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ORIGINAL ARTICLE
Adult congenital heart disease

Assessment of aortic and cerebral haemodynamics and vascular brain injury with 3 and 7 T magnetic resonance imaging in patients with aortic coarctation

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Aims

Coarctation of the aorta (CoA) is characterized by a central arteriopathy resulting in increased arterial stiffness. The condition is associated with an increased risk of stroke. We aimed to assess the aortic and cerebral haemodynamics and the presence of vascular brain injury in patients with previous surgical CoA repair.

Methods and results

Twenty-seven patients with CoA (median age 22 years, range 12–72) and 25 age- and sex-matched controls (median age 24 years, range 12–64) underwent 3 T (heart, aorta, and brain) and 7 T (brain) magnetic resonance imaging scans. Haemodynamic parameters were measured using two-dimensional phase-contrast images of the ascending and descending aorta, internal carotid artery (ICA), basilar artery (BA), middle cerebral artery (MCA), and perforating arteries. Vascular brain injury was assessed by rating white matter hyperintensities, cortical microinfarcts, lacunes, and microbleeds. Pulse wave velocities in the aortic arch and descending aorta were increased and ascending aortic distensibility was decreased in patients with CoA vs. controls. Patients with CoA showed a higher mean flow velocity in the right ICA, left ICA, and BA and a reduced distensibility in the right ICA, BA, and left MCA. Haemodynamic parameters in the perforating arteries, total cerebral blood flow, intracranial volumes, and vascular brain injury were similar between the groups.

Conclusion

Patients with CoA show an increased flow velocity and reduced distensibility in the aorta and proximal cerebral arteries, which suggests the presence of a generalized arteriopathy that extends into the cerebral arterial tree. No substantial vascular brain injury was observed in this relatively young CoA population, although the study was inadequately powered regarding this endpoint.

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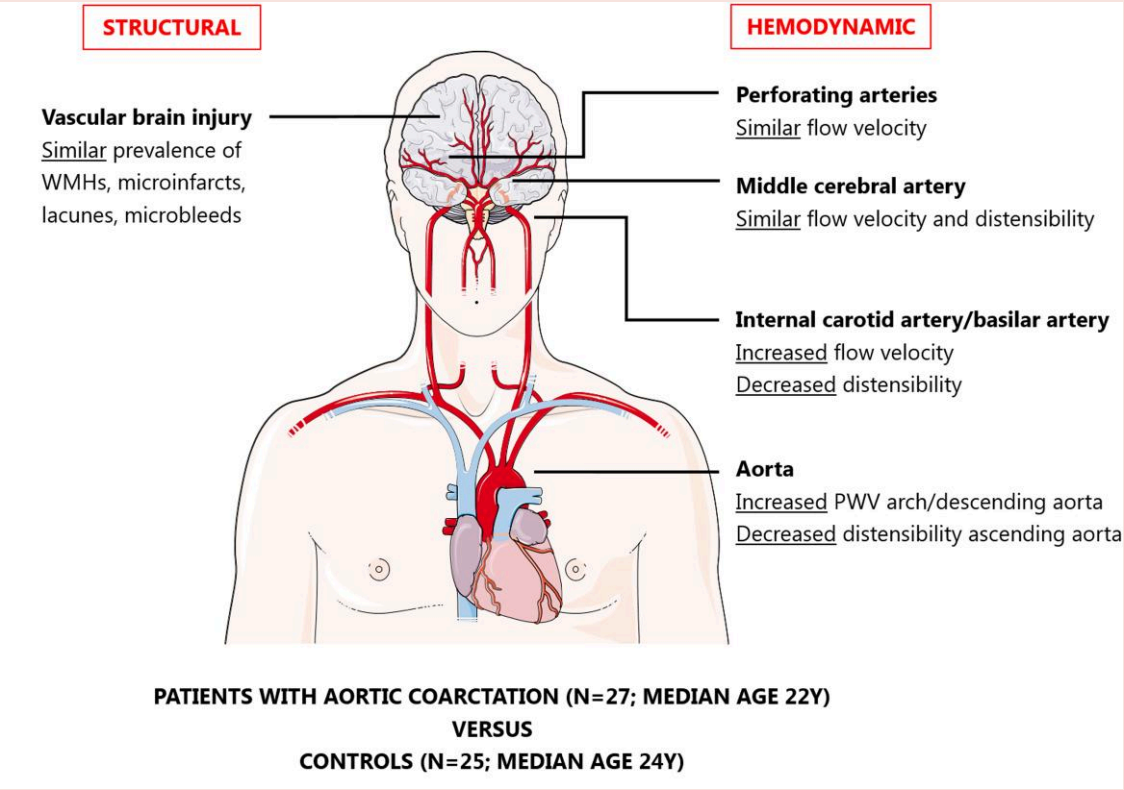
Graphical Abstract



Graphical summary of the main findings in this study. This figure was created using an image from Servier Medical Art (smart.servier.com). PWV, pulse wave velocity; WMH, white matter hyperintensity.

Keywords Congenital heart disease • Aortic coarctation • 7 T MRI • Cerebrovascular disease

Introduction

Coarctation of the aorta (CoA) is a congenital, focal stenosis of the aortic isthmus, affecting ~4 of 10 000 newborns.[1] Nowadays, most patients undergo surgical repair in the first months after birth. Coarctation of the aorta is characterized by a central arteriopathy, resulting in increased arterial stiffness of the prestenotic aorta, even after an anatomically successful repair.[1,2] Microscopic evaluation has revealed that this is caused by pronounced elastin fragmentation and accumulation of collagen.[3] Increased arterial stiffness may induce several pathological changes. It augments the left ventricular (LV) afterload, resulting in LV hypertrophy and potentially fibrosis. Furthermore, the dampening of the arterial pulse wave, also known as the Windkessel effect, is impaired.[4] Deterioration of this protective mechanism may result in end-organ damage.[5] Increased arterial stiffness is also associated with hypertension, which is frequently observed in patients with repaired CoA and predisposes for vascular brain injury.[1]

Importantly, patients with CoA are at an increased risk of haemorrhagic and ischaemic stroke, despite successful CoA repair.[6,7] According to a recent study, patients with CoA experience haemorrhagic and ischaemic stroke on average 29 and 16 years earlier, respectively, than patients without CoA.[8] In particular, subarachnoid haemorrhage is frequent.[7] This may be partly related to the high prevalence of intracranial aneurysms, which are present in ~10% of adults with CoA as opposed to 2% in the general population.[9,10] Despite the high incidence of stroke, little is known about the characteristics of the cerebral circulation in this specific patient population and its role in the pathogenesis of stroke. In this exploratory case–control study, we used 3 and 7 T magnetic resonance imaging (MRI) to evaluate haemodynamic parameters in the aorta and the proximal and distal segments of the cerebral arterial tree in patients with previously repaired CoA. Furthermore, we assessed the presence and extent of vascular brain injury.

Methods

Study population

In this cross-sectional case–control study, patients ≥12 years of age with previous surgical repair of CoA were included. Hereafter, these patients will be referred to as 'patients with CoA'. Controls, defined as subjects with no history of cardiovascular disease, were frequency-matched by age and sex in a 1:1 ratio to patients. Exclusion criteria for patients with CoA and controls were a history of stroke or intellectual disability, current pregnancy, and the presence of a contraindication for MRI. All subjects completed the Questionnaire for Verifying Stroke-Free Status.[11] A specific exclusion criterion for patients with CoA was the presence of an associated congenital defect or syndrome other than a bicuspid aortic valve (BAV), closed/small ventricular septal defect, atrial septal defect, or patent foramen ovale. Patients with CoA were also excluded when they had a history of aortic stent implantation (due to potential MRI artefacts) or when there was current evidence of recoarctation. Written informed consent was provided by all subjects. The study was approved by the institutional review board (number 19-417).

Study procedures

In all subjects, blood pressure (BP) measurements were performed on the right arm and right leg. Hypertension in subjects >16 years was defined as a systolic BP ≥140 mmHg, diastolic BP ≥90 mmHg, and/or any anti-hypertension medication.[12] In subjects ≤16 years, reference values were based on the 95th percentile for age, sex, and height.[13] Patients with CoA additionally underwent 24 h ambulatory BP monitoring, which was classified according to ESC guidelines for subjects >16 years and ESH guidelines for subjects ≤16 years.[12,13] Clinical data, including comorbidities, prior interventions, and use of anti-hypertensive medication, were extracted from medical records.

All subjects underwent two MRI scans: a combined cardiac, aortic, and brain MRI scan on a 3 T Philips Ingenia Elition scanner (Philips Healthcare, Best, The Netherlands), and a brain MRI scan on a 7 T Philips Achieva scanner (Philips Healthcare). The imaging parameters of these MRI scans are provided in Supplementary material online, *Table S1*. The maximal duration between both scanning sessions was 6 months.

Cardiac and aortic imaging

Cardiac and aortic evaluation was performed with 3 T MRI to assess LV volumes, LV ejection fraction, aortic pulse wave velocity (PWV), and aortic distensibility. The cardiac cines were analysed using Qmass (Medis Medical Imaging, Leiden, The Netherlands). The cardiac-gated two-dimensional (2D) phase-contrast images were analysed on the scanner console using the Philips scanner software (R5.1.7). Based on these analyses, aortic PWV was calculated (i) between the ascending and the proximal descending aorta, both measured at the level of the pulmonary bifurcation, (ii) between the proximal descending aorta and the aorta at diaphragm level, and (iii) between the ascending aorta and the aorta at diaphragm level, as previously described.[2,14] Ascending aortic distensibility was calculated according to the following formula: $(A_{max}–A_{min})/(A_{min} \times (BP_{systolic}–BP_{diastolic}))$.[2] In this formula, A_{max} and A_{min} refer to the maximal and minimal lumen area (mm^2) and the right arm BP measurement was used as proxy for the local intraluminal pulse pressure. Cardiac and aortic analyses were performed independently by two trained operators.

Brain imaging

Cerebral haemodynamic parameters were assessed from the 3 and 7 T 2D phase-contrast images in the following cerebral arteries: the C3 segment of the right and left internal carotid artery (ICA), the basilar artery (BA), the M1 segment of the right and left middle cerebral artery (MCA), and the perforating arteries in the basal ganglia and centrum semiovale. For analysis of the ICA (3 T), BA (3 T), and MCA (7 T), vessel contours were automatically detected and propagated over the cardiac cycle using Qflow (Medis Medical Imaging), as illustrated in *Figure 1*. Correct contour propagation was individually verified and, if necessary, manually adjusted blinded to the presence of CoA. Measurements were excluded when the quality criteria were not met, i.e. the slice planning was not perpendicular to the arteries and/or the contour was unstable over the cardiac cycle. Analysis of the perforating arteries (7 T) was performed according to previously described methods.[15,16] These analyses were conducted independently by two trained operators. The following parameters were assessed in the examined arteries: mean flow velocity, velocity pulsatility index (PI), mean flow, and distensibility. Velocity PI was calculated by dividing the difference between maximal and minimal flow velocity by the mean flow velocity over the cardiac cycle.[16]

Arterial spin labelling and T1-weighted images were used to quantify total white matter and grey matter cerebral blood flow (CBF). Cerebral blood flow was estimated using BASIL software and corrected for partial volume effects.[17] Intracranial volumes were measured by voxel-based morphometry on 3 T T1-weighted images using CAT12 software.[18] Vascular brain lesions were assessed by experienced raters. White matter hyperintensity burden was determined on the FLAIR sequence using the Fazekas scale.[19] The presence of lacunes (on 3 T T1-weighted and FLAIR images) and microbleeds (on 7 T T2* images) was rated according to the STRIVE criteria.[20] Cortical microinfarcts were rated on 3 T T1-weighted, FLAIR, and SWI images according to previously published rating criteria.[21]

Statistical analyses

Velocity PI at 7 T MRI was used for sample size calculation. Recently, this was assessed in patients with lacunar stroke or intracerebral haemorrhage (mean velocity PI: 1.045 ± 0.12) and in controls (mean velocity PI: 0.94).[16] Based on these data, we expected to need 21 subjects per group ($\alpha = 0.05$; $\beta = 0.20$). Taking into account a margin of error, we decided to include 25 patients with CoA and 25 controls in the study.

Baseline characteristics were compared between patients with CoA and control subjects using the independent-samples *t*-test, Mann–Whitney *U* test, or Fisher's exact test, where appropriate. Cardiac/aortic parameters and haemodynamic parameters in the cerebral arteries were compared between both groups using the independent-samples *t*-test. Multiple linear regression was performed to adjust for age, sex, and the presence of hypertension, since these variables may impact haemodynamic measurements based on physiological concepts and/or prior reports.[22] Residual analyses were conducted to evaluate whether the assumptions of linearity, normality, and homoscedasticity were met. Variance inflation factor values were reviewed to detect potential multicollinearity. A similar regression model was created for the association between CoA and intracranial volumes. All analyses were performed using IBM SPSS Statistics 25 (Armonk, NY, USA). A *P*-value of <0.05 was considered statistically significant.

Results

Baseline characteristics

Of the 25 included patients with CoA, 2 patients had an incomplete data set. As prespecified in the study protocol, these patients were replaced but their available data were used for analysis. Therefore, a total of 27 patients with CoA and 25 controls were included. A flow diagram is provided in *Figure 2*. Baseline characteristics of all participants are displayed in *Table 1*. The median age was 22 years (range 12–72) in patients with CoA and 24 years (range 12–64) in controls. Patients were more frequently hypertensive and more likely to use anti-hypertensive medication when compared with controls.

Cardiac and aortic parameters

In *Table 2*, cardiac and aortic parameters are presented (adjusted analyses in Supplementary material online, *Table S2*). There were no differences in LV volumes and ejection fraction between patients with CoA and controls. Pulse wave velocity in the aortic arch (5.9 vs. 4.9 m/s, $P = 0.03$), descending aorta (5.7 vs. 4.6 m/s, $P = 0.03$), and total thoracic aorta (5.6 vs. 4.7 m/s, $P = 0.004$) were increased in patients with CoA vs. controls. Inversely, distensibility of the ascending aorta was reduced in patients vs. controls (6.1×10^{-3} vs. 8.5×10^{-3} $mmHg^{-1}$, $P = 0.02$).

Haemodynamic parameters in the cerebral arteries

Table 3 provides the haemodynamic parameters in various segments of the cerebral arterial tree (adjusted analyses in Supplementary material online, *Table S3*). The mean flow velocity was higher in the right ICA (30.5 vs. 24.1 cm/s, $P = 0.02$), left ICA (29.8 vs. 23.0 cm/s, $P = 0.006$), and BA (33.6 vs. 28.5 cm/s, $P = 0.007$) in patients with CoA vs. controls, whereas the distensibility was lower in the right ICA (6.5×10^{-3} vs. 8.6×10^{-3} $mmHg^{-1}$, $P = 0.048$) and BA (6.6×10^{-3} vs. 12.6×10^{-3} $mmHg^{-1}$, $P < 0.001$). Similarly, in the right and left MCA, a higher mean flow velocity and lower distensibility were observed in patients with CoA, although only the lower distensibility in the left MCA reached statistical significance (2.7×10^{-3} vs. 4.4×10^{-3} $mmHg^{-1}$, $P = 0.001$). Coarctation of the aorta was not associated with altered velocity PI or mean flow in the ICA, BA, and MCA. The mean lumen area over the cardiac cycle was decreased in the ICAs and BA compared with controls, but no

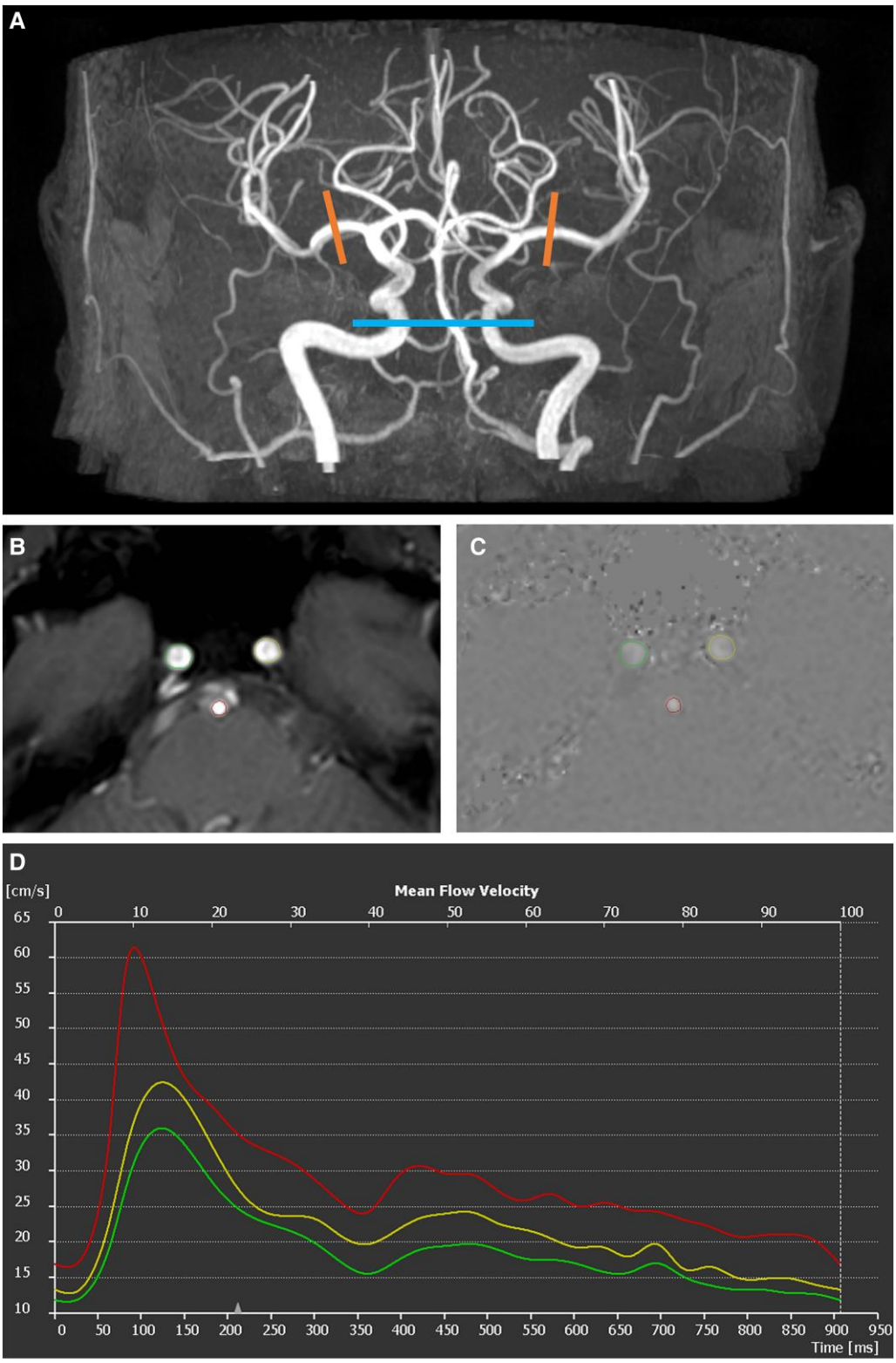


Figure 1 Planning and contour detection for haemodynamic measurements of the internal carotid arteries, basilar artery, and middle cerebral arteries. (*A*) Phase-contrast angiography (coronal view) showing the slice planning used for measurements of the internal carotid arteries and basilar artery at C3 level (blue) and the middle cerebral arteries at the M1 segment (orange). (*B* and *C*) Contours were automatically detected and propagated over the cardiac cycle (green, right internal carotid artery; yellow, left internal carotid artery; red, basilar artery). (*D*) Corresponding flow velocity curves in the three cerebral arteries are mentioned above.

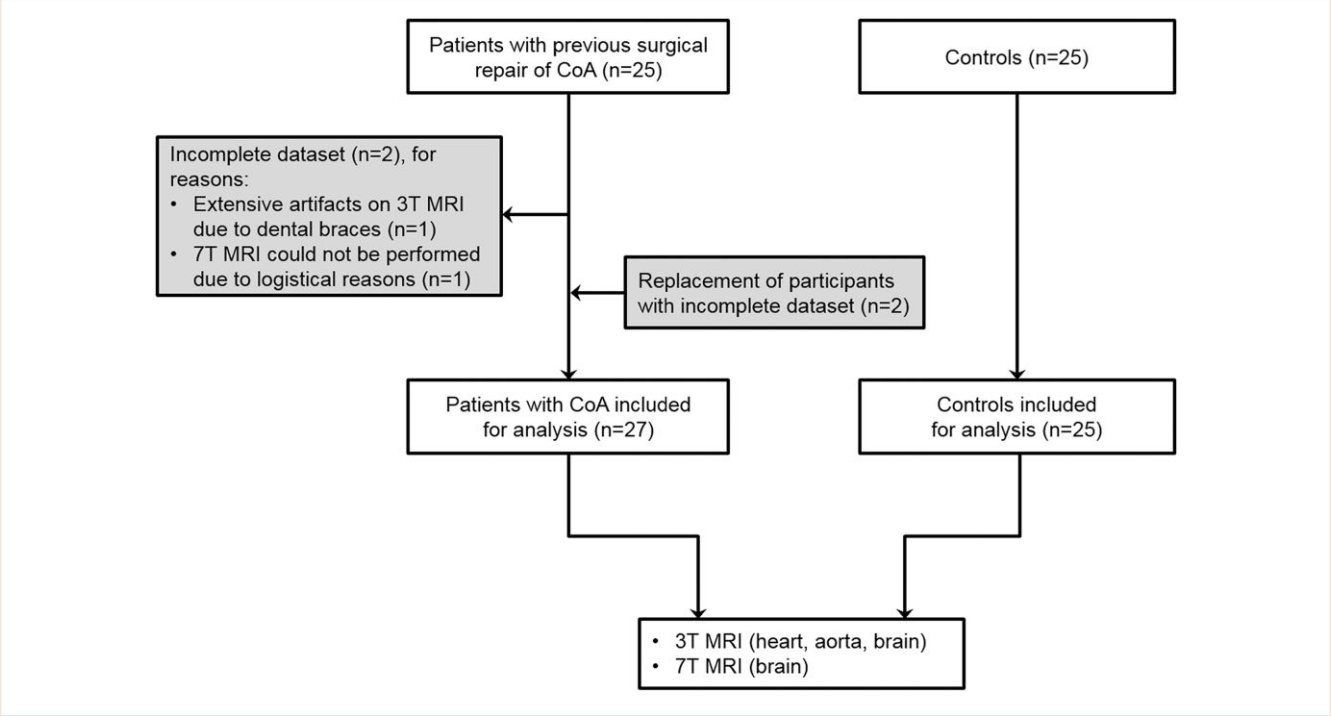


Figure 2 Flow diagram of the study population.

Table 1 Baseline characteristics

	CoA ($n = 27$)	Control ($n = 25$)	*P*-value
Age (years)	22 (12–72)	24 (12–64)	0.65
Female sex	10 (37)	7 (28)	0.56
BMI (kg/m^2)	22.9 ± 3.8	22.1 ± 2.9	0.39
Hypertension	17 (63)	6 (24)	**0.006**
Use of any AHM	6 (22)	0	**0.02**
SBP (mmHg)	136 ± 13	127 ± 15	**0.04**
DBP (mmHg)	81 ± 8	79 ± 10	0.32
Pulse pressure (mmHg)	54 ± 13	48 ± 13	0.12
Arm-leg SBP gradient (mmHg)	−5 ± 14		
Age at initial CoA repair (years)	0 (0–28)		
Type of initial CoA repair			
End-to-end anastomosis	19 (70)		
Patch angioplasty	5 (19)		
Subclavian flap angioplasty	1 (4)		
Surgery, technique unknown	2 (7)		
Intervention for recurrent CoA	5 (19)		
Bicuspid aortic valve	13 (48)		
Ventricular septal defect	6 (22)		

Bold values represent $P < 0.05$.
Data are presented as mean ± standard deviation (SD), median (range), or number (percentage). Groups were compared using the independent-samples *t*-test, Mann–Whitney *U* test, or Fisher's exact test, where appropriate.
AHM, anti-hypertensive medication; BMI, body mass index; DBP, diastolic blood pressure; SBP, systolic blood pressure.

decrease was observed in the MCAs (see Supplementary material online, *Table S4*).

In the perforating arteries, no differences between patients with CoA and controls were found in the mean flow velocity and velocity PI (*Table 3*). Additionally, patients and controls were comparable with regard to the number of detected perforating arteries in the basal ganglia (25 ± 8 vs. 25 ± 6, respectively; $P > 0.99$) and centrum semiovale (72 ± 15 vs. 74 ± 16, respectively; $P = 0.64$).

Subgroup analyses in patients with CoA showed no difference in the mean flow velocity and distensibility in the ICA and BA between patients with and without BAV, although patients with BAV tended to have a lower mean flow velocity in the right ICA, left ICA, and BA (see Supplementary material online, *Table S5*). Similarly, hypertension status and age at initial CoA repair were not associated with haemodynamic parameters in the ICA and BA (see Supplementary material online, *Tables S6* and *S7*, respectively).

Total cerebral blood flow

White matter CBF was 25.6 ± 5.1 mL/100 g/min in patients with CoA and 24.3 ± 5.9 mL/100 g/min in controls ($P = 0.42$). Grey matter CBF values were 50.4 ± 10.6 and 51.4 ± 10.4 mL/100 g/min, respectively, for patients with CoA and controls ($P = 0.74$). When corrected for age, sex, and the presence of hypertension, CoA diagnosis was not associated with altered white matter CBF nor grey matter CBF.

Presence of vascular brain injury

The prevalence of white matter hyperintensities, cortical microinfarcts, lacunes, and microbleeds was low in patients with CoA and controls with no substantial differences between the groups (*Table 4*). No patient had an occlusive lesion of the carotid arteries. As an incidental finding, a 9 mm left ICA bifurcation aneurysm was detected on a 7 T T1-weighted image in a 43-year-old male patient with CoA (*Figure 3*). Due to the

Table 2 Cardiac and aortic parameters in patients with coarctation of the aorta and controls

	CoA	Control	Unadjusted *P*-value	Adjusted *P*-value
LV ejection fraction (%)	57 ± 3	57 ± 5	0.56	0.27
LV mass index (g/m^2)	46 ± 11	48 ± 11	0.48	0.51
LV end-diastolic volume (mL/m^2)	96 ± 12	103 ± 17	0.10	0.44
LV end-systolic volume (mL/m^2)	41 ± 7	45 ± 10	0.12	0.25
PWV aortic arch (m/s)	5.9 ± 2.2	4.9 ± 1.1	**0.04**	**0.03**
PWV descending aorta (m/s)	5.7 ± 2.0	4.6 ± 1.6	**0.03**	**0.03**
PWV total thoracic aorta (m/s)	5.6 ± 1.5	4.7 ± 1.1	**0.02**	**0.004**
Distensibility ascending aorta (10^{-3} mmHg^{-1})	6.1 ± 4.1	8.5 ± 3.6	**0.03**	**0.02**

Bold values represent $P < 0.05$.
Data are presented as mean ± SD. Groups were compared using the independent-samples *t*-test (unadjusted *P*-values). Multiple linear regression was performed to adjust for age, sex, and the presence of hypertension (adjusted *P*-values).
LV, left ventricular; PWV, pulse wave velocity.

substantial risk of rupture as determined by the consulted neurologist, the patient underwent successful surgical clipping of the aneurysm.

Intracranial volumes

No association was observed between CoA diagnosis and intracranial volumes (see Supplementary material online, *Table S8*). However, although non-significant, patients with CoA tended to have a lower white matter volume ($\beta = -21.4$ cm^3, $P = 0.08$), lower grey matter volume ($\beta = -16.1$ cm^3, $P = 0.28$), and higher cerebrospinal fluid volume ($\beta = 11.0$ cm^3, $P = 0.40$).

Discussion

In this study, we performed a detailed assessment of the aortic and cerebral haemodynamics and the presence of vascular brain injury in patients with CoA. The combination of two complementary high-field strength MRI scans (3 and 7 T) allowed for an analysis of the entire arterial vascular tree from the central aorta to the proximal and distal cerebral arteries. Our results indicate that patients with CoA have an increased flow velocity and decreased distensibility in the aorta and proximal cerebral arteries. In this relatively young cohort of patients with CoA, no substantial vascular brain injury was observed, although the study was underpowered to detect differences in this endpoint. A graphical summary of the main results is presented in graphical abstract.

Haemodynamics from the proximal aorta to the distal cerebral arteries

Over the last few decades, we have learned that CoA is not an isolated condition but should rather be considered as a central arteriopathy. Multiple studies have reported on the structural and haemodynamic abnormalities in the aorta proximal of the CoA.[2,3,23] Elastin fibre fragmentation results in increased aortic stiffness and increased PWV.[2,3] Distal vascular beds are also affected. The brachial arteries were found to be less responsive to flow and nitroglycerine and the retinal arteries show pronounced corkscrew-shaped tortuosity.[24,25] Although the involvement of the cerebral arteries seemed likely, especially in the light of the increased risk of stroke, no detailed assessment of the cerebral arterial tree had been performed in this patient population.[6,7] In this study, we found an increase in the mean flow velocity and a decrease in distensibility in the ICA and BA. These findings suggest that these proximal cerebral arteries are involved in the complex, generalized arteriopathy observed in CoA. In the MCA, a similar increase in mean flow velocity and decrease in distensibility was seen, although not all associations reached statistical significance. This is in line with the higher resistive index in the MCA in a previous study.[26] Interestingly, the perforating arteries appeared unaffected. This may be largely attributable to the cerebral autoregulation, which ensures adequate and constant blood flow in these small cerebral arteries. However, as the perforating arteries are too small to reliably assess the arterial wall characteristics, the presence of a local vasculopathy cannot be excluded.

The aetiology of the altered cerebral haemodynamics remains unclear. Specifically, it is unknown whether these changes are inherent to the structural condition of CoA and thus already present during prenatal development, or attributable to secondary processes such as chronic hypertension, or a combination of both. Increased aortic stiffness has already been identified in the neonatal phase and could not be resolved by adequate early surgical repair, which suggests an inborn aetiology.[23] On the other hand, the impaired elasticity that we observe in the proximal cerebral arteries is also seen in individuals with chronic hypertension.[27] Additionally, an important role of hypertension is suggested by the increased carotid intima-media thickness and the high incidence of haemorrhagic stroke relative to ischaemic stroke observed in this patient population.[6,7,28] Our subgroup analyses showed that cerebral haemodynamics in patients with CoA was not associated with age at initial repair nor the presence of hypertension, although the study was not adequately powered for these analyses. Interestingly, patients with an associated BAV tended to have a lower flow velocity in the ICA and BA. This finding is likely attributable to the eccentric blood flow and resulting energy loss within the ascending aorta in patients with BAV.[29,30]

We observed a decreased lumen area of the ICA and BA in patients with CoA, which may explain the increased flow velocity in these arteries. To our knowledge, this has not been described before. We hypothesize that this is due to vessel wall thickening secondary to hypertension, which is in line with the increased carotid intima-media thickness found in this patient population.[28] However, the possibility of an abnormal prenatal development of these arteries cannot be ruled out.

Vascular brain injury

It is plausible that the altered cerebral haemodynamics in patients with CoA could contribute to vascular brain injury, as increased carotid stiffness is strongly associated with cardiovascular risk and atherosclerosis.[31] However, in contrast to previous studies, we observed no substantial vascular brain injury (including small vessel disease)

Table 3 Haemodynamic parameters in the cerebral arteries in patients with coarctation of the aorta and controls

	Mean flow velocity (cm/s)				Velocity PI			
	CoA	Control	Unadjusted *P*-value	Adjusted *P*-value	CoA	Control	Unadjusted *P*-value	Adjusted *P*-value
Right ICA	30.5 ± 8.8	24.1 ± 8.7	**0.02**	**0.02**	0.97 ± 0.20	1.06 ± 0.17	0.11	0.10
Left ICA	29.8 ± 8.9	23.0 ± 7.6	**0.007**	**0.006**	1.01 ± 0.25	1.09 ± 0.23	0.25	0.06
Basilar artery	33.6 ± 6.5	28.5 ± 5.6	**0.004**	**0.007**	0.88 ± 0.21	0.92 ± 0.21	0.56	0.18
Right MCA, M1 segment	48.2 ± 6.9	45.8 ± 7.7	0.25	0.32	0.69 ± 0.11	0.68 ± 0.10	0.83	0.90
Left MCA, M1 segment	46.2 ± 7.6	43.6 ± 8.1	0.26	0.30	0.69 ± 0.12	0.68 ± 0.15	0.67	0.80
Perforating arteries BG	3.7 ± 0.6	3.8 ± 0.5	0.56	0.68	0.28 ± 0.10	0.30 ± 0.07	0.49	0.46
Perforating arteries CS	1.1 ± 0.4	1.0 ± 0.2	0.42	0.62	0.27 ± 0.10	0.27 ± 0.09	0.94	0.81
	Mean flow (mL/s)				**Distensibility ($\times 10^{-3}$ mmHg^{-1})**			
	CoA	Control	Unadjusted *P*-value	Adjusted *P*-value	CoA	Control	Unadjusted *P*-value	Adjusted *P*-value
Right ICA	4.6 ± 1.5	5.2 ± 2.2	0.32	0.50	6.5 ± 2.8	8.6 ± 5.5	0.13	**0.048**
Left ICA	4.3 ± 1.7	4.6 ± 1.9	0.57	0.70	6.8 ± 3.1	9.2 ± 6.3	0.12	0.08
Basilar artery	2.3 ± 0.8	2.6 ± 0.8	0.23	0.28	6.6 ± 2.6	12.6 ± 6.7	**<0.001**	**<0.001**
Right MCA, M1 segment	2.7 ± 0.7	2.8 ± 0.6	0.85	0.76	2.5 ± 1.1	3.1 ± 2.1	0.22	0.09
Left MCA, M1 segment	2.5 ± 0.6	2.7 ± 0.6	0.23	0.87	2.7 ± 1.2	4.4 ± 2.3	**0.003**	**0.001**
Perforating arteries BG	NA	NA	NA	NA	NA	NA	NA	NA
Perforating arteries CS	NA	NA	NA	NA	NA	NA	NA	NA

Bold values represent $P < 0.05$.
Data are presented as mean ± SD. Groups were compared using the independent-samples *t*-test (unadjusted *P*-values). Multiple linear regression was performed to adjust for age, sex, and the presence of hypertension (adjusted *P*-values).
BG, basal ganglia; CS, centrum semiovale; ICA, internal carotid artery; MCA, middle cerebral artery; NA, not applicable; PI, pulsatility index.

Table 4 Presence of vascular brain injury, i.e. white matter hyperintensities, cortical microinfarcts, lacunes, and microbleeds

	CoA	Control
Fazekas score for periventricular WMH	*n* = 26	*n* = 25
0	23 (88)	22 (88)
1	2 (8)	3 (12)
2	1 (4)	0
3	0	0
Fazekas score for deep WMH	*n* = 26	*n* = 25
0	21 (81)	21 (84)
1	4 (15)	4 (16)
2	1 (4)	0
3	0	0
No. of cortical microinfarcts	*n* = 24	*n* = 25
0	24 (100)	24 (96)
1	0	1 (4)
2	0	0
No. of lacunes	*n* = 26	*n* = 25
0	26 (100)	25 (100)
1	0	0
2	0	0
No. of cerebral microbleeds	*n* = 25	*n* = 25
0	23 (92)	25 (100)
1	1 (4)	0
2	1 (4)	0

Data are presented as number (percentage).
WMH, white matter hyperintensities.

compared with controls. This is an important finding, since recent data indicate that the hazard of haemorrhagic and ischaemic stroke in patients with CoA is 12.5–17.3 and 4.0 times higher, respectively, in comparison with the general population.[6,7] Furthermore, stroke occurs ~20 years earlier in patients with CoA compared with patients without CoA.[8] However, there may be an important effect of era. Patients with CoA from these previous studies generally underwent surgical repair with less sophisticated techniques and at a later age, thus being exposed longer to the adverse effects of CoA with increased blood pressure proximal to the aortic narrowing. In contrast, most patients in our study underwent early and technically advanced repair. This may partly explain the low incidence of vascular brain injury observed in our study, which is a reassuring finding for the current generation of patients with CoA. Preserved cerebral autoregulation may also (partly) prevent vascular brain injury in this relatively young cohort. However, hypertension, diabetes mellitus, and hypercholesterolaemia are known risk factors for a future decline in cerebral autoregulation.[32–34] This illustrates the importance of reducing the cumulative effects of (modifiable) risk factors other than CoA during lifetime follow-up. Alternative causes of stroke in patients with CoA should also be considered. Although none of the patients in this study had documented atrial arrhythmias, it was previously shown that the prevalence of supraventricular tachycardia is more than 10-fold higher in patients with CoA compared with individuals <50 years from the general population.[35] Importantly, considering the normal LV dimensions and function in our patients, there was no evidence of adverse arterio-ventricular interaction.

Limitations

One of the limitations of this study is that no systematic assessment of intracranial aneurysms was performed due to the relatively small sample size. Additionally, although mean flow velocity and distensibility in the ICA and BA were different between patients with CoA and controls, our study may have been underpowered to detect differences

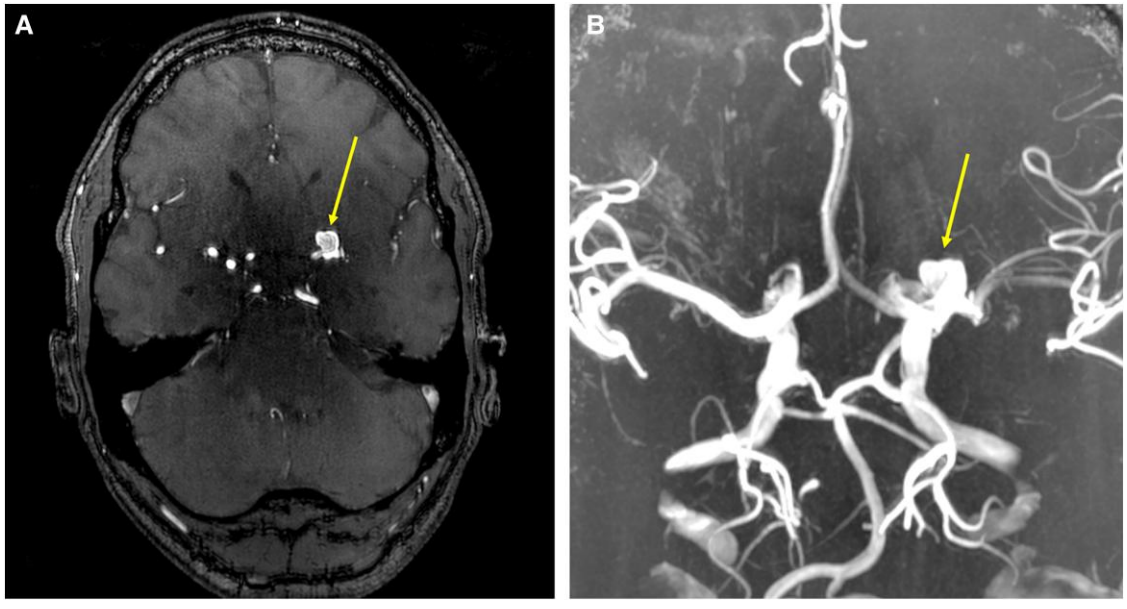


Figure 3 A 9 mm bifurcation aneurysm of the left internal carotid artery in a 43-year-old male patient with coarctation of the aorta. (*A*) The aneurysm was incidentally detected on a 7 T T1-weighted image (transversal view). (*B*) Subsequently, phase-contrast angiography was performed (coronal view). The aneurysm is indicated by the yellow arrows. The patient underwent successful neurosurgical clipping of the aneurysm.

in these parameters in the MCA. Another limitation is that the study population consisted mainly of children and young adults, which limits the conclusions that can be drawn regarding older patients with CoA. This is particularly relevant to vascular brain injury, which is expected to increase with age. Furthermore, our findings cannot be directly extrapolated to patients who underwent stent implantation for native or recurrent CoA, as these patients were excluded from this study.

Conclusions

In this exploratory study using 3 and 7 T MRI, patients with CoA showed an increased flow velocity and reduced distensibility in the aorta and proximal cerebral arteries. These findings support the hypothesis that CoA is characterized by a generalized arteriopathy that extends into the cerebral arterial tree. We found no evidence of substantial vascular brain injury in this relatively young CoA population, although the study was inadequately powered regarding this endpoint. Due to the large hypertensive burden and the increased risk of stroke demonstrated by previous studies, close follow-up and adequate risk factor control remain of the utmost importance.

Lead author biography

Timion A. Meijs graduated from a medical school in 2017 at Utrecht University, The Netherlands. In 2022, he obtained his PhD degree at the Department of Adult Congenital Heart Disease at University Medical Center Utrecht. He is currently working as a cardiologist in training at Amsterdam University Medical Center.

Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

Supplementary material

Supplementary material is available at *European Heart Journal Open* online.

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