Vascular Wall Changes and Arterial Functions in Children with Surgically Repaired Aortic Coarctation

Nilüfer Çetiner, Elif Erolu, Neslihan Baran Him, Berna Şaylan Çevik, and Figen Akalın

1Department of Pediatric Cardiology, Koç University, Faculty of Medicine, İstanbul, Turkey
2Department of Pediatric Cardiology, Koşuyolu Highly Specialized Training and Research Hospital, İstanbul, Turkey
3Department of Pediatrics, Marmara University, Faculty of Medicine, İstanbul, Turkey
4Department of Pediatric Cardiology, Marmara University, Faculty of Medicine, İstanbul, Turkey

ABSTRACT

Objective: We investigated arterial functions by measuring carotid–intima–media thickness, flow-mediated dilatation of the brachial artery, and distensibility and stiffness of the abdominal aorta as early indicators of cardiovascular risk in children followed up after coarctation repair.

Materials and Methods: Twenty patients with successful repair of coarctation and 27 healthy children were investigated. Two-dimensional echocardiographic images, and carotid and brachial ultrasound studies were performed.

Results: The ages of the study group ranged from 5.3 to 22 years, and those of the control group from 7 to 17 years. The age at time of surgery was between 0.23 and 257 months. Average follow-up duration after repair was between 11 and 257 months. The stiffness index of the abdominal aorta was significantly higher in patients with coarctation repair than controls (mean = 0.625 ± 0.41, mean = 0.11 ± 0.73; P = .007). Flow-mediated dilatation of the brachial artery in the first minute decreased significantly among the patients (mean = 4.5 ± 2.7, mean = 6.9 ± 4.5; P = .005). Age of the patients had a negative correlation with distensibility of the abdominal aorta (r = −0.572; P = .008) and a positive correlation with stiffness of abdominal aorta (r = 0.566, P = .009).

Conclusion: This study suggested that vascular wall changes in children and adolescents can be seen even after successful coarctation repair and may progress toward overt atherosclerosis at older ages.

Keywords: aortic stiffness index, arterial elasticity, carotid intima–media thickness, coarctation of aorta, flow-mediated dilatation

INTRODUCTION

Coarctation of the aorta (CoA) is a treatable condition with excellent early surgical results. However, previous reports have suggested that long-term morbidity may occur despite successful correction. Patients undergoing repair for aortic coarctation are known to be capable of becoming hypertensive at a young age. Systemic hypertension is recognized as a major adverse prognostic factor during rest and exercise. Systemic hypertension may develop during long-term follow-up even in the absence of residual or recurrent coarctation. The constancy or repetition of hypertension after correction has been connected to a late operation time, the presence of remaining occlusion, a suboptimal aortic arch form, and ambiguous neuro–humoral mechanisms occurring before correction. In addition, histological abnormalities of the arterial wall, especially cystic medial necrosis, have been
demonstrated in patients with coarctation. These arterial wall changes may also cause abnormal hemodynamics and abnormalities of arterial functions even in the peripheral arterial tree, which may lead to early atherosclerosis.2-4

Various non-invasive diagnostic methods have been used to evaluate the risk of cardiovascular disease (CVD) in recent years. Adult reports suggest that endothelial dysfunction is one of the earliest indicators of vascular changes at an early stage. Various studies have evaluated endothelial dysfunction by measuring brachial flow-mediated dilatation (FMD).5,6 Additionally, peripheral arterial elasticity may be a premature marker of atherosclerosis. Aortic distensibility and the stiffness index (SI) have been used in cardiology clinics as a non-invasive method for detecting early atherosclerosis in adults.7

Carotid–intima–media thickness (CIMT) has been utilized as a non-invasive procedure for testing premature or subclinical atherosclerotic changes in both children and adults. It has also been utilized as a useful indicator of atherosclerosis for both coronary and peripheral arteries.8,9

Despite successful repair at a young age, CoA has been associated with an increased risk of arterial hypertension, early-onset CVD, and premature mortality. Therefore, we aimed to evaluate the arterial functions in children after aortic coarctation repair and determine the risk factors which may be related with impaired arterial functions.

MATERIALS AND METHODS

Patients
This study was conducted in 2014 and 2015 at the Pediatric Cardiology Department outpatient clinics, Turkey. The study group included 20 patients who had undergone successful surgical repair of coarctation between 1993 and 2013 and who were recruited retrospectively. No patients had evidence of recoarctation at their most recent visit (defined as >20 mmHg pressure gradient by measuring upper and lower limb non-invasive blood pressure). Hypertension was defined as systolic and/or diastolic blood pressure (sBP/dBP) above the 95th percentile of Task Force on Blood Pressure Control in Children reference values. Seven (35%) patients in the study group were hypertensive (6 received antihypertensive drugs). Eleven patients with a bicuspid aortic valve had no important aortic valve stenosis or regurgitation. The control group included 20 patients who had undergone successful repair at a young age, CoA has been associated with an increased risk of arterial hypertension, early-onset CVD, and premature mortality. Therefore, we aimed to evaluate the arterial functions in children after aortic coarctation repair and determine the risk factors which may be related with impaired arterial functions.

Echocardiography
We performed 2D, M-mode, and Doppler studies using a Philips IE33-model echocardiography device (Andover, Md, USA) equipped with a 5-MHz transducer by the same physician in the patients and controls. End-systolic diameter of the left ventricle/end-diastolic diameter of left ventricle (LVEDD), end-diastolic diameter of posterior wall (LVPWD), left atrial, and aortic root diameters were measured. Systolic functions of LV were computed by the M-mode method. Left ventricular mass (LVM) was computed utilizing the Devereux modified method \[LVM \frac{1}{1.04} \left(\text{IVSTD} + \text{LVIDD} + \text{LVPWD} \right) - \text{LVIDD}^3 - 13.6 \text{g},\] where IVSTD is the interventricular septum end-diastolic thickness, LVIDD is the left ventricular internal dimension at end-diastole, and LVPWD is the left ventricular posterior wall end-diastolic thickness.14 The LVM index was calculated by dividing the LVM value from 2.7 degrees by the “height.” If the value yielded was greater than 38 g/m2.7, this was regarded as left ventricular hypertrophy (LHV). Standard techniques recommended by the American Society of Echocardiography were used for measurements.15

Systolic and diastolic diameters of the abdominal aorta at the diaphragm level (in subcostal abdominal long-axis view) were obtained at the peak of the R wave for systolic diameter and end of T wave for diastolic diameter at simultaneously recorded electrocardiograms, and 3 measurements were averaged for each diameter. Abdominal aortic elasticity measures were applied as previously defined by Lacombe et al16:

Aortic strain (%) = 100 × (systolic aortic diameter – diastolic aortic diameter)/diastolic aortic diameter;

Aortic distensibility (cm² dyn⁻¹) = 2 × (aortic strain)/(aortic pulse pressure).

Brachial Artery Ultrasound Studies
All ultrasound studies were performed with a Philips IE33 echocardiography device equipped with L-11-MHz linear transducer by the same physician in all cases. In order to reduce the effect of external stimuli, all studies were carried out quietly in a temperature-controlled room (24–26°C). The participant laid supine on a couch in that room. Right brachial artery thickness was evaluated from B-mode ultrasound images at rest and during reactive hyperemia. Following 10 minutes’ rest, a straight, non-branching segment of the brachial artery above the antecubital fossa was determined and analyzed in longitudinal form. Brachial artery diameter was initially recorded after depth and gain settings were regulated. A pneumatic cuff was then inflated to above 50 mmHg on the upper arm for 5 minutes and then released. After cuff deflation, brachial artery thickness was measured at every 30 seconds for 3 minutes in the end-diastolic phase. Flow-mediated
dilatation was calculated as the percentage change in diameter from baseline to the highest value after cuff deflation. The average of 3 sequential measures was adopted as the final measurement.17

**Carotid Ultrasound Studies**

The studies were performed using a Philips IE33 echocardiography machine (Philips Medical Systems) equipped with an L11-3 MHz linear transducer by the same physician in all cases as described in the literature.18 The common carotid artery images used for assessment were obtained while the patient was in a supine position with the head turned to the left. Images were acquired at the end-diastolic phase simultaneously with the tip of R-wave on electrocardiograms. The neck vessel was first shown in a cross-sectional plane, after which the transducer was rotated clockwise to a longitudinal plane. Measurements were obtained when the longitudinal distance of the common carotid artery walls was visible for at least 10 mm on both sides. Measurement of CIMT was performed at the far wall of the carotid artery, Carotid–intima–media thickness was defined as the distance between 2 bright lines measured edge to edge. An average CIMT value was obtained from 3 separate video-loop measurements.18,19

The same echocardiographic measurements were performed in the control group. The difference between the groups for each parameter was subjected to statistical comparisons.

**Statistical Analysis**

All statistical analyses were performed using the Statistical Package for Social Sciences, version 22.0 software (SPSS Inc.; Chicago, IL, USA). The variables were compared using the Mann–Whitney U test. Categorical variables were analyzed with the χ² and Fisher’s exact tests. Spearman’s correlation analysis was used to evaluate the relations between variables. The results were evaluated at a 95% confidence interval, and significance was set at P ≤ 0.05.

### RESULTS

**Patient Characteristics**

The study group consisted of 7 (35%) girls and 13 (65%) boys, and the control group of 7 (24%) girls and 23 (76%) boys. Patients’ ages ranged from 5.3 to 22 years (mean ± SD = 12.6 ± 5) and control group ages ranged from 7 to 17 years (mean ± SD = 12.2 ± 2.5). Operative time ranged from 0.23 months to 257 months (mean ± SD = 62 ± 7, median = 36 months). Mean follow-up time after coarctation repair was between 11 months and 257 months (mean ± SD = 88.92 ± 65.1). End-to-end anastomosis was performed for coarctation repair in 18 patients, the subclavian flap technique was employed in 1 case, and 1 patch aortoplasty in another. The Z score for height in the patient group (mean ± SD = −1.19 ± 1.9) was significantly lower than that in the control group (mean ± SD = −0.135 ± 1.3, P = 0.05). Systolic blood pressure in the patient group (mean ± SD = 116.6 ± 18.7 mmHg) was significantly higher than the controls (mean ± SD = 106.7 ± 7.6 mmHg, P = 0.028). Age, height, weight, body mass index (BMI), and diastolic blood pressures did not vary significantly between the 2 groups (Table 1).

**Echocardiographic Features**

Left ventricular hypertrophy was present in 9 patients (45%) during the postoperative period. Interventricular septal diameter, LVPWDd, and left ventricular mass index (LVMI) were significantly higher in the patient group than in the control group (P = 0.04, P = 0.032, and P = 0.05, respectively). M-mode measurements exhibited no difference in terms of LVEDd, ejection fraction, and shortening fraction between the patient and the control group (Table 2).

**Aortic Elasticity Parameters**

The Z score for the abdominal aorta was higher among the patients than in the controls (P = 0.001). Aortic strain and aortic

---

**Table 1. Clinical Features of the Patients and the Control Group**

|                          | Patients (n = 20) | Control (n = 27) | P     |
|--------------------------|------------------|-----------------|-------|
| Female/male              | 7/13             | 6/21            | .344a |
| Age (years)              | 12.6 ± 5.0       | 12.0 ± 2.5      | .666a |
| Weight (kg)              | 39.1 ± 17.95     | 43.9 ± 1.5      | .344a |
| Height (cm)              | 139.5 ± 19.7     | 149.0 ± 15.2    | .05b  |
| Height Z score           | −1.19 ± 0.9      | 0.35 ± 1.3      | .05b  |
| BMI (kg/m²)              | 18.8 ± 3.7       | 19.2 ± 4.2      | .79b  |
| BMI Z score              | 0.002 ± 1.01     | 0.0048 ± 0.29   | .877b |
| Systolic blood pressure at rest (mmHg) | 116.6 ± 18.7     | 106.7 ± 7.6     | .028b |
| Diastolic blood pressure at rest (mmHg) | 67.2 ± 7.9       | 67.3 ± 8.3      | .973b |
| Index of systolic blood | 0.9 ± 0.11       | 0.85 ± 0.06     | .038b |
| Age of operation (months) | 62 ± 7 (0.23–257) | 88.92 ± 65.1 (11–254) |     |
| Follow-up duration (months) | 365 (11–254)     | 88.92 ± 65.1 (11–254) |     |
| Primary procedure         |                  |                 |       |
| End-to-end               | 18               |                 |       |
| Subclavian flap          | 1                |                 |       |
| Patch aortoplasty        | 1                |                 |       |
| Preoperative pressure gradient (mmHg) | 67.7 ± 23.2 (30–120) |                 |       |

SD, standard deviation; F, female; M, male; BMI, body mass index.

aChi-square–Fisher’s exact test; bMann–Whitney U test.
distensibility were lower in the patients, although these differences were not statistically significant ($P = .109$ and $P = .206$, respectively). The aortic SI was higher (mean $0.41$, $0.625 = P$ healthy children ($0.446$) (Figure 1A and B). Arterial elasticity parameters, CIMT, and FMD did not vary significantly between sex and follow-up period.

**DISCUSSION**

The present study suggests that postoperative abnormalities in arterial physiology and structural wall changes may be seen even after successful coarctation repair in children and adolescents. The reasons for this can be multifactorial, such as systemic hypertension, increased LVMI, preoperative pressure gradient, operation time, and length of postoperative follow-up.

Previous studies have shown that cardiovascular morbidity and mortality following successful surgical repair of aortic coarctation may occur in the long term after surgery. In a study conducted in the early 1990s, the 30-year results after coarctation repair of the patients were examined and revealed that up to 25% of patients could experience death due to complications of hypertensive disease. Left ventricular hypertrophy after correction of coarctation is probably caused by a combination of various factors, such as permanent mild hypertension, increment afterload from small residual gradients, exercise-stimulated gradients or hypertension, bicuspid aortic valve with progressive stenosis, and early coronary disease. Echocardiography in the present study revealed higher diameters of the diastolic interventricular septum, diastolic left ventricular posterior wall, and LVMI values than in the control group. Left ventricular hypertrophy was detected in 45% of the patients. This may be a result of the presence of increased left ventricular afterload in this patient group. The resting arterial blood pressure measurements of patients without re-coarctation showed that 25% had pre-hypertension and 10% had hypertension. The continuity or repetition of hypertension after correction has been associated with the older age at correction, the presence of remaining occlusion, a suboptimal aortic arch shape, ambiguous neuro-humoral mechanisms started before repair, and surgical technique. End-to-end anastomosis was performed on 90% of our patients, and patients with re-coarctation were not included. The persistence of arterial hypertension may cause the development of other cardiac complications, such as premature coronary artery disease through intimal proliferation in the coronary arteries and atherosclerosis. In recent years, long observational studies have shown that even after successful CoA repair, patients still suffer from arterial hypertension, atherosclerosis, ischemic heart disease, and chronic heart failure. Studies in the literature reveal that aortic coarctation is a generalized vascular disease, not a simple mechanical obstruction.

Aortic stiffness and distensibility have been described as useful parameters for detecting early atherosclerosis in adults using non-invasive methods. The SI of the abdominal aorta increases with hypertension, age, smoking, atherosclerosis, obesity and in patients with thalassemia, Marfan syndrome, and Kawasaki disease. In the present study, the arterial SI

---

**Table 2.** Echocardiographic Characteristics of the Patients and the Control Group

|                      | Patients Group (n = 20) | Control Group (n = 27) | $P$   |
|----------------------|------------------------|------------------------|-------|
| IVSD (mm)            | 0.81 ± 0.12            | 0.72 ± 0.1             | .04   |
| LVED (mm)            | 4.17 ± 0.73            | 4.08 ± 0.44            | .480  |
| LVPWd (mm)           | 0.62 ± 0.19            | 0.71 ± 0.14            | .032  |
| EF (%)               | 68.90 ± 6.69           | 67.8 ± 4.6             | .54   |
| SF (%)               | 38.35 ± 5.07           | 36.6 ± 3.6             | .143  |
| LV mass (g)          | 91.5 ± 39.4            | 94.76 ± 22             | .830  |
| LVMI (g/cm)          | 36.5 ± 10.2            | 32.24 ± 6.2            | .05   |

IVSD, interventricular septum end-diastolic diameter; LVED, left ventricle end-diastolic diameter; LVPWd, left ventricular posterior wall end-diastolic diameter; EF, ejection fraction; FS, shortening fraction; LV, left ventricle; LVMI, left ventricle mass index.

**Table 3.** Carotid–Intima–Media Thickness, Abdominal Artery Elasticity Parameters, Flow-Mediated Dilatation of the Brachial Artery, and Z Scores of the Abdominal Aorta in the Postoperative Patients and the Control Group

|                      | Patients Group (n = 20) | Control Group (n = 27) | $P$   |
|----------------------|------------------------|------------------------|-------|
| Z scores (Abd. Aorta)| -0.24 ± 1.12           | -1.73 ± 0.63           | .001  |
| CIMT                 | 0.58 ± 0.06            | 0.53 ± 0.06            | .448  |
| Aortic strain        | 10.9 ± 7.4             | 8.9 ± 8.8              | .109  |
| Aortic SI            | 11.5 ± 8.4             | 6.2 ± 4.1              | .007  |
| Aortic Dis           | 18.5 ± 6.1             | 20.9 ± 5.5             | .206  |
| FMD (firstmin) (%)   | 4.5 ± 2.7              | 6.9 ± 4.5              | .005  |
| FMD (thirdmin) (%)   | 9.2 ± 3.8              | 9.35 ± 3.9             | .604  |

Abd. Aorta, abdominal aorta; CIMT, carotid–intima–media thickness; SI, stiffness index; Dis, distensibility; FMD, flow-mediated dilatation.

*Mann–Whitney U test.*
was significantly higher and arterial distensibility was insignificantly lower in the patient group compared to the control group. Another adult study involving 30 postoperative coarctation patients without hypertension and 28 patients with hypertension identified arterial hypertension as a risk factor for increased arterial stiffness. The result from this study may be associated with the patients being younger and the short-term follow-up period. On the other hand, aging is known to have a strong effect on arterial functional properties. Some adult studies reported that the aorta more rapidly stiffens with aging. In the present study, similar to some other studies, we found that the distensibility of abdominal aorta was higher and arterial stiffness was lower in the younger group.

Increased CIMT is another marker of atherosclerosis in adults and adolescents. Previous studies have demonstrated that early structural vascular alterations lead to atherosclerosis due to ongoing subclinical inflammation. Most scientists believe that these alterations are outcomes of acute dysfunction of the endothelium and inflammation of the vascular wall. Carotid–intima–media thickness has been higher in the patient group compared to the control group in the present study, although the difference was not statistically significant. Previous studies have suggested that CIMT increases with age and the advance of atherosclerosis. However, we could not find a significant correlation between CIMT and age. These results may be associated with the relatively small number of patients and the short-term follow-up period.

Flow-mediated dilatation is an early endothelium-dependent marker of endothelial dysfunction and may be associated with an increased inflammatory process involving the endothelium and a useful indicator of atherosclerosis. Flow-mediated brachial artery dilatation in the first minute decreased significantly in patients with coarctation repair, but FMD decreased insignificantly in the third minute. Cohen et al showed that age at the time of surgical repair was the most significant predictor of hypertension and long-time survival, with the best outcomes analyzed in patients undergoing surgery before the age of 9 years. However, our study showed no relationship between the risk factors such as operation time, age and FMD.

**CONCLUSION**

This study has certain limitations. The number of children and the postoperative follow-up period were not adequate to evaluate increasing risk of atherosclerotic CVD. Therefore, there is a need for comprehensive studies with larger numbers of patients with longer follow-up periods.

Although successful coarctation repair was efficient in reducing pressure gradient and in controlling systemic arterial hypertension, it may not be able to prevent the structural and functional damage of features of the peripheral arteries, such as arterial stiffness, FMD, and CIMT. This result of arterial elasticity suggested that children exhibit detectable vascular wall changes following coarctation repair, which may start and progress toward overt atherosclerosis at older ages. Close monitoring for systemic hypertension, LVH, and recurrence of coarctation, early medical treatment or timely re-intervention, and elimination of other preventable risk factors for atherosclerotic heart disease will improve long-term results in this patient group.
E.E., B.Ş.C.; Analysis and/or Interpretation – N.Ç., B.Ş.C., N.B.H.; Literature Review – N.Ç., E.E., N.B.H.; Writing Manuscript – N.Ç., F.A.; Critical Review- F.A., N.Ç.

**Conflict of Interest:** The authors have no conflict of interest to declare.

**Financial Disclosure:** The authors declared that this study has received no financial support.

**REFERENCES**

1. Freed MD, Rocchini A, Rosenthal A, Nadas AS, Castaneda AR. Exercise-induced hypertension after surgical repair of coarctation of the aorta. *Am J Cardiol*. 1979;43(2):253-258. [CrossRef]

2. Cohen M, Fuster V, Steele PM, Driscoll D, McGoon DC. Coarctation of the aorta: long-term follow-up and prediction of outcome after surgical correction. *Circulation*. 1989;80(4):840-845. [CrossRef]

3. Anderson R, Baker EJ, Macartney FJ, Rigby ML, Shinebourne EA, Tynan M, eds. *Paediatric Cardiology*. 2nd ed. London: Churchill Livingstone; 2002.

4. Bower C, Ramsay JM. Congenital heart disease: a 10-year cohort. *J Paediatr Child Health*. 1994;30(5):414-418. [CrossRef]

5. Samánek M, Vórivsková M. Congenital heart disease among 815,569 children born between 1980 and 1990 and their 15-year survival: a prospective Bohemia survival study. *Pediatr Cardiol*. 1999;20(6):411-417. [CrossRef]

6. Clarkson PM, Nicholson MR, Barratt-Boyes BG, Neutze JM, Whitelock RM. Results after repair of coarctation of the aorta beyond infancy: a 10 to 28 year follow-up with particular reference to late systemic hypertension. *Am J Cardiol*. 1983;51(9):1481-1488. [CrossRef]

7. Tanous D, Benson LN, Horlick EM. Coarctation of the aorta: evaluation and management. *Curr Opin Cardiol*. 2009;24(6):509-515. [CrossRef]

8. de Divitiis M, Rubba P, Calabrò R. Arterial hypertension and cardiovascular prognosis after successful repair of aortic coarctation: a clinical model for the study of vascular function. *Nutr Metab Cardiovasc Dis*. 2005;15(5):382-394. [CrossRef]

9. Corretti MC, Anderson TJ, Benjamin EJ, et al. Guidelines for the ultrasound assessment of endothelial-dependent flow-mediated vasodilation of the brachial artery: a report of the International Brachial Artery Reactivity Task Force. *J Am Coll Cardiol*. 2002;39(2):257-265. [CrossRef]

10. Kadono T, Sugiyama H, Hoshiai M, et al. Endothelial function evaluated by flow-mediated dilatation in pediatric vascular disease. *Pediatr Cardiol*. 2005;26(4):385-390. [CrossRef]

11. O’Rourke MF, Staessen JA, Vlachopoulos C, Duprez D, Plante GE. Clinical applications of arterial stiffness: definitions and reference values. *Am J Hypertens*. 2002;15(5):426-444. [CrossRef]

12. Touboul PJ, Hennerici MG, Meairs S, et al. Mannheim carotid intima-media thickness and plaque consensus (2004-2006-2011). An update on behalf of the advisory board of the 3rd, 4th and 5th watching the risk symposia, at the 13th, 15th and 20th European Stroke Conferences, Mannheim, Germany, 2004, Brussels, Belgium, 2006, and Hamburg, Germany, 2011. *Cerebrovasc Dis*. 2012;34(4):290-296. [CrossRef]

13. Lorenz MW, Markus HS, Bots ML, Rosvall M, Sitzer M. Prediction of clinical cardiovascular events with carotid intima-media thickness: a systematic review and meta-analysis. *Circulation*. 2007;115(4):459-467. [CrossRef]

14. Devereux RB, Alonso DR, Lutas EM, et al. Echocardiographic assessment of left ventricular hypertrophy: comparison to necropsy findings. *Am J Cardiol*. 1986;57(6):450-456. [CrossRef]

15. Sahin DJ, DeMaria A, Kisslo J, Weyman A. The committee on M-mode standardization of the American Society of Echocardiography: results of a survey of echocardiographic measurements. *Circulation*. 1978;58(6):1072-1083. [CrossRef]

16. Lacombe F, Dart A, Dewar E, Jennings G, Cameron J, Laufer E. Arterial elastic properties in man: a comparison of echo-Doppler indices of aortic stiffness. *Eur Heart J*. 1992;13(8):1040-1045. [CrossRef]

17. Järvisalo MJ, Rönnergård L, Volanen I, et al. Brachial artery dilatation responses in healthy children and adolescents. *Am J Physiol Heart Circ Physiol*. 2002;282(1):H87-H92. [CrossRef]

18. Wendelhag I, Gustavsson T, Suurküla M, Berglund G, Wikström J. Ultrasound measurement of wall thickness in the carotid artery: fundamental principles and description of a computerized analysing system. *Clin Physiol*. 1991;11(6):565-577. [CrossRef]

19. Riley WA, Evans GW, Sharrett AR, Burke GL, Barnes RW. Variation of common carotid artery elasticity with intimal-medial thickness: the ARIC Study. *Atherosclerosis Risk in Communities. Ultrasound Med Biol*. 1997;23(2):157-164. [CrossRef]

20. Toro-Salazar OH, Steinberger J, Thomas W, Rocchini AP, Carpenter B, Moller JH. Long-term follow-up of patients after coarctation of the aorta repair. *Am J Cardiol*. 2002;89(5):541-547. [CrossRef]

21. Oliver JM, Gallego P, Gonzalez A, Aroca A, Bret M, Mesa JM. Risk factors for aortic complications in adults with coarctation of the aorta. *J Am Coll Cardiol*. 2004;44(8):1641-1647. [CrossRef]

22. Heger M, Willfort A, Neunteufel T, et al. Vascular dysfunction after coarctation repair is related to the age at surgery. *Int J Cardiol*. 2005;99(2):295-299. [CrossRef]

23. Seirafl PA, Warner KG, Geggel RL, Payne DD, Cleveland RJ. Repair of coarctation of the aorta during infancy minimizes the risk of late hypertension. *Ann Thorac Surg*. 1998;66(4):1378-1382. [CrossRef]

24. Conte S, Lacour-Gayet F, Serraf A, et al. Surgical management of neonatal coarctation. *J Thorac Cardiovasc Surg*. 1995;109(4):663-674; discussion 674-675. [CrossRef]

25. Chobanian AV, Lichtenstein AH, Nilakhe V, Haudenschild CC, Drago R, Nickerson C. Influence of hypertension on aortic atherosclerosis in the Watanabe rabbit. *Hypertension*. 1989;14(2):203-209. [CrossRef]

26. Cook SC, Ferketich AK, Raman SV. Myocardial ischemia in asymptomatic adults with repaired aortic coarctation. *Int J Cardiol*. 2009;133(1):95-101. [CrossRef]

27. Swan L, Kraidly M, Vonder Mühll I, Collins P, Gatzoulis MA. Surveillance of cardiovascular risk in the normotensive patient with repaired aortic coarctation. *Int J Cardiol*. 2010;139(3):283-288. [CrossRef]

28. Forbes TJ, Moore P, Pedra CA, et al. Intermediate follow-up following intravascular stenting for treatment of coarctation of the aorta. *Catheter Cardiovasc Interv*. 2007;70(4):569-577. [CrossRef]

29. Swan L, Ashrafian H, Gatzoulis MA. Repair of coarctation: a higher goal? *Lancet*. 2002;359(9310):977-978. [CrossRef]

30. Van Popel NE, Grobbbee DE, Bots ML, et al. Association between arterial stiffness and atherosclerosis: the Rotterdam Study. *Stroke*. 2001;32(2):454-460. [CrossRef]

31. Nollen GJ, Meijboon LJ, Groenink M, et al. Comparison of aortic elasticity in patients with the Marfan syndrome with and without aortic root replacement. *Am J Cardiol*. 2003;91(5):637-640. [CrossRef]

32. Mahmud A, Feely J. Arterial stiffness is related to systemic inflammation in essential hypertension. *Hypertension*. 2005;46(5):1118-1122. [CrossRef]

33. Rög B, Okálska M, Dziezicz-Oleksy H, et al. Arterial stiffness in adult patients after coarctation of aorta repair and with bicuspid aortic valve. *Acta Cardiol*. 2019;74(6):517-524. [CrossRef]

34. Ciccone MM, Bilianou E, Balbarini A, et al. Task force on: ‘Early markers of atherosclerosis: influence of age and sex’. *J Cardiovasc Med*. 2013;14(10):757-766. [CrossRef]

35. Paini A, Bouthuyrie P, Calvet D, Tropeano AI, Laloux B, Laurent S. Carotid and aortic stiffness: determinants of discrepancies. *Hypertension*. 2006;47(3):371-376. [CrossRef]
36. McEniery CM, Yasmin HIR, Hall IR, et al. Normal vascular aging: differential effects on wave reflection and aortic pulse wave velocity: the Anglo–Cardiff Collaborative Trial (ACCT). J Am Coll Cardiol. 2005;46(9):1753-1760. [CrossRef]

37. Poredos P. Intima-media thickness: indicator of cardiovascular risk and measure of the extent of atherosclerosis. Vasc Med. 2004;9(1):46-54. [CrossRef]

38. Ishizu T, Ishimitsu T, Yanagi H, et al. Effect of age on carotid arterial intima-media thickness in childhood. Heart Vessels. 2004;19(4):189-195. [CrossRef]

39. Park SH, Chung JW, Lee JW, Han MH, Park JH. Carotid artery involvement in Takayasu’s arteritis: evaluation of the activity by ultrasonography. J Ultrasound Med. 2001;20(4):371-378. [CrossRef]

40. Peru H, Altun B, Doğan M, Kara F, Elmaci AM, Oran B. The evaluation of carotid intima-media thickness in children with familial Mediterranean fever. Clin Rheumatol. 2008;27(6):689-694. [CrossRef]

41. Howard G, Sharrett AR, Heiss G, et al. Carotid artery intimal-medial thickness distribution in general populations as evaluated by B-mode ultrasound. ARIC Investigators. Stroke. 1993;24(9):1297-1304. [CrossRef]

42. Brili S, Tousoulis D, Antoniades C, et al. Evidence of vascular dysfunction in young patients with successfully repaired coarctation of aorta. Atherosclerosis. 2005;182(1):97-103. [CrossRef]