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Predictors of left ventricular reverse remodelling after coarctation of aorta intervention

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Aims Several coarctation of aorta (COA) severity indices are used for timing of COA intervention, and to define severity of residual coarctation post-intervention. However, it is unclear how many of these COA indices are required in order to recommend intervention, and what degree of residual coarctation results in suboptimal recovery of the left ventricle (LV). Our aim was to assess the correlation between different COA indices and effects of chronic LV pressure overload (LV hypertrophy, diastolic, and systolic dysfunction), and to determine the effect of residual coarctation on LV reverse remodelling after COA intervention.

Methods and results COA severity indices were defined as Doppler COA gradient, systolic blood pressure (SBP, upper-to-lower-extremity SBP gradient, aortic isthmus ratio. LV remodelling indices were defined as LV mass index (LVMI), LV global longitudinal strain (LVGLS), e' and E/e'. LV reverse remodelling was defined as the difference between indices obtained pre-intervention and 5-year post-intervention (delta LVMI, e', E/e', LVGLS).

Of the COA indices analysed in 546 adult COA patients, aortic isthmus ratio had the strongest correlation with LVMI (β ± standard error -28.3 ± 14.1, $P < 0.001$), LVGLS (1.51 ± 0.42, $P = 0.005$), e' (3.11 ± 1.10, $P = 0.014$), and E/e' (-13.4 ± 6.67, $P = 0.008$). Residual aortic isthmus ratio also had the strongest correlation with LV reverse remodelling, and residual aortic isthmus ratio <0.7 was predictive of suboptimal LV reverse remodelling post-intervention.

Conclusion Considering the known prognostic implications of LV remodelling and reverse remodelling in response to pressure overload, these results support the use of aortic isthmus ratio for timing of COA intervention, and for prognostication post-intervention.

Keywords coarctation of aorta • left ventricular mass index • systolic blood pressure • left ventricular pressure overload

Introduction

Coarctation of aorta (COA) is the primary diagnosis in >10% of adults with congenital heart disease.[1] It results in left ventricular (LV) pressure overload because of mechanical obstruction at the aortic isthmus, vascular and endothelial dysfunction, and LV outflow tract obstruction in the setting of associated left-sided lesions.[2–5] Chronic LV pressure overload subsequently leads to LV hypertrophy, a mismatch between myocardial oxygen demand and supply, and apoptosis with replacement fibrosis.[6] These pathologic changes result in alteration in the viscoelastic properties, effective operative compliance, and contractile function of the LV manifested clinically as diastolic dysfunction and/or systolic dysfunction.[6] LV hypertrophy, diastolic dysfunction, and systolic dysfunction are well-established predictors of cardiovascular mortality.[7]

Because of the known adverse effects of chronic LV pressure overload, the American College of Cardiology and the European Society of Cardiology have outlined practice guidelines with indications for intervention in adults with COA.[8,9] These indications are based on the following COA severity indices: Doppler mean COA gradient, systolic blood pressure (SBP), upper-to-lower extremity systolic blood pressure (ULE-SBP) gradient, exercise induced hypertension, and aortic isthmus ratio.[8,9] However, there are limited data about how well these COA severity indices correlate with LV pressure

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overload. Such data would guide clinicians in deciding on which COA severity metric to prioritize when deciding on the timing of intervention.

The goal of COA intervention is to relieve aortic isthmus stenosis, and ideally, the patient should have no residual coarctation (residual aortic isthmus stenosis). Unfortunately, some patients do have some degree of residual coarctation after COA intervention.[10,11] Currently, there is no consensus about the severity of residual coarctation that is *acceptable* to describe successful repair. Such data would guide prognostication after COA intervention.

The purpose of this study was to assess the correlation between the different COA severity indices and the downstream effects of chronic LV pressure overload (LV hypertrophy, diastolic dysfunction, and systolic dysfunction) and to determine the effect of residual coarctation on LV reverse remodelling after COA intervention.

Methods

Study population

Adult patients (age ≥ 18 years) with a diagnosis of COA who had echocardiographic and cardiac cross-sectional imaging assessment were identified from the Mayo Adult Congenital Heart Disease (MACHD) Registry. The MACHD Registry contains data of all adults with congenital heart disease that received care at the Mayo Clinic Enterprise, from 1 January 1985 to 31 December 2018. A prior study has been[12] published using the same cohort. The Mayo Clinic Institutional Review Board approved this study and waived informed consent for patients that provided research authorization. From this cohort, we excluded the following patients: (i) Patients with significant aortic valve disease defined as the presence of a prosthetic aortic valve, native aortic valve peak velocity >2 m/s or >mild aortic regurgitation. (ii) Patients with significant mitral valve disease defined as the presence of a prosthetic mitral valve, native mitral valve mean gradient >3 mmHg or >mild mitral regurgitation. (iii) Patients with aberrant origin of right subclavian artery.

Study objectives

The primary objective was to assess the correlation between COA severity indices and LV remodelling indices. We assessed LV remodelling using LV mass index (LVMI) as a measure of LV hypertrophy; LV global longitudinal strain (LVGLS) as a measure of LV systolic function; and tissue Doppler early velocity (e') and ratio of mitral inflow early velocity and tissue Doppler early velocity (E/e') as measures of LV diastolic function.[13] These indices were based on the echocardiogram performed at baseline (first clinical evaluation within the study period).

The secondary objective was to assess the effect of residual coarctation on LV reverse remodelling among patients that underwent COA intervention. LV reverse remodelling indices were calculated as the difference between the values obtained at baseline (pre-intervention) and 5-year post-intervention (delta LVMI, e', E/e', LVGLS). Exploratory analysis was performed to determine the cut-off point (threshold) for residual coarctation that predicted suboptimal LV reverse remodelling at 5-year post-intervention. Suboptimal LV reverse remodelling was defined as the absence of reverse LV remodelling at 5-year post-intervention (no change in LV remodelling indices from baseline to 5-year post-intervention).

Predictor variables

For the primary objective, we used the COA severity indices stipulated in the American and European guidelines for the management of adults with congenital heart disease as the predictor variables.[8,9] The severity indices were Doppler mean (peak) gradient, SBP, ULE-SBP gradient, and aortic isthmus ratio. The predictor variables were obtained from the echocardiogram and cross-sectional imaging performed at baseline (first clinical evaluation within the study period).

The secondary objective was based on a subgroup analysis of patients that underwent COA intervention, and had at least 5 years of follow-up post-intervention. The patients who required re-intervention within 5 years were excluded from this analysis. For the patients that met the inclusion criteria for the subgroup analysis, we assessed residual coarctation using indices [Doppler mean (peak) gradient, ULE-SBP gradient, and aortic isthmus ratio] obtained within 12-month post-intervention. Because of the potential confounding effect of post-operative pain and anaemia on SBP and Doppler assessment, we analysed only echocardiograms performed between 3 and 12 months post-intervention during ambulatory clinical evaluation.

The SBP was measured in the right arm, and ULE-SBP gradient was calculated as: SBP from the right arm minus SBP from the leg. Continuous wave Doppler was obtained across the aortic isthmus (site of COA), and only Doppler signals with optimal alignment defined as angle of insonation <20° were analysed for this study. Doppler peak velocity and time velocity integral were used to calculate *uncorrected* peak gradient (maximum instantaneous gradient) and mean gradients, respectively.[13] Chest computed tomographic angiogram and magnetic resonance angiogram were reviewed, and thoracic aortic dimensions were measured as previously described.[10,14] Aortic isthmus ratio was determined as a ratio of the aortic isthmus (the smallest COA diameter) divided by the diameter of the descending aorta at the level of the diaphragm.[10,14] Collateral vessels were considered to be present or absent based on review of the imaging report.

Outcome variables

For diastolic function assessment, we used the average of the septal and lateral e' when both variables were available, and we used either septal or lateral e' in patients that had only one variable recorded.[15,16] LVMI was calculated using end-diastolic linear measurements of the interventricular septum, LV inferolateral wall thickness, and LV internal diameter derived from 2D echocardiography measured at the tissue–blood interphase.[17] LV speckle tracking strain imaging was obtained using Vivid E9 and E95 (General Electric Co, Fairfield, CT, USA) with M5S and M5Sc-D transducers (1.5–4.6 MHz) at frame rate of 40–80 Hz.[18] Image analysis and offline measurements were performed in all patients by two experienced sonographers (J.W. and K.T.).

Statistical analysis

Multivariate linear regression analysis was used to assess the correlation between COA severity indices and LV remodelling indices using stepwise backwards selection, and a threshold of $P < 0.1$ was required to remain in the model. Doppler mean and peak gradient were not used in the same model because of collinearity. First, we constructed the multivariate regression models using Doppler mean gradient, and then we substituted Doppler mean gradient with Doppler peak gradient. All regression models were adjusted for age, sex, LV ejection fraction, history of hypertension, use of antihypertensive medication (modelled as yes vs. no), and age at the time of initial COA repair because these variables were known to be associated with LV remodelling. In the patients without prior COA repair, the current age was substituted for the age of COA repair.

Similarly, linear regression analysis was used to assess the correlation between residual coarctation indices and LV reverse remodelling indices. These models were adjusted for age, sex, LV ejection fraction, history of hypertension, use of antihypertensive medication, haemoglobin, and type

of COA intervention. Receiver operating characteristic curves were used to determine the threshold of residual coarctation that predicted suboptimal LV reverse remodelling. Multivariate logistic regression analysis was used to assess the correlation between residual coarctation and suboptimal LV reverse remodelling using the cut-off points generated from the receiver operating characteristic curves. Similarly, these models were adjusted for age, sex, LV ejection fraction, history of hypertension, use of antihypertensive medication, haemoglobin, and type of COA intervention. Reproducibility of the indices of COA severity was assessed using interclass correlation (ICC) and 95% confidence interval (CI). All statistical analyses were performed with JMP software (version 14.1.0; SAS Institute Inc., Cary, NC, USA).

Results

Of 546 patients that met the inclusion criteria, 144 (26%) and 402 (74%) had native and recurrent COA, respectively. *Table 1* shows the baseline characteristics of the cohort. Of the 402 patients that had prior COA repair, the initial COA intervention was surgical ($n = 365$), stent therapy ($n = 33$), and balloon dilation only ($n = 4$). The median age at time of initial COA repair was 7 (0.9–17) years, and 288 of the 402 patients (72%) had COA repair prior to age 18 years. *Table 2* shows the COA severity indices and LV remodelling indices at baseline.

COA severity indices and LV remodelling

Of all the COA severity indices analysed, there was a correlation between aortic isthmus ratio and all four domains of LV remodelling indices (*Table 3*). SBP correlated with LVMI and LVGLS but not with e′ or *E*/e′. Doppler peak gradient correlated with LVMI and LV e′ but not with LVGLS or *E*/e′ (*Table 3*). In a model substituting Doppler mean gradient for Doppler peak gradient, the Doppler mean gradient had a correlation with LV e′ but not with any of other LV remodelling metric.

Residual coarctation and LV reverse remodelling post-intervention

Of the 546 patients, 172 (32%) patients underwent COA intervention (stent $n = 44$, surgery $n = 128$) within the study period. Of these 172 patients, 165 (96%) patients had echocardiogram and cross-sectional imaging within 12 months from the time of COA intervention, 165 patients, 100 (61%) patients had follow-up beyond 5 years without any COA re-interventions during follow-up (Supplementary data online,*Figure S1*). There were no significant differences between the patients with vs. without 5-year follow-up (Supplementary data online, *Table S1*).

Among the 100 patients with 5-year follow-up (stent $n = 21$, surgery $n = 79$), the residual Doppler peak gradient was 16 ± 8 mmHg, Doppler mean gradient was 8 ± 4 mmHg, and aortic isthmus ratio was 0.83 ± 0.11. ULE-SBP gradient data were only available in 68 patients, and the residual ULE-SBP gradient was 2 (0–9) mmHg. The LV reverse remodelling indices at 1, 3, and 5 years are shown in Supplementary data online, *Table S2*. At 5-year post-intervention, there was a significant change in LVMI [delta LVMI -7.2 (-8.2 to -6.3) g/m^2], LVGLS [delta LVGLS 2.6 (2.3–2.9) %], and e′ [delta e′ 1.7 (1.4–2.0) cm/s], but not in *E*/e′ [delta *E*/e′ -0.1 (-0.3 to 0.1)]. There was a correlation between residual aortic isthmus ratio and delta LVMI ($r = 0.46$, $P = 0.002$), and delta e′ ($r = 0.41$, $P = 0.031$) but not *E*/e′ or LVGLS. Similarly, there was a correlation between residual Doppler peak gradient and delta LVMI ($r = -0.39$, $P = 0.009$), and delta e′ ($r = -0.33$, $P = 0.026$), but not *E*/e′ or LVGLS. In a model substituting residual Doppler mean gradient for residual Doppler peak gradient, the residual Doppler mean gradient had a correlation with only delta e′ ($r = -0.30$, $P = 0.047$). There was no correlation between residual ULE-SBP gradient and any LV reverse remodelling metric. These suggest that residual aortic isthmus ratio and Doppler peak gradient were associated, to some extent, with post-intervention LV reverse remodelling.

Exploratory analysis showed that residual aortic isthmus ratio <0.7 was the optimal cut-off point to predict suboptimal LV reverse remodelling post-intervention for LVMI [area under the curve (AUC) 0.776] and for e′ (AUC 0.682). Similarly, residual Doppler peak gradient >29 mmHg was the optimal cut-off point to predict suboptimal LV reverse remodelling post-intervention for LVMI (AUC 0.659) and

Table 1 Baseline characteristics ($N = 546$)

Age (years)	**33 ± 9**
Male	334 (61%)
Body mass index (kg/m^2)	26 ± 4
Body surface area (m^2)	1.9 ± 0.3
Hypertension diagnosis	326 (60%)
Bicuspid aortic valve	309 (57%)
NYHA II–IV	214 (39%)
Medications	
Beta blockers	142 (26%)
Calcium channel blockers	59 (11%)
ACEI/ARB	129 (24%)
Thiazide	47 (9%)
Hydralazine	3 (0.5%)
Any BP medication	341 (62%)
Echocardiography	
LV end-diastolic dimension (mm)	49 ± 6
LV end-systolic dimension (mm)	30 ± 5
LV ejection fraction (%)	62 ± 7
LV septal wall thickness (mm)	9 ± 2
LV posterior wall thickness (mm)	10 ± 2
Aortic valve peak velocity (m/s)	1.4 ± 0.3
COA peak velocity[a] (m/s)	2.7 ± 0.5
Cross-sectional imaging data	
Mid ascending aorta (mm)	30 ± 7
Distal ascending aorta (mm)	25 ± 6
Proximal aortic arch (mm)	19 ± 7
Distal aortic arch (mm)	19 ± 8
Aortic isthmus (mm)	14 ± 5
Proximal descending aorta (mm)	22 ± 7
Descending aorta at diaphragm (mm)	20 ± 5

Data were presented as mean ± standard deviation or number (%).
ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin-II receptor blocker; COA, coarctation of aorta; LV, left ventricle; LVMI, left ventricular mass index; SBP, systolic blood pressure; ULE, upper-to-lower extremity.
[a]COA peak gradient represents *uncorrected* maximum instantaneous gradient.

Table 2 COA severity and LV remodelling indices at baseline (*N* = 546)

COA severity indices	
SBP (mmHg)	132 ± 19
ULE-SBP gradient (mmHg)	14 (0-29)
COA mean gradient (mmHg)	16 ± 9
COA peak gradient (mmHg)	29 ± 11
Aortic isthmus ratio	0.73 ± 0.22
Collateral vessels	48 (9%)
LV remodelling indices	
LVMI (g/m^2)	99 ± 21
LVGLS (%)	18 ± 4
LV e′ (cm/s)	10 ± 4
LV *E*/e′	11 ± 3

Data were presented as mean ± standard deviation, median (interquartile range), or count (%).
COA, coarctation of aorta; *E*, mitral inflow Doppler early velocity; e′, mitral annular Doppler tissue early velocity; LV, left ventricle; LVGLS, left ventricular global longitudinal strain; LVMI, left ventricular mass index; SBP, systolic blood pressure; ULE, upper-to-lower extremity.

for e′ (AUC 0.617). After multivariate adjustments, residual aortic isthmus ratio < 0.7 was predictive of suboptimal LV reverse remodelling for LVMI [odds ratio (OR) 3.54, 95% CI 1.22–5.18, *P* = 0.018] and for e′ (OR 2.16, 95% CI 1.09–4.11, *P* = 0.032). Doppler peak gradient >29 mmHg was predictive of suboptimal LV reverse remodelling for LVMI (OR 2.62, 95% CI 1.03–4.96, *P* = 0.039) but not for e′. There was excellent inter-observer (ICC 0.93, 0.91–0.95) and intra-observer correlation (ICC 0.95, 0.93–0.97) for aortic isthmus ratio. There was good inter-observer (ICC 0.89, 0.87–0.91.) and intra-observer correlation (ICC 0.92, 0.90–0.94) for Doppler peak gradient.

Discussion

The American College of Cardiology and the European Society of Cardiology have proposed a number of COA severity indices that should prompt a referral for intervention.[8,9] These indices can broadly be classified as metrics of physiologic severity (Doppler mean gradient, SBP, and ULE-SBP) or anatomic severity (aortic isthmus ratio). However, there are no data about the relative contributions of these COA indices to LV pressure overload and LV remodelling. Furthermore, some patients have residual coarctation (residual aortic isthmus stenosis) after COA intervention, and there are limited data

Table 3 Multivariate predictors of LV remodelling

	Full model		Final model	
Predictors of LVMI	**β coefficient ± SE**	***P***	**β coefficient ± SE**	***P***
Doppler peak gradient, per 5 mmHg	0.42 ± 0.49	0.2	—	
SBP, per 5 mmHg	0.63 ± 0.42	0.045	0.61 ± 0.37	0.034
ULE-SBP gradient, per 5 mmHg	0.18 ± 0.19	0.2		
Aortic isthmus ratio	-23.6 ± 14.2	<0.001	-28.3 ± 14.1	<0.001
Presence of collateral vessels	2.54 ± 4.59	0.6		
Predictors of LV e′				
Doppler peak gradient, per 5 mmHg	-0.18 ± 0.06	0.022	-0.19 ± 0.02	0.016
SBP, per 5 mmHg	-0.33 ± 0.39	0.4		
ULE-SBP gradient, per 5 mmHg	0.13 ± 0.24	0.3		
Aortic isthmus ratio	3.26 ± 1.36	0.007	3.11 ± 1.10	0.014
Presence of collateral vessels	-2.41 ± 3.17	0.2		
Predictors of LV *E*/e′				
Doppler peak gradient, per 5 mmHg	0.14 ± 0.26	0.4		
SBP, per 5 mmHg	0.30 ± 0.31	0.1		
ULE-SBP gradient, per 5 mmHg	0.27 ± 0.32	0.3		
Aortic isthmus ratio	-12.9 ± 6.44	0.009	-13.4 ± 6.67	0.008
Presence of collateral vessels	2.91 ± 4.22	0.3		
Predictors of LVGLS				
Doppler peak gradient, per 5 mmHg	-0.49 ± 0.51	0.2		
SBP, per 5 mmHg	-0.52 ± 0.21	0.002	0.53 ± 0.11	0.001
ULE-SBP gradient, per 5 mmHg	-0.35 ± 0.42	0.4		
Aortic isthmus ratio	1.43 ± 0.25	0.028	1.51 ± 0.42	0.005
Presence of collateral vessels	-1.16 ± 1.72	0.6		

Regression models were adjusted for age, sex, LV ejection fraction, history of hypertension, and age at the time of initial COA repair.
E, mitral inflow Doppler early velocity; e′, mitral annular Doppler tissue early velocity; LV, left ventricle; LVGLS, left ventricular global longitudinal strain; LVMI, left ventricular mass index; SBP, systolic blood pressure; SE, standard error; ULE, upper-to-lower extremity.

about the degree of residual coarctation that results in suboptimal LV reverse remodelling. The current study addressed some of these knowledge gaps.

COA results in LV pressure overload, and LV hypertrophy occurs as an adaptive response to LV pressure overload, in order to maintain (normalize) wall stress.[7,19] However, this *adaptive* response becomes *mal-adaptive* in the setting of chronic LV pressure overload resulting in increased LV mass (hypertrophy), impaired LV myocardial relaxation and compliance (diastolic dysfunction), and reduced contractility (systolic dysfunction).[5,7,19] Of the different COA severity indices analysed in the study, aortic isthmus ratio had the best correlation with the severity of these pathologic changes in the LV (LV remodelling) as measure by LV hypertrophy, LV diastolic, and LV systolic dysfunction. This suggests that longitudinal monitoring of COA patients using aortic isthmus ratio provides the most accurate reflection (as compared with other COA severity indices) of LV *mal-adaptive* response to chronic LV pressure overload, and may potentially be used to determine the optimal timing for intervention in order to prevent irreversible LV dysfunction.

The current study also showed that residual coarctation as measured by aortic isthmus ratio had the strongest correlation (as compared with other COA severity indices) with LV reverse remodelling post-intervention. Although an inverse correlation between the residual coarctation and LV reverse remodelling is intuitive and expected, the current study describes (for the first time) a threshold beyond which LV reverse remodelling was unlikely to occur. Studies conducted in patients with aortic stenosis and systemic hypertension have shown that absence of LV reverse remodelling after medical or surgical intervention is associated with reduced long-term survival.[7,20,21] The current study did not assess the prognostic implication of residual coarctation or suboptimal LV reverse remodelling. However, we postulated that the long-term adverse effect of residual LV pressure overload due to residual coarctation would be similar to that of aortic stenosis and hypertension.[7,20,21] Based on this assumption, the ideal COA intervention should be the technique (surgical or transcatheter) that is most likely to result in a residual aortic isthmus ratio >0.7 and residual COA peak gradient <29 mmHg.

Several studies have reported outcomes in adults with native and recurrent COA, [11,22–24] and these studies provide the foundation for the current guideline recommendations.[8,9] Although these studies provide very important clinical information, they assessed the predictive value of selected COA indices (in isolation) without controlling for the effect of all other COA severity indices, as well as other factors such as aortic stenosis that can impact LV remodelling. Additionally, the previous studies do not provide data about the effect of residual coarctation on reverse remodelling of LV structure and function after intervention. The current study addressed some of these limitations.

Clinical implications

Based on the results of the current study demonstrating a strong correlation between aortic isthmus ratio and LV remodelling indices, and the results of previous studies showing the prognostic importance of aortic isthmus size on cardiovascular outcomes during pregnancy, we expect that our results will help simplify (at least to some extent) risk stratification in patients with COA. Aortic isthmus ratio can easily be obtained from non-invasive cross-sectional imaging. It is not subjected to the limitations of using Doppler COA gradients in patients with long segment stenosis and those with suboptimal windows, because these conditions increase the margin of error with these techniques. Doppler COA gradients, SBP, and ULE-SBP gradients are still very important, and hence will provide complementary data to guide management.

Another important take home point from this study is that it provides some guidance (threshold) for the definition of successful COA intervention, because the patients with residual coarctation above this threshold had suboptimal LV reverse remodelling. Further studies are required to validate the proposed cut-off points in a different population, and to determine if timing of COA intervention and the assessment of adequacy of COA intervention based on aortic isthmus ratio will result in improved long-term survival in this population.

Limitations

The rationale for the current study was based on the assumption that LV remodelling reflects the composite effect of chronic LV pressure overload, and LV reverse remodelling reflects adequacy of relief of LV pressure overload. The current study did not provide data to support the postulation that LV remodelling or suboptimal LV reverse remodelling will result in mortality on long-term follow-up. However, these concepts have been well studied in patients with systemic hypertension and aortic stenosis, and we do suspect that the prognostic implications of LV remodelling would not be different in COA patients.

Another interesting observation was that although the guidelines recommend the use of Doppler mean gradient, our study showed that Doppler peak gradient (but not Doppler mean gradient) was associated with LVMI. Unfortunately, we do not have simultaneous invasive haemodynamic data in the study, and hence we cannot comment on which of the Doppler gradients actually correlate with invasive haemodynamic indices and reflects end-systolic arterial pressure load on the LV. The current study did not assess the effect of exercise induced hypertension on LV remodelling because exercise data were not available in all patients.

Conclusion

Of all the COA severity indices stipulated in the guidelines, aortic isthmus ratio had the strongest correlation with LV remodelling, and residual aortic coarctation as measured by aortic isthmus ratio also had a correlation with LV reverse remodelling after intervention. Aortic isthmus ratio is independent of loading conditions, and can be obtained by non-invasive cross-sectional imaging. Cross-sectional imaging is one of the routine imaging evaluations that is performed in this population, and provides information about COA severity as well as thoracic aortic size and the presence of aneurysm and pseudo-aneurysm that can occur in this population. These results can potentially improve and simplify patient selection for COA intervention, determine the optimal type of intervention based on anatomy, and for prognostication after intervention.

Supplementary data

Supplementary data are available at *European Heart Journal - Cardiovascular Imaging* online.

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References

1. Zomer AC, Vaartjes I, van der Velde ET, de Jong HM, Konings TC, Wagenaar LJ *et al.* Heart failure admissions in adults with congenital heart disease; risk factors and prognosis. *Int J Cardiol* 2013;**168**:2487–93.
2. Rinnstrom D, Dellborg M, Thilen U, Sorensson P, Nielsen NE, Christersson C *et al.* Left ventricular hypertrophy in adults with previous repair of coarctation of the aorta; association with systolic blood pressure in the high normal range. *Int J Cardiol* 2016;**218**:59–64.
3. Vriend JW, Mulder BJ. Late complications in patients after repair of aortic coarctation: implications for management. *Int J Cardiol* 2005;**101**:399–406.
4. Leandro J, Smallhorn JF, Benson L, Musewe N, Balfe JW, Dyck JD *et al.* Ambulatory blood pressure monitoring and left ventricular mass and function after successful surgical repair of coarctation of the aorta. *J Am Coll Cardiol* 1992;**20**:197–204.
5. de Divitiis M, Pilla C, Kattenhorn M, Donald A, Zadinello M, Wallace S *et al.* Ambulatory blood pressure, left ventricular mass, and conduit artery function late after successful repair of coarctation of the aorta. *J Am Coll Cardiol* 2003;**41**:2259–65.
6. Nishimura RA, Borlaug BA. Diastology for the clinician. *J Cardiol* 2019;**73**:445–52.
7. Levy D, Garrison RJ, Savage DD, Kannel WB, Castelli WP. Prognostic implications of echocardiographically determined left ventricular mass in the Framingham Heart Study. *N Engl J Med* 1990;**322**:1561–6.
8. Stout KK, Daniels CJ, Aboulhosn JA, Bozkurt B, Broberg CS, Colman JM *et al.* 2018 AHA/ACC guideline for the management of adults with congenital heart disease: a report of the American College of Cardiology/American Heart Association Task Force on clinical practice guidelines. *J Am Coll Cardiol* 2019;**73**:e81–192.
9. Baumgartner H, Bonhoeffer P, De Groot NM, de Haan F, Deanfield JE, Galie N *et al.*; Endorsed by the Association for European Paediatric Cardiology (AEPC). ESC guidelines for the management of grown-up congenital heart disease (new version 2010): the Task force on the management of Grown-up Congenital Heart Disease of the European Society of Cardiology (ESC). *Eur Heart J* 2010;**31**:2915–57.
10. Forbes TJ, Kim DW, Du W, Turner DR, Holzer R, Amin Z *et al.* Comparison of surgical, stent, and balloon angioplasty treatment of native coarctation of the aorta: an observational study by the CCISC (Congenital Cardiovascular Interventional Study Consortium). *J Am Coll Cardiol* 2011;**58**:2664–74.
11. Hager A, Kanz S, Kaemmerer H, Schreiber C, Hess J. Coarctation long-term assessment (COALA): significance of arterial hypertension in a cohort of 404 patients up to 27 years after surgical repair of isolated coarctation of the aorta, even in the absence of restenosis and prosthetic material. *J Thoracic Cardiovasc Surg* 2007;**134**:738–45.
12. Egbe AC, Qureshi MY, Connolly HM. Determinants of left ventricular diastolic function and exertional symptoms in adults with coarctation of aorta. *Circ Heart Fail* 2020;**13**:e006651.
13. Mitchell C, Rahko PS, Blauwet LA, Canaday B, Finstuen JA, Foster MC *et al.* Guidelines for performing a comprehensive transthoracic echocardiographic examination in adults: recommendations from the American Society of Echocardiography. *J Am Soc Echocardiogr* 2019;**32**:1–64.
14. Forbes TJ, Garekar S, Amin Z, Zahn EM, Nykanen D, Moore P *et al.*; Congenital Cardiovascular Interventional Study Consortium (CCISC). Procedural results and acute complications in stenting native and recurrent coarctation of the aorta in patients over 4 years of age: a multi-institutional study. *Catheter Cardiovasc Interven* 2007;**70**:276–85.
15. Nagueh SF, Smiseth OA, Appleton CP, Byrd BF 3rd, Dokainish H, Edvardsen T *et al.* Recommendations for the evaluation of left ventricular diastolic function by echocardiography: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr* 2016;**29**:277–314.
16. Caballero L, Kou S, Dulgheru R, Gonjilashvili N, Athanassopoulos GD, Barone D *et al.* Echocardiographic reference ranges for normal cardiac Doppler data: results from the NORRE Study. *Eur Heart J Cardiovasc Imag* 2015;**16**:1031–41.
17. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L *et al.* Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr* 2015;**28**:1–39.e14.
18. Voigt JU, Pedrizzetti G, Lysyansky P, Marwick TH, Houle H, Baumann R *et al.* Definitions for a common standard for 2D speckle tracking echocardiography: consensus document of the EACVI/ASE/Industry Task Force to standardize deformation imaging. *J Am Soc Echocardiogr* 2015;**28**:183–93.
19. Reddy YNV, Andersen MJ, Obokata M, Koepp KE, Kane GC, Melenovsky V *et al.* Arterial stiffening with exercise in patients with heart failure and preserved ejection fraction. *J Am Coll Cardiol* 2017;**70**:136–48.
20. Thanassoulis G, Lyass A, Benjamin EJ, Larson MG, Vita JA, Levy D *et al.* Relations of exercise blood pressure response to cardiovascular risk factors and vascular function in the Framingham Heart Study. *Circulation* 2012;**125**:2836–43.
21. Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M *et al.*; ESC Scientific Document Group. ESC/ESH guidelines for the management of arterial hypertension. *Eur Heart J* 2018;**39**:3021–104.
22. Morgan GJ, Lee KJ, Chaturvedi R, Bradley TJ, Mertens L, Benson L. Systemic blood pressure after stent management for arch coarctation implications for clinical care. *JACC Cardiovasc Interv* 2013;**6**:192–201.
23. Krieger EV, Clair M, Opotowsky AR, Landzberg MJ, Rhodes J, Powell AJ *et al.* Correlation of exercise response in repaired coarctation of the aorta to left ventricular mass and geometry. *Am J Cardiol* 2013;**111**:406–11.
24. Jimenez-Juan L, Krieger EV, Valente AM, Geva T, Wintersperger BJ, Moshonov H *et al.* Cardiovascular magnetic resonance imaging predictors of pregnancy outcomes in women with coarctation of the aorta. *Eur Heart J Cardiovas Imaging* 2014;**15**:299–306.