gradient of ≥45 mm Hg. Aortic regurgitation was assessed according to the usual criteria,[4] based on an overall assessment of jet width in the left ventricular outflow tract, signal intensity and depth, regurgitation slope, and left ventricular size. We considered aortic root and/or ascending aorta dilation[5] to exist when the indexed diameter was >21 mm/m^2. Aortic dilation was defined as dilation of at least 1 of these 2 segments.

Qualitative variables were compared by the χ^2 or Fisher's exact test, where applicable. Quantitative variables were compared with Student *t* test. Logistic regression analysis was used to determine the independent factors related to aortic dilation, introducing as a block the variables with *P*<.10 in the univariate analysis and applying the stepwise method. Linear correlations between age/aortic transvalvular gradient, age/aortic diameter, and aortic transvalvular gradient/aortic diameter were analyzed. Statistically significant differences were considered to exist when *P*<.05.

RESULTS

Sixty-three patients were diagnosed with BAV. The clinical characteristics are shown in Table 1. Aortic coarctation was diagnosed or known in 3 cases.

Valvular Dysfunction

The most frequent functional alterations were aortic regurgitation (44%) and double aortic lesion (38%) (Table 2). The distribution of the various lesions according to age is presented in Figure 1. The same data is shown in the subset of patients with severe valvular dysfunction in Figure 2. Only 17 patients (27%) had little or no functional alteration. Patients with isolated aortic regurgitation were younger than those with aortic stenosis, whether isolated or associated with regurgitation (40±15 vs 54±13 years; *P*=.0001). With increasing age, we observed a decline in the proportion of patients with isolated aortic regurgitation and a rise in the proportion of patients with double aortic lesion and aortic stenosis (Figures 1 and 2). There was an acceptable linear relationship between age and transvalvular aortic gradient (*r*=0.4; *P*=.001).

Aortic Dilation

The mean diameters of the aortic root and ascending aorta are shown in Table 1. Dilation was detected in the aortic root in 26 cases (37%) and in the ascending aorta in 33 cases (52%). Aortic dilation was present in 41 patients (65%), including 10 of the 17 (59%) patients with no functional alterations or with mild valvular dysfunction. In the univariate analysis, age and aortic stenosis, when considered both as a qualitative and quantitative variable (mean

TABLE 1. **Clinical Characteristics of 63 Patients With Bicuspid Aortic Valve**

Age, years	46±16
Weight, kg	74±13
Height, cm	168±10
Body surface area, m^2	1.83±0.2
Aortic root, mm	38±7
Aortic root, mm/m^2	21±4
Ascending aorta, mm	41±9
Ascending aorta, mm/m^2	23±5
Men	52 (83%)
Hypertension	14 (22%)
Diabetes mellitus	4 (6%)
Ischemic heart disease	3 (5%)
Stroke	3 (5%)
Peripheral vascular disease	4 (6%)

TABLE 2. **Functional Alterations of the Aortic Valve in 63 Patients With Bicuspid Aortic Valve**

	n (%)
Aortic regurgitation	28 (44)
Severe	13
Aortic stenosis	6 (10)
Severe	3
Double lesion	24 (38)
Severe regurgitation	7
Severe stenosis	4
Severe double lesion	1
No functional abnormalities	5 (8)

TABLE 3. **Univariate Analysis of Variables Related to Aortic Dilation**

Variable	Aortic Dilation		*P*
	Yes (n=41)	No (n=22)	
Age, years	52±13	36±16	<.0001
Weight, kg	74±10	72±18	.65
Height, cm	168±9	169±10	.55
Body surface area, m^2	1.84±0.16	1.83±0.23	.87
Men	34 (83%)	18 (80%)	.35
Hypertension	9 (22%)	5 (23%)	.75
Vascular disease*	7 (18%)	3 (14%)	.78
Aortic stenosis	25 (61%)	5 (23%)	.003
Aortic transvalvular gradient, mm Hg	24±20	8±7	<.0001
Aortic regurgitation (≥1/4)	34 (83%)	18 (84%)	.9
Severe aortic regurgitation (≥3/4)	13 (31%)	8 (37%)	.56

*Vascular disease indicates ischemic heart disease, stroke, or peripheral vascular disease.

TABLE 4. **Correlation of Aortic Root and Ascending Aorta Diameters With Age**

	R	*P*
Aortic root, mm	0.59	.0001
Aortic root, mm/m^2	0.54	.0001
Ascending aorta, mm	0.54	.0001
Ascending aorta, mm/m^2	0.45	.0001

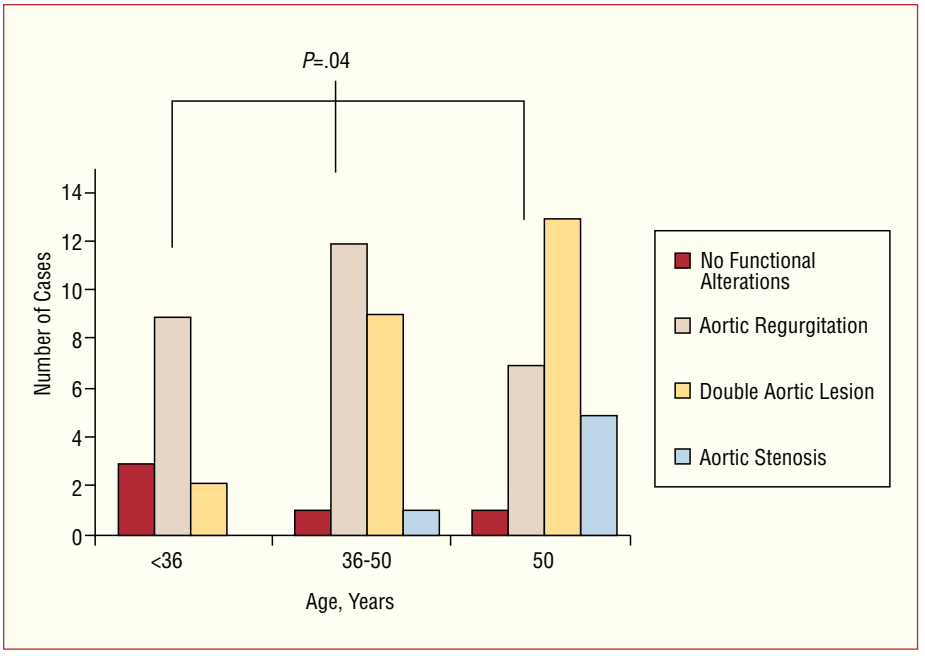

Figure 1. Distribution of functional aortic valve abnormalities according to age and number of cases.

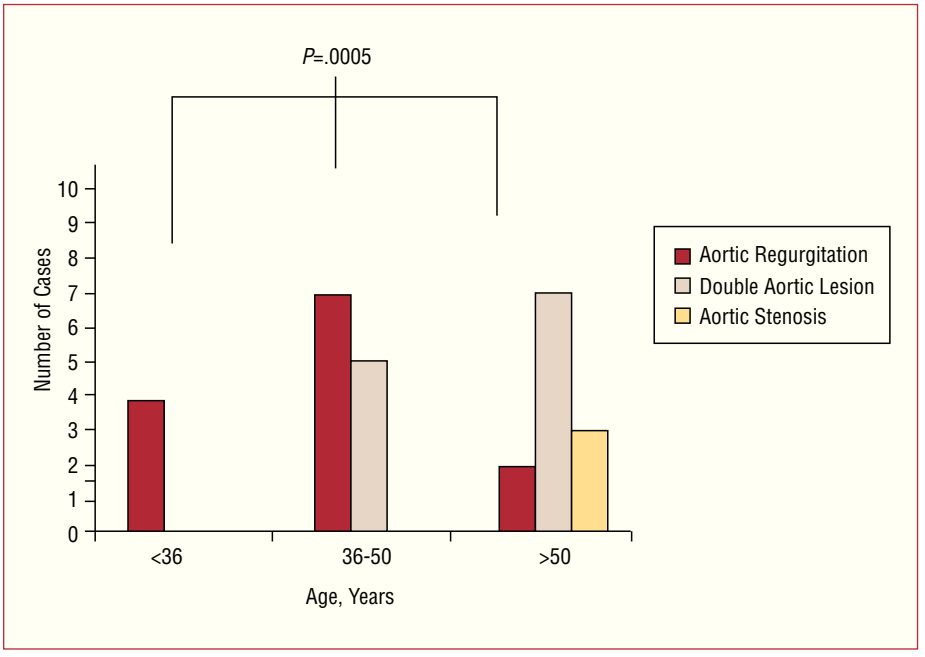

Figure 2. Distribution of severe functional aortic valve abnormalities according to age and number of cases.

transvalvular gradient), were found to be related to aortic dilation (Table 3). Patients with dilation were older than patients without dilation (52±13 vs 34±16 years; *P*<.0001); 29 of the 35 (83%) patients older than 45 showed dilation. In the logistic regression, age (odds ratio [OR] =1.06 per year; *P*=.01) and aortic stenosis (mean transvalvular gradient) (OR=1.07 per mm Hg; *P*=.03) were maintained as variables related to aortic dilation. A good linear relationship was observed between age and the aortic root and ascending aorta diameter (Table 4), but not between aortic transvalvular gradient and these diameters.

DISCUSSION

Aortic Valve Dysfunction

Several authors have described the functional alterations detected by echocardiography in BAV patients. Hahn et al[6] reported a predominance of aortic regurgitation, whereas stenosis was the most frequent finding in 2 recent studies among pediatric patients with BAV.[7,8] Nevertheless, there may be some bias in these series because the patients were from referral hospitals with cardiac surgery departments and were studied retrospectively.

In our study we observed a high prevalence of aortic regurgitation, which was the most frequent valvular dysfunction in patients less than 50 years old. Aortic regurgitation in patients with BAV is considered to be primarily the result prolapse or retraction of 1 of the valves (usually, the one with the raphe)[9] and the consequences of aortic root and ascending aorta dilation on valve function.[10]

In particular, we highlight the relationship between aortic stenosis and age. In patients older than 50 with BAV, stenosis is mainly due to an accelerated degenerative process in the abnormal valve.[11] This would explain the smaller percentage of patients with isolated aortic regurgitation and the resulting higher percentage of patients with double aortic lesion we observed with ageing.

Aortic Dilation

Histological alterations in the aortic tunica media indicative of a degenerative process have been reported in patients with BAV[12]; this would lead to aortic wall weakness and subsequent dilation.

In our study, age and aortic stenosis were independent factors related to aortic dilation. Increasing age has been linked to degeneration of the tunica media, which makes the vessel susceptible to a loss of distensibility and dilation due to increased circumferential stress.[13,14] Our results indicate that the known degenerative process of the aortic media described in patients with BAV is favored by ageing. With respect to aortic stenosis, although BAV is associated with aortic dilation,[6,15] aortic stenosis has been described as contributing to dilation whether or not there are functional alterations.[6] We have observed that this dilation is more frequent as the degree of stenosis is higher. The turbulent flow generated by stenosis appears to contribute to dilation.[16] Furthermore, we found that significant valvular dysfunction is not necessarily associated with aortic dilation, since more than half the patients with no functional alterations or with mild valvular dysfunction presented aortic dilation.

CONCLUSIONS

In patients with BAV diagnosed in a general hospital after childhood, aortic regurgitation is the most frequent functional abnormality among the younger patients. Aortic stenosis is usually detected in older patients and typically associated with regurgitation. Aortic dilation is common and is related to age and aortic transvalvular gradient. Since most patients with BAV develop valvular dysfunction and aortic dilation, we believe that long-term clinical and echocardiographic follow-up should be undertaken, even though significant alterations are not found at the time of diagnosis.

REFERENCES

1. Vasan RS, Larson MG, Levy D. Determinants of echocardiographic aortic root size. The Framingham Heart Study. Circulation. 1995;91:734-40.
2. Stewart BF, Suscovick D, Lind BK, Gardin JM, Gottdiener JS, Smith VE, et al. Clinical factors associated with calcific aortic valve disease. J Am Coll Cardiol, 1977;29:630-4.
3. Brandemburg RO, Tajik AJ, Edwards WD, Reeder GS, Shub C, Seward JB. Accuracy of 2-dimensional echocardiographic diagnosis of congenitally bicuspid aortic valve: echocardiographic-anatomic correlation in 115 patients. Am J cardiol. 1983;51:1469-73.
4. Roman MJ, Devereux RB, Kramer-Fox R, O'loughlin J. Two-dimensional echocardiographic aortic root dimensions in normal children and adults. Am J cardiol. 1989;64:507-52.
5. Gill EA, Pittenger B, Otto CM. Evaluación de la severidad y decisiones quirúrgicas en las valvulopatías. Rev Esp Cardiol. 2003; 56:900-14.
6. Hahn RT, Roman MJ, Mogtader AH, Devereux RB. Association of aortic dilation with regurgitant, stenotic and functionally normal bicuspid aortic valves. J Am Coll Cardiol. 1992;19:283-8.
7. Fernandes SM, Sanders SP, Khairy P, Jenkins KJ, Gauvreau K, Lang P, et al. Morphology of bicuspid aortic valve in children and adolescents. J Am Coll Cardiol. 2004;44:1648-51.
8. Gurvitz M, Chang RK, Drant S, Allada V. Frequency of aortic root dilation in children with a bicuspid aortic valve. Am J Cardiol. 2004;94:1337-40.
9. Stewart WJ, King ME, Gillam LD, Guyer DE, Weyman AE. Prevalence of aortic valve prolapse with bicuspid aortic valve and its relation to aortic regurgitation: a cross-sectional echocardiographic study. Am J Cardiol. 1984;54:1277-82.
10. Alegret JM, Palazón O, Duran I, Vernis JM. Factors related to aortic regurgitation in the presence of a dilated aortic root. Am J Cardiol. 2005;95:417-20.
11. Otto CM. Calcification of bicuspid aortic valves. Heart. 2002;88: 321-2.
12. Veinot JP. Congenitally bicuspid aortic valve and associated aortic medical disease. Ann Thorac Surg. 2001;71:1067-8.
13. Schlatmann TJ, Becker AE. Histologic changes in the normal aging aorta: implications for dissecting aortic aneurysm. Am J Cardiol. 1977;39:13-20.
14. Okamoto RJ, Xu H, Kouchoukos NT, Moon MR, Sundt TM. The influence of mechanical properties on wall stress and distensibility of the dilated ascending aorta. J Thorac Cardiovasc Surg. 2003;126:842-50.
15. Alegret JM, Duran I, Palazón O, Vernis JM, Ameijide A, Rabassa A, et al. Prevalence of and predictors of bicuspid aortic valves in patients with dilated aortic roots. Am J Cardiol. 2003;91:619-23.
16. Robicsek F, Thubrikar MJ, Cook JW, Fowler B. The congenitally bicuspid aortic valve: how does it function? Why does it fail? Ann Thorac Surg. 2004;77:177-85.