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RESEARCH ARTICLE

Prevalence and Characteristics of Ascending Aorta Dilatation in Pediatric Patients with Bicuspid Aortic Valve and Aortic Valve Stenosis: A Cross-Sectional Analysis

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ABSTRACT

Objective: We aim to examine the prevalence and characteristics of ascending aorta (AA) dilatation in pediatric patients, specifically focusing on its relationship with the bicuspid aortic valve (BAV) and aortic valve stenosis (AS). We also seek to identify potential risk factors and clinical implications of AA dilatation within this population.

Materials and Methods: In this retrospective cross-sectional study, 71 pediatric patients who underwent echocardiography between 2010 and 2022 were analyzed. AA dilatation is seen in connective tissue disorders and in BAV. Our objective was to look at the potential diagnoses for pediatric AA dilatation, focusing on associated aortic valve diseases. Patients with genetic syndromes, congenital heart defects, or other cardiac conditions were excluded. Aortic measurements were taken using standard techniques, and z-scores were calculated. Statistical analyses were performed to evaluate associations between aortic dilatation, valvular conditions, and other variables.

Results: The median age of 71 patients was 9 years (1 day–18 years). AA dilation was common in patients with AS (36%) and BAV (47%). Isolated aortic root dilation was observed in 49% of cases. AA z-scores were statistically higher in BAV patients (p=0.034), but no difference was found in aortic root z-scores between BAV and non-BAV patients (p=0.117). AA z-scores correlated with aortic root z-scores and BAV presence (p=0.037, p=0.033). Patients with AS had smaller aortic root z-scores compared to those without AS (p=0.003). Smaller aortic root z-scores were also found in patients with both AS and BAV compared to those without either condition (p=0.0001). We could not find a statistically significant difference in AA dilatation in patients with and without AS.

Conclusion: AA dilatation is a significant concern in pediatric patients with BAV, especially when AS is present. Routine echocardiography is essential for monitoring and early detection of aortic dilatation. Further studies are needed to understand the long-term implications and to optimize diagnostic approaches.

Keywords: Ascending aorta dilatation, bicuspid aortic valve, children

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INTRODUCTION

Congenital heart defects (CHDs) are a prominent cause of ascending aorta (AA) dilatation, although other conditions can also contribute.[1–4] The most common CHD, bicuspid aortic valve (BAV), shares histological abnormalities in the AA similar to those found in connective tissue disorders such as Marfan syndrome, Loeys-Dietz syndrome, and Ehlers-Danlos syndrome type IV. These syndromic conditions are associated with AA dilatation, leading to aortic dissection. Unlike aortic valve stenosis (AS) and regurgitation, de novo AA dilatation is typically observed in the presence of BAV.[5–7] Numerous biological variables, including exercise capacity, are correlated with AA dilatation, acting as potential confounders or contributors in patient evaluation.[8] Accurate assess-

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ment of pathologic AA dilatation thus requires consideration of biological variables such as age, height, body surface area (BSA), and gender to eliminate the influence of known confounders. However, the literature on the differential diagnosis of AA dilatation in children is limited.

This study aims to examine the prevalence and characteristics of AA dilatation in pediatric patients, focusing on its relationship with BAV and AS. We also seek to identify potential risk factors and clinical implications of AA dilatation within this population.

MATERIALS and METHODS

Our study is a single-center, retrospective, cross-sectional analysis conducted between 2010 and 2022. We included 71 patients for whom echocardiographic imaging and medical records were available in the hospital database. The study received approval from the Clinical Research Ethics Committee of Uskudar University (Date: April 28, 2023, No: 61351342/Nisan 2023-08) and adhered to the Helsinki Declaration.

Exclusion Criteria

Patients with genetic syndromes, CHDs, a history of coronary artery disease, endocarditis, autoimmune illness, or hypertension under medical treatment were excluded. Additionally, those diagnosed with Marfan, Loeys-Dietz, or Ehlers-Danlos syndromes during the follow-up period were also excluded. We received professional assistance from hospital data-recording staff.

Inclusion Criteria

We analyzed echocardiographic reports of patients with AS, BAV, and small patent foramen ovales. Due to the study's retrospective nature, individual patient consent was not required. All data were de-identified to protect patient privacy.

Data Collection

Measurements were taken from the initial echocardiographic reports of patients diagnosed with AA dilatation, following the guidelines of the American Society of Echocardiography.[9,10] The aortic annulus was measured in systole, while the aortic root and proximal AA were measured in diastole, using the leading-edge-to-leading-edge technique. Due to the lack of a standardized aortic root measurement protocol for the pediatric population, we adopted this approach.[9,10] BSA was calculated using Haycox's formula.[11]

Outcome Measures

We assessed the aortic root, AA, and z-scores for each patient. Z-scores were calculated using online calculators based on nomograms by Gautier et al.[10] AA dilatation was defined as an AA measuring 1.1–1.5 times the normal size.

Aortic Stenosis Classification

If the peak Doppler gradient was unavailable, AS was categorized as trivial (gradient ≤15 mm Hg), mild (15–35 mm Hg), moderate (35–65 mm Hg), or severe (gradient >65 mm Hg) based on the echocardiographic report.

Statistical Analysis

All data were analyzed using SPSS 17 (version 17; SPSS Inc., Chicago, IL, USA). For continuous variables, overall statistics were expressed as the median and interquartile range (first quartile, third quartile), and for categorical variables, frequency and percentage. The Shapiro-Wilk test was used to determine whether the data was normal. The median (interquartile range) is displayed individually for data that are not normally distributed. Independent t-tests and Mann-Whitney tests are utilized for normally distributed and non-normally distributed data, respectively. The Mann–Whitney U test was used to examine the distributions of continuous variables among severity groups, and the Chi-square test was used to evaluate the proportions of categorical variables. Statistics were considered significant at p=0.05.

RESULTS

Data were collected from 71 patients (73.2% male) out of 1,245 charts reviewed. The median age, according to echocardiography was 9 years, ranging from 1 day to 18 years.

Aortic Dilatation Characteristics

AA dilatation was observed in association with AS in 36% (26/71) of cases and with BAV in 47% (34/71) of cases (Fig. 1). Isolated aortic root dilatation was seen in 49% (35/71) of patients. AA z-scores were significantly higher in patients with BAV compared to those without (p=0.034) (Fig. 2), but there was no significant difference in aortic root z-scores between these groups (p=0.117).

In a univariate analysis among the 71 individuals with AA dilatation, no demographic or clinical characteristic correlated with the severity of dilatation (z-score). AA z-scores were, however, correlated with aortic root z-scores and BAV (p=0.037 and p=0.033, respectively) (Table 1).

Aortic root z-scores were significantly smaller in patients with AS than in those without AS (p=0.003). Furthermore, patients with both AS and BAV showed significantly smaller aortic root z-scores than those without either condition (p<0.0001). Aortic root z-scores correlated with AA z-scores and AS (p=0.037 and p=0.003, respectively).

Table 1. Echocardiographic and clinical data of the patients with ascending aorta dilatation

	Total n	Normal aortic valve median (25–75th)	Bicuspid valve median (25–75th)	Aortic valve stenosis median (25–75th)
Patients (n)	71	35	34	26
Age (year)		10 (0.35–12.0)	8.5 (1.87–11.25)	9.25 (1.5–12.25)
Male/female	52/19	28/9	24/10	18/8
Aortic root z scores		1 (1.00–1.7)	1 (1.0–1.18)	1 (1.0–1.0)*β
Ascending aorta z scores		2.1 (1.5–2.72	2.35 (2.0–3.1)&	2.35 (2.1–2.85)

*: Mann Whitney U test used for comparison of patients with and without stenotic aortic valve p=0.003; β: Mann Whitney U test used for comparison of patients with aortic stenosis and bicuspid aortic valve with patients having normal aortic valve anatomy; &: Mann Whitney U test used for comparison of patients with and without bicuspid aortic valve p=0.034. Z scores were measured according to the nomograms provided from Gautier M, et al. Nomograms for aortic root diameters in children using two-dimensional echocardiography. Am J Cardiol 2010;105:888–94.

DISCUSSION

Our study shows that 47% of children with BAV experience AA dilatation during follow-up, as indicated by a z-score >2. The severity of dilatation tends to worsen in the presence of AS. BAV was the most common diagnosis associated with AA dilatation in our study. Given its prevalence of 1–2% in the general population, BAV is considered the most common congenital heart defect (CHD), affecting over 70% of cases in men.[12,13] Patients with BAV should be regularly monitored for valve stenosis, insufficiencies, and AA size, as they are at risk for serious complications like aortic dissection and rupture.[14] Consistent with existing literature, our study had a high proportion of male subjects (73.2%).[15]

AA Dilation

We found that children with BAV showed elevated z-scores for AA dilatation, specifically limited to the aortic root. Research by Blais et al.[16] demonstrated that AA dilatation in BAV patients progresses gradually during childhood but at a rate without significant clinical implications, except in cases of aortic valve dysfunction. Valve dysfunction significantly increased the rate of dilatation; for those with mild regurgitation, the likelihood of developing a considerably dilated AA increased more than 3.5-fold. In our study, we found that patients with BAV had more dilated AA than those without BAV, although we lacked longitudinal data. Monitoring BAV patients for AA dilatation is crucial.

Existing data on the relationship between adult BAV and AA dilatation are inconsistent.[16,17] While Nistri et al.[18] report minimal dilatation of the aortic annulus, sinuses, and sinotubular junction in adults with BAV, Hahn et al.[19] observed increased dimensions in these areas. Few studies have explored the causes of proximal aorta dilatation in children. Warren et al.[20] analyzed 88 patients and found a mean advancement rate of 0.390 z-score units/year for AA dilatation

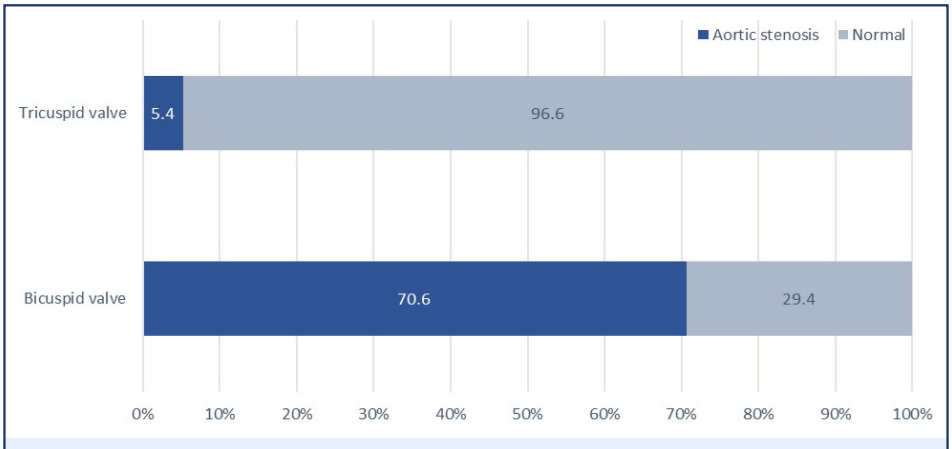

Figure 1. Proportions of aortic valve stenosis among tricuspid and bicuspid aortic valve patients

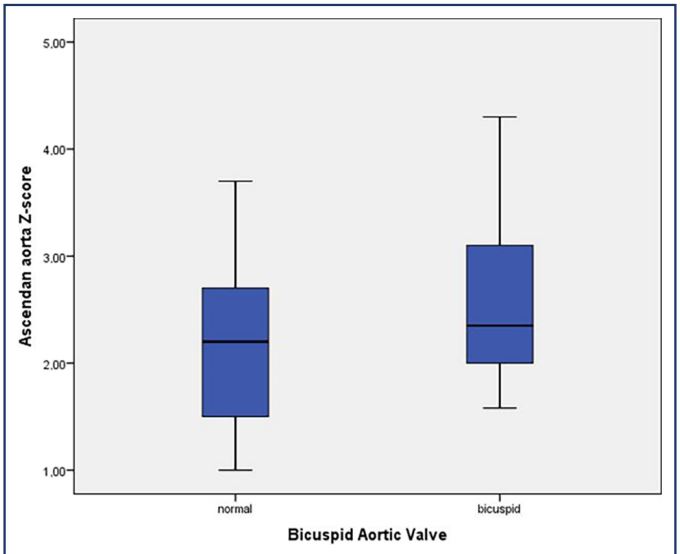

Figure 2. Graphical illustration of ascending aorta z-scores according to anatomy of aortic valve

in children with BAV, concluding that dilatation is progressive, a finding consistent with our results.

Aortic Root Dilatation and AS

We found that patients with aortic stenosis (AS) had smaller aortic root z-scores than those without stenosis. In addition, individuals with both AS and BAV had significantly lower aortic root z-scores than those without either condition. In our study, aortic root z-scores were correlated with AA z-scores and AS. We could not find a statistically significant difference in AA dilatation in patients with and without AS. Blais et al.[16] reported that among juvenile BAV patients – the largest cohort studied with long-term follow-up – the rate of AA dilatation significantly increased with valvular dysfunction. They projected that the likelihood of developing a significantly dilated AA rose more than 3.5-fold with severe regurgitation and more than 9-fold when AS and BAV were present.

This contrasts with other studies claiming that AA dilatation is not correlated with the severity of stenosis. We believe the discrepancy arises from the methodology. Instead of using absolute aortic diameters or measurements adjusted for body size, which can introduce significant biases, we utilized z-scores, shown to be uncorrelated with age and body size.[21]

Our study, being a retrospective cross-sectional design, offers a snapshot in time and uses transthoracic echocardiography (TTE) as the primary imaging method. TTE is convenient and cost-effective but may have limitations in image quality. While cardiac computed tomography angiography is often used for thoracic aorta studies due to its higher quality, it comes with the disadvantage of radiation exposure.[22] Cardiovascular magnetic resonance offers even higher-quality imaging without radiation exposure but is more expensive and less accessible.[23]

Ascending aortic dilatation that extends to aneurysms may be fatal due to their liability to dissect or rupture.[24] The ascending part of the aorta is more elastic than the descending part due to its greater concentration of elastic fibers. An ascending aortic aneurysm is an enlargement (in width and/or in length) of a weakened area in the AA and is mostly associated with degenerative changes in elastic media. The aortic wall then loses its strength and elasticity, becoming aneurysmal; it may then dissect or rupture.

There's also a link between ascending aortic aneurysms and abnormal aortic valves, like bicuspid or unicuspid types.[25] These valve anomalies and the tendency for aneurysm development may stem from the same developmental irregularities. The aneurysms are further exacerbated by post-stenotic dilation in those with stenotic bicuspid or unicuspid aortic valves.[26] Given that there were no cases of aortic dissections, ruptures, or interventions in our dataset, our study offers valuable insights but lacks longitudinal data for drawing more comprehensive conclusions, which is the limitation of this study. The choice of imaging technique can have implications for both diagnosis and longitudinal tracking, and there's no universal "gold standard," which presents a challenge for comparing results across studies.

CONCLUSION

We examined AA dilatation in pediatric patients with a focus on BAV and AS. Using a retrospective design and echocardiography, we found that 47% of children with BAV had AA dilatation. AA dilatation was more severe when AS was also present. However, AS alone did not show a statistically significant correlation with AA dilatation. Our study highlights the need for ongoing monitoring of pediatric patients with BAV for the risks of AA dilatation and potentially severe complications like aortic dissection or rupture. We suggest that the choice of imaging technique can influence diagnosis and tracking, underscoring our study's limitations, including its cross-sectional nature and absence of longitudinal data. Overall, our study appears to make a significant contribution to the existing body of literature, highlighting the prevalence and risks of AA dilation in children with BAV and emphasizing the need for ongoing monitoring.

Disclosures

Ethics Committee Approval: The study was approved by the Uskudar University Non-interventional Research Ethics Committee (No: 61351342, Date: 28/04/2023).

Informed Consent: Written informed consent was obtained from all patients.

Peer-review: Externally peer reviewed.

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REFERENCES

1. Cozijnsen L, Braam RL, Waalewijn RA, Schepens MA, Loeys BL, Van Oosterhout MF, et al. What is new in dilatation of the ascending aorta? Review of current literature and practical advice for the cardiologist. Circulation 2011;123:924–8. [CrossRef]
2. Cecconi M, Nistri S, Quarti A, Manfrin M, Colonna PL, Molini E, et al. Aortic dilatation in patients with bicuspid aortic valve. J Cardiovasc Med (Hagerstown) 2006;7:11–20. [CrossRef]
3. Guntheroth WG. A critical review of the American College of Cardiology/American Heart Association practice guidelines on bicuspid aortic valve with dilated ascending aorta. Am J Cardiol 2008;102:107–10. [CrossRef]
4. Fernandes S, Khairy P, Graham DA, Colan SD, Galvin TC, Sanders SP, et al. Bicuspid aortic valve and associated aortic dilatation in the young. Heart 2012;98:1014–9. [CrossRef]
5. Jain D, Dietz HC, Oswald GL, Maleszewski JJ, Halushka MK. Causes and histopathology of ascending aortic disease in children and young adults. Cardiovasc Pathol 2011;20:15–25. [CrossRef]
6. Ward C. Clinical significance of the bicuspid aortic valve. Heart 2000;83:81–5. [CrossRef]
7. Braverman AC, Güven H, Beardslee M, Makan M, Kates AM, Moon MR. The bicuspid aortic valve. Curr Probl Cardiol 2005;30:470–522. [CrossRef]
8. Iskandar A, Thompson PD. A meta-analysis of aortic root size in elite athletes. Circulation 2013;127:791–8. [CrossRef]
9. Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, et al. European Association of Echocardiography Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. J Am Soc Echocardiogr 2005;18:1440–63. [CrossRef]
10. Gautier M, Detaint D, Fermanian C, Aegerter P, Delorme G, Arnoult F, et al. Nomograms for aortic root diameters in children using two-dimensional echocardiography. Am J Cardiol 2010;105:888–94. [CrossRef]
11. Haycock GB, Schwartz GJ, Wisotsky DH. Geometric method for measuring body surface area: a height-weight formula validated in infants, children, and adults. J Pediatr 1978;93:62–6. [CrossRef]
12. Prapa M, Pepper J, Gatzoulis MA. Congenital cardiovascular malformations. Abnormality of the aortic root. In: Allen HD, Shaddy RE, Penny DJ, Feltes TF, Cetta F, eds. Moss and Adams' Heart Disease in Infants, Children and Adolescents. Including the Fetus and Young Adult. 9th ed. Amsterdam: Wolters Kluwer; 2016. p. 871–80.
13. Steinberger J, Moller JH, Berry JM, Sinaiko AR. Echocardiographic diagnosis of heart disease in apparently healthy adolescents. Pediatrics 2000;105:815–8. [CrossRef]
14. Basso C, Boschello M, Perrone C, Mecenero A, Cera A, Bicego D, et al. An echocardiographic survey of primary school children for bicuspid aortic valve. Am J Cardiol 2004;93:661–3. [CrossRef]
15. Cecconi M, Manfrin M, Moraca A, Zanoli R, Colonna PL, Bettuzzi MG, et al. Aortic dimensions in patients with bicuspid aortic valve without significant valve dysfunction. Am J Cardiol 2005;95:292–4. [CrossRef]
16. Blais S, Dumas LM, Fournier A, Dallaire F, Dahdah N. Long-term risk factors for dilatation of the proximal aorta in a large cohort of children with bicuspid aortic valve. Circ Cardiovasc Imaging 2020;13:e009675.
17. Gurvitz M, Chang RK, Drant S, Allada V. Frequency of aortic root dilatation in children with a bicuspid aortic valve. Am J Cardiol 2004;94:1337–40. [CrossRef]
18. Nistri S, Sorbo MD, Marin M, Palisi M, Scognamiglio R, Thiene G. Aortic root dilatation in young men with normally functioning bicuspid aortic valves. Heart 1999;82:19–22. [CrossRef]
19. 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. [CrossRef]
20. Warren AE, Boyd ML, O'Connell C, Dodds L. Dilatation of the ascending aorta in paediatric patients with bicuspid aortic valve: frequency, rate of progression and risk factors. Heart 2006;92:1496–500. [CrossRef]
21. Dallaire F, Bigras JL, Prsa M, Dahdah N. Bias related to body mass index in pediatric echocardiographic Z scores. Pediatr Cardiol 2015;36:667–76.
22. Brenner DJ, Hall EJ. Computed tomography--an increasing source of radiation exposure. N Engl J Med 2007;357:2277–84. [CrossRef]
23. Burman ED, Keegan J, Kilner PJ. Aortic root measurement by cardiovascular magnetic resonance: specification of planes and lines of measurement and corresponding normal values. Circ Cardiovasc Imaging 2008;1:104–13. [CrossRef]
24. Davies RR, Goldstein LJ, Coady MA, Tittle SL, Rizzo JA, Kopf GS, et al. Yearly rupture or dissection rates for thoracic aortic aneurysms: simple prediction based on size. Ann Thorac Surg 2002;73:17–27. [CrossRef]
25. Nistri S, Sorbo MD, Basso C, Thiene G. Bicuspid aortic valve: abnormal aortic elastic properties. J Heart Valve Dis 2002;11:369–74. [CrossRef]
26. Della Corte A, Bancone C, Quarto C, Dialetto G, Covino FE, Scardone M, et al. Predictors of ascending aortic dilatation with bicuspid aortic valve: a wide spectrum of disease expression. Eur J Cardiothorac Surg 2007;31:397–404. [CrossRef]