Serial Magnetic Resonance Imaging for Aortic Dilation in Tetralogy of Fallot With Pulmonary Stenosis

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Aortic dilation occurs in patients with repaired tetralogy of Fallot (TOF), but the rate of growth is incompletely characterized. The aim of this study was to assess the rates of growth of the aortic root and ascending aorta in a cohort of pediatric and adult patients with sequential magnetic resonance angiography Magnetic Resonance Imaging (MRI) data. Using serial MRI data from pediatric and adult patients with repaired TOF, we performed a retrospective analysis of the rates of growth and associations with growth of the aortic root and ascending aorta. Patients with pulmonary atresia or absent pulmonary valve were excluded. Between years 2005 to 2021, a total of 99 patients were enrolled. A follow-up MRI was performed an average of 5.9 ± 3.7 years from the initial study. For the cohort aged ≥16 years, the mean rate of change in diameter was 0.2 ± 0.5 mm/year at the ascending aorta and 0.2 ± 0.6 mm/year at the sinus of Valsalva. For the entire cohort, the mean change in cross-sectional area indexed to height at the ascending aorta was 7 ± 12 mm^2/m/year and at the sinus of Valsalva was 10 ± 16 mm^2/m/year. Younger age was associated with higher rates of growth of the sinus of Valsalva while the use of β blockers or angiotensin-converting enzyme inhibitors was associated with a slower rate of growth. There were no cases of aortic dissection in this cohort. We conclude that serial MRI demonstrates a slow rate of growth of the aorta in the TOF. **(Am J Cardiol 2023;191:92−100)**

Tetralogy of Fallot (TOF) is the most common cyanotic heart lesion,[1] and management of long-term co-morbidities is of increasing importance, given the excellent long-term survival after repair.[2] Aortic root dilation has been described in patients with a repaired TOF, with a prevalence between 14% and 87%, depending on the age of the cohort and the criteria used to define dilation.[3−6] A suspected etiology for increased aortic growth in the TOF is increased flow through the aorta before repair. In addition, histologic findings, such as loss of lamellar units, fibrosis, and cystic medial necrosis, and increased aortic stiffness may also predispose these patients to aortic dilation.[7−12] These changes may also lead to a rare aortic dissection that has also been reported late after TOF repair.[13] Consequently, centers that care for adults with a repaired tetralogy perform aortic valve or root procedures on a small number of patients because of aortic dilation.[14−16] Although previous reports have identified the presence of aortic root dilation in this population, there are limited longitudinal studies to help guide the monitoring of aortic root dimensions in either pediatric or adult congenital populations.[13] This study provides a single-center experience on aortic root dilation in patients with a repaired TOF with pulmonary stenosis who have undergone at least 2 cardiac magnetic resonance angiography (MRI) studies. We assessed the rate of aortic root dilation and examined the risk factors for dilation over time. We expanded on previous studies by including a subset of pediatric patients, providing values of cross-sectional area (CSA) normalized by height and providing a greater sample size.

Methods

The Indiana University Institutional Review Board approved this retrospective cohort study. An internal database derived from electronic medical record data was queried for patients of all ages with a repaired TOF who underwent at least 2 clinically indicated MRIs at least 6 months apart, between January 1, 2005 and January 1, 2021. Demographic information, and the cardiac anatomy, previous cardiac surgeries, genetic diagnoses, medications, and pregnancy

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history, were obtained from chart review. In the case of >2 MRI studies, the first and the most recent MRIs were analyzed. Patients with TOF with associated anomaly (i.e., pulmonary atresia, absent pulmonary valve syndrome, or common atrioventricular canal), double outlet right ventricle, or bicuspid aortic valve were excluded from this study.

MRI exams were performed using a Siemens 1.5 T Avanto scanner (Siemens, Inc., Erlangen, Germany). A single investigator trained in advanced imaging for pediatric cardiology performed the measurements of the aortic root and ascending aorta and was blinded to the patient and the date of the study. The majority (71%) of measurements were obtained using a respiratory navigator-gated and electrocardiogram-triggered whole heart sequences obtained in diastole, with the remainder (29%) obtained using 3-dimensional balanced steady-state free precession technique when the former sequence was not obtained. We independently evaluated studies with both sequences (n = 45) in a blinded random manner and found that the measurements were not significantly different (p = 0.56 to 0.88 for the ascending aorta and sinus of Valsalva measurements), providing support for use of either sequence.

The analysis was performed using CVI42 platform (Circle Cardiovascular Imaging, Alberta, Canada) using multiplanar reformatting to obtain measurements perpendicular to the blood flow and using inner lumen-to-inner lumen technique. The oblique coronal, oblique sagittal, and the greatest cusp to commissure dimension at the sinus of Valsalva were measured. The ascending aorta was measured in oblique coronal and sagittal planes.

We separately analyzed the subset of patients aged ≥16 years because the majority of somatic growth is achieved by this age. The absolute measurements of the aortic root and ascending aorta diameters were used for the analysis of patients aged ≥16 years. The observed-to-expected ratios were calculated using normative diameters based on age, body surface area, and gender at the ascending aorta and sinus of Valsalva for patients aged >16 years.[17,18]

The estimated CSAs of the sinus of Valsalva and ascending aorta were calculated using the formula for area of an ellipse, with the diameters obtained in the oblique coronal and sagittal views. The CSA of the ascending aorta and sinus of Valsalva were indexed to height to account for ongoing growth in patients aged <16 years. A CSA of >10 cm^2/m was used as a threshold for severe aortic root dilation.[19]

Summary statistics for continuous and categorical variables were expressed as means and medians with SDs and counts with percentages. Bivariate regression models of rates of change of aortic size were fit for the primary outcomes: rate of growth of the aorta between the initial and most recent MRI. Residual plots were examined to assess the model assumptions of normality of error terms and homogeneity of variance. Variables, which were significant at the 0.3 level in the bivariate models, were considered eligible for inclusion in a multiple regression model. Stepwise variable selection with entry criteria of 0.30 and staying criteria of 0.10 was used to reach the final model for each outcome. All the data were analyzed using SAS/STAT 9.4 software 2016 by SAS Institute Inc, Cary, North Carolina. The figures were produced using R Core Team (2021; R: a language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria: https://www.R-project.org).

Results

There were 103 patients with a repaired TOF with pulmonary stenosis and sequential cardiac MRIs in our database; 3 patients were excluded because of the time intervals between studies of 6 months or less and 1 patient was excluded because of presence of bicuspid aortic valve, leaving 99 patients included in analysis. The mean age at the time of the first MRI was 21 ± 12 years and 46% were male (Table 1). A total of 57 patients were aged ≥16 years at the time of their first MRI. The average age of patients aged ≥16 years at the first MRI was 28 ± 11 years and 40% were male. The mean time interval between the first and most recent MRI was 6 ± 4 years.

Overall, the average age at the time of complete repair was 2.5 ± 2 years; 48 were aged ≤2 years, with 27 being aged ≤1 year. There were 40 patients aged >2 years at the time of the complete repair (age at complete repair was unavailable for 11 patients). There were 47 patients (49%) who underwent staged repair. Regarding the type of surgical repair, 14% (n = 14) had a valve-sparing repair, 59% (n = 58) had a transannular patch, with 50% (n = 29) of these having a monocusp valve, and 3% (n = 3) had a conduit placement. Data on the type of initial, definitive surgical repair were missing for 24% of patients. All patients had a complete repair before the time of the first MRI. The majority of patients (77%) had a left-sided aortic arch. There were no patients with aortic dissection and no patient required intervention on the aortic valve or aortic root.

In the population of patients aged ≥16 years, the baseline mean diameter of the ascending aorta was 2.9 ± 0.5 cm and at the sinus of Valsalva, the mean diameter was 3.3 ± 0.5 cm. The mean observed-to-expected ratio for the ascending aorta in the cohort aged ≥16 years was 1.1 ± 0.3 for boys and 1.0 ± 0.1 for girls at the first MRI. At the sinus of Valsalva, the mean observed-to-expected ratio was 1.2 ± 0.2 for men and 1.2 ± 0.1 for women (Table 2).

For the entire cohort, including children, the mean baseline ascending aorta CSA indexed to height was 3.5 ± 1.2 cm^2/m and the mean CSA of the sinus of Valsalva indexed to height was 4.8 ± 1.3 cm^2/m (Table 2).

Only 3 patients (all aged ≥16 years) had an aortic root over 4 cm at the sinus of Valsalva on the baseline study. There were 4 patients (4%) who had more than a trivial aortic valve insufficiency defined as aortic reverse to forward flow ratio of >5%.

Follow-up MRI was performed an average of 5.9 ± 3.7 years from the initial study. For the cohort aged ≥16 years, the mean diameter at the ascending aorta on the most recent MRI was 3.0 ± 0.5 cm. The mean diameter at the sinus of Valsalva was 3.4 ± 0.4 cm. The mean rate of change was 0.2 ± 0.5 mm/year at the ascending aorta and 0.2 ± 0.6 mm/year at the sinus of Valsalva (Table 2). The rate of growth did not differ in the very small subset of patients who had an aortic root >4.0 cm at the sinus of Valsalva on the baseline study. Figure 1 depicts the diameters

Table 1
Demographic and baseline information for the entire cohort and for the cohort ≥ 16 years old

Variable		Total population n=99	Cohort≥16 y Old n=57
Age (years) at MRI1	Mean±SD	20.8±11.7	27.6±10.9
	Median (range)	17.4 (3.9, 58.0)	24.9 (16.0, 58.0)
Gender	Male	45 (45.5%)	23 (40.4)
	Female	54 (54.5%)	34 (59.7)
Height (m) at MRI1	Mean±SD	1.6±0.2	1.7±0.1
	Median (range)	1.6 (0.9, 1.9)	1.7 (1.5, 1.9)
Weight (kg) at MRI1	Mean±SD	61.4±23.2	72.5±17.3
	Median (range)	62.6 (15.9, 116.6)	68.95 (37.7, 116.6)
BSA at MRI1	Mean±SD	1.6±0.4	1.8±0.2
	Median (range)	1.7 (0.6, 2.3)	1.8 (1.3, 2.3)
Age at complete repair (years)	Mean±SD	2.5±2.2	3.6±2.5
	Median (range)	1.7 (0.0, 10.0)	3.0 (0.4, 10.0)
Staged repair	No	50 (51.6%)	25 (45.5%)
	Yes	47 (48.5%)	30 (54.6%)
Age at Shunt Placement (years)	N	37	21
	Mean±SD	0.7±1.1	1.0±1.3
	Median (range)	0.3 (0.01, 4.7)	0.46 (0.01, 4.71)
Diabetes		3 (3.0%)	1 (1.8%)
Hypertension		10 (10.1%)	9 (15.8%)
Smoker or former smoker		4 (4.0%)	4 (7.0%)
β blocker		23 (23.2%)	19 (33.3%)
ACE/ARB medicine		12 (12.1%)	10 (17.5%)
Aortic arch side	Left	76 (76.8%)	42 (73.7%)
	Right	23 (23.2%)	15 (26.3%)
History of pulmonary valve replacement	No	42 (44.7%)	24 (45.3%)
	Yes	52 (55.3%)	29 (54.7%)

of the ascending aorta and sinus of Valsalva by age for the entire cohort aged ≥16 years, whereas Figure 2 links these diameters to each patient to assess rate of growth for each patient.

The observed-to-expected ratio at the ascending aorta at the follow-up MRI was 1.0 ± 0.2 for boys and 1.0 ± 0.1 for girls. The observed-to-expected ratio at the sinus of Valsalva was 1.2 ± 0.1 for men and 1.2 ± 0.1 for women (Table 2). No patient had an observed-to-expected ratio >1.5 at the ascending aorta. Only 1 patient had an observed-to-expected ratio >1.5 at the sinus of Valsalva.

For the entire cohort, the mean CSA indexed to height at follow-up was 3.9 ± 1.3 cm^2/m at the ascending aorta and 5.3 ± 1.3 cm^2/m at the sinus of Valsalva. The mean change in the CSA indexed to height at the ascending aorta was 7 ± 12 mm^2/m/year and at the sinus of Valsalva was 10 ± 16 mm^2/m/year (Table 2). Figure 3 depicts the CSA indexed to height of the ascending aorta and sinus of Valsalva by age for the entire older cohort, whereas Figure 4 links these indexed areas to each patient to assess rate of growth for each patient.

Of note, there were no cases of aortic dissection or need for surgical intervention on the aortic root in this cohort.

For the cohort of patients aged ≥16 years, a history of pulmonary valve replacement was marginally associated with a slower rate of growth of the ascending aorta. After a stepwise variable selection, only the history of pulmonary value replacement was selected for inclusion in a multiple regression model and this was again marginally associated with slower rates of growth at the ascending aorta (Table 3).

Variables associated with the rate of growth of the sinus of Valsalva for the cohort aged ≥16 years on the bivariate analysis included age at the initial MRI; age at the time of complete repair; and the presence of a β blocker, angiotensin-converting enzyme (ACE) inhibitor, or angiotensin receptor blocker (ARB). These were all negatively associated with the rate of growth at the sinus of Valsalva. After stepwise variable selection, age at the first MRI and history of staged repair were selected for inclusion in a multiple regression model, with increasing age significantly associated with slower growth (Table 4).

For the entire cohort, including those aged <16 years, a history of pulmonary valve replacement was marginally associated with a higher rate of growth of the CSA indexed to height of the sinus of Valsalva in bivariate and multivariable analysis (Table 5).

There were no statistically significant associations of any variable with the rate of growth of the CSA indexed to height of the ascending aorta.

Gender, staged repair, hypertension, aortic arch sidedness, and tobacco use were not significantly associated with growth of the ascending aorta or sinus of Valsalva.

Discussion

This study used a large database of patients with a repaired TOF to examine the rates of aortic root dilation using MRI studies. This study is unique because of the large cohort of patients with MRI data, longitudinal evaluation, and inclusion of children in the analysis with the novel use of aortic CSA. We found at the baseline MRIs a low

Table 2
Measurements of the aortic root and ascending aorta with rates of change for the entire cohort and for the cohort ≥16 years old

	MRI 1 mean, cm	MRI 2 mean, cm	Absolute change mean, cm	Rate of change/year mean, mm/y
Cohort ≥16 y old				
Ascending aorta diameter	2.9 (0.5)	3.0 (0.5)	0.13 (0.18)	0.2 (0.5)
Observed: expected ratio, ascending aorta	M: 1.1 (0.3) F: 1.0 (0.1)	M: 1.0 (0.2) F: 1.0 (0.1).		
Sinus of Valsalva diameter	3.3 (0.5)	3.4 (0.4)	0.13 (0.18)	0.2 (0.6)
Observed : expected ratio, SoV	M: 1.2 (0.2) F: 1.2 (0.1)	M: 1.2 (0.1) F: 1.2 (0.1).		
Entire cohort	**MRI 1 mean, cm^2/m**	**MRI 2 mean, cm^2/m**	**absolute change mean, cm^2/m**	**rate of change/year mean, $mm^2/m/y$**
Ascending aorta CSA/Ht	3.5 (1.2)	3.9 (1.3)	0.4 (0.5)	7 (12)
Sinus of Valsalva CSA/ht	4.8 (1.3)	5.3 (1.3)	0.5 (0.6)	10 (16)

[a]Data are expressed as mean (SD).

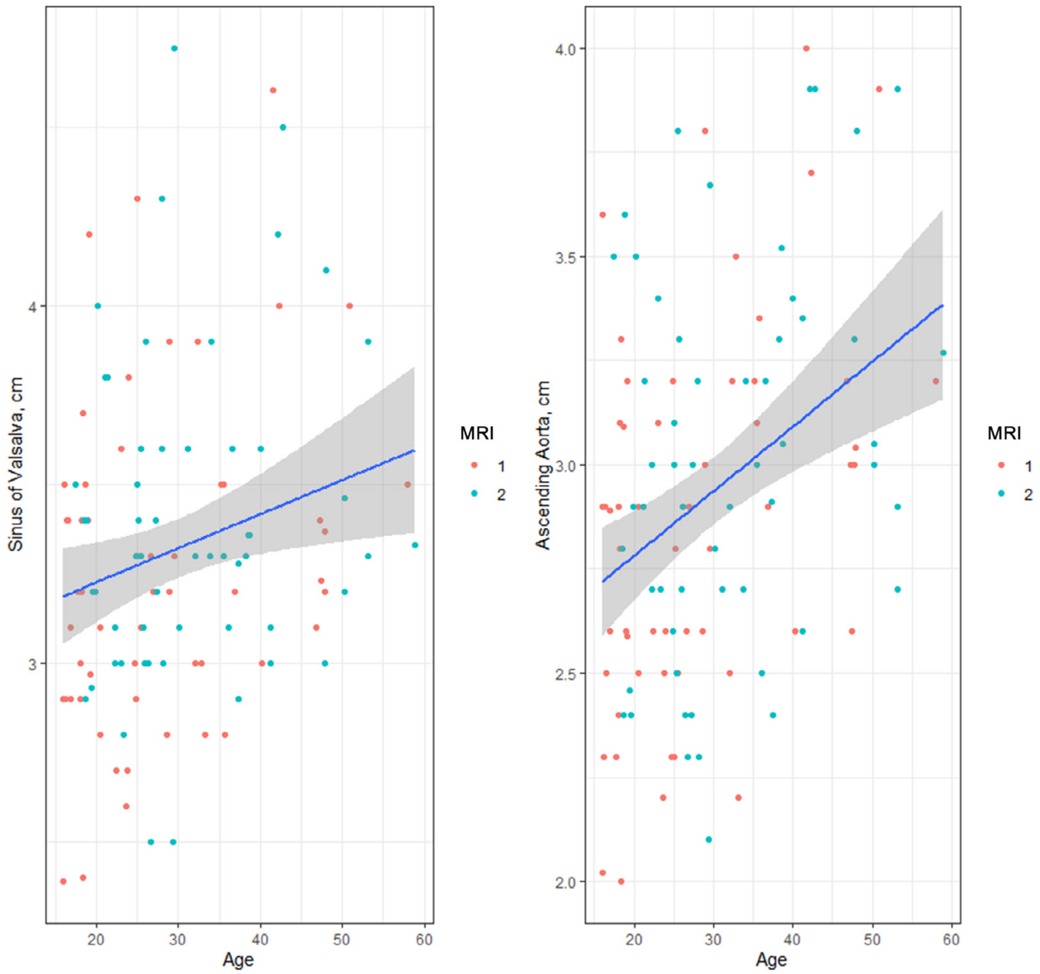

Figure 1. Diameters of the sinus of Valsalva (left) and ascending aorta (right) by age. The shaded area represents the 95th confidence intervals for the regression line.

incidence of significant aorta dilation. The rates of growth of both the ascending aorta and sinus of Valsalva were also low, and no patient in this study had an aortic dissection.

At baseline evaluation, the subset aged >16 years had aortas that were at least marginally above expected size (observed : expected ratio >1.0 in 95% at the sinus of Valsalva and 50% at the ascending aorta); however, clinically relevant dilation was rare, with an observed : expected ratio >1.5 in only 1 patient at the sinus of Valsalva and 1 patient at the ascending aorta. Similarly, the absolute diameter at

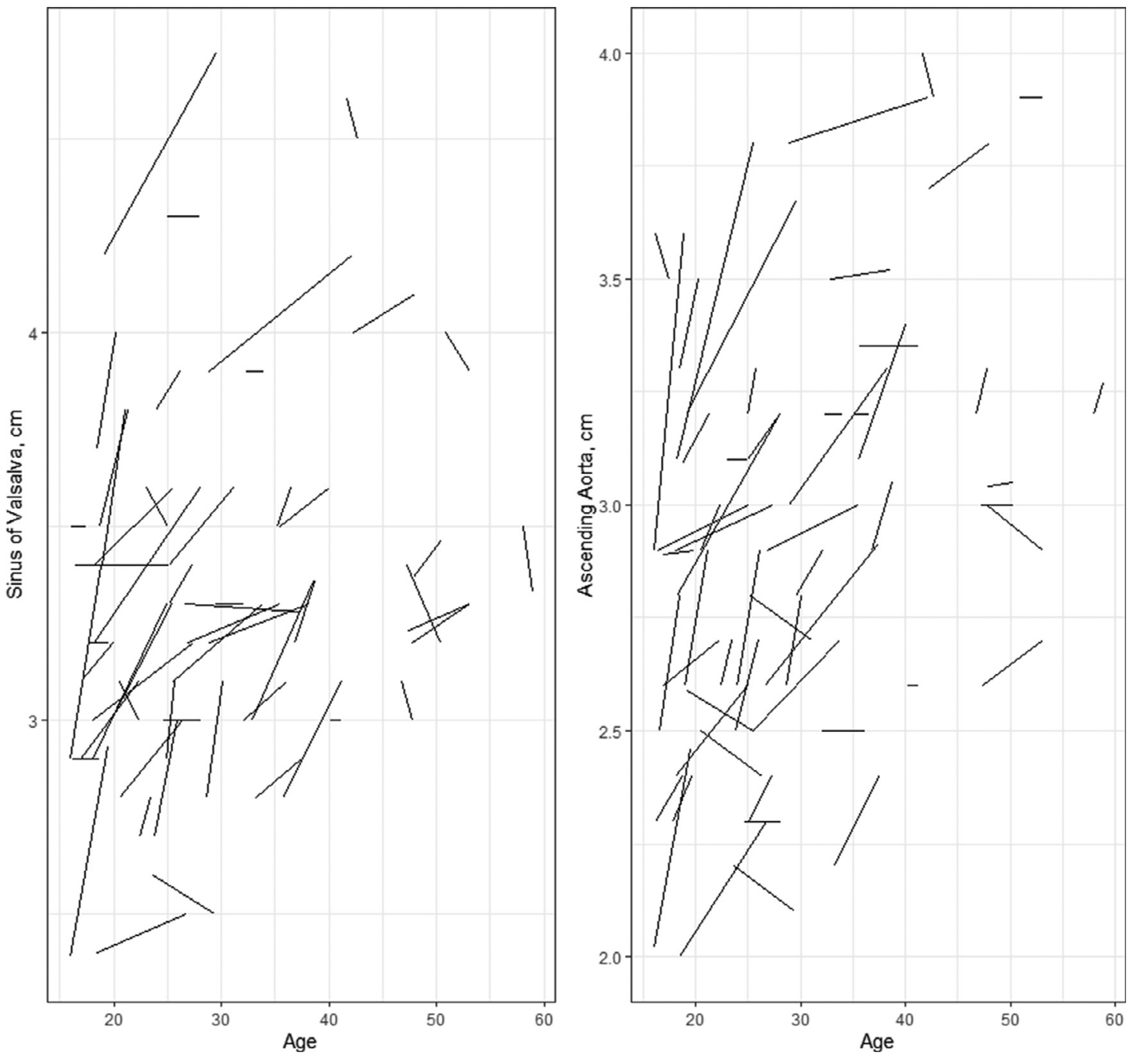

Figure 2. Change in diameter of the sinus of Valsalva (left) and ascending aorta (right) over time linked by patient.

the sinus of Valsalva of >4 cm was found in only 3 patients (3%) at the initial MRI and 5 (5.1%) at the time of the most recent MRI in this older cohort.

A notable finding in this study was that the baseline measurements of the sinus of Valsalva and ascending aorta were smaller than some previous reports of 3.3 to 4.4 cm at the aortic root and 3.1 to 4.4 cm at the ascending aorta.[4,6,7,20] Our study intentionally evaluated a homogenous population of patients TOF with pulmonary stenosis. We excluded patients with TOF with pulmonary atresia, who have been shown to have larger aorta size than those with pulmonary stenosis, perhaps because of larger aortic roots because of greater degree of conotruncal rotation during development.[4,7,21,22] In addition, a cohort of slightly younger patients than previous studies may account for this finding because aorta size has been correlated to increasing age.[17,18] Finally, previous works support the idea that aortic root size is associated with later age at repair and may normalize after early repair.[7,11,12,23] This study's population had an overall relatively young age at complete repair (mean 2.5 years, 27% in infancy), which perhaps also contributed to the low baseline measurements.

Previous studies have demonstrated that the CSA to height ratio may be a useful measure of the aorta that accounts for both aortic elliptical shape, and body habitus variations.[19,24−26] A CSA indexed to height >10 cm^2/m has previously been reported to be independently correlated with the risk of death in patients with dilated aortic roots in adults with trileaflet aortic valve and no underlying structural heart disease,[19] bicuspid aortic valves,[24,25] and Marfan syndrome.[26]

This novel evaluation has not been well evaluated in a repaired TOF population. A previous study evaluated the aorta CSA/height (ht) ratio in an adult population that was older than our total population and with a later age of complete repair.[6] They found an average CSA/height (ht) ratio at the sinus of Valsalva of 6.0 ± 1.9 cm^2/m and at the ascending aorta of 4.8 ± 2.1 cm^2/m, with 3 patients having a ratio >10 cm^2/m at either location.[6] These values are larger than our findings of baseline aortic CSA/ht ratio at the aortic root of 4.8 ± 1.3 cm^2/m and ascending aorta of 3.5 ± 1.2 cm^2/m, with no patients having aortic CSA/ht ratio >10 cm^2/m. Although this finding may be reassuring based on the predictive value of aortic CSA/ht in the

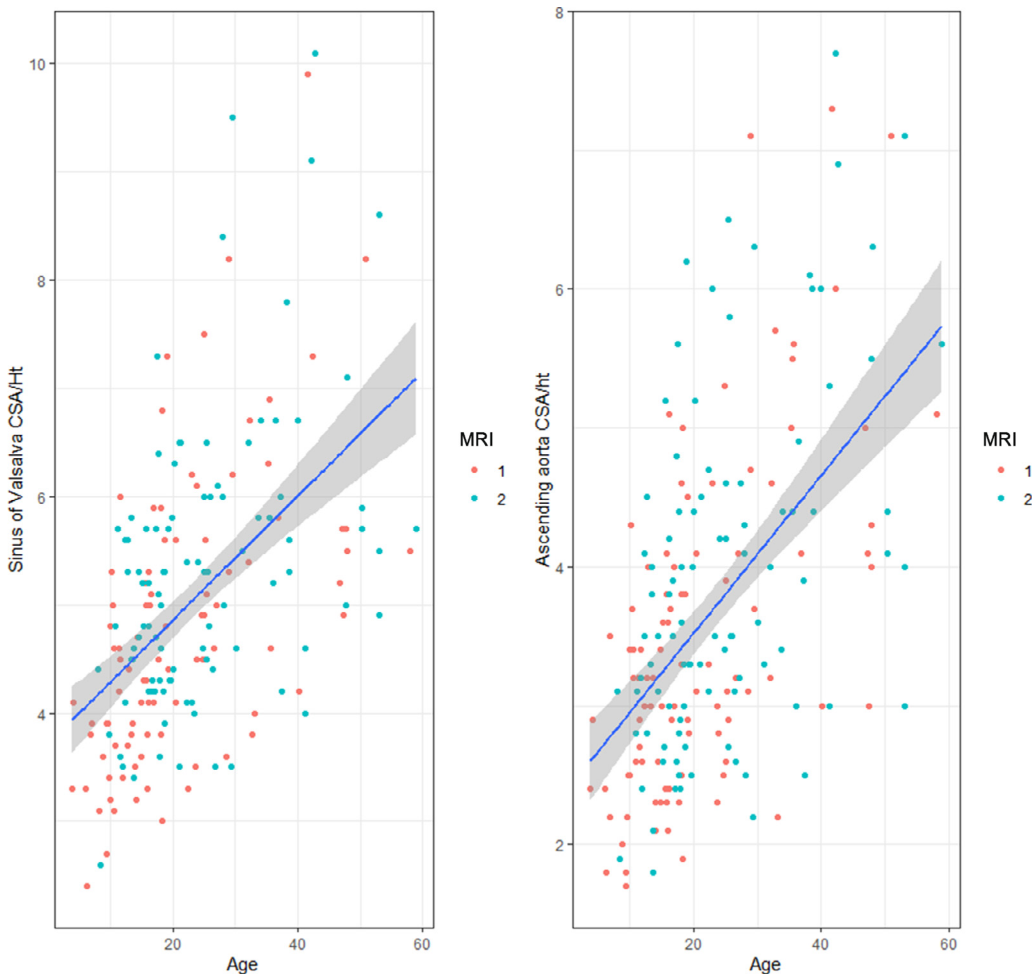

Figure 3. Cross-sectional areas indexed to height of the sinus of Valsalva (left) and ascending aorta (right) by age. The shaded area represents the 95th confidence intervals for the regression line.

Marfan or aortic valve disease populations, it is difficult to draw conclusions in this setting because the utility of this threshold has not been fully studied in patients with TOF. However, it does provide updated CSA/ht values in a larger, younger, and more modern TOF population.

The rate of growth of the aortic root and ascending aorta in our older population was low (0.2 ± 0.5 mm/year at the ascending aorta and 0.2 ± 0.6 mm/year at the sinus of Valsalva), which echoes findings of previous studies[6,7] of 0.23 to 0.5 mm/year or 0.6 mm over 2 years at the aortic root and 0.3 to 0.37 mm/year at the sinus of Valsalva.[6,22,27] Although echocardiography has shown rates of growth of 0.03 to 1.7 mm/year at the aortic root,[7,20] MRI may be superior in imaging the aorta without limitation from acoustic windows. We also take advantage of the 3-dimensional capabilities of MRI to report the measurement of change per year of the CSA/ht of the entire population of 7 ± 12 mm^2/m/year at the ascending aorta and 10 ± 16 mm^2/m/year at the sinus of Valsalva. A small subset (8 patients at the ascending aorta, 11 patients at the sinus of Valsalva) had a slight decrease in aortic measurements over time; the absolute change was an average of 1.2 mm at the ascending aorta and 1.3 mm at the sinus of Valsalva. This likely highlights the technical measurement variability.

In our multivariable analysis, younger age at the time of the initial MRI was associated with an increased rate of growth at the sinus of Valsalva. Previous studies have demonstrated that the rate of growth of the aortic root tends to be higher in the first several years after surgery than later in childhood.[12,21,23] These studies emphasized the importance of repair in infancy in preventing future aortic root dilation. In our cohort, the mean age of repair was 2.5 ± 2.2 years and 48.5% underwent staged repair as a strategy to preserve the pulmonary valve. Even in this setting, we found that severe aortic root dilation was rare. Other studies in adult populations[4] either did not find age to be a significant predictor of aortic root dilation or found that older age was associated with increased aortic root dilation.[4,6]

The use of β blockers, ACE inhibitors, or ARBs was associated with a slower rate of growth at the sinus of Valsalva. In this cohort, the indication for starting these medications was not assessed but may be of interest to investigate in a future study. Beta blockers and ARBs have been shown to be protective against aortic root dilation in patients with Marfan syndrome and those with aortopathy related to a bicuspid aortic valve.[28,29] A prospective study evaluating losartan in patients with a repaired TOF did not show significant effect of treatment.[27] Given our small

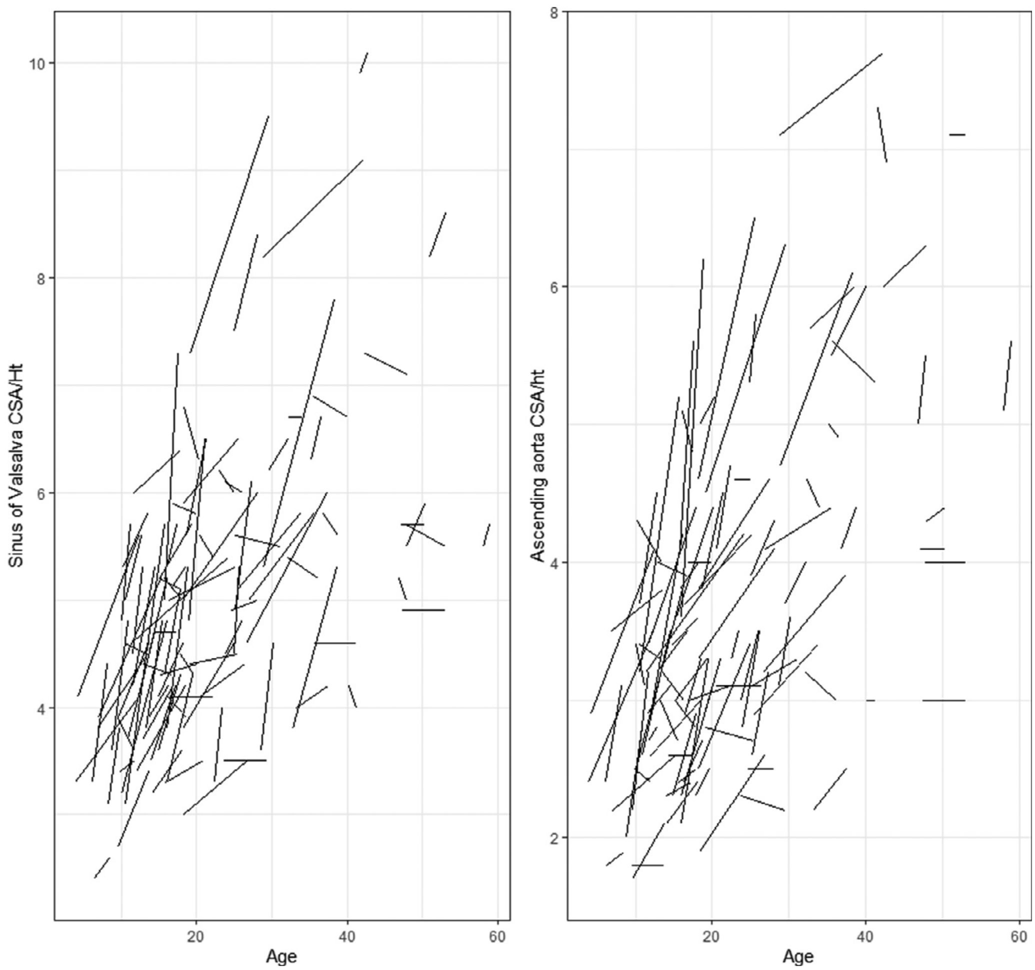

Figure 4. Change in the cross-sectional area indexed to height of the sinus of Valsalva (left) and ascending aorta (right) over time linked by patient.

Table 3
Variables associated with growth of the ascending aorta diameter in the cohort≥16 y old

Variable label	Bivariate model			Multivariable model			
	Estimate (std error)	95% CI	p Value	Estimate (std error)	95% CI	p Value	R-square
Pulmonary valve replacement	−0.023 (0.011)	(−0.046, 0.000)	0.0469	−0.023 (0.011)	(−0.05, 0.00)	0.047	0.08
Age at MRI 1	−0.001 (0.001)	(−0.002, 0.000)	0.125				
Female	−0.014 (0.011)	(−0.037, 0.009)	0.23				
Height at MRI 1	0.076 (0.060)	(−0.046, 0.197)	0.217				
Weight at MRI 1	0.000 (0.000)	(−0.001, 0.001)	0.761				
Age at complete repair	−0.004 (0.003)	(−0.009, 0.002)	0.182				
BSA at MRI 1	0.012 (0.025)	(−0.038, 0.062)	0.624				
Staged repair	0.013 (0.011)	(−0.010, 0.036)	0.255				
Age at shunt placement	−0.006 (0.007)	(−0.022, 0.009)	0.405				
Diabetes	−0.030 (0.042)	(−0.114, 0.053)	0.472				
Hypertension	−0.009 (0.015)	(−0.039, 0.021)	0.556				
Smoker or former smoker	−0.027 (0.021)	(−0.069, 0.016)	0.215				
β blocker	−0.014 (0.012)	(−0.038, 0.009)	0.223				
ACE/ARB medicine	−0.002 (0.015)	(−0.032, 0.029)	0.920				
Right aortic arch	−0.005 (0.013)	(−0.030, 0.020)	0.697				
Aortic valve regurgitant fraction	−0.042 (0.137)	(−0.316, 0.233)	0.761				

sample size and retrospective study design, we cannot draw conclusions about the protective effect against aortic root dilation in those with TOF.

A history of pulmonary valve replacement was marginally associated with a higher rate of growth at the sinus of Valsalva as measured by CSA/ht for the entire cohort. The

Table 4
Variables associated with growth of the sinus of XXX valsalva diameter in the cohort ≥16 years old

Variable label	Bivariate model			Multivariable model			
	Estimate (std error)	95% CI	p Value	Estimate (std error)	95% CI	p Value	R-square
Age at MRI1	−0.002 (0.001)	(−0.004, −0.001)	0.0009	0.00 (0.00)	(0.00, −0.00)	0.0019	0.217
Staged repair	−0.028 (0.017)	(−0.062, 0.005)	0.0972	−0.02 (0.02)	(−0.05, 0.01)	0.2461	
Female	−0.018 (0.017)	(−0.052, 0.015)	0.2775				
Height(m) at MRI1	0.021 (0.088)	(−0.156, 0.198)	0.8143				
Weight at MRI1	0.000 (0.000)	(−0.001, 0.000)	0.3360				
Age at complete repair	−0.011 (0.004)	(−0.018, −0.004)	0.0038				
BSA at MRI1	−0.022 (0.038)	(−0.097, 0.054)	0.5683				
Age at shunt placement	0.002 (0.004)	(−0.007, 0.011)	0.6353				
Diabetes	0.032 (0.063)	(−0.094, 0.157)	0.6154				
Hypertension	−0.040 (0.022)	(−0.084, 0.004)	0.0716				
Smoker or former smoker	−0.002 (0.032)	(−0.067, 0.063)	0.9548				
β blocker	−0.035 (0.017)	(−0.069, −0.001)	0.0448				
ACE/ARB medicine	−0.055 (0.020)	(−0.096, −0.014)	0.0089				
Right aortic arch	0.016 (0.019)	(−0.022, 0.053)	0.4040				
Aortic valve regurgitant fraction	−0.034 (0.207)	(−0.449, 0.381)	0.8699				
History of pulmonary valve replacement	−0.001 (0.017)	(−0.035, 0.034)	0.9690				

Table 5
Variables associated with growth of the sinus of Valsalva as measured by CSA/Ht for the entire cohort

Variable label	Bivariate model			Multivariable model			
	Estimate (std error)	95% confidence interval	p Value	Estimate (std error)	95% confidence interval	p Value	R-square
History of pulmonary valve replacement	0.06 (0.03)	(0.00, 0.13)	0.0527	0.069 (0.031)	(0.01, 0.13)	0.0313	0.086
Age at MRI1	0.00 (0.00)	(0.00, 0.00)	0.2365				
Female	−0.04 (0.03)	(−0.10, 0.02)	0.2068				
Height(m) at MRI1	0.01 (0.08)	(−0.15, 0.18)	0.8796				
Weight at MRI1	0.00(0.00)	(0.00, 0.00)	0.4437				
Age at complete repair	−0.01 (0.01)	(−0.02, 0.01)	0.2209				
BSA at MRI1	−0.03 (0.04)	(−0.11, 0.05)	0.4876				
Staged repair	−0.01 (0.03)	(−0.07, 0.05)	0.7048				
Age at shunt placement	−0.01 (0.03)	(−0.06, 0.04)	0.7626				
Diabetes	0.00 (0.09)	(−0.18, 0.17)	0.9759				
Hypertension	−0.01 (0.05)	(−0.11, 0.09)	0.7888				
Smoker or former smoker	−0.04 (0.08)	(−0.20, 0.11)	0.5801				
β blocker	0.01 (0.04)	(−0.06, 0.08)	0.8295				
ACE/ARB medicine	−0.05 (0.05)	(−0.14, 0.04)	0.3082				
Right aortic arch	0.02 (0.04)	(−0.06, 0.09)	0.6325				
Aortic valve regurgitant fraction	0.01 (0.48)	(−0.95, 0.97)	0.9824				

surgical strategy at our institution favors aggressively preserving the native pulmonary valve. With greater degrees of conotruncal rotation, it is possible that the aorta becomes larger, whereas the right ventricular outflow tract becomes smaller. Therefore, it is possible that the patients with more severe pulmonary stenosis who were unable to have a valve-preserving initial surgical repair and ultimately required pulmonary valve replacement had relatively larger aortic roots that grew over time. However, this association with pulmonary valve replacement did not hold for the sinus of Valsalva for the cohort aged ≥16 years.

Limitations

This study is a retrospective report from a single institution; these findings may not be representative of all adult congenital heart disease programs and may be prone to selection bias in terms of which patients had clinical indications for obtaining MRIs.

The surgical practice at our institution is to stage repair of patients requiring intervention aged <120 days in effort to allow growth and preserve the pulmonary valve.[30] Because our dataset may include a higher proportion of staged repairs than other centers, our results may not be applicable across all centers. In addition, data regarding surgical repair were missing on 24% of patients in this cohort. This cohort does not include patients with pulmonary atresia or bicuspid aortic valve and, as such, does not assess rates of growth in this potentially higher risk cohort. Attempts were made to limit confirmation bias by blinding the MRI reader to patient information, including the study date.

Conclusions

The rate of growth of the ascending aorta and sinus of Valsalva in patients with a repaired TOF with pulmonary stenosis is low, 0.2 ± 0.5 mm/year at the ascending aorta and 0.2 ± 0.6 mm/year at the sinus of Valsalva. In addition, severe dilation of the aortic root is rare, with an observed-to-expected ratio of >1.5 being observed in only 1 patient at the sinus of Valsalva. Younger age was associated with higher rates of growth of the sinus of Valsalva, whereas the use of β blockers or ACE inhibitors was associated with a slower rate of growth. There were no cases of aortic dissection or need for surgical intervention on the aortic root in this cohort. The findings of this study utilizing MRI data in a population of repaired TOF, including adults and children, are reassuring that severe dilation of the aortic root is rare in a younger, modern cohort and adverse events were not noted. Further study will be needed to predict factors that may predict the exceedingly rare complication of aortic dissection in this population.

Disclosures

The authors have no conflicts of interest to declare.

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