

Progression of aortic valve dysfunction in 51 adult patients with congenital bicuspid aortic valve: assessment and follow up by Doppler echocardiography

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Abstract

Objective—To assess the pattern and progression of aortic valve dysfunction by serial Doppler echocardiographic examinations in ambulatory adult patients with congenital bicuspid aortic valve.

Design and setting—Retrospective analysis of patients referred for Doppler echocardiography over a four year period.

Subjects—Fifty one adult patients with echocardiographic diagnosis of congenital bicuspid aortic valve had serial Doppler echocardiographic studies at least six months apart. There were 40 men and 11 women with a mean age of 36 years.

Main outcome measure—Doppler echocardiographic values of aortic valve dysfunction. Cardiac events including endocarditis and aortic valve replacement were also evaluated.

Result—Coarctation was present in five patients. 31 (61%) patients had a functionally normal bicuspid aortic valve defined as a mean gradient <25 mm Hg and mild regurgitation. Significant aortic regurgitation was present in 15 patients (moderate in 12 and severe in three). Three patients had isolated aortic stenosis and two patients had combined aortic valve dysfunction. At a median follow up of 21 months (range six to 46 months), six patients had aortic valve surgery (one for aortic stenosis, three for aortic regurgitation, and two for endocarditis). Only 22 patients (43%) continued to have a functionally normal aortic valve.

Conclusion—In this cohort of fairly young patients, aortic regurgitation is more common than aortic stenosis. Progression of aortic valve dysfunction occurs in patients with pre-existing valve dysfunction and even in those with normal aortic valve function at the initial echocardiographic examination.

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judged clinically to have functionally normal aortic valves. The clinical impressions were corroborated by phonocardiography and M mode echocardiography. Recent studies showed that cross sectional echocardiography is more sensitive and specific in detecting BAV.²⁻⁴ Furthermore, Doppler echocardiography has been found to be a reliable tool in assessing the severity of valve dysfunction.⁵

In surgical pathological series⁶⁻⁸ and necropsy studies,⁹⁻¹¹ aortic stenosis (AS) seems to be the most frequent fate of patients with a BAV. Pure aortic regurgitation (AR) and combined AS and AR are less common. The pattern of aortic valve dysfunction in ambulatory BAV patients has not, however, been well defined, and there is no study that reports the progression of aortic valve function in these patients using current diagnostic techniques. The purposes of our study were therefore to determine the pattern of aortic valve dysfunction and to assess the progression of aortic valve dysfunction in a cohort of ambulatory adult patients with a BAV by serial Doppler echocardiographic examination.

Patients and methods

PATIENT POPULATION

Echocardiographic findings in patients diagnosed to have a BAV in our echocardiographic laboratory between March 1985 and March 1989 were reviewed. The aortic valve is imaged in the short axis view to make the commissure visible. The excursion of the BAV has the appearance of a fish mouth with the conjoint cusp moving as one piece distinguishing it from a tricuspid aortic valve.²⁻⁴ In patients with densely calcified aortic valves, the number of cusps can be difficult to determine with certainty. These patients tend to be old and were excluded from this study. Only patients with clear echocardiographic evidence of BAV were included, and they had to have had two Doppler echocardiograms at least six months apart. When more than two studies were performed, the two studies with the greatest intervening time interval were used.

Aortic stenosis is present when the mean transvalvar Doppler pressure gradient is > 25 mm Hg. Measurement of AR was based on mapping the extent of a diastolic turbulent signal within the left ventricle by pulsed wave

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To date there is only one published report concerning the natural history of bicuspid aortic valve (BAV).¹ It is based primarily on clinical diagnosis, and follow up was restricted to the subgroup of patients with a BAV

Doppler¹² or the width of the diastolic colour flow image of AR relative to the left ventricular outflow tract.¹³ For this analysis, 1 + AR is mild, 2 + moderate, and 3 + and 4 + AR were grouped together and classified as severe regurgitation because of the few patients with these last two grades of regurgitation. Patients with $\leq 1 +$ AR and < 25 mm Hg transvalvar systolic gradient were considered to have normally functioning aortic valves. Aortic coarctation was imaged from the suprasternal window and the pressure gradient obtained by the continuous wave Doppler technique.¹⁴

Results

During the study period, 208 patients were diagnosed by echocardiography to have BAV. One hundred patients were excluded because Doppler examination to assess aortic valve function was not performed. In the remaining 108 patients, 57 were excluded because there were no serial studies. Thus only 51 patients with serial echocardiographic examinations at least six months apart were analysed. There were 40 men and 11 women, with a mean age of 36 (range 21 to 67) years. They had an average of three Doppler echocardiographic studies and a median follow up of 21 (range six to 46) months. In the 57 patients (36 men and 21 women) who had Doppler examination but were excluded because of no serial studies, the mean age was 39 (range 18 to 74) years.

INITIAL FINDINGS

Figure 1 shows the pattern of aortic valve involvement in the 108 patients who had Doppler assessment.

FIFTY-ONE PATIENTS WITH FOLLOW UP STUDIES

Most patients (31 of 51) had a functionally normal aortic valve, although trivial to mild AR was detected in 20 of these patients (fig 2). Significant aortic regurgitation present in 15 patients (moderate in 12 and severe in three) was the most common valve dysfunction found in our cohort of fairly young patients. Three patients had AS with mean

aortic gradients of 30, 30, and 40 mm Hg. Combined AS and AR was present in two patients; both had moderate AR and their aortic gradients were 31 and 35 mm Hg.

Coarctation was present in five patients; four had functionally normal aortic valves (three had previous surgical repair with no residual coarctation gradient and one with no previous surgery had a coarctation gradient of 25 mm Hg), and one had moderate AR and a 64 mm Hg coarctation gradient after surgical repair.

Other associated cardiac anomalies were membranous ventricular septal defect and ventricular septal aneurysm, each in one patient.

FIFTY-SEVEN PATIENTS WITHOUT FOLLOW UP STUDIES

The pattern of aortic valve dysfunction was similar in the 57 patients who did not have follow up Doppler echocardiographic studies, with 35 having a functionally normal aortic valve (fig 2). Significant AR was present in 12 patients, AS in eight patients, and combined AS and AR in two patients. Also coarctation was detected in six patients.

FOLLOW UP DATA

During follow up, the patients with functionally normal aortic valves decreased from 31 to 22 (fig 3). Of the nine patients with initial normally functioning BAV who showed progression four developed AS, two AR, and three had aortic valve surgery (one for severe AR and two for endocarditis).

Two of three patients with severe AR had aortic valve replacement. Three patients progressed to have severe AR. Thus at follow up there were four patients with severe AR.

In the three patients with AS, one had surgical dilatation of the aortic valve and one developed combined aortic valve dysfunction. There was no change in the two patients with combined aortic valve dysfunction.

Three patients had endocarditis during the follow up, leading to aortic surgery in two patients. The remaining patient developed AR after successful medical treatment for endocarditis. The infecting organisms were

Figure 1 Pattern of aortic valve dysfunction in 108 adult ambulatory patients as determined by Doppler echocardiography. AR, aortic regurgitation; AS, aortic stenosis.

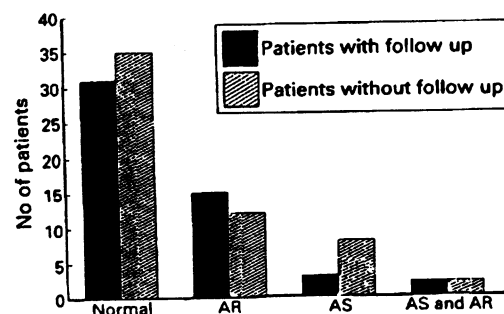
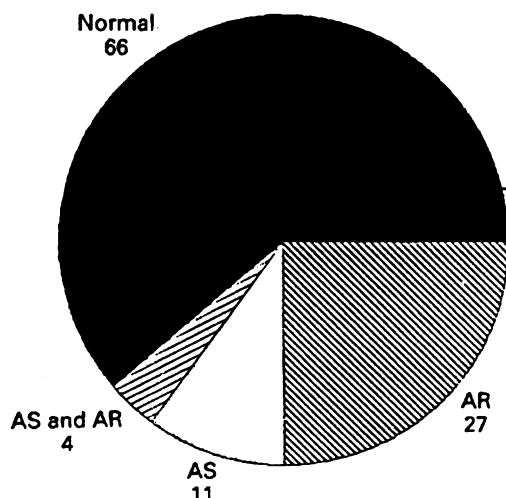
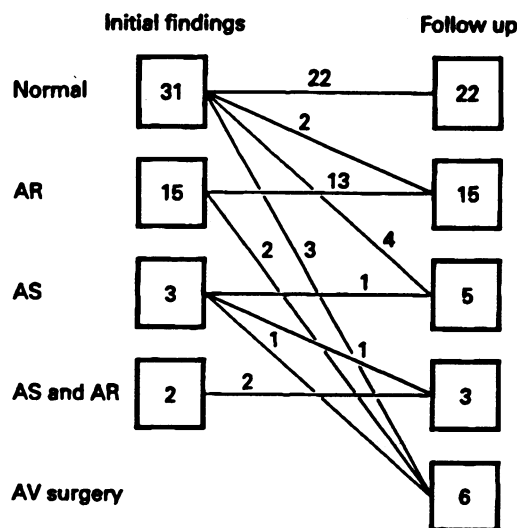


Figure 2 Aortic valve dysfunction in patients with and without follow up Doppler echocardiographic studies. Abbreviations as in fig 1.

Figure 3 Progression of aortic valve dysfunction in 51 patients with congenital bicuspid aortic valve with a median follow up of 21 months. AR, aortic regurgitation; AS, aortic stenosis; AV, aortic valve.



Streptococcus viridens in two patients and *Staphylococcus aureus* in one patient.

Discussion

Although BAV is the most common congenital valvar malformation, identification of this condition during life can be difficult. Echocardiography, particularly cross sectional studies, can reliably identify the characteristic morphological features of BAV, and is superior to clinical examination in the detection of patients with BAV.²⁻⁴ Early studies based largely on clinical findings should be re-evaluated in the modern era of Doppler echocardiography.

FUNCTIONAL SIGNIFICANCE OF BAV

The functional significance of BAV has been uncertain. Necropsy series suggest a high frequency of severe aortic valvar abnormalities, likely as a result of case selection.⁹⁻¹¹ Evidence for this is given by a very high incidence of infective endocarditis reported in these studies. In the study by Fenoglio *et al*, 77% of cases with AR had endocarditis.¹⁰

Contrary to the study by Roberts in which AS was the most usual cause of dysfunction,⁹ our study shows that AR is the most common valve dysfunction in patients with a BAV. This difference is likely to be a result of case selection and perhaps, more importantly, the younger age of our study population. Aortic stenosis accounted for about 70% of cases in Roberts' series and the average age in these patients was 49 years; 13% had AR and they were considerably younger with an average age of 31 years.⁹ Results presented by Fenoglio *et al* are similar.¹⁰ In a study of pathology after surgery from the Mayo Clinic calcific AS was more common than AR in about 20% of patients with a BAV, but the mean age at surgery was 20 years younger in those presenting with AR.¹⁵

It seems that during life, particularly in the first 50 years, a BAV will function normally, and in those with dysfunction AR is more common on account of cuspal prolapse or

Development of aortic valve dysfunction and other complications in patients with normally functioning bicuspid aortic valves

	Mills <i>et al</i> ¹		Our study ¹
	Whole group No (%)	Age > 20 No (%)	No (%)
Total	41 (100)	20 (100)	31 (100)
No change	26 (63)	8 (40)	22 (71)
AS	6 (15)	4 (20)	4 (13)
AR	5 (12)	4 (20)	2 (6)
AS and AR	1 (2)	1 (5)	0 (0)
AV surgery	3 (7)	3 (15)	3 (10)
Endocarditis	3 (7)	3 (15)	2 (6)
Deaths	5 (12)	5 (25)	0 (0)

*The totals do not equal the added category numbers because some patients were classified into more than one category. AR, aortic regurgitation; AS, aortic stenosis; AV, aortic valve.

infective endocarditis. Beyond the age of 50, the tendency for calcification of the valve progresses eventually leading to AS. Thus the pattern of aortic dysfunction in patients with a BAV will depend largely on the age of these patients.

In ambulatory patients who are young as in our patients, AR is more common than AS. Furthermore, AR is more likely to be detected by Doppler echocardiography, as used in our study, than by clinical examination alone.

PROGRESSION OF VALVE DYSFUNCTION

Although patients with a BAV susceptible to serious complications such as endocarditis, aortic dissection and aortic aneurysm,¹⁶⁻¹⁸ the frequency of development of aortic valve dysfunction is more common. In the study by which Mills *et al* based largely on clinical findings alone, about two thirds of their patients showed no progression over a mean follow up of 10.9 years.¹ This result seems to be very different from our study which showed that only 43% of patients had normal BAV in a much shorter follow up of 21 months.

Major differences exist between the two studies in the method of diagnosis and follow up and the patient population. Doppler echocardiography was used in this study and is more sensitive than clinical, phonocardiographic, and M mode echocardiographic evaluation particularly in the detection of AR. This accounts for the higher incidence of AR in our study. The patient population in the study of Mills *et al* included paediatric patients (table).¹ Indeed 21 of 41 patients were under 20 years old, and only those with a normally functioning aortic valve were followed up. The paediatric patients had a much lower incidence of development of valve dysfunction. Eighteen of 21 patients under the age of 20 compared with only eight of 20 patients over that age showed no change during follow up in their study. This is likely to be related to the rare occurrence of calcification of the valve cusps, which in their study was the major marker for valve dysfunction, in the younger patients.

When only patients over the age of 20 and with a normally functioning BAV are compared, it becomes apparent that there is a higher frequency of valve dysfunction with a

longer follow up in the patients reported by Mills *et al* compared with our series (table). These data are consistent with the pathological finding that cuspal calcification is a common and progressive process in adult BAV patients, and seems to be the major cause of valve dysfunction.^{1 9 10} Our data show that in adult patients with a BAV, significant progression of aortic valve dysfunction can occur in a short time, even in those with a normally functioning BAV at the start.

The patients with a BAV are clearly at risk for endocarditis, which often leads to rapid progression of aortic valve dysfunction.^{1 7 8} Antibiotic prophylaxis for endocarditis is crucial in these patients.

LIMITATIONS

In this study we have attempted to provide information regarding development and progression of aortic valve dysfunction with the sensitive tool, Doppler echocardiography. It could be argued that this technique may be overly sensitive leading to overestimation of valve dysfunction. This is unlikely as in all six patients who had aortic valve surgery, preoperative catheterisation and surgical findings confirmed the Doppler echocardiographic assessment in every case. The study population may not be representative of patients with a BAV in general. It is more difficult to differentiate a BAV from a tricuspid aortic valve in older patients because of the presence of calcification, and this accounts for an over-representation of young patients in our study. Although it is possible that patients with significant aortic valve dysfunction are more likely to be referred for echocardiographic assessment, and patients with progression are more likely to have follow up studies, our data suggest otherwise. Most patients who had Doppler studies (66 of 108 patients) had a functionally normally BAV, and the pattern of aortic valve dysfunction was similar in those with and without serial echocardiographic follow up. Furthermore, progression of aortic valve dysfunction was found in those with pre-existing valve dysfunction as well as in those with a normally functioning BAV. A prospective study of

patients with a BAV identified by screening a large population would be needed to remove any potential referral bias.

The follow up period is short in this study because application of Doppler echocardiography in valvar disease is a recent development. A long-term follow up study with this technique will likely provide a better insight into the natural history of BAV. Development of AS will be likely to assume more importance with a longer follow up.

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