Coronary Artery Dilatation and Aortic Outflow Tract Enlargement in Children with Unicommissural Aortic Valves

M.J. Faber[2], J.S. Zeiger[3], P.J. Spevak[1], J.I. Brenner[1] and W.J. Ravekes[1]

(1) Division of Pediatric Cardiology, John Hopkins Hospital, Brady 520, 600 N. Wolfe Street, Baltimore, MD 21287, USA
(2) Erasmus Medical Centre—Sophia Children s Hospital, Rotterdam, The Netherlands
(3) Department of Biostatistics, Johns Hopkins Hospital, 600 N. Wolfe Street, 21287 Baltimore, MD, USA

W.J. Ravekes
Email: wravekes@jhmi.edu
Phone: (410) 955-5517
Fax: (410) 955-0897

Published online: 18 November 2004

Abstract: We evaluated the aortic outflow tract (AOT) and coronary artery dimensions in pediatric patients with unicommissural aortic valves. A retrospective review of an echocardiographic database identified 37 patients with unicommissural aortic valves. A total of 115 echocardiograms were reviewed, and the right coronary artery (RCA), left main coronary artery (LM), left anterior descending coronary artery aortic valve annulus, aortic root, sinotubular junction (STJ), and ascending aorta were measured and z scores determined. The aortic stenosis peak gradient and the amount of aortic regurgitation (AR) were also measured. The RCA diameter (z score, 1.85 ± 1.8, $p = 0.03$) and LM diameter (z score, 1.74 ± 1.47, $p = 0.04$) are significantly dilated, as are all the AOT measurements: aortic annulus (2.02 ± 1.9, $p = 0.02$), aortic root (2.25 ± 1.9, $p = 0.02$), STJ (2.22 ± 1.74, $p = 0.01$), and ascending aorta (4.38 ± 2.03, $p < 0.001$). Longitudinal follow-up showed that there was no significant variation over time in any variable. The AOT measurements were significantly correlated with each other. A trend was found in which an increasing amount of AR gave an increase in AOT measurements. The aortic gradient was not significantly associated with any measurement. Our study population demonstrated significant dilatation of the RCA and LM as well as the AOT. The dilatation of the AOT structures is likely caused by the same mechanism that accounts for the AOT dilatation in patients with bicommissural aortic valves. Dilatation of the coronary arteries may represent an intrinsic abnormality in the vessel wall. Further studies are needed to define possible changes.

Keywords: Aortic valve - Aortic root - Congenital heart disease

Work was performed at Johns Hopkins Hospital, Baltimore, MD 21287, USA.

Unicommissural aortic valve (UAV), described by Edwards [2] in 1958, is a rare form of congenital heart disease accounting for approximately 1–5% of all congenital aortic valvar stenosis [1, 9]. UAV consists of an abnormal aortic valve with only one leaflet with an eccentrically located commissure. Patients with UAV often need to undergo valve replacement with an autograft (Ross procedure), which requires coronary artery explantation. There have been a few descriptive case series on patients with UAVs [3, 10], but systematic investigation concerning coronary artery and aortic outflow tract involvement in this condition has not yet been described. UAVs are in some ways similar to bicommissural aortic valves, which have been described to have abnormalities in the aortic outflow tract [4, 5, 6]. Coronary artery dimensions have not been described in either unicommissural or bicommissural aortic valves. This study examines whether coronary artery and aortic outflow tract dimensions, adjusted for body surface area (BSA), are larger in patients who have UAVs than in the general population. Coronary dilatation, if present, would be important in perioperative planning and care with aortic valvuloplasty, aortic valve replacement, or the Ross procedure. The gradient across the aortic valve as well as the amount of aortic regurgitation (AR) were also taken into account. Multivariate analysis of the different measures as well as longitudinal data on individual patients were examined.

Methods

A retrospective review of the pediatric echocardiography laboratory database at Johns Hopkins Hospital (Baltimore, MD, USA) was performed for all patients coded with (UAVs). Patients with complex congenital heart disease, unclear morphology of the aortic valve, and/or inadequate imaging were excluded. All subjects had to have at least one echocardiogram with adequate imaging of the coronary arteries and the aortic valve annulus, aortic root, sinotubular junction, and ascending aorta, which comprise the aortic outflow tract (AOT). Aortic valve peak instantaneous gradient was calculated and the amount of AR determined. AR if present, was graded as trivial, mild, moderatre, or severe based on quantitative and qualitative criteria as previously published [11, 13]. For statistical purposes, these grades were assigned discrete variables of 1, 2, 3, or 4. Serial echocardiograms were reviewed when available to assess longitudinal data for each patient and the study group as a whole. No further echocardiograms were analyzed once a patient had undergone surgical valvuloplasty or aortic valve replacement.

The review of the echocardiograms was performed by two investigators (M.J.F. and W.J.R.) using a Phillips (Andover, MA, USA) Model 5500 cardiac ultrasound machine with electronic calipers calibrated to the depth markers recorded on the echocardiograms. Comparison of duplicate measurements of the coronary arteries and AOT by both investigators on the same study showed less that 5% interobserver variability. In patients with multiple echocardiograms, studies for analysis were selected based on image quality and to allow for at least a 1-month time interval between studies.

The coronary arteries were measured from a parasternal short-axis view in mid-diastole with frame-by-frame review to find the largest diameter of each coronary artery. The aortic valve annulus, aortic root, sinotubular junction, and ascending aorta diameter were measured from a parasternal long-axis view during midsystole.

Coronary artery and AOT absolute measurements were converted to a z score based on the patients BSA using widely accepted pediatric population normal values as included in the Waveform Pediatric Echo program (program and z scores regression originally supplied by S. Colan, Children s Hospital, Boston, MA, USA). Mean z scores for all variables were computed for each measurement for each visit by averaging the individual z score for each patient who had a measurement available. Correlations were performed between all measurements using a Bonferoni correction. Since the null hypothesis was that coronary artery dimensions are larger in patients who have UAVs than in the general population, all p values are one-tailed.

Aortic regurgitation was categorized as none, trivial, mild, moderate, and severe. For the purpose of analysis, these qualitative descriptors were assigned discrete variables, 0–4. Polytomous logistic regression was used to examine how AR affects coronary artery and AOT measurements.

Results

A total of 40 patients diagnosed with UAVs were found in the pediatric echocardiography database at Johns Hopkins Hospital. Upon review, 2 patients were found to have bicommissural aortic valves and 1 patient had severe endocarditis involving the aortic valve, so that 37 patients met enrollment criteria. A total of 115 echocardiograms were reviewed; follow-up ranged from one to eight separate echocardiograms. The male:female ratio was 34:3. Additional patient characteristics are shown in Table 1.

Table 1: Characteristics of 37 patients with unicommissural aortic valves at first echocardiogram

	Minimum	Maximum	Median

	Minimum	Maximum	Median
Age (years)	0.01	27.4	10.4
Body surface area (m^2)	0.18	1.99	1.07
Gradient (mmHg)	10	87	36
Follow-up (years)	0	6	1.46

There was minimal variation in mean z scores for each measurement over time (only three patients had more than five visits; thus, we included only the first five visits) (Fig. 1). Because of this finding, and because all patients had at least one echocardiogram, we based the further statistics on the first echocardiogram.

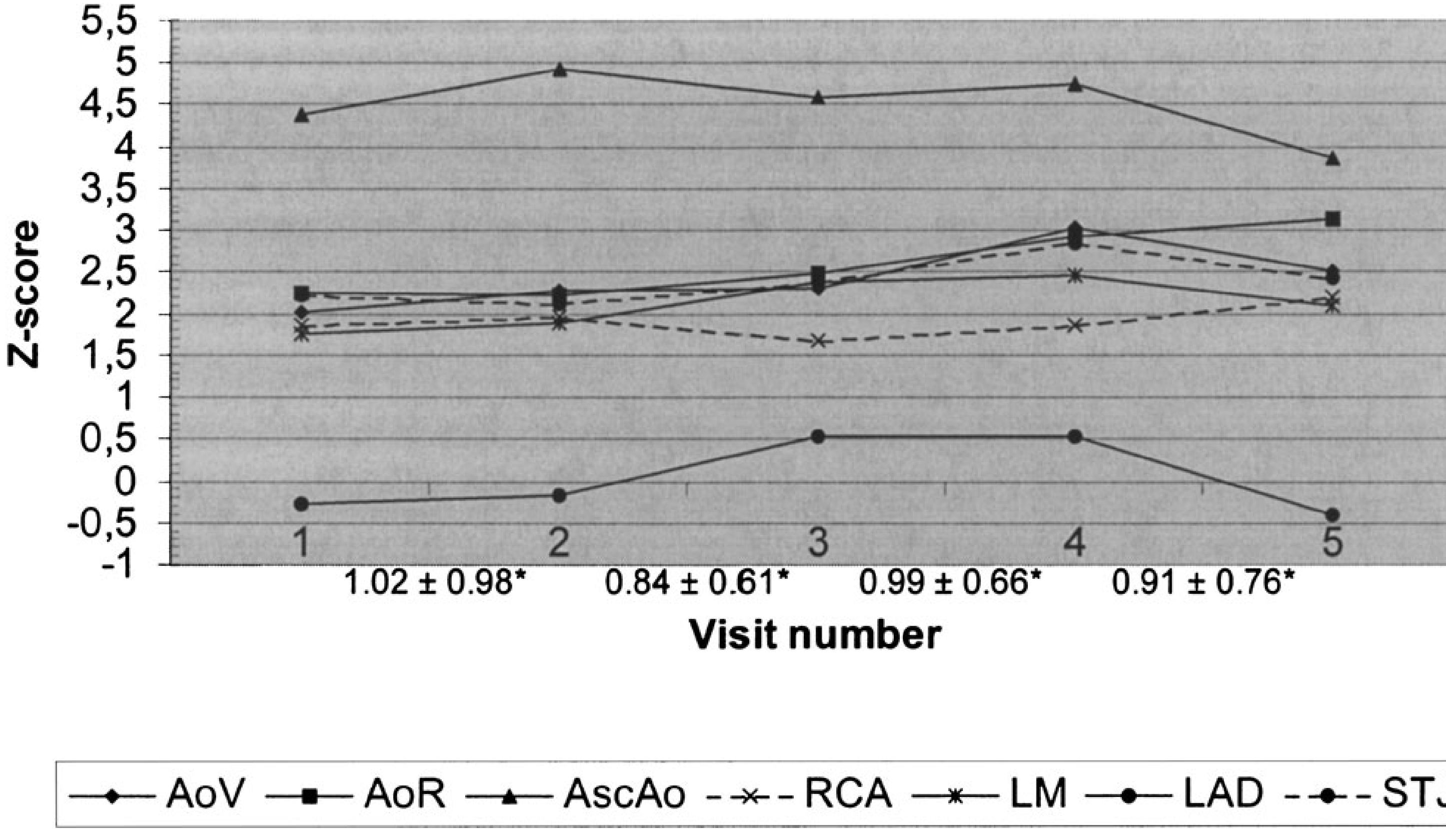

Figure 1 Variability in z scores in a follow-up period of five echocardiograms performed on 37 patients with unicommissural aortic valves. AoV, aortic valve annulus; AoR, aortic root; STJ, sinotubular junction; AscAo, ascending aorta; RCA, right coronary artery; LM, left main coronary artery; LAD, left anterior descending coronary artery. *Time interval between the visits in years (mean ± SD).

None of the patients presented with an abnormal coronary artery branching pattern. There was significant dilatation of the left main coronary artery (mean z score, 1.74; SD, 1.47; $p = 0.04$). There was also significant dilatation of the right coronary artery (mean z score, 1.85; SD, 1.8; $p = 0.03$). The left anterior descending coronary artery was not significantly dilated (Table 2). Measurements of the aortic valve annulus (mean z score, 2.02; SD, 1.9; $p = 0.02$), aortic root (mean z score, 2.25, SD, 1.62; $p = 0.01$), sinotubular junction (mean z score, 2.22, SD, 1.74, $p = 0.01$), and ascending aorta all showed significant dilatation. The ascending aorta has the greatest dilatation (mean z score, 4.38; SD, 2.03; $p < 0.001$) (Table 3).

Table 2: Coronary artery measurements performed on 37 patients with unicommissural aortic valve[a]

	Mean absolute measure (cm)	Mean *z* score	*p* value
Right coronary artery	0.32 ± 0.10	1.85 ± 1.80	0.03
Left main coronary artery	0.36 ± 0.08	1.74 ± 1.47	0.04
Left anterior descending artery	0.22 ± 0.06	–0.28 ± 1.42	NS

NS, not significant.

[a]Based on the first echocardiogram.

Table 3: Aortic outflow tract measurements performed on 37 patients with unicommissural aortic valve[a]

	Mean absolute measure (cm)	Mean *z* score	*p* value
Aortic valve annulus	1.90 ± 0.58	2.02 ± 1.91	0.02
Aortic root	2.61 ± 0.75	2.25 ± 1.62	0.01
Sinotubular junction	2.21 ± 0.69	2.22 ± 1.74	0.01
Ascending aorta	2.66 ± 0.81	4.38 ± 2.03	<0.001

[a]Based on the first echocardiogram.

The AOT variables are correlated with each other (Table 4). The coronary arteries are not correlated with any other measurement. The polytomous logistic regression indicated that the aortic valve annulus, aortic root, and sinotubular junction dimensions increase as the severity of aortic regurgitation increases (Table 5). This was not seen for the ascending aorta or the coronary arteries. Analysis of the aortic stenosis gradient showed that although the gradient is negatively correlated with some of the variables, it did not reach statistical significance. The aortic stenosis gradient was also not correlated with the degree of aortic regurgitation.

Table 4: Correlations between aortic outflow tract measurements based on the first echocardiogram

	AoV	AoR	STJ	AscAo	RCA	LM	LAD
AoV	1.0000						
AoR	**0.6574***	1.0000					
STJ	**0.6882***	**0.8169***	1.0000				
AscAo	**0.5624***	**0.5321**†	**0.5638***	1.0000			
RCA	–0.1645	0.0264	–0.2372	0.1817	1.0000		
LM	0.0963	0.2011	0.1214	0.1631	0.3284	1.0000	
LAD	–0.0682	0.1074	0.0727	–0.1342	0.2158	0.1923	1 .0000

AoV, aortic valve annulus; AoR, aortic root; STJ, sinotubular junction; AscAo, ascending aorta; RCA, right coronary artery; LM, left main coronary artery; LAD, left anterior descending coronary artery.
*$p < 0.01$ using a Bonferoni correction.

† $p < 0.05$ using a Bonferoni correction.

Table 5: Polytmous logistic regression analysis of aortic outflow tract dimension and aortic regurgitation

Aortic regurgitation	Trivial	Mild	Moderate	Severe
AoV	z = –1.0 (±0.34) p = 0.313 95% Cl =0.119–1.97	z = –0.31(±0.32) p = 0.76 95%Cl = 0.436–1.83	z = 0.76 (±0.50) p = 0.45 95%Cl = 0.636–2.79	z = 2.13 (±0.183) p = 0.03 95%Cl = 1.09–9.84
Aortic root	z = –1.08 (±0.30) p = 0.41 95%Cl = 0.097–1.73	z = –0.41 (±0.33) p = 0.76 95%Cl = 0.457–1.93	z = 0.92 (±0.62) p = 0.35 95%Cl = 0.71–2.81	z = 2.61 (±1.62) p = 0.01 95%Cl = 1.3–9.8
STJ	z = –1.32 (±0.27) p = 0.186 95%Cl = 0.058–1.73	z = –0.11 (±0.36) p = 0.915 95% Cl = 0.464–1.99	z = 0.712 (±0.49) p = 0.476 95% Cl = 0.625–2.73	z = 1.84 (±1.03) p = 0.066 95% Cl = 0.945–5.57
Ascending aorta	z = –0.95 (±0.33) p = 0.341 95% Cl = 0.182–1.80	z = 0.54 (±0.32) p = 0.59 95% Cl = 0.675–1.98	z = 1.31 (±0.42) p = 0.189 95% Cl = 0.829–2.57	z = 1.13 (±0.52) p = 0.26 95% Cl = 0.741–2.96

AoV, aortic valve annulus; STJ, sinotubular junction

Discussion

Our data show that the left main coronary artery and right coronary artery are both significantly dilated in patients with UAVs. The etiology of the dilatation in the right coronary artery and left main coronary artery is uncertain. One theory is that an eccentric jet of aortic stenosis is directed toward the right coronary cusp and the ostium of the right coronary artery, causing dilatation secondary to a hemodynamic jet effect. However, this seems unlikely given that the right coronary artery dilatation does not correlate with the aortic stenosis peak instantaneous gradient and that the left coronary artery is also dilated. Dilatation of the coronary arteries may represent an intrinsic abnormality in the vessel wall similar to the previously described abnormalities in the media of the aortic wall of patients with bicommissural aortic valves. Dilatation of the coronary arteries may also be in response to changes in left ventricle mass or increased wall stress. Unfortunately, not all echocardiograms had wall stress analysis performed or adequate images for accurate retrospective calculation of the left ventricular mass. This possible correlation will be examined in future prospective research on this cohort of patients.

The aortic valve annulus, aortic root, sinotubular junction, and ascending aorta are all significantly dilated. The degree of dilatation did not regress or progress during the study period. This implies that the first echocardiogram is predictive of the degree of dilatation of these structures and frequent repeated measurements may not be necessary, at least during the time frame of the study. We found a significant correlation between the dilated AOT structures, meaning that dilatation of one structure may be predictive of dilatation of other structures. No significant correlation could be found between the dilatation of the AOT structures and the coronary arteries. A trend was found in which an increasing amount of AR gives an increase in AOT dimensions.

Bicommissural aortic valves have a well-known association with dilatation of AOT structures. This study shows that this process also occurs in patients with UAVs McKusick et al. [8] reported initially in 1957 that the dilatation was due to cystic medial necrosis caused by altered hemodynamics due to the aortic valvular disease. Other authors also support the theory that aortic wall changes are mainly the consequence of hydraulic laws [5, 12]. In 1972, McKusick [17] revised his opinion that hemodynamics were the causative factor in the onset of Erdheim s medial necrosis. Reports by Hanh et al. [4] and Keane et al. [6] show that the AOT dilatation is more likely to be caused by an intrinsic abnormality. We believe that the same intrinsic process that causes AOT dilatation in patients with bicommissural aortic valves occurs in patients with UAVs and may also affect the coronary arteries. In our opinion hemodynamic jets are less likely to cause a dilatation of the right and left main coronary artery because of the bilateral dilatation observed. An intrinsic process is more likely to account for the bilateral dilation. The extreme male:female ratio also suggests an underlying intrinsic genetic abnormality. An intrinsic abnormality of the coronary artery vessel wall is important to identify since many patients with UAVs progress to autograft valve replacement that requires explantation and reimplantation of the coronary arteries as part of the Ross procedure. The dilatation of the coronary arteries is not likely to have an influence on the technique used for the Ross procedure, although it may be of some importance to have this knowledge in advance to the surgery.

Study Limitations

There are several study limitations. First, this study is retrospective in design and mean follow-up was limited to 18 months, with maximum follow-up of 6 years. Measurements of the coronary arteries and occasionally the AOT were taken offline, and in certain cases echocardiographic windows were of insufficient quality to allow for accurate measurements. However, in cases in which clear delineation of the vessel could not be made, these measurements were excluded. This report documents only a single center s experience and may not reflect that of other pediatric cardiology centers. Lastly, although there are several proposed mechanisms for the coronary artery dilatation in this population, none have been proven and remain questions for further investigation.

Conclusions

We present the largest study of patients with UAVs to date. By our review of the literature, this is also the first study to follow this patient population longitudinally. There is significant dilatation of the right coronary artery and left main coronary artery, which has not previously been reported. The etiology of this coronary artery dilation remains unclear, but it does not appear to be secondary to the degree of aortic stenosis or regurgitation. In addition, there is significant dilatation of the AOT structures. The severity of dilatation of these structures remains stable over time. Our data suggest that these changes are not related to hemodynamic stress secondary to aortic stenosis, but an association of dilatation with increasing AR was found. Further studies are needed to better define possible changes in the media of these vessels and to clarify the extreme male predominance and the potential association with genetic disorders.

References

1. Datta, BN, Bhusnurmath, B, Khattri, HN et al. (1988) "Anatomically isolated aortic valve disease. Morphologic study of 100 cases at autopsy" Jpn Heart J 29: 661-670

2. Edwards, JE (1958) "Pathologic aspects of cardiac valvular insufficiencies" Arch Surg 77: 634-649

3. Falcone, MW, Roberts, WC, Morrow, AG, Perloff, JK (1971) "Congenital aortic stenosis resulting from a unicommissural valve" Circulation 44: 272-280

4. Hahn, RT, Roman, MJ, Mogtader, AH, Devereux, RB (1992) "Association of aortic dilatation with regurgitant, stenotic and functionally normal bicuspid aortic valves" J Am Coll Cardiol 19: 283-288

5. Holman, E (1954) "The obscure physiology of post-stenotic dilatation: its relation to the development of aneurysms" J Thorac Surg 28: 109-133

6. Keane, MG, Wiegers, SE, Plappert, T et al. (2000) "Bicuspid aortic valves are associated with aortic dilation out of proportion to coexistent valvular lesions" Circulation 102: 35-39

7. McKusick, VA (1972) "Association of congenital bicuspid aortic valve and Erdheim s cystic medial necrosis" Lancet 1: 1026-1027

8. McKusick, VA, Logue, RB, Bahnson, HT (1957) "Association of aortic valvular disease and cystic medial necrosis of the ascending aorta" Report of four instances. Circulation 16: 188

9. Peterson, MD, Roach, RM, Edwards, JE (1985) "Types of aortic stenosis in surgically removed valves" Arch Pathol Lab Med 109: 829-832

10. Roberts, WC, Morrow, AG (1965) "Congenital aortic stenosis produced by a unicommissural valve" Br Heart J 27: 505-510

11. Snider, AR (1997) Echocardiography in Pediatric Heart Disease, 2, Mosby-Year Book, St. Louis, pp 177-190

12. Stebhens, WE (1996) "Structural and architectural changes during arterial development and the role of hemodynamics" Acta Anat 157: 261-274

13. Zoghbi, WA et al. (2003) "Recommendations for evaluation of the severity of native valvular regurgitation with two-dimensional and Doppler echocardiography" J Am Soc Echocardiogr 16: 777-802