Research Article

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Evaluation of Both Aortic Diameters (Annulus, Sinus of Valsalva, Ascending Aorta) and Z-Scores in Patients with Bicuspid Aortic Valve, Aortic Valve Prolapse, and Mitral Valve Prolapse

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Abstract

Objectives: The aim of this study is to evaluate echocardiographically (and determine pathology if there is any) the diameters and Z-scores of aortic annulus, sinus of valsalva and ascending aorta in patients with bicuspid aortic valve, aortic and mitral valve prolapse and healthy children.

Materials and Methods: This retrospective cross-sectional study includes three hundred and fifty patients with bicuspid aortic valve, aortic and mitral valve prolapse and healthy children. One hundred and ninety of them (54.3%) are non-syndromic, non-operated, hemodynamically stable patients. One hundred and sixty (45.7%) are heathy control group. Three hundred and fifty of 0-18 (average 10.47) years old patients are boys (58.6%) and 150 are girls (42.9%). Aortic annulus, sinus of valsalva and ascending aorta were measured on the parasternal long axis view. The indexed values were obtained by dividing all measured parameters by body surface area. The Z-scores and percentile values are calculated for each group.

Results: Average indexed aortic annulus value is 1.59 cm/m^2; sinus of Valsalva value is 2.27 cm/m^2 and ascending aortic value is 2.07 cm/m^2 in our study. Average aortic annulus Z-score is 0.4; sinus of valsalva Z-score is 0.08 and ascending aorta Z-score is 0.15.

Conclusion: In the present study, children aged between 0.33-17.8 years, mean aortic diameters were determined in three levels. According to the nomogram we used in our study, our dilation rate was 33.6% in the patient group, 21.4% in the entire patient group, and 6.9% in the control group.

Keywords: Aortic valve, ascending aorta, bicuspid aortic valve, mitral valve prolapse, aortic valve prolapse, children, Z-scores, congenital heart defects

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Introduction

Bicuspid aortic valve (BAV) is one of the most common congenital malformations that may accompany isolated or congenital heart diseases. Although the incidence of isolated BAVs has been reported to be 1% in the general population, its prevalence reaches 0.5-0.8% in healthy school children and young adults and 50-85% in patients with aortic coarctation[1-4]. Mitral valve prolapse (MVP), which can be defined as the extension of the valve leaflets into the left atrium, and in which echocardiographic variations are common, is a disease spectrum in which the incidence has been reported generally between 1% and 5%[5,6].

Aortic valve prolapse (AVP), which can be defined as the prolapse of one or more leaflets of the aortic valve, is a pathology often encountered with congenital heart diseases such as ventricular septal defect (VSD) and tetralogy of Fallot.

While aortic dilatation, which predisposes to life-threatening rupture, dissection, and mortality, is frequently encountered in adults, especially in syndromic patients, the rates of dilatation in children are not clear[7,8]. Nomograms and Z-score formulas designed for all cardiac structures, which vary according to the age, gender, and body surface area (BSA) of the patients, are very helpful in determining aortic dilatation[9-14].

The purposes of this cross-sectional study are; determination of diameters and Z-score percentile values of the aortic annulus (Aoa), sinus of Valsalva, and ascending aorta, patients with non-syndromic, isolated BAV, AVP and MVP, comparison with normal healthy children, and determination of dilatation rates, if any.

Materials and Methods

Ethical committee approval was obtained from the Manisa Celal Bayar University Faculty of Medicine Health Sciences Ethics Committee (approval no.: 20.478.486/1821, date: 03.05.2023). Informed consent was taken from the family of the patients.

Patients

A total of 350 patients, [aged 0.33-17.8 years (10.47±4.23)], 152 girls (43.4%), and 198 boys (56.6%) who applied to the pediatric cardiology clinic of Manisa City Hospital between June 2020 and June 2022 with complaints of chest pain, palpitations, fatigue, fainting, and murmurs were retrospectively examined.

Anthropometric measurements, blood pressure values, physical examination, and electrocardiogram records of the patients were accessed. BSAs of the patients were calculated. Polyclinic file records of patients diagnosed with BAV, AVP, MVP, mitral valve regurgitation (MR), aortic valve regurgitation (AR), and aortic valve stenosis (AS) were examined. Echocardiography reports were evaluated retrospectively. Patients whose Aoa, sinus Valsalva (SoV), and ascending aorta (Asc ao) diameters were all recorded and included in the study. Those whose diameter measurements were recorded at one or two levels and whose dysrhythmia was detected were excluded from the study. Among the patients with normal echocardiography findings with functional murmur, the patients whose Aoa, SoV, and Asc ao diameters were all recorded constituted the control group. Patients with patent foramen ovale (PFO) or secundum, small atrial septal defect (ASD) (<3 mm), and small, muscular, clinically hemodynamically insignificant VSD were included in the control group. Patients with Marfan, Loeys-Dietz, Turner, Down, Alagille syndrome, patients with hemodynamically significant congenital heart disease, those who underwent surgery because of that reason, and patients with acquired rheumatic heart disease and hypertension were excluded from the study. Echocardiographic examination of a single application during the study period was included. Repeated measurements within the study period were excluded from the study.

Patients were grouped according to their diagnosis.

Group 1 (n=160) patients diagnosed with an innocent murmur with normal echocardiography findings (Patients with hemodynamically insignificant PFO/ASD/very small VSD were also included in this group).

Group 2 (n=60) patients with BAV, AVP, and AR-AS. Group 3 (n=100) patients with MVP and MR.

Group 4 (n=30) was classified as patients with coexisting aortic and mitral valve pathologies.

Patients were also scored according to the coexistence of their existing pathologies with BAV, AVP, MVP, MR, AR, AS, and aortic dilatation. Namely:

AVP: 1 point, AVP+AR: 2 points, AVP-AR-AS: 3 points, MVP: 1 point, MVP+MR: 2 points, BAV: 4 points, BAV-AVP: 5 points, BAV-AS-AR: 6 points, aortic dilatation at BAV+1 level: 7 points, aortic dilatation at BAV+2 level: 8 points, aortic dilatation at BAV+3 level: 9 points.

According to their scores, Group 1: Patients with scores between 0 and 7 points, Group 2: Patients with scores between 8 and 14 points.

Patient group: Group 1: BAV, AVP, MVP, AR, MR, AS, aortic dilatation.

Control group: Group 2: Patients with normal echocardiography findings.

Echocardiography

Echocardiographic recordings were created by the same investigator (Dr. Ş.P.) using the Philips Afiniti 50 C (Release 3.0, Philips healthcare, 3000 minuteman road, Andower MA01810 USA) device, using S4-2, S8-3 mHz probes. M-mode, 2 D, color Doppler, continuous wave Doppler, pulsed wave, left ventricular systolic and diastolic diameters, interventricular septum diastolic diameter, left ventricular posterior wall diastolic diameter, aortic root and left atrium diameters, peak and mean aortic gradient measurements in the presence of aortic stenosis by Doppler echocardiography, whether aortic regurgitation is existent or not, its definition with color Doppler, its degree, the status of the aortic valve in parasternal short and long axis examination, fusion type, the status of mitral valve leaflets in parasternal long axis examination, the presence and degree of mitral valve insufficiency, annulus, sinus of Valsalva, ascending aorta in parasternal long axis examination were measured as recommended by Lopez et al.[15]. The aortic valve Doppler values were measured from the apical-4 chamber and suprasternal windows. Peak and mean gradient values were recorded. Index values were obtained by dividing the aortic diameters at the three levels by BSA. A schematic parasternal echocardiographic image where the measurements were made is shown in Figure 1. The echocardiographic image of BAV is shown in Figure 2.

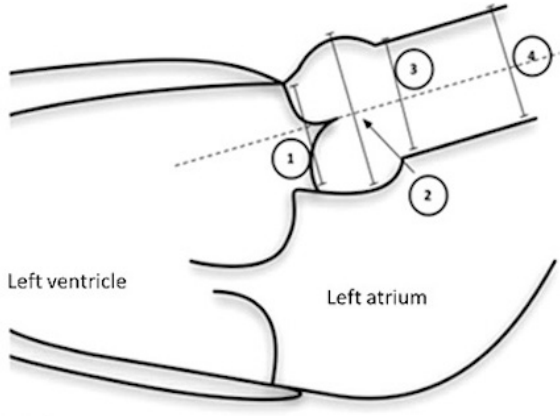

Figure 1. The parasternal long axis schematic view of echocardiographic aortic diameters

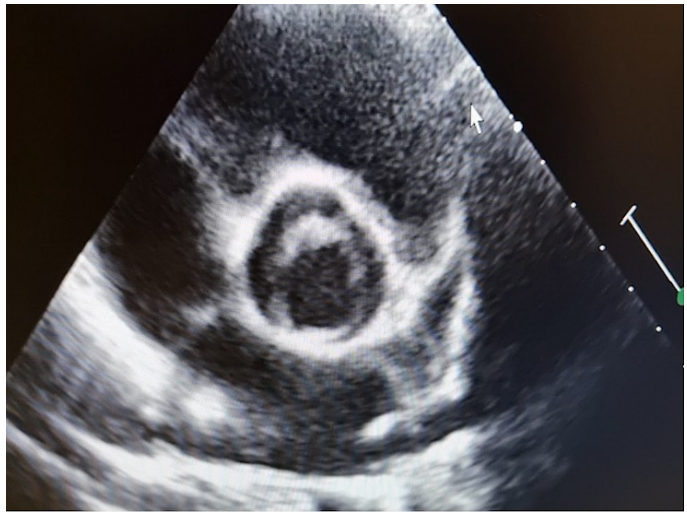

Figure 2. The echocardiographic parasternal short-axis view of bicuspid aortic valve

Innocent murmurs were detected in 7617 of 10938 patients evaluated by echocardiography (69%). Of these, 3371 patients had congenital heart disease. Z-scores and BSA values (according to Haycock formula) were determined by Cantinotti et al.[10] (http://parameterz.com).

Statistical Analysis

All statistical analyses were conducted using SPSS 15.0 (SPSS for Windows v.15.0; IBM- SPSS Inc, Chicago, IL, USA). Independent samples t-test was used to compare parametric values, and Pearson correlation test and linear regression analysis were used to evaluate the correlation between the variables. Continuous variables were recorded as mean ± standard deviation (SD). P-value <0.05 was considered statistically significant.

Results

Innocent murmurs were detected in 7617 of 10938 patients (69%) who were evaluated with echocardiography between June 2020 and 2022. Of the 350 patients included in the study, 152 were female (43.4%) and 198 were male (56.6%). Group 1 (Patient Group): 190 patients (54.3%), Group 2 (Control Group): 160 patients (46.7%). The basic characteristics of the patients are presented in Table 1. Z-scores of the patients' aortic diameters and BSA (according to the Haycock formula) were prepared according to the study of Cantinotti et al.[10] (http://parameterz.com).

Table 1. Basic characteristic properties of the all patients

	Minimum	Maximum	Mean	SD
Age (year)	0.33	17.8	10.47	4.23
Weight (kg)	6.66	86	36.32	16.89
Height (cm)	63	193	140.71	26.44
BSA (m^2)	0.34	2.02	1.16	0.37
Aoa (cm)	0.84	2.64	1.74	0.31
Aoa/m^2 (cm/m^2)	0.99	3.02	1.59	0.36
Z-score Aoa	-3.12	4.51	0.40	1.02
SoV (cm)	1.23	3.62	2.27	0.48
SoV/m^2 (cm/m^2)	1.25	4.54	2.07	0.53
Z-score SoV	-2.74	5.85	0.086	1.15
Asc ao (cm)	1.05	3.51	2.07	0.41
Asc ao/m^2 (cm/m^2)	1.15	5.02	1.91	0.49
Z-score Asc ao	-2.21	6.29	0.15	1.26
ARr	11.8	27.7	16.3	0.24

SD: Standard deviation, BSA: Body surface area, Aoa: Aortic annulus, SoV: Sinus valsalva, Asc ao: Ascending aorta, ARr: Aortic Root ratio

The minimum, maximum, mean, and SD values of demographic and echocardiographic data of the patient and control groups are displayed in Table 2. When the patient and control groups were compared using the independent samples t-test, no statistically significant difference was detected between the two groups in terms of gender, Z-score SoV, Asc ao/m^2, and Z-score Asc ao. The distribution of the patients' current pathologies according to the scores received is displayed in Tables 3a and 3b. The percentile values of patients in Groups 1 and 2 are presented in Table 4.

There were 28 patients (14.7%) who scored 1 point, 85 patients (44.7%) who scored 2 points, 6 patients (3.2%) who scored 3 points, 17 patients (8.9%) who scored 4 points, 13 patients (6.8%) who scored 5 points, 17 patients (8.9%) who scored 6 points, 9 patients (4.7%) who scored 7 points, 6 patients (3.2%) who scored 8 points, 3 patients (1.6%) who scored 9 points, 2 patients (1.1%) who scored 10 points, and 3 patients (1.6%) who scored over 10 points.

When the patient group is examined; There were 20 patients with Aoa Z-score ≥2 and 3 patients with Z-score ≥3. There were 14 patients with a SoV Z-score ≥2 and 2 patients with a Z-score ≥3. There were 15 patients with an Asc ao Z-score of ≥2 and 10 patients with a Z-score of ≥3. There were 49 patients with a Z-score 2.0-2.99, 15 patients with a total Z-score ≥3. In the patient group (Group 1), the total dilatation rate was 33.6%. In all patients (Group 1+2), the total dilatation rate was 18.3 %. Z-score values and the ratio of dilatation are presented in Figures 3-5.

When the control group is examined; There were 6 patients with Aoa Z-score ≥2, 2 patients with SoV Z-score ≥2, and 3 patients with Asc ao Z-score ≥2. The patient with a Z-score ≥3 was not in the control group. There were 11 patients with a Z-score >2, and the dilation rate was 6.87%. In all patients (Group 1+2), the total dilatation rate was 21.4%. There were 75 patients with a Z-score of

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Table 2. The demographic and echocardiographic data of the patient and control groups

		Minimum	Maximum	Mean±SD	p-value
Age (year)	Group 1 (n=190)	0.7	17.50	11.38±3.73	0.001
	Group 2 (n=160)	0.33	17.80	9.45±4.57	
Weight (kg)	Group 1 (Patient)	9.5	84.00	39.19±15.36	0.001
	Group 2 (Control)	6.66	86.00	33.17±18.10	
Height (cm)	Group 1	68	193.00	147.5±23.22	0.001
	Group 2	63	180.00	133±28.08	
BSA (m^2)	Group 1	0.45	1.97	1.23±0.33	0.001
	Group 2	0.34	2.02	1.07±0.39	
Aoa (cm)	Group 1	1.01	2.63	1.82±0.28	0.001
	Group 2	0.84	2.64	1.64±0.32	
Aoa/m^2 (cm/m^2)	Group 1	0.99	3.02	1.54±0.32	0.009
	Group 2	1.02	2.94	1.64±0.39	
Z -score Aoa	Group 1	-3.12	4.51	0.54±1.1	0.005
	Group 2	-2.28	2.25	0.23±0.09	
SoV (cm)	Group 1	1.3	3.62	2.35±0.39	0.001
	Group 2	1.23	3.29	2.17±0.41	
SoV/m^2 (cm/m^2)	Group 1	1.25	3.83	2.00±0.46	0.001
	Group 2	1.29	4.55	2.2±0.59	
Z-score SoV	Group 1	-2.74	5.85	0.13±1.29	0.427
	Group 2	-2.35	2.96	0.036±0.96	
Asc ao (cm)	Group 1	1.37	3.51	2.19±0.41	0.001
	Group 2	1.05	2.82	1.94±0.38	
Asc ao/m^2 (cm/m^2)	Group 1	1.15	5.02	1.86±0.49	0.099
	Group 2	1.21	3.67	1.95±0.49	
Z-score Asc ao	Group 1	-2.21	6.29	0.36±1.45	0.099
	Group 2	-2.12	2.63	0.07±0.95	

SD: Standard deviation, BSA: Body surface area, Aoa: Aortic annulus, SoV: Sinus Valsalva, Asc ao: Ascending aorta

Table 3a, b. The distribution of the patients' pathologies according to the scores

Diagnosis	Score (a)	Score (b)	n	%
AVP	1	1	28	14.7
MVP	1	2	85	44.7
AVP+AR	2	3	6	3.2
AVP+AR+AS	3	4	17	8.9
MVP+MR	2	5	13	6.8
BAV	4	6	17	8.9
BAV+AVP	5	7	9	4.7
BAV+AR+AS	6	8	6	3.2
BAV+Aort dilatation-1 level	7	9	3	1.6
BAV+Aort dilatation-2 level	8	10	2	1.1
BAV+Aort dilatation-3 level	9	>10	3	1.6
		>10	3	1.6

AVP: Aortic valve prolapse, AR: Aortic valve regurgitation, AS: Aortic valve stenosis, MVP: Mitral valve prolapse, MR: Mitral valve regurgitation, BAV: Bicuspid aortic valve

>2 (64 patients in Group 1, and 11 patients in Group 2). The range of aortic measurements of the studies performed by Spaziani et al.[16] is shown in Table 5. The Z-score measurements and the rate of dilatation are shown in Table 6. The ratios of aortic dilatations in Group 1 are shown in bar graphics (Figures 3-5).

Discussion

Isolated BAV, one of the most common congenital malformations in both children and adolescents, is generally a benign lesion; however, in a small proportion of patients, it causes valve dysfunction that is significant enough to require surgical or interventional treatment. Again, because aortic dilatation and progression have been reported in childhood, careful echocardiographic follow-ups are valuable[16].

Table 4. Percentile values of patients

	5p	10p	25p	50p	75p	95p
Aoa Group 1 (n=190)	1.36	1.46	1.62	1.83	2.02	2.32
Aoa Group 2 (n=160)	1.1	1.22	1.43	1.63	1.85	2.2
Aoa/m²-Group 1	1.16	1.21	1.3	1.46	1.71	2.17
Aoa/m²-Group 2	1.14	1.21	1.36	1.59	1.81	2.54
Z-score Aoa-Group 1	-1.02	-0.69	-0.09	0.42	1.18	2.32
Z-score Aoa-Group 2	-1.29	-0.94	-0.33	0.22	0.91	1.94
SoV-Group 1	1.71	1.82	2.12	2.36	2.57	3.05
SoV-Group 2	1.51	1.68	1.89	2.19	2.45	2.98
SoV/m²-Group 1	1.43	1.51	1.66	1.89	2.24	2.9
SoV/m²-Group 2	1.48	1.55	1.75	2.11	2.50	3.61
Z-score SoV-Group 1	-1.89	-1.51	-0.65	0.01	0.92	2.37
Z-score SoV-Group 2	-1.54	-1.18	-0.62	0.09	0.79	1.58
Ass ao-Group 1	1.6	1.72	1.87	2.19	2.41	2.91
Ass ao-Group 2	1.39	1.48	1.64	1.97	2.21	2.61
Asc ao/m²-Group 1	1.32	1.4	1.53	1.75	2.09	2.81
Asc ao/m²-Group 2	1.3	1.38	1.63	1.88	2.18	3.05
Z-score Asc ao-Group 1	-1.7	-1.35	-0.77	0.2	1.29	3.07
Z-score Asc ao-Group 2	-1.79	-1.4	-0.72	-0.11	0.59	1.5

Aoa: Aortic annulus, SoV: Sinus Valsalva, Asc ao: Ascending aorta

In a study involving a large pediatric population diagnosed with BAV, aged between 0 and 20 years, the strongest predictors of progressive dilatation of the proximal ascending aorta were severe aortic stenosis and moderate/severe aortic regurgitation[17]. In contrast, a rather slow rate of aortic dilatation has been reported in

Table 5. The range of aortic measurements

	Level	Median	Range	Median age
Kaiser et al.[20]	SoV (mm)	20.7	13.8-31.8	9 (2-20) year
Children without cardiovascular disease	Asc Ao (mm)	18	12.0-26.7	
Spaziani et al.[16]	Aoa (mm)	17	10.0-30.0	9.18 (5-18) year
Children with BAV	SoV (mm)	22.5	14-38	
	Asc Ao (mm)	22	12.0-41.0	
This study	Aoa (mm)	18.2	10.1-26.3	11.38 (0.7-17.7) year
Patient group	SoV (mm)	23.5	13-36.2	
	Asc Ao (mm)	21.9	13.7-35.1	
Control group	SoV (mm)			
	Asc Ao (mm)			

Aoa: Aortic annulus, SoV: Sinus Valsalva, Asc ao: Ascending aorta, BAV: Bicuspid aortic valve

Table 6. The Z-score measurements

		Mean Z-score±SD	Prevalence of a Z-score ≥2
Merkx et al.[19]	SoV	-0.2±1.5	8±2
n=234			
Mean age: 6.1	STJ	0.3±1.8	15±2
	Asc Ao	0.8±1.7	24±3
Total dilatation			19.30%
Our study (Patient group)	Aoa	0.54±1.1	25
n=190			
Mean age: 11.38	SoV	0.13±1.29	18
	Asc Ao	0.36±1.45	35
Total dilatation			33.6%

SD: Standard deviation, Aoa: Aortic annulus, SoV: Sinus Valsalva, Asc ao: Ascending aorta

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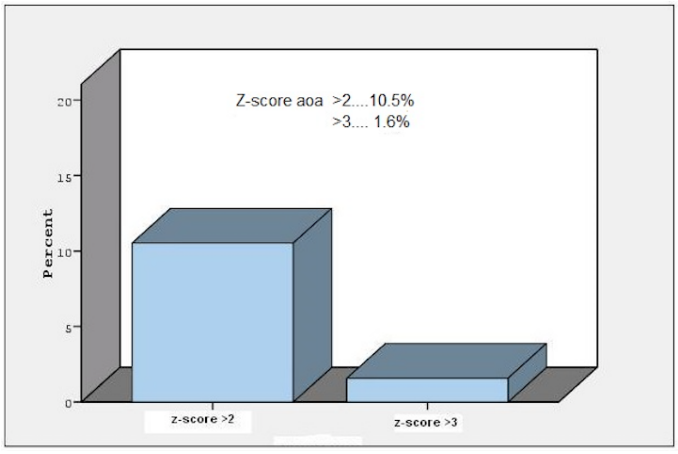

Figure 3. The ratio of dilatation of aortic annulus in Group 1

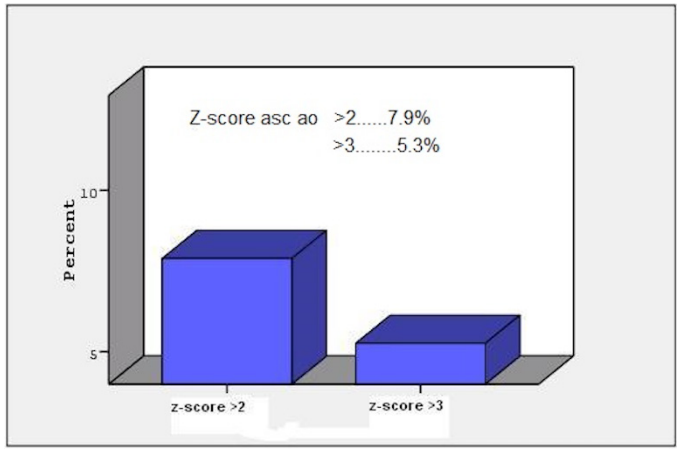

Figure 5. The ratio of dilatation of ascending aorta in Group 1

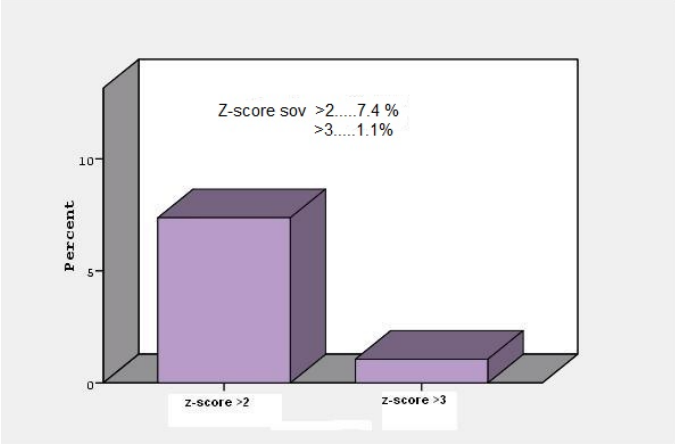

Figure 4. The ratio of dilatation of sinus of valsalva in Group 1

children with a normally functioning BAV, regardless of the type of leaflet fusion[17]. However, it is also interesting that significant dilatations, thought to be related to degeneration of the aortic wall, have been reported in young patients with normally functioning BAVs without hemodynamic stress[17]. Patients who did not have hemodynamically significant congenital heart disease, those who did not have genetic diseases such as Marfan, Turner, or Loeys-Dietz, and those who did not undergo an interventional or surgical procedure were included in our study. Because there were no syndromic patients in our study, it was thought that it would be interesting to determine the presence of aortic dilatation only in patients with BAV and aortic and mitral valve prolapse.

In the reports of Zanjani and Niwa[18] aortic dilatation and aortopathy in congenital heart diseases were examined and it was emphasized that although it is less serious than Marfan syndrome, it is not a benign disease, its pathophysiology is complex and not yet fully understood, and aortic diameter measurements should be made with special care[18].

In a study conducted by Merkx et al.[19], aortic diameters were retrospectively examined in a group of patients with syndromic (Turner, 22q11 deletion, etc.) and congenital heart disease (Coarctation of aorta, VSD, PDA, ASD, hypoplastic aortic arch) accompanying BAV. Z-scores were determined by two different methods, Gautier et al.[11] and Campens et al.[12], and it was emphasized that there was no need for rupture, dissection, or protective aortic intervention[19].

While the Z-score mean value was found to be -0.2 ±1.5/0.3±1.8 according to Gautier at the SoV/ascending aorta level, the value was 0.6±1.5/1.4±2.2 according to Dampens. Again, in the study of Merkx et al.[19], in a total of 234 patients, 8 patients with SoV Z-score >2 and 24 patients with ascending aorta Z-score >2 were reported[19]. In our study, the Z-score mean value in the patient group was 0.13±1.29 for SoV and 0.36±1.45 for the ascending aorta level, while there were 16 patients with SoV Z-score >2 and 25 patients with ascending aorta Z-score >2.

Kaiser et al.[20] also evaluated the aortic diameters of 53 patients with a mean age of 9 years without cardiovascular disease by contrast-enhanced CMR angiography and reported the mean diameter of the SoV as 20.7 mm and the mean diameter of the Asc ao as 18 mm. In our study, the average age of the control group (the group without any cardiovascular anomalies) was 9.45 years. The mean SoV diameter was found to be 21.7±4.1 mm, and the mean ASC diameter was 19.4±3.8 mm. These figures were compatible with the MR angiography measurements of Kaiser et al.[20]. Wozniak-Mielczarek et al.[21] reported that the most common cardiovascular anomaly was aortic root dilatation with a rate of 81.19% in their study including children and adults with Marfan syndrome (44 children, 57 adults, a total of 101 patients). When only patients in the pediatric age group were examined, the average aortic root diameter was reported as 31.54±6.5 (17-46 mm) and the average Z-score was 2.57±1.26[21]. In our study, the average SoV diameter in the patient group was 23.5±3.9 mm and the average Z-score was 1.3±12.9.

Wozniak-Mielczarek et al.[22] reported the development of a new screening tool for aortic root dilatation in their study involving 193 children with Marfan and Marfan-like syndrome. In their study, the average age was 12.3 years, the average height was 160 cm, and the average body weight was 45 kg. They obtained the value they called Aortic Root ratio (ARr) by dividing the aortic root diameter (mm) by the patient's height (cm) and multiplying it by 100. In measurements calculated by two different techniques: the leading edge technique in end diastole and the inner edge technique in mid-systole, the average ARr was reported as 18.09±3.9 (12.3-35.6) to 17.78±3.85 (12.3-34.2), respectively. The optimal cut-off value calculated for aortic root dilatation has been reported as ≥18.7[22]. In our study, using the inner edge technique, the average ARr was calculated as 16.3±0.0.24 (11.8-27.7) in the whole group, 16.1±2 (11-24) in our patient group, and 16.59±2 (12-27) in our control group. It is a lesion that can accompany some congenital heart diseases in studies conducted on children and adults with Marfan syndrome. In a study reporting that isolated MVP is an independent determinant of aortic root diameter in the general population; That the average age was 37.9 years and the aortic root diameter was 30.4±0.1 mm in patients with MVP (n=637) and 29.5±0.1 mm in the control group (n=627) was reported[23].

Conclusion

In this cross-sectional and retrospective study, Aoa, sinus of Valsalva, and ascending aorta diameters, index values, Z-scores, and percentiles were determined in patients diagnosed with BAV without any additional congenital heart disease or syndrome between the ages of 0.3 and 17.8 years and in the control group.

Aortic dilatation increases with age. Dilatation rates vary depending on the nomograms used. According to the nomogram we used in our study, our dilatation rate was 33.6% in the patient group, 21.4% in the all patient group, and 6.9% in the control group.

This study emphasizes that the dilation rate determined should be considered in the control group of patients without hypertension and any syndrome or without a family history of aortopathy. In addition, this study underlines that aortic diameters should be measured in routine echocardiographic examinations and repeated during follow-ups for the aforementioned patients in the control group.

Ethics

Ethics Committee Approval: Ethical committee approval was obtained from the Manisa Celal Bayar University Faculty of Medicine Health Sciences Ethics Committee (approval no.: 20.478.486/1821, date: 03.05.2023).

Informed Consent: Informed consent was taken from the family of the patients.

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