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ORIGINAL ARTICLE

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Disease progression and variation in clinical practice for isolated bicuspid aortic valve in children

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Abstract

Background: Disease progression of an isolated bicuspid aortic valve (BAV) in children is poorly understood and adult management guidelines may not be applicable. Thus, we sought to evaluate disease progression of pediatric isolated BAV and its relationship to current management practices.

Methods: Children with a BAV and ≤mild aortic stenosis (AS) and/or aortic regurgitation (AR) at the time of initial evaluation were included in this retrospective cohort study (1/2005-12/2014). Outcomes included change in *z*-scores for aortic root and ascending aorta diameters, cardiac interventions, adverse outcomes, recommended follow-up interval, and frequency of cardiac imaging studies at each follow up evaluation, as well as AS/AR severity at final evaluation. Outcomes were analyzed using generalized mixed-effect models with subject and provider clustering.

Results: BAV disease progression was evaluated in 294 subjects over 4.1 ± 2.4 (range 0.2-9.5) years. Ascending aorta *z*-scores increased by 0.1/year ($P < .001$) but aortic root diameter *z*-scores were unchanged. AS and/or AR progressed to >mild in 9 (3%), 1 subject underwent cardiac intervention, and none had a major complication. Management was evaluated in 454 subjects (1343 encounters) with 27 different cardiologists. The average recommended follow-up interval was 1.5 ± 0.9 years. Younger age at diagnosis, greater aortic root or ascending aorta *z*-score at diagnosis, ≥mild AS/AR at follow-up, and earlier diagnosis era were associated with shorter recommended follow-up interval ($P < .001$ for all). Imaging was obtained at 87% of follow-up encounters and was associated with age at encounter with children ≥12 years most frequently imaged ($P < .001$). Provider accounted for 14% of variability in recommended follow-up interval and 24% of imaging variability ($P < .001$ for both).

Conclusions: We found little to no evidence of disease progression in children with an isolated BAV. Given the low risk, close follow-up and frequent cardiac imaging for BAV surveillance may not be warranted for children.

KEYWORDS

aortopathy, bicuspid aortic valve, pediatrics, practice variation

1 | INTRODUCTION

Bicuspid aortic valve (BAV) is the most common congenital cardiac lesion in the general population with a prevalence of 0.5%–2%.[1,2] Guidelines for the management of adults and adolescents with an isolated BAV recommend clinical follow-up with cardiac imaging every 2 years. There are no guidelines for the management of younger children with an isolated BAV.[3,4]

Children with a BAV have fewer adverse outcomes, including no reported cases of aortic dissection, and fewer cardiac interventions for aortic valve dysfunction and/or aortic dilation compared to adults.[5–8] Therefore, extrapolation from adult guidelines may lead to more frequent than necessary follow-up encounters and inappropriate use of cardiac imaging. Targeting children with higher risk for disease progression is limited by conflicting reports regarding the influences of BAV morphology and aortic valve dysfunction on aortic dilation.[5–16] The aims of this study are to assess the disease progression of an isolated BAV during childhood and to assess associations between disease progression and current management practices (follow-up intervals and frequency of cardiac imaging).

2 | METHODS

This single-center retrospective cohort study was approved by the Institutional Review Board at the University of Utah and Intermountain Healthcare. Subjects less than 18 years old with an isolated BAV [≤mild aortic stenosis (AS) and/or aortic regurgitation (AR)] at initial diagnosis evaluated from 01/2005 to 12/2014 were included.

The echocardiographic database (Syngo Dynamics, Siemens Medical Solutions USA, Inc., Ann Arbor, Michigan) was searched using the keyword "bicuspid aortic valve" to obtain a list of potentially eligible subjects. Inclusion and exclusion criteria were confirmed by review of the electronic medical record (EMR). Study data were collected and managed using REDCap electronic data capture tools hosted at the University of Utah.[17]

Data collection included the recommended follow-up interval for each encounter, type of imaging study performed [echocardiogram or cardiac magnetic resonance imaging (CMR)], sex, age at diagnosis, age at each encounter and at each imaging study, presence of a genetic syndrome, era of diagnosis (earlier, 01/01/2005 to 12/31/2009 vs later, 01/01/2010 to 12/31/2014), interventions (aortic valve surgery, aortic root surgery, and aortic balloon valvuloplasty), history of aortic dissection and/or endocarditis, and death. Imaging data collected included *z*-scores for aortic root and ascending aorta diameter, BAV morphology, and severity of AS and/or AR. AS category was categorized based on mean gradients: (1) no stenosis, <10 mm Hg, (2) mild, 10–25 mm Hg, (3) moderate, 25–40 mm Hg, and (4) severe, >40 mm Hg.[18] AR was graded as none, mild, moderate, or severe based on the characteristics of the color Doppler jet.[19] The diameters of the aortic root and ascending aorta were measured from inner edge-to-inner edge during maximum systolic expansion in the parasternal long axis view, and were indexed to normative *z*-scores by body surface area.[20,21] When imaging information was not provided in the report, the original images were retrieved and measurements were made according to these standards. Pediatric cardiology management data collected included recommended clinic follow-up interval, frequency of testing for echocardiograms, CMR, electrocardiograms, and chest x-rays; and cardiac medications.

Subjects were excluded from the BAV disease progression analysis for (1) genetic syndrome or (2) imaging inadequate to assess change in either aortic root or ascending aorta dimensions. Subjects were excluded from the analysis of practice management if (1) their pediatric cardiologist had seen less than five subjects with an isolated BAV during the study period, or (2) no follow-up interval recommendations were documented.

Continuous variables were summarized using means (standard deviations, SDs) or medians (interquartile ranges, IQRs), as appropriate. Categorical variables were summarized using frequencies and percentages.

Ordinal generalized linear mixed effect regression was used to analyze the recommended follow-up interval outcome, which was categorized as: 0–1 year, 1–2 years, 2–3, or >3 years; such that greater odds ratios corresponded to shorter follow-up intervals. The secondary outcome, frequency of cardiac imaging, was analyzed using logistic mixed effects regression with Laplace estimation. Provider and subject level random intercepts were included for both outcome models. Model results were reported as unadjusted and adjusted odds ratios (ORs with 95% confidence intervals, CIs) and *P* values. The adjusted models included age group at diagnosis (<2 years, 2–12 years, and ≥12 years), era of diagnosis, sex, genetic syndrome, and baseline values for aortic root *z*-score, ascending aorta *z*-score, and AS and AR severity. Provider and subject variation was estimated from unadjusted and adjusted multilevel regression models using the intraclass correlation coefficient (ICC) formula for the logit.[22,23]

Aortic root and ascending aorta *z*-scores were analyzed as change from baseline to each follow-up using linear mixed effect models. Unadjusted and adjusted models with unstructured covariance matrices were run for each outcome to account for correlation within providers and subjects. The adjusted models included factors that may influence management decisions including age group at diagnosis, follow-up time in years, sex, BAV morphology, and baseline values for aortic root *z*-score, ascending aorta *z*-score, AS, and AR. The change in aortic root *z*-score per year and ascending aorta *z*-score per year was also determined, and descriptive statistics were performed. Model coefficients, 95% CIs and *P* values were reported from the unadjusted and adjusted models. Fisher's exact tests were used to compare subject characteristics (coded as categorical variables) with the outcomes of >mild AS and >mild AR. The outcomes aortic dissection, endocarditis, and death were analyzed with descriptive statistics.

All statistical analyses were performed using Statistical Analysis Software version 9.4 (SAS Institute Inc., Cary, North Carolina). All tests were two-tailed and statistical significance was evaluated at the .05 level.

3 | RESULTS

There were 294 subjects included in the disease progression analysis and the 454 subjects included in the practice variation analysis

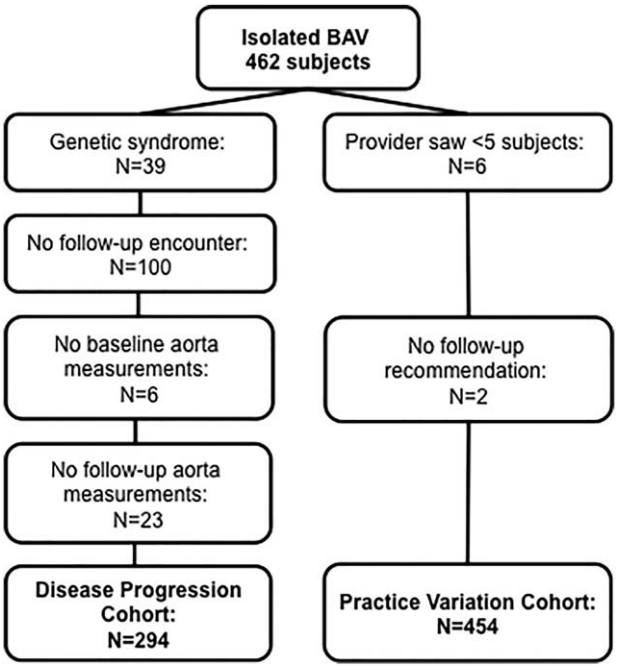

FIGURE 1 Inclusion and exclusion for practice variation and disease progression cohorts. This figure describes the criteria leading to selection for the practice variation and disease progression cohorts

(Figure 1). The majority were male, and at baseline had normal aortic root and ascending aorta *z*-scores with no AS or AR (Table 1). At the time of diagnosis, about a third of subjects were <2 years of age, and about half were 2–12 years of age with the remainder >12 years of age. The mean duration of follow-up for the disease progression group was 4.1 ± 2.4 (range 0.2–9.5) years.

3.1 | Changes in aortic root *z*-score

There was no significant change in the aortic root *z*-score during follow-up (Table 2), and no significant change in the aortic root *z*-score/year within age groups <2 years, 2–12 years, and >12 years (Figure 2). On multivariable analysis adjusted for follow-up time, subjects with an aortic root >2 at baseline demonstrated a significant decrease in aortic root *z*-score at follow-up encounters compared to those with a normal baseline aortic root *z*-score (Table 2). Compared to those diagnosed at <2 years of age, those aged 2–12 years and >12 years had significant decreases of 0.5 and 0.4, respectively, in their aortic root *z*-score ($P < .05$ for each) at any follow-up encounter.

3.2 | Changes in ascending aorta *z*-score

On average, the ascending aorta *z*-score increased by 0.1/year of follow-up ($P < .01$, Table 3). Subjects with either a mildly dilated ascending aorta at baseline (*z*-score 2–4) or a moderate to severely dilated ascending aorta (*z*-score >4) had a significant decrease in ascending aorta *z*-score compared to those with a normal ascending aorta at baseline ($P < .01$, Table 3). Compared to subjects diagnosed at <2 years of age, those aged 2–12 years and those >12 years had a significant decrease of 0.4 and 0.8, respectively, in their ascending aorta *z*-score at any follow-up encounter ($P < .05$ for each). The change in ascending aorta *z*-score/year of follow-up was relatively flat for all 3 age groups within 5 years from diagnosis (Figure 3). Beyond 5 years from diagnosis, those diagnosed at <2 years of age demonstrated an increase in ascending aorta *z*-score. Overall, wider confidence intervals were seen for the last 2–3 years of follow-up for each age group since relatively few subjects represented these later time points.

3.3 | Subjects with rapid aortic dilation

There were 35 subjects (12%) with >0.5 *z*-score/year aortic root or ascending aorta growth, 6 subjects (2%) with >0.5 *z*-score/year growth of both the aortic root and ascending aorta, 16 subjects (6%) with >0.5 *z*-score/year aortic root growth, and 25 subjects (9%) with >0.5 *z*-score/year ascending aorta growth. Of the subjects with rapid aortic dilation, 19/35 (54%) subjects progressed from nondilated to dilated aortic root or ascending aortas, 2 subjects (6%) had a dilated ascending aorta at diagnosis (ascending aorta *z*-score at diagnosis: 2.1–2.4, ascending aorta *z*-score at last follow-up: 2.9–6.6), and the remainder of subjects started with a normal aortic root and ascending aorta *z*-score, which remained in normal range at the end of the follow-up period.

TABLE 1 Baseline characteristics of study cohort

Characteristic	Disease progression cohort frequency (%) N = 294	Practice variation cohort frequency (%) N = 454
Sex (male)	230 (78%)	336 (74%)
Age at diagnosis		
<2 years	103 (35%)	142 (31%)
≥2–<12 years	159 (54%)	242 (53%)
≥12–18 years	32 (11%)	70 (15%)
Diagnosis era (1/1/2010–12/31/2014)	121 (41%)	236 (52%)
Aortic root *z*-score		
<2	241 (82%)	320 (70%)
≥2–<4	50 (17%)	59 (13%)
≥4	3 (1%)	3 (1%)
Missing	0	72 (16%)
Ascending aorta *z*-score		
<2	175 (60%)	242 (53%)
2–4	92 (31%)	102 (22%)
≥4	27 (9%)	25 (6%)
Missing	0	85 (19%)
Aortic regurgitation		
None	251 (85%)	390 (86%)
Mild	43 (15%)	64 (14%)
Aortic stenosis		
None	234 (80%)	374 (82%)
Mild	60 (20%)	80 (18%)
Valve morphology		
Right/Left fusion	208 (70%)	315 (69%)
Right/Noncoronary fusion	83 (28%)	131 (29%)
Not determined	3 (1%)	8 (2%)

TABLE 2 Characteristics associated with the change in aortic root *z*-score at follow-up

Characteristics	Univariable analysis		Multivariable analysis	
	z-score change (95% CI)	*P* value	*z*-score change (95% CI)	*P* value
Follow-up time (years)	−0.02 (−0.04, 0.01)	.23	−0.02 (−0.05, 0.01)	.13
Sex (ref: female)	0.1 (−0.2, 0.4)	.42	0.2 (−0.1, 0.4)	.24
Bicuspid aortic valve morphology (ref: right/non)		.49		.76
Right/left	−0.1 (−0.4, 0.1)	.29	−0.07 (−0.3, 0.2)	.54
Unknown	0.2 (−0.9, 1.4)	.70	0.2 (−0.9, 1.3)	.77
Age at diagnosis (ref: <2 years)		<.001		<.001
≥2–<12 years	−0.5 (−0.7, −0.3)	<.001	−0.5 (−0.7, −0.2)	<.001
≥12 years	−0.5 (−0.8, −0.1)	.013	−0.4 (−0.8, −0.1)	.019
Baseline aortic root *z*-score (ref: <2)		<.001		<.001
≥2–<4	−0.6 (−0.9, −0.3)	<.001	−0.6 (−0.8, −0.2)	<.001
≥4	−1.4 (−2.4, −0.4)	.008	−1.4 (−2.4, −0.4)	<.001
Baseline ascending aorta *z*-score (ref: <2)		.64		.76
≥2–<4	−0.1 (−0.3, 0.1)	.40	0.03 (−0.2, 0.3)	.81
≥4	−0.1 (−0.5, 0.3)	.54	0.1 (−0.2, 0.5)	.46
Baseline aortic gradient (ref: none)	0.1 (−0.1, 0.4)	.36	−0.2 (−0.4, 0.1)	.24
Baseline aortic regurgitation (ref: none)	−0.2 (−0.5, 0.1)	.13	−0.08 (−0.4, 0.2)	.59

3.4 | Valve function changes

In the disease progression cohort, the 9/294 subjects (3%) with >mild AS and/or >mild AR at the last encounter were more likely to have had mild AS or mild AR, respectively, at baseline (Table 4). The presence of >mild AR at the last encounter was significantly associated with a dilated aortic root at baseline.

3.5 | Outcomes

Only 1 subject with minimal aortic valve dysfunction (no AS and mild AR) at diagnosis (age 8 years) underwent aortic valve repair and aortic root replacement for moderate AR with progressive left ventricular, aortic root, and ascending aorta dilation at age 16 years. There were no aortic dissections, episodes of endocarditis, or deaths in our cohort.

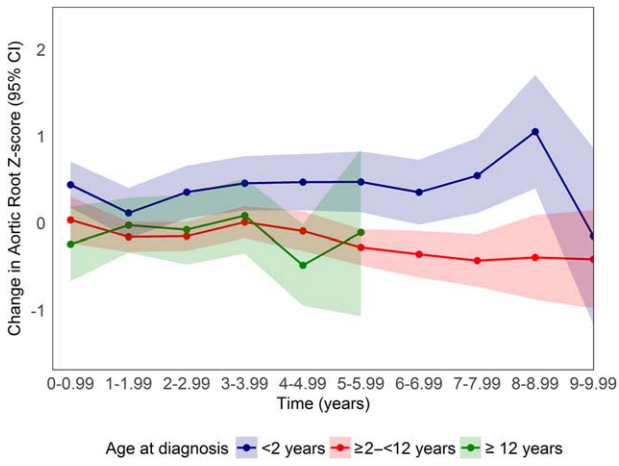

FIGURE 2 Change in aortic root *z*-scores at follow-up over time (years). The change in the aortic root *z*-score is plotted over time from baseline, in years. This change in aortic root *z*-score is stratified by the age at diagnosis (<2 years, ≥2–<12 years, and ≥12 years)

3.6 | Follow-up and provider recommendations

There were 454 subjects evaluated by 27 pediatric cardiologists during 1343 encounters, including 889 follow-up encounters. The average recommended follow-up interval between clinic visits was 1.5 ± 0.9 years. The average recommended follow-up interval for each age group was 1.2 ± 0.8 years for age <2 years, 1.7 ± 0.9 years for 2–12 years, and 1.4 ± 0.9 years for ≥12 years. At follow-up visits, 87% had either an echocardiogram (766/774 imaging studies, 99%) or a CMR (8/774 imaging studies, 1%). Other testing performed at follow-up encounters included electrocardiograms (542/889 encounters, 61%) and chest x-rays (27/889 encounters, 3%).

Provider alone accounted for modest, but significant variability in recommended follow-up interval (ICC 14%, $P < .001$) in the adjusted ordinal logistic regression model. Other factors associated with a shorter recommended follow-up interval included age <2 years, later diagnosis era, mild AR or AS at diagnosis, and greater aortic root and ascending aorta *z*-score at any follow-up study. Sex and genetic syndrome were not associated with the recommended follow-up interval (Table 5).

Provider variation in cardiac imaging at follow-up was also significant (ICC 24%, $P < .001$) in our adjusted logistic regression model. Age was also associated with the likelihood of imaging at follow-up. Compared to subjects <2 years old, children aged ≥2 years were more likely to have an imaging study at follow-up. Furthermore, adolescents were more likely be imaged in follow-up compared to children aged 2–12 years (OR: 9.3, 95% CI: 1.2–71.7). Genetic syndrome, sex, and diagnosis era were not associated with imaging at follow-up (Table 6).

TABLE 3 Characteristics associated with the change in ascending aorta *z*-score at follow-up

Characteristics	Univariable analysis		Multivariable analysis	
	z-score change (95% CI)	*P* value	*z*-score change (95% CI)	*P* value
Follow-up time (years)	0.1 (0.1, 0.2)	<.001	0.1 (0.1, 0.2)	<.001
Sex (ref: female)	0.1 (−0.2, 0.4)	.41	−0.2 (−0.1, 0.5)	.13
Bicuspid aortic valve morphology (ref: right/non)		.80		.93
Right/left	−0.06 (−0.3, 0.2)	.66	0.04 (−0.2, 0.3)	.73
Unknown	−0.4 (−1.6, 0.9)	.58	−0.07 (−1.3, 1.1)	.91
Age at diagnosis (ref: <2 years)		<.001		<.001
≥2–12 years	−0.4 (−0.6, −0.1)	<.001	−0.4 (−0.6, −0.2)	<.001
≥12 years	−0.8 (−1.2, −0.4)	<.001	−0.7 (−1.1, −0.2)	<.001
Baseline aortic root *z*-score (ref: <2)		.11		.50
≥2–<4	−0.2 (−0.6, 0.1)	.12	0.03 (−0.3, 0.3)	.87
≥4	−0.9 (−2.1, 0.3)	.14	−0.6 (−1.7, 0.4)	.25
Baseline ascending aorta *z*-score at baseline (ref: <2)		<.001		<.001
≥2–<4	−0.4 (−0.7, −0.2)	<.001	−0.4 (−0.7, −0.2)	<.001
≥4	−0.9 (−1.3, −0.5)	<.001	−0.8 (−1.2, −0.4)	<.001
Baseline aortic stenosis (ref: none)	0.04 (−0.2, 0.3)	.77	−0.03 (−0.3, 0.3)	.83
Baseline aortic regurgitation (ref: none)	−0.1 (−0.4, 0.2)	.62	0.2 (−0.2, 0.5)	.31

3.7 | Medical therapy

Only 11 subjects received cardiac medications during the study period, including beta-blocker (N = 1), angiotensin receptor blocker (N = 4), and angiotensin converting enzyme inhibitor (N = 7). Dual therapy was used in 1 subject (beta-blocker and an angiotensin converting enzyme inhibitor).

4 | DISCUSSION

This study demonstrates that children with an isolated BAV had little disease progression through adolescence and adverse outcomes were rare. Despite the lack of disease progression, these children were seen and imaged frequently in cardiology clinic. Although significant, pediatric cardiology provider variation accounted for a relatively small proportion of the overall practice variation. As expected, valve dysfunction, aortic root and ascending aorta dilation, age at encounter, and an earlier diagnosis era significantly influenced management decisions.

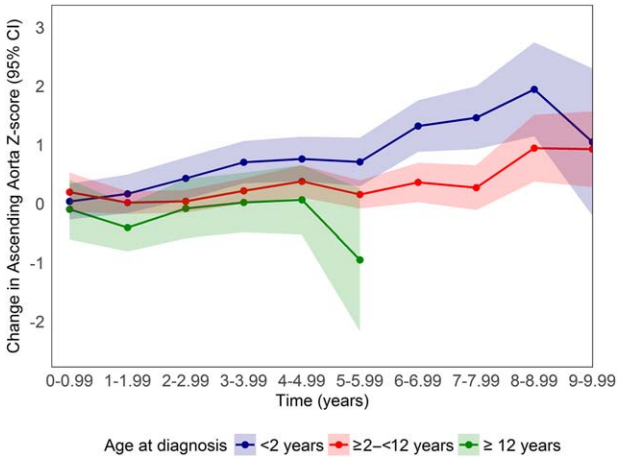

FIGURE 3 Change in ascending aorta *z*-scores at follow-up over time (years). The change in the ascending aorta *z*-score is plotted over time from baseline, in years. This change in ascending aorta *z*-score is stratified by the age at diagnosis (<2 years, ≥2–<12 years, and ≥12 years)

The most important findings of our study are that, for children with an isolated BAV, disease progression is uncommon and adverse events are rare. Only 3% of the subjects developing >mild AS or AR, and only 1 patient required surgical intervention (8 years after initial diagnosis for progressive AR, LV enlargement, and aortic dilation). There were no episodes of aortic dissection, endocardtitis, or death in our study. Mahle et al. found an event rate of 0.004/patient-year in children with an isolated BAV, including catheterization and surgical aortic valve interventions and one case of endocarditis.[6] Disease progression in children in other reports has been similar to that demonstrated in the current study with few adverse outcomes.[8] No aortic dissections have been reported in the pediatric population.[6,7,24] Compared to previous studies[5,6,8] which included children with varying degrees of valve dysfunction (>mild AS or AR) at baseline or other major cardiac defects, the disease progression described in the current study may be slower because ≤mild valve dysfunction at diagnosis was part of the inclusion criteria.[5,6,8] Although adults with an isolated BAV have an increased risk of aortic aneurysms, aortic dissection, and aortic valve or aortic interventions compared to the general population,[7] these adverse outcomes are far less prevalent in children.[6–8]

In terms of aortic dilation, we found no significant change in the aortic root *z*-score, only a small change in ascending aorta *z*-score during the study period, and only a minority of patients demonstrating rapid aortic dilation. Our findings are similar to those reported previously with the average ascending aorta *z*-score increasing by

TABLE 4 Characteristics associated with ≥mild aortic valve dysfunction at follow-up

Characteristic	Aortic regurgitation at last encounter *P* value	Aortic stenosis at last encounter *P* value
Sex	>.99	.30
Age at diagnosis	.56	.15
Bicuspid aortic valve morphology	>.99	>.99
Baseline aortic stenosis (none vs mild)	>.99	<.001
Baseline aortic regurgitation at diagnosis (none vs mild)	.011	>.99
Baseline aortic root *z*-score	.005	.45
Baseline ascending aorta *z*-score	.06	>.99

0.06 ± 0.01 to 0.4/year.[5,8,10,15] Thus, the rate of aortic dilation is slower in children than in adults. Adults with a BAV have demonstrated an average increase of 1.0 mm/year in aortic root and ascending aorta diameters.[25] Aortic dilation by age group at presentation has not been previously reported, and while the current study shows that children <2 years of age at baseline had relatively greater aortic dilation, the vast majority of these patients had aortic root and ascending aorta *z*-scores that were at most mildly dilated.

Despite the rarity of adverse outcomes for children with an isolated BAV compared to adults, the children in this cohort were followed even more frequently than recommended by the adult/adolescent guidelines, and the vast majority of encounters (87%) included cardiac imaging. Younger children had more frequent follow-up, but less frequent imaging. Although it appears contradictory, the shorter follow-up interval may be due to concern about rapid progression of aortic valve dysfunction (detectable by auscultation) rather than aortic dilation (detectable only with imaging) in younger patients. This hypothesis is supported by the higher frequency of echocardiograms in adolescents where the development of aortic aneurysms and possible aortic dissection may be the primary concern. Adolescents may also have more imaging to determine appropriate exercise recommendations since current guidelines recommend sports restriction for patients with a dilated aorta or >mild aortic valve dysfunction.[26] Although both infancy and adolescence are characterized by rapid somatic growth, the changes in aortic valve function and aortic dilation were not pronounced during either period.

Provider variance contributed, albeit modestly, to practice variation, and may be partly explained by inconsistent data regarding risk factors for aortic valve dysfunction and aortic dilation. In fact, data regarding whether BAV morphology, AS, and AR are risk factors for aortic dilation and aortic valve dysfunction are conflicting in prior reports.[5–16] This study showed that BAV morphology and the degree of AS or AR at the time of initial encounter were unrelated to aortic dilation. Although baseline aortic root and ascending aorta *z*-score influenced the change observed in these respective dimensions, those with a dilated aortic root or ascending aorta at baseline actually had, on average, a decrease in their aortic root or ascending aorta *z*-score over time compared to those with normal dimensions. This conflicting data

TABLE 5 Factors associated with a shorter recommended follow-up interval (years)

Factor	Univariable analysis Odds ratio (95% CI)	*P* value	Multivariable analysis Odds ratio (95% CI)	*P* value
Age at encounter (ref: <2 years)		<.001		<.001
≥2–<12 years	0.2 (0.1, 0.3)	<.001	0.3 (0.2, 0.4)	<.001
≥12 years	0.3 (0.2, 0.5)	<.001	0.4 (0.3, 0.8)	.007
Diagnosis era (ref: 1/1/05–12/31/09)	1.9 (1.3, 2.8)	.002	2.2 (1.5, 3.1)	<.001
Sex (ref: male)	1.3 (0.8, 2.0)	.25	1.2 (0.8, 1.8)	.32
Genetic syndrome (ref: yes)	1.2 (0.6, 2.6)	.57	0.8 (0.4, 1.6)	.52
Aortic regurgitation (ref: none)		<.001		<.001
Mild	1.8 (1.2, 2.9)	<.007	1.6 (1.0, 2.5)	.04
>Mild	7.1 (2.4, 21.1)	<.001	4.5 (1.4, 14.3)	.01
Aortic stenosis (ref: none)		<.001		<.001
Mild	4.3 (3.0, 6.1)	<.001	4.1 (2.8, 6.0)	<.001
>Mild	10.9 (3.6, 33.4)	<.001	15.6 (4.4, 55.4)	<.001
Aortic root *z*-score	1.3 (1.1, 1.5)	<.001	1.3 (1.1, 1.4)	<.002
Ascending aorta *z*-score	1.4 (1.2, 1.5)	<.001	1.3 (1.1, 1.4)	<.001

TABLE 6 Characteristics associated with a cardiac imaging study performed at follow-up

	Univariable analysis		Multivariable analysis	
Characteristics	**Odds ratio (95% CI)**	***P* value**	**Odds ratio (95% CI)**	***P* value**
Age at encounter (ref: <2 years)		<.001		<.001
2–12 years	2.2 (1.5, 3.4)	<.001	2.2 (1.4, 3.4)	<.001
≥13 years	21.4 (2.8, 164.5)	.003	20.5 (2.7, 157.6)	<.001
Diagnosis era (ref: 1/1/05–12/31/09)	0.9 (0.6, 1.4)	.68	1.0 (0.6, 1.5)	.91
Sex (ref: male)	1.8 (1.1, 2.9)	.025	1.6 (0.9, 2.6)	.052
Genetic syndrome (ref: no)	1.0 (0.4, 2.2)	.93	0.7 (0.3, 1.7)	.47

from prior reports of risk factors leading to aortic valve dysfunction and aortic dilation likely contribute substantially to provider variance and overall management practices. Further studies are needed to improve understanding of the longer-term natural history of a BAV to inform practice guidelines in children.

This study is limited by the retrospective single-center design and the relatively small number of individuals with longer-term follow-up. Few subjects received cardiac medication (n = 11) and the indication for medical therapy was not always clear therefore, no meaningful analysis of the impact on disease progression could be performed. While aortic root dilation at baseline and aortic valve dysfunction were significantly associated with >mild AR at last encounter, the numbers analyzed were small. Health insurance and other factors that impact access to care and the frequency of recommended clinic and imaging follow-up were not addressed in this study.

Follow-up intervals and the performance of cardiac imaging in this cohort of pediatric patients with an isolated BAV were more frequent than recommended by the ACC/AHA adult congenital and valve guidelines,[3,4] and are not well-supported by evidence since both valvar disease and related aortopathy appear to progress slowly during childhood. Based on the findings of this study, less frequent clinic follow-up and cardiac imaging may be appropriate for a child with an isolated BAV.

CONFLICT OF INTEREST

None.

AUTHOR CONTRIBUTIONS

Concept/Design, Data Collection, Data analysis/interpretation, Drafting article, Critical revision of article: Melissa Yamauchi

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