Original Article

Aortic Dilatation at Different Levels of the Ascending Aorta in Patients with Bicuspid Aortic Valve

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Abstract

Introduction: Bicuspid aortic valve (BAV) is the most common form of adult congenital heart disease. When compared to patients with a normal trileaflet aortic valve, dilatation of the aortic root and the ascending aorta (Asc Ao) are the common findings in patients with BAV, with consequent higher risk of developing aortic aneurysm, aortic dissection and rupture. We aim to determine the site of the Asc Ao where maximum dilatation occurs in Asian adult patients with BAV. Materials and Methods: All subjects underwent full echocardiography examination. The diameter of the Asc Ao was measured at 3 cm, 4 cm, 5 cm, 6 cm and 7 cm from the level of aortic annulus to the Asc Ao in 2D from the parasternal long-axis view. Results: A total of 80 patients (male/female: 45/35; mean age: 45.3 ± 16.2 years) with congenital BAV and 30 normal control group (male/female: 16/14; mean age: 45.9 ± 15.1 years) were enrolled. The indexed diameters of the Asc Ao were significantly larger than the control group. In patients with BAV, maximum dilatation of Asc Ao occurred around 6 cm distal to the aortic annulus. Conclusion: In patients with BAV, dilatation of Asc Ao is maximal at the mid Asc Ao region around 6 cm distal to the aorta annulus.

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Introduction

Bicuspid aortic valve (BAV) is the most common form of adult congenital heart disease.[1-4] When compared to patients with a normal trileaflet aortic valve, dilatation of the aortic root and the ascending aorta (Asc Ao) are the common findings in patients with BAV, with consequent higher risk of developing aortic aneurysm, aortic dissection and rupture.[5-8]

The dilatation of any or all segments of the proximal aorta from the aortic root to the aortic arch, called bicuspid aortopathy, is present in approximately 50% of affected persons[9-12] and is a challenging clinical issue. There is not only marked variability in the phenotype of bicuspid aortopathy, but also the presence and severity of the aortic dilation appear to be independent of the degree of valvular dysfunction.[13-16]

Limited data is available on the site of the Asc Ao where maximum dilatation occurs. We aim to determine the site of the Asc Ao where maximum dilatation occurs in adult Asian patients with BAV. This is important in the serial follow-up of BAV patients with dilated Asc Ao to ensure that the region of maximal dilatation is not overlooked and is accurately measured at each follow-up echo study.

Materials and Methods

All adult patients aged from 19 to 70 years old on follow-up at the National Heart Centre, Singapore who were diagnosed with BAV were recruited into the study. In addition, normal controls who had echocardiography done for evaluation of murmurs, other cardiac symptoms and subsequently found to be normal were retrospectively studied for comparison. Patients with aortic coarctation, transposition of the great

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arteries or other congenital cardiac defects, connective tissue disorders like Marfans, Ehlers-Danlos syndrome type IV and Loeys-Dietz syndrome etc. were excluded. Patients with BAV and systolic blood pressure (SBP) of more than 140 mmHg, and those with more than moderate aortic stenosis (AS)[17] and aortic regurgitation (AR)[18] were also excluded. The ethics committee of our hospital and the local research ethics committee had approved this study.

All patients underwent full transthoracic echocardiograms. Echocardiography was performed with Philips iE33 and GE Vivid7 equipped with 2.5 MHz transducers (including 2D, M-mode and color Doppler). The zoom function was used when the aorta was scanned and the commissures were carefully examined. The diameters of the Asc Ao were measured at 3 cm (distance from the centre point of the perpendicular line drawn at the level of aortic annulus to the Asc Ao), 4 cm, 5 cm, 6 cm and 7 cm levels (Figs. 1A and 1B). The image was obtained by 2D in the parasternal long-axis view, perpendicular to the long axis of the vessel, from leading edge to leading edge during end-systole.[19] The indexed diameter (ID) was obtained after correction for body surface area. Dilatations of Asc Ao were defined as an ID greater than the mean +2SD of the values found in controls.

Intra- and Inter-Observer Viability Test

The results of 20 participants were randomly selected and repeat analyses were independently performed by 2 investigators who were each blinded to the other's results. Intra- and inter-observer reproducibility of echocardiographic derived measurements were assessed by calculating the mean difference and standard deviation between the results, with the percentage variability equal to the mean of the absolute values of the differences between the 2 measurements divided by their mean.

Statistic Analysis

All data was analysed using Stata version 13. Continuous data were summarised as mean ± SD. Categorical variables are presented as a count and percentage. The statistical significance of the difference of continuous variables between patients with BAV and normal control group was assessed by student's t-test. Differences in continuous variables among groups were calculated using one-way analysis of variance (ANOVA). Comparing to the dilation at 6 cm distal to aortic annulus, we assessed the sensitivity and specificity at 3 cm, 4 cm, 5 cm and 7 cm.

Results

The data was collected over a 72-month period from December 2007 to December 2013. A total of 200 BAV patients (200/7650 from our database, 2.6%) during the study period and 30 age-matched normal controls with normal tricuspid aortic valves (mean age: 45.9 ± 15.1 years) were retrospectively studied. Out of the 200 BAV patients, only 80 patients (male/female: 45/35, mean age: 45.3 ± 16.2 years) were included in our study after excluding patients with SBP ≥140 mmHg, and those with more than moderate aortic stenosis and regurgitation. The clinical characteristics are shown in Table 1. There is no significant differences between patients with BAV and normal controls in their clinical characteristics. We were not able to measure all the diameters of Asc Ao in all 80 patients with BAV. The

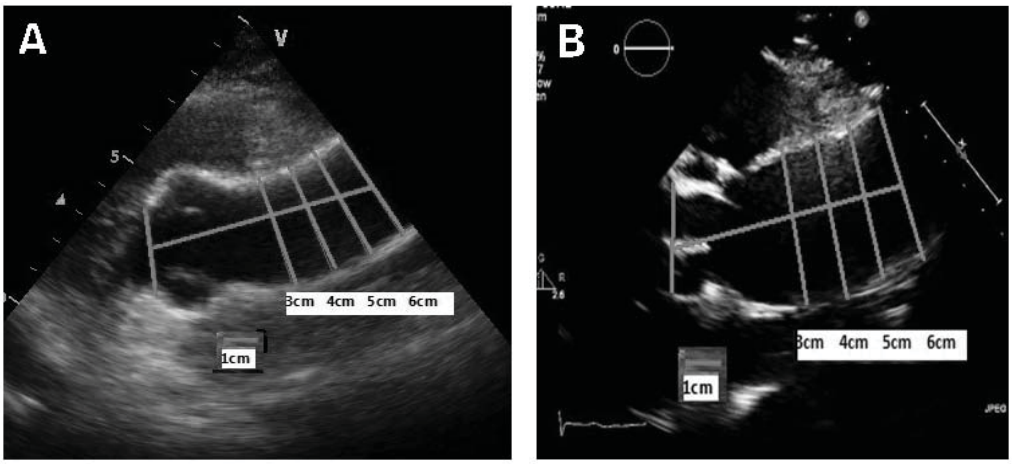

Fig. 1. Measurements of the diameter of Asc Ao at 3 cm, 4 cm, 5 cm and 6 cm from the aortic annulus. Slide A) is of a normal control with diameters of Asc Ao at 3.09 cm, 3.19 cm, 3.25 cm and 3.26 cm at 3 cm, 4 cm, 5 cm and 6 cm from the aortic annulus. Slide B) is of a patient with BAV with diameters of Asc Ao at 3.89 cm, 3.91 cm, 4.07 cm and 4.08 cm at 3 cm, 4 cm, 5 cm and 6 cm from the aortic annulus. The maximal diameter is at the site of 5 cm and 6 cm from the aortic annulus.

Table 1. Clinical Characteristics and Echocardiographic Parameters between BAV Patients and Controls

	BAV Patients (n = 80)	Normal Controls (n = 30)	*P* Value
Age (years)	45.3 ± 16.2	45.9 ± 15.1	NS
Height (cm)	163.2 ± 9.2	164.8 ± 8.5	NS
Weight (kg)	61.0 ± 12.5	64.6 ± 12.1	NS
BSA (m^2)	1.7 ± 0.2	1.7 ± 0.2	NS
Male	45 (56.3%)	16 (53%)	NS
SBP (mmHg)	120.8 ± 13.0	120.4 ± 13.5	NS
DBP (mmHg)	71.6 ± 8.6	73.8 ± 8.6	NS
HR (beat/min)	74.7 ± 15.8	73.6 ± 9.3	NS
LVEF (%)	64.5 ± 7.6	65.2 ± 6.7	NS
LV diastolic dimension (cm)	4.6 ± 0.6	4.4 ± 0.5	NS
LV systolic dimension (cm)	2.7 ± 0.5	2.5 ± 0.4	NS
Aortic velocity (m/s)	1.9 ± 0.6	1.1 ± 0.2	<0.05
Indexed diameter of ascending aorta (cm/m^2)	1.86 ± 0.39	1.59 ± 0.21	<0.05
Indexed diameter of sinus of valsalva (cm/m^2)	1.91 ± 0.58	1.62 ± 0.56	<0.05
Indexed diameter of sinotubular junction (cm/m^2)	1.65 ± 0.53	1.48 ± 0.18	<0.05

BAV: Bicuspid aortic valve; BSA: Body surface area; DBP: Diastolic blood pressure; HR: Heart rate; LV: Left ventricle; LVEF: Left ventricular ejection fraction; NS: Not significant; SBP: Systolic blood pressure

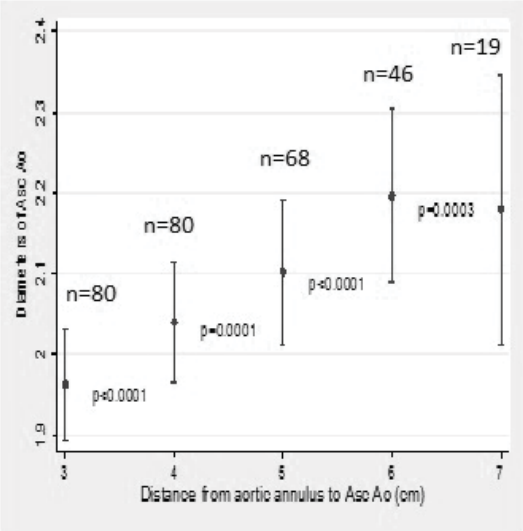

Fig. 2. Indexed diameter of Asc Ao at 3 cm, 4 cm, 5 cm, 6 cm and 7 cm from the aortic annulus (mean) and 95% CI.

respective number of patients in which the measurement was able to be performed at the various distance were 80 (3 cm), 80 (4 cm), 68 (5 cm), 46 (6 cm) and 19 (7 cm) as shown in Table 2. In normal controls, the respective number in which the measurement was able to be performed at the various distance were 30 (3 cm), 30 (4 cm), 28 (5 cm), 25 (6 cm) and 20 (7 cm).

The most common region of dilated Asc Ao and the largest ID of Asc Ao are at around 6 cm distal to the aortic annulus, and the ID of Asc Ao were significantly larger in patients with BAV compared with the normal controls at the same levels of Asc Ao (Table 2). Taking the index of 6 cm as the gold standard, sensitivity and specificity at various distances from aortic annulus to Asc Ao were 83.3%, 90.9% at 3 cm, 87.5%, 90.9% at 4 cm, 100%, 100% at 5 cm, 90%, and 100% at 7 cm, respectively. The ID of Asc Ao and 95% CI are shown in Figure 2. There were significant differences among the groups (Group 3 to Group 4, Group 4 to Group 5, Group 5 to Group 6 and Group 6 to Group 7).

Intra-and Inter-Observer Variability

The intra-observer percentage variability was 8.13 ± 2.41% and inter-observer percentage variability was 6.31 ± 3.52% for the diameter index of Asc Ao.

Discussion

BAV is not just a valvular disorder but is also associated with aortopathy and higher incidence of aortic aneurysm, aortic dissection and rupture,[4,5] which are major causes of

Table 2. Indexed Diameter and Dilatation of the Ascending Aorta at Different Sites

Distance from Aortic Annulus to the Asc Ao	3 cm (n1 = 80) (n2 = 30)	4 cm (n1 = 80) (n2 = 30)	5 cm (n1 = 68) (n2 = 28)	6 cm (n1 = 46) (n2 = 25)	7 cm (n1 = 19) (n2 = 20)
Dilated Asc Ao (BAV) (n)	33	32	33	24	9
Dilated Asc Ao (BAV) (% based on diameter measurable)	41.3%	40.0%	48.5%	52.2%	47.3%
Indexed diameter of Asc Ao (BAV) (cm/m^2)	1.96 ± 0.32	2.04 ± 0.34	2.10 ± 0.38	2.20 ± 0.37	2.18 ± 0.37
Indexed diameter of Asc Ao (controls) (cm/m^2)	1.58 ± 0.22	1.59 ± 0.22	1.60 ± 0.26	1.60 ± 0.23	1.60 ± 0.24

ASc Ao: Ascending aorta; BAV: Bicuspid aortic valve; n1: Number of patients; n2: Number of controls

morbidity and mortality. Patients with BAV have larger aortic dimensions than patients with a normal trileaflet aortic valve.[7,8] Aortic dilatation can occur anywhere between the aortic root and the aortic isthmus, but most commonly occurs in the Asc Ao in BAV disease.[6] Some studies reported that the prevalence of dilatation of the Asc Ao among persons with a BAV ranges from 20% to 84%. [9,10,20-25] This differentiation is related to different study populations, assessment methods, aortic size thresholds and age. But few studies focused on finding the region or site of the Asc Ao at where maximal aortic dilatation occurs.

Bauer M et al[26] reported that the diameter of the Asc Ao in patients with BAV and dilation was significantly larger than in those with a tricuspid aortic valve and dilation. In addition, distances between aortic valve level and point of maximum diameter of the Asc Ao at the outer and inner curves of the vessel in patients with BAV without dilatation were greater than those of the coronary artery disease group. Our study also found that the diameters of Asc Ao in patients with BAV are significantly larger than normal controls at all different sites of the Asc Ao.

In our study, we demonstrated that the indexed aortic dimensions at the sinus of Valsalva, sinotubular junction and Asc Ao in patients with isolated BAV were larger than in normal controls. Our study also found that the maximal dilatation of Asc Ao was at mid-Asc Ao (around 5 cm to 6 cm distal to the aortic annulus), which is probably a combination of haemodynamic and histological changes of the ascending aortic wall in patients with BAV.

Some studies have reported differences in histological and haemodynamic findings of the ascending aortic wall between patients with bicuspid and tricuspid aortic valves.[27,28] Bauer et al reported that patients with a BAV had thinner elastic lamellae of the aortic media and greater distances between the elastic lamellae than patients with a tricuspid aortic valve.[27]

In a study by Viscardi et al[28] looking at ascending aortic flow in patients with BAV, they found asymmetrical distribution of velocity flow towards the convexity region of the mid-Asc Ao and symmetrical blood flow in the distal Asc Ao. On the contrary, blood flow in patients with tricuspid aortic valve was symmetrical in each aortic segment. Comparison between bicuspid and tricuspid models showed asymmetrical and higher flow velocity in bicuspid models. Both the histological and haemodynamic flow changes may contribute to the site of maximal ascending aortic dilatation in this subset of patients.

The ascending aortic diameter and the extention of aortic dilation in the BAV group were found to be significantly associated with patient age, gender and body surface area.[29-32] The 2 groups of patients in our study were matched with respect to age, sex, and body surface area to eliminate these confounding factors and hence our result showing the site of maximal dilatation at 6 cm distal to the aortic annulus is consistent and in agreement with the asymmetrical flow pattern and histological changes in the Asc Ao of BAV patients.

Clinical Implication

Transthoracic echocardiography (TTE) is commonly performed for serial follow-up of Asc Ao dilatation in patients with BAV. It is important to consistently measure the Asc Ao diameter at the site of maximum dilatation during serial echo examinations. In our study, we found that the largest dilatation of Asc Ao occurred at around 6 cm distal to the aortic annulus. The highest percentage is also around 6 cm distal to the aortic annulus. The measurements made at aortic levels at 6 cm would be able to determine the existence of aortic dilatation. Hence, the sensitivity and specificity made at other aortic levels besides 6 cm were also calculated, using 6 cm as the gold standard. High sensitivity and specificity are also found at around 5 cm distal to the aortic annulus. This finding suggests that in patients with BAV, there is a need to measure the diameter not only at the proximal Asc Ao, but also at the mid-part of the Asc Ao (around 5 cm to 6 cm distal to the aortic annulus) where maximum dilatation commonly occurs. Although visualisation of the mid-distal Asc Ao may be difficult in most adults, more than 50% were still measurable in our cohort. Consistent measurement at the same site of maximum Asc Ao dilatation will allow for more accurate monitoring of progressive Asc Ao dilatation in patients with BAV.

Limitations

In our study, each group had a relatively small sample size, particularly those groups at around 6 cm and 7 cm distal to the aortic annulus and normal controls. Due to limited echo window, our sample sizes in this study were sufficient for statistical analysis, but this fact limits the statistical power of our analysis. AR and AS showed different impact on aortic dilatation in different levels of the Asc Ao: the diameter of aortic sinus is affected by AR severity, whereas AS severity shows a linear relationship with the diameter of the tubular portion. For the present study, BAV patients with more than moderate AR and AS were excluded to minimise the effect of valve dysfunction. In addition, in aorta that is tortuous or meandered, there is further inherent limitation in the measurement of the entire length of the Asc Ao; hence the number of possible measurements at increasing distance from the annulus become smaller, especially at 6 cm to 7cm distances from aortic annulus. Other cardiac imaging modalities, including computed tomography (CT) and magnetic resonance

imaging (MRI), may be better for the accurate evaluation of the entire thoracic aorta. We did not try to measure the distal Asc Ao and aortic arch for more complete evaluation and analysis of site of maximal dilatation, because they were not easily seen in some adult patients. So, they were not measured in all patients with BAV.

Conclusion

In our cohort of mainly Asian patients with BAV, Asc Ao dilatation occurs and is maximal at the mid-part of the Asc Ao around 5 cm to 6 cm distal to the aortic annulus. This information is important to ensure that the maximum dilatation of the Asc Ao is measured and documented in each and subsequent echo study performed for serial follow-up of these BAV patients.

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