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The Impact of a Bicuspid Aortic Valve on Aortic Geometry and Function in Patients with Aortic Coarctation: A Comprehensive CMR Study

Laura Schweikert¹, Dominik Gabbert¹, Sylvia Krupickova² and Inga Voges^{1,*}

¹Department of Congenital Heart Disease and Paediatric Cardiology, University Hospital Schleswig-Holstein, Kiel, Germany

²Royal Brompton Hospital, London, UK

*Corresponding Author: Inga Voges. Email: inga.voges@uksh.de

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ABSTRACT

Background: An isolated bicuspid aortic valve (BAV) is associated with structural and functional abnormalities of the aorta and the left ventricle (LV). Although ~50% of patients with aortic coarctation (CoA) have a BAV, less is known about its impact on LV function and aortic geometry and function in CoA patients. In this cardiovascular magnetic resonance imaging (CMR) study, we analysed markers of LV and aortic function as well as aortic geometry in a large cohort of CoA patients with a BAV and compared them with CoA patients with a tricuspid aortic valve (TAV). **Methods:** We included 48 patients with a BAV (18.4 ± 9.3 years) and 45 patients with TAV (20.7 ± 9.9 years). LV volumes, mass and ejection fraction as well as aortic distensibility, pulse wave velocity (PWV) were measured from standard cine CMR and phase-contrast CMR images. 2-dimensional CMR feature tracking (2D-CMR-FT) was performed to measure longitudinal, circumferential and radial strain and strain rate of the LV. Aortic arch geometry was classified as romanica, gothic and crenel. **Results:** LV volumes, mass and ejection fraction as well as aortic distensibility and PWV did not significantly differ between the BAV and the TAV group. There was also no significant difference for LV global longitudinal, radial and circumferential strain and strain rate between both groups. Patients with a BAV had more commonly a gothic aortic arch compared to TAV patients, but this difference was not statistically significant (22 vs. 14, $p = 0.2$). Ascending and descending aortic distensibility correlated with LV mass in the entire patient group ($p < 0.001$). Global longitudinal, circumferential and radial strain (GLS, GCS, GRS) and global longitudinal and circumferential strain rate (GLSR, GCSR) correlated with LV ejection fraction ($p < 0.001$). **Conclusion:** Our data suggest that the presence of a BAV does not adversely impact LV and aortic function in children and young adults with CoA. The correlation of global circumferential, longitudinal and radial strain values with LV ejection fraction demonstrates that 2D-CMR-FT might provide additional information related to ventricular function in CoA patients.

KEYWORDS

Aortic coarctation; bicuspid aortic valve; cardiovascular magnetic resonance; feature tracking

1 Introduction

Patients with aortic coarctation (CoA) are at risk for late complications associated with increased cardiovascular morbidity and mortality [1]. This not only includes a postoperative persisting arterial hypertension [2] and residual aortic obstruction but also left ventricular dysfunction [3–5].



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About 50% of CoA patients have a bicuspid aortic valve (BAV) which is associated with structural and functional abnormalities of the aorta including aortic root and ascending aortic dilatation, reduced aortic elasticity and abnormal aortic blood flow patterns [6–8]. In a recent study in patients with aortic valve stenosis, it was demonstrated that patients with BAV have increased left ventricular (LV) volumes and a larger LV outflow tract diameters to patients with a tricuspid aortic valve (TAV) [9].

However, less is known about patients with both, CoA and BAV. Frandsen et al. [10] reported that CoA patients with TAV often have smaller aortic root and ascending aortic diameters compared to CoA patients with BAV. But concrete information about the influence of a BAV on aortic elasticity as well as on LV size, function and mass in CoA patients is scarce.

Cardiovascular magnetic resonance (CMR) imaging is routinely used for the follow up in repaired CoA patients and allows detailed assessment of aortic and LV function and geometry. Regional LV myocardial function and deformation can be assessed with 2-dimensional CMR feature tracking (2D-CMR-FT) [11].

The aim of this CMR study, was to compare CoA patients with a BAV to those with a TAV regarding: (1) LV size and global function, (2) LV regional function and deformation using 2D-CMR-FT, (3) aortic distensibility and pulse wave velocity (PWV) and (4) aortic geometry.

2 Materials and Methods

We consecutively included all patients with repaired CoA who underwent CMR imaging between 2009 and 2019. Exclusion criteria were evidence of a mitral valve stenosis (mean gradient >8 mmHg), moderate or severe aortic stenosis and more than mild aortic or mitral valve regurgitation. Clinical, demographic and surgical data were obtained from the patients' medical records. The study was approved by the local ethics committee (Nr. D566/19, Date of Approval 09/12/2019). Informed consent from patients or parents was obtained as appropriate.

2.1 CMR Acquisition

CMR studies were performed using a 3.0-Tesla or 1.5 Tesla scanner (Philips Medical Systems, Netherlands) with a dedicated coil for cardiac imaging. Standard steady-state free precession (SSFP) sequences were used to acquire short axis cine stacks, axial cine stacks, 4-chamber-views and aortic arch views.

To measure aortic PWV we applied two-dimensional phase-contrast flow imaging with through-plane velocity encoding and retrospective ECG gating at three locations as previously described [12]: 1) ascending aorta (AAo), 2) proximal descending aorta (DAo) and 3) DAo.

2.2 CMR Analysis

All CMR analyses were performed using a dedicated CMR software (Medis Suite MR, Medis Medical Imaging Systems, Leiden, The Netherlands).

LV volumetry was performed using short axis cine stacks. First, end-diastolic and end-systolic time points were defined. Second, endo- and epicardial contours in all slices showing the left ventricle at end-diastole were drawn; at end-systole only endocardial contours were defined. LV volumes (LV end-diastolic volume, LVEDV; LV end-systolic volume, LVESV; LV stroke volume, LVSV) and LV mass were automatically calculated by the software.

2D-CMR-FT was performed to measure longitudinal, circumferential and radial strain and strain rate of the LV. Global longitudinal strain (GLS) and strain rate (GLSR) as well as regional longitudinal strain values were measured from the acquired 4-chamber views. Global circumferential and radial strain and strain rate values (GCS, GCSR, GRS, GRSR) as well as regional strain and strain rate values were obtained from short axis cine images. Regional strain and strain rate values are reported according to the American Heart association 17-segment-model [13].

PWV in the aortic arch and descending thoracic aorta was measured as described before by one of the authors [12,14].

Aortic distensibility was measured from CMR cine images in the ascending aorta, aortic isthmus and descending thoracic aorta by using the following formula [14,15]:

$$\text{Distensibility}(10^{-3} \text{ mmHg}^{-1}): (A_{\max} - A_{\min})/[A_{\max} \times (P_{\max} - P_{\min})]$$

with A_{\max} and A_{\min} representing the maximal and minimal cross-sectional area and P_{\max} and P_{\min} being the systolic and diastolic blood pressure.

Aortic arch shape was assessed by visual inspection of aortic arch views and classified as: (1) gothic, (2) romanesque and (3) crenel [16].

2.3 Statistics

Statistical analysis was performed using MedCalc Version 19.6 (MedCalc statistical software, Mariakerke, Belgium). Data was adequately evaluated according to their distribution by T-test or Mann-Whitney-U-Test. To measure the associations between variables Spearman rank correlation was used. Chi-squared test for the comparison of proportions was performed to test for the difference in distribution of categorical variables. A p value of 0.05 was considered to be statistically significant.

3 Results

Patient characteristics are shown in [Tab. 1](#). In total, 93 patients were included in this study of which, 48 (52%) had a BAV and 45 (48%) had a TAV.

Table 1: Patient characteristics

Parameters	All (n = 93)	CoA-BAV (n = 48)	CoA-TAV (n = 45)	p -value*
Age (y)	19.5 ± 9.6	18.4 ± 9.3	20.7 ± 9.9	0.21
Weight (kg)	60.8 ± 24.9	56.1 ± 22.5	65.9 ± 26.6	0.06
Height (cm)	171 (60–196)	170 (60–196)	173 (86–190)	0.32
BMI (kg/m ²)	21.0 (13.6–36.7)	20.4 (13.6–36.7)	23.1 (13.8–36.6)	0.06
BSA (m ²)	1.7 (0.3–2.4)	1.7 (0.3–2.3)	1.8 (0.6–2.4)	0.09
Heart rate (1/min)	73.5 (41–149)	72 (41–149)	75 (52–120)	0.39
MAP (mmHg)	85.0 (60.3–108.3)	83.7 (60.3–108.3)	85.5 (65.7–128.3)	0.82
Medication (n)				
–ACE inhibitor	9	5	4	
–ARB (n)	4	0	4	
–Betablocker	10	3	7	
–Hydrochlorothiazide	2	1	1	
–Amlodipin	2	1	1	
–Allopurinol	1	0	1	
–L-Thyroxin	1	1	0	
–ASA	1	0	1	
–Oral contraceptives	3	4	0	
–Methyphenidate	1	1	1	

Note: Values are mean ± standard deviation or median with range.

ACE, Angiotensin converting enzyme inhibitor; ARB, Angiotensin receptor blocker; ASA, Acetylsalicylic acid; BMI, Body mass index; BP, blood pressure; BSA, Body surface area; MAP, mean arterial pressure.

*Comparison between CoA patients with BAV to those with TAV.

22 patients were treated for arterial hypertension. None of the patients had more than mild aortic stenosis or regurgitation (as assessed by CMR).

3.1 Ventricular, Volumes Mass and Ejection Fraction

There was no difference in LV volumes, mass and ejection fraction between the two groups (all $p > 0.05$, [Tab. 2](#)). A higher LV mass was associated with a lower aortic distensibility at all three levels (ascending aorta: $r = -0.38$, $p < 0.01$; aortic isthmus: $r = -0.25$, $p < 0.05$; descending aorta: -0.44 , $p < 0.01$; [Figs. 1A](#) and [1B](#)). No association between blood pressure and LV mass was found.

Table 2: Markers of LV and aortic function

Parameters	All (n = 92)	CoA-BAV (n = 47)	CoA-TAV (n = 45)	p-value*
LVEDV (ml)	150.8 ± 54.8	146.9 ± 55.2	148.1 ± 54.6	0.50
LVEDVi (ml/m ²)	89.2 (50.5–152.2)	88.7 (50.5–148.1)	85.4 (58.9–152.2)	0.41
LVESV (ml)	55.9 ± 24.7	55.4 ± 23.9	56.4 ± 25.7	0.85
LVESVi (ml/m ²)	31.1 (14.0–70.8)	33.4 (16.8–55.8)	29.4 (14.0–70.8)	0.19
LVSV (ml)	95.2 ± 33.2	92.0 ± 33.5	98.5 ± 32.9	0.37
LVSVi (ml/m ²)	55.9 (33.7–92.3)	57.9 (33.7–92.3)	55.6 (33.7–81.3)	0.62
LVMM (g)	97.6 ± 41.3	92.6 ± 37.0	102.8 ± 45.2	0.25
LVMMi (g/m ²)	56.5 (31.8–126.1)	57.8 (33.8–88.1)	54.8 (31.8–126.1)	0.75
LVEF (%)	63.8 ± 6.4	62.3 ± 5.7	64.6 ± 7.1	0.28
Distensibility (10 ⁻³ mmHg ⁻¹)				
–AAo	11.4 ± 7.8	11.5 ± 8.7	11.4 ± 6.8	0.94
–Isthmus	9.6 ± 8.0	9.8 ± 8.4	9.4 ± 7.6	0.83
–DAo	11.4 ± 10.1	11.4 ± 11.7	11.1 ± 8.0	0.79
PWV aortic arch (m/s)	3.7 (1.2–8.5)	3.2 (2.0–8.5)	3.7 (1.2–8.3)	0.72
PWV DAo (m/s)	5.0 (1.9–15.7)	5.0 (1.9–15.7)	5.0 (2.0–14.2)	0.90
Max. aortic area (mm ²)				
–AAo	647.4 ± 253.4	680.0 ± 283.7	614.0 ± 216.4	0.23
–Isthmus	294.9 ± 184.8	287.3 ± 211.9	303.5 ± 150.8	0.26
–DAo	264.7 ± 112.7	252.2 ± 111.3	277.5 ± 114.3	0.34
Aortic arch geometry				
–Romanic	44	19	25	
–Gothic	36	22	14	
–Crenel	36	6	6	

Note: Values are mean ± standard deviation or median with range.

DAo, descending aorta; LVEDV, left ventricular end-diastolic volume; LVEDVi, indexed left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume; LVESVi, indexed left ventricular end-systolic volume; LVSV, left ventricular stroke volume; LVSVi, indexed left ventricular stroke volume; LVMM, left ventricular myocardial mass; LVMMi, indexed left ventricular myocardial mass; LVEF, left ventricular ejection fraction; PWV, pulse wave velocity.

*Comparison between CoA patients with BAV and CoA patients with TAV.

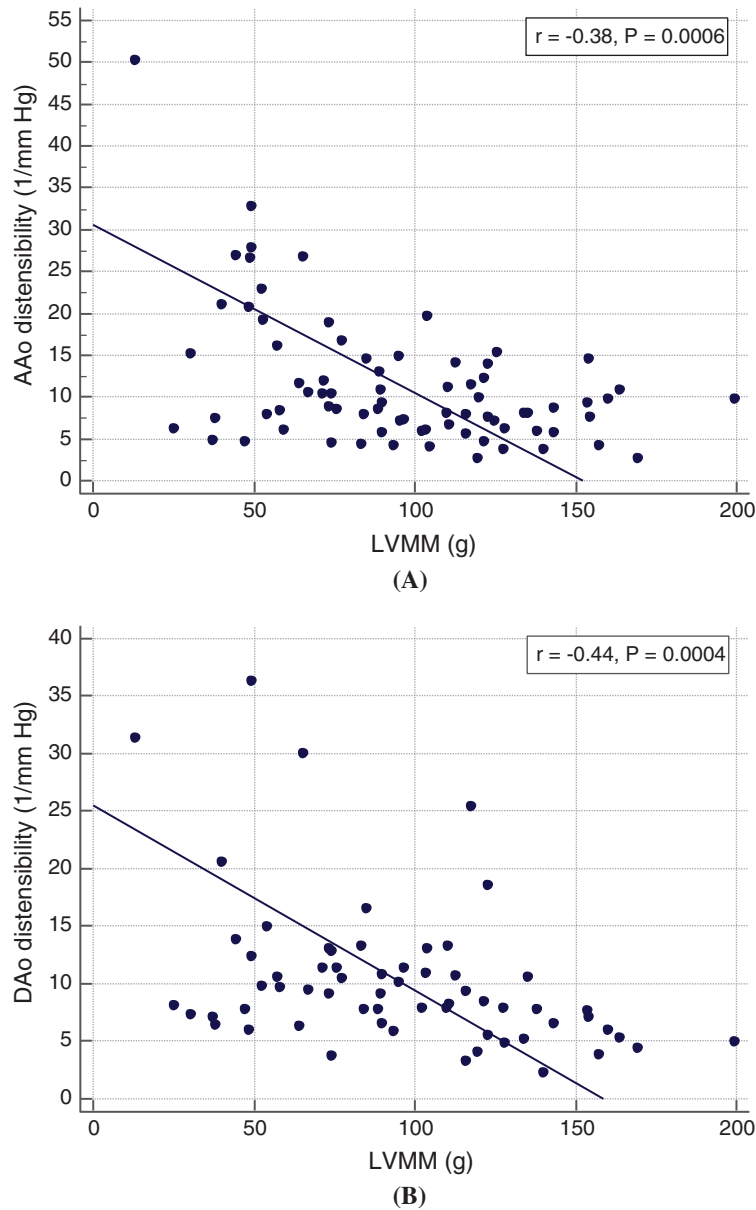


Figure 1: Relationship between LV mass (LVMM) and ascending (A) and descending (B) aortic distensibility

3.2 2D-CMR-FT Results

Global strain and strain rate values were not different between BAV and TAV patients (Tab. 3). Global longitudinal, circumferential and radial strain (GLS, GCS, GRS) and global longitudinal and circumferential and radial strain rate (GLSR, GCSR) correlated with LV ejection fraction ($r = 0.30$ – 0.39 ; all $p < 0.01$; Figs. 2A–2C).

3.3 Aortic Elasticity and Geometry

The aortic elasticity parameters PWV and distensibility did not differ between BAV and TAV patients (Tab. 2). PWV was significantly higher in the descending aorta compared to aortic arch PWV

($p < 0.001$). Aortic isthmus distensibility was significantly lower compared to distensibility in the ascending aorta ($p = 0.025$). There was a trend towards a lower isthmus distensibility compared to the descending aortic distensibility ($p = 0.05$).

Table 3: CMR feature tracking analysis

Parameters	All (n = 92)	CoA-BAV (n = 47)	CoA-TAV (n = 45)	p-value*
GLS (%)	-25.2 (-14.6 to -44.2)	-24.8 (-17.4 to -41.6)	-25.5 (-14.6 to -44.2)	0.60
GLSR (1/s)	-1.4 (-0.6 to -4.6)	-1.3 (-0.6 to -2.5)	-1.5 (-0.8 to -4.6)	0.17
GCS (%)	-36.6 ± 6.6	-35.9 ± 6.8	-37.6 ± 6.4	0.23
GCSR (1/s)	-2.1 (-0.8 to -4.4)	-1.9 (-0.8 to -4.2)	-2.1 (-1.2 to -4.4)	0.13
GRS (%)	74.9 (13.9–184.1)	74.4 (13.9–124.7)	76.4 (50.6–184.1)	0.68
GRSR (1/s)	2.1 (1.2–3.6)	2.1 (1.2–3.6)	2.1 (1.4–3.6)	0.96

Note: Values are mean ± standard deviation or median with range.

GLS, global longitudinal strain; GLSR, global longitudinal strain rate; GCS, global circumferential strain; GCSR, global circumferential strain rate; GRS, global radial strain; GRSR, global radial strain rate.

*Comparison between CoA patients with BAV to those with TAV.

The distribution of aortic geometry as well as aortic cross-sectional areas from distensibility measurements are shown in [Tab. 2](#). Patients with a BAV had more commonly a gothic aortic arch compared to non-BAV patients, but this difference was not statistically significant (22 vs. 14, $p = 0.2$). Cross-sectional areas of the AAo were higher and cross-sectional areas of the descending aorta (isthmus and DAo) were lower in BAV patients compared to TAV patients. However, these findings were not statistically significant. In addition, in patients with a BAV cross-sectional areas of the BAV patients were more often above the 95th centile compared to TAV patients (16 BAV vs. 6 TAV patients) [17].

4 Discussion

We assessed the influence of a bicuspid aortic valve on LV and aortic functional parameters in a relatively large cohort of CoA patients and could demonstrate:

1) LV size, mass, ejection fraction, global strain values and aortic elasticity parameters are not different between CoA patients with a BAV and a TAV.

2) Global longitudinal, circumferential and radial strain values correlate with LV ejection fraction.

To our knowledge, this is the first study comparing LV size as well as LV and aortic functional parameters between CoA patients with TAV and BAV. Previous studies in CoA patients found larger aortic diameters in BAV compared to TAV patients and this was independent from arterial hypertension. The authors concluded that their findings suggest that aortopathy in BAV patients is a reflection of the BAV but not the CoA phenotype [9]. Our results, did not demonstrate any differences in aortic elasticity between BAV and TAV patients supporting the assumption that the CoA phenotype but not the valve phenotype is mainly responsible for an increased aortic stiffness [4,18]. In particular, intrinsic structural abnormalities of the aortic wall in CoA patients might be important in this context [19].

Frandsen et al. [10] reported differences in LV size and morphology between with BAV and TAV stenosis. We evaluated LV volumes and mass and did not find any differences between the two study groups which again suggests that the valve phenotype in CoA patients does not seem to have a major influence on cardiovascular changes. However, we could demonstrate that a higher aortic distensibility is associated with a higher LV mass in the entire patient group emphasizing that arterial changes have an impact on LV morphology [20]. The differences to the study by Frandsen et al. [10] might be explained

by the fact that their patient group was significantly older than our patient cohort. Furthermore, in our patient group there were no relevant aortic valve lesions with the need for intervention.

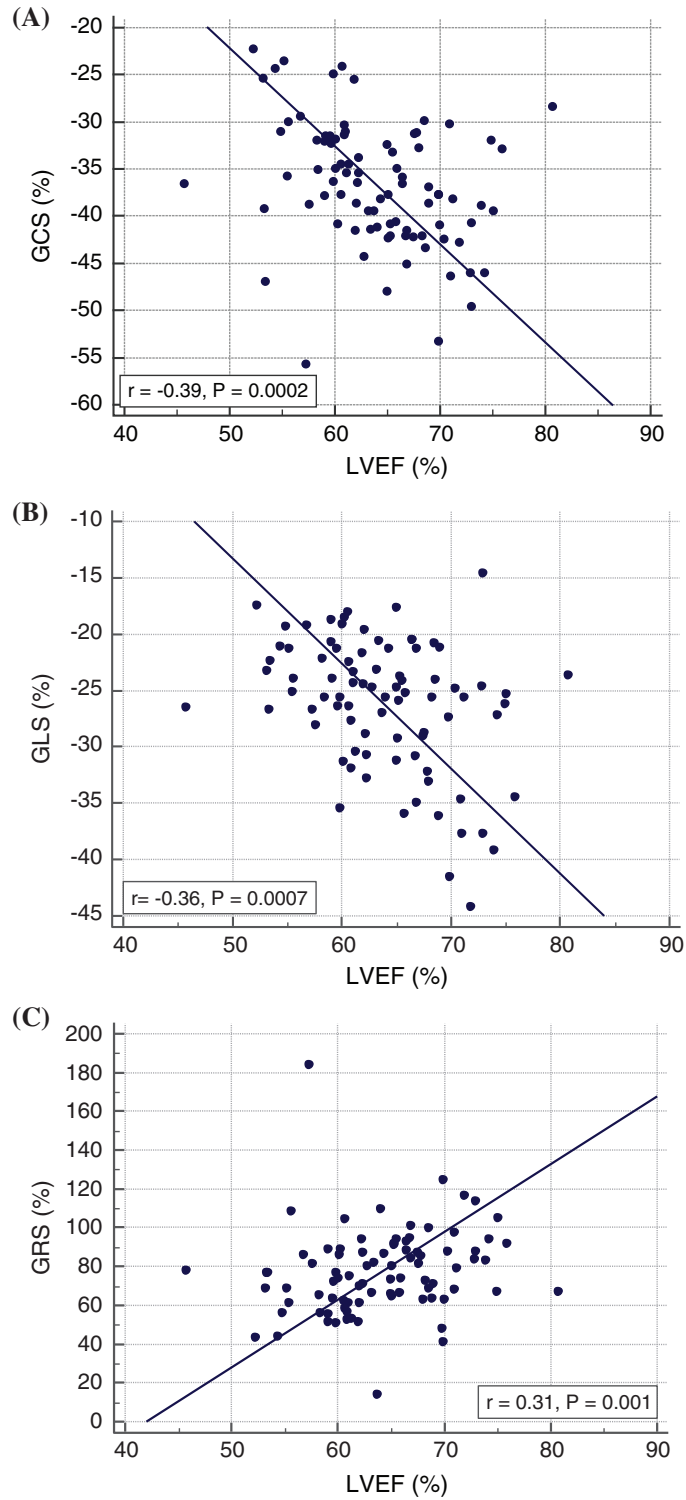


Figure 2: Relationship between LVEF and global strain values

In this study we also compared ventricular function and deformation markers and did not demonstrate differences between TAV and BAV CoA patients. Our results are similar to a CMR study by Stefek et al. [21] who did not find any differences in LV volumetric indices and LV strain between pediatric BAV patients with normal valve function and pediatric TAV patients. No similar studies in CoA patients have been performed according to our knowledge. Studies in CoA patients analysing LV function and myocardial deformation compared patients with healthy controls and used CMR-FT and speckle tracking echocardiography. Kutty et al. found reduced global longitudinal and radial strain values with a normal LVEF in CoA patients compared to healthy subjects [22]. Others could demonstrate that adult CoA patients have an impaired LV GLS compared to controls whereas LV ejection fraction did not differ between patients and controls [23].

We demonstrated that LVEF correlates with GCS, GLS and GRS as well as with GLSR, GCSR and we therefore believe that 2D-CMR-FT can be helpful in assessing LV function in CoA patients. Similar relationships between EF and strain values have been shown by other groups [24,25]. However, correlations between myocardial deformation parameters and EF are controversially discussed and recently a mathematical model has been presented to describe the relationship between LVEF, GCS and GLS [26].

4.1 Limitations

This study has a few limitations. Due to the retrospective nature of the study not all measures were available in some patients and this potentially could have had an impact on our study results. The retrospective study design also did not allow us to describe the detailed BAV phenotype.

We did not include a control group due to ethical reasons as this would have meant to prospectively recruit healthy subjects including children. In addition, GLS was only measured from the 4-chamber view and this might have impacted our global strain results. Finally, we did not assess in detail the influence on blood pressure on aortic and ventricular measurements.

5 Conclusions

Our results suggest that the valve phenotype in CoA patients does not have an impact on LV and aortic function as well as on LV morphology in a relatively young cohort of children and younger adults. However, thorough long-term follow up is needed as BAV patients likely have a higher risk for the development of relevant valve lesions predisposing them to morphological and functional LV changes. Global circumferential, longitudinal and radial strain values correlate with LV ejection fraction demonstrating that 2D-CMR-FT might be useful in assessing ventricular function and deformation in CoA patients.

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Conflicts of Interest: The authors declare that they have no conflicts of interest to report regarding the present study.

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