Peripheral Blood Flow Responses to Exercise After Successful Correction of Coarctation of the Aorta

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Objectives. The purpose of this study was to characterize peripheral flow kinetics in response to progressive discontinuous maximal exercise in 10 patients who underwent repair of coarctation of the aorta and 11 age-matched healthy adolescents.

Background. An impairment of leg blood flow has been suggested on the basis of exaggerated femoral muscle lactate accumulation in patients with successful repair of coarctation. Few data are available describing blood flow kinetics of the exercising leg in such patients.

Methods. Duplex ultrasound provided transcutaneous measurements of peak systolic and end-diastolic flow velocities of the femoral, humeral and renal arteries at rest and immediately after mild, moderate and maximal exercise intensities for computation of mean velocity, resistance index and femoral blood flow.

Results. Femoral mean velocity and femoral blood flow increased linearly with exercise intensity in both groups, but the slope of this increase was significantly lower in patients. Similarly, humeral mean velocity increased significantly less in patients than in control subjects. Femoral resistance index sharply decreased from that at rest (patients [mean ± SE] 1.4 ± 0.04; control subjects 1.4 ± 0.03) to mild exercise intensity in both groups (patients 0.69 ± 0.03; control subjects 0.72 ± 0.03). A further decrease was observed at maximal exercise in patients (0.60 ± 0.04, p = 0.08) but not in control subjects (0.69 ± 0.02).

Conclusions. These observations suggest that despite a greater exercise-induced femoral vasodilation, patients with successful correction of coarctation of the aorta demonstrate an impaired lower limb blood flow in response to strenuous dynamic exercise. In the absence of stenosis at rest, this alteration could result from exaggerated flow turbulence in the descending aorta distal to the site of correction because of loss of elasticity at the site of the resection of the coarcted segment.

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Despite successful surgical repair of coarctation of the aorta, abnormal upper and lower limb arterial pressure responses to pharmacological challenges and dynamic exercise have been reported (1–4). Thus, even in the absence of significant residual coarctation or recoarctation, upper limb blood pressure determinations have provided evidence for postoperative hypertension in 10% to 30% of patients at rest and in 30% to 65% of patients during exercise (5–8). Furthermore, in patients with an absent gradient at rest, an arm–leg blood pressure gradient has been reported during moderate and intensive dynamic exercise (1,4,9,10). Possible mechanisms for the observed hypertension include exaggerated peripheral vasoconstrictor tone, hyperdynamic cardiac output or a combination of both (11–15). Hyperkinetic ventricular systolic function has also been reported both at rest and during dynamic exercise (13,14) in patients with successful correction of coarctation of the aorta and was found to persist even after a postoperative period of 2 to 27 years (15). Abnormal vascular reactivity in resistance vessels anatomically positioned proximal to the site of coarctation of the aorta has also been reported using both xenon-133 clearance (11) and venous occlusion plethysmography (16).

There is to date little information concerning the peripheral limitations to exercise in these patients. A potential impairment in leg blood flow during dynamic exercise has previously been suggested (17) on the basis of plasma and muscle lactate determinations showing exaggerated muscle lactate accumulation in the exercising limb of men with successful correction of coarctation of the aorta in childhood. However, there is, to our knowledge, no report of upper and lower limb flow kinetics in response to exercise in patients with successful correction of coarctation of the aorta. The purpose of the present investigation was therefore to evaluate peripheral blood flow kinetics in response to submaximal and maximal exercise in a group of patients with successful correction of coarctation of the aorta in excellent clinical condition and in a group of healthy age-matched control subjects.

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Methods

Subjects. Patients were recruited from a cohort of children regularly followed up at our pediatric cardiology unit. The research protocol was approved by the research committee of our institution, and all participants gave written informed consent to participate in the study (parental consent was obtained for subjects <18 years old). A group of 10 patients (8 boys, 2 girls) with successful correction of coarctation of the aorta were investigated (mean [±SE] age 15.0 ± 1.4 years, range 8 to 21). The operation had been carried out at a mean age of 4.5 ± 1.14 years, resulting in a mean postsurgical period of 9.3 ± 1.5 years. No patient had associated intracardiac defects or any signs of aortic restenosis, as determined by physical examination, upper and lower limb blood pressure measurement or electrocardiographic (ECG) and echocardiographic evaluations. Asymptomatic control subjects were 11 healthy children (8 boys, 3 girls) closely matched for age (patients 15.0 ± 1.4 years old, control subjects 16.7 ± 1.6 years old) and body surface area (patients 1.51 ± 0.1 cm², control subjects 1.58 ± 0.08 cm²).

Surgical repair was performed by means of angioplasty in six patients and end-to-end anastomosis in four. Echocardiographic examination revealed a pressure gradient across the site of coarctation repair (isthmus) of <25 mm Hg in nine patients, and 1 patient had a gradient of 35 mm Hg. An arm–leg pressure gradient >15 mm Hg measured by sphygmomanometry was found in only one patient (20 mm Hg). All patients were normotensive at rest.

Experimental protocol. Each test took place in an air-conditioned laboratory, where room temperature was maintained between 19 and 23°C. Subjects presented to the laboratory in a 2-h postprandial state. They rested in the supine position for 30 min before evaluation of arterial flow velocity in the femoral, humeral and renal arteries, in that order. Posterior tibial and brachial artery systolic pressure were then measured by Doppler.

Supine cycling exercise was performed using a Quinton cardiac stress table, with the head of the patient resting at an angle of 20° from horizontal. A discontinuous graded exercise protocol was used to allow recording of blood flow kinetics immediately on release of cycling resistance. Subjects performed two 5-min submaximal work loads of mild and moderate intensities, respectively, and a final maximal exercise session. Submaximal work loads were set to achieve ~45% to 55% (mild) and 70% to 80% (moderate) of maximal predicted heart rate, respectively. After exercise, Doppler evaluation was performed in the following order: femoral flow, tibial and brachial systolic pressures, humeral and renal artery velocity waveforms. All recordings were obtained with subjects in the supine position and were completed within 3 min of exercise termination.

Upper limb arterial blood pressure was obtained with a mercury sphygmomanometer with a cuff of appropriate size in the supine position, before exercise as well as during the last minute of each work load. Right posterior tibial and brachial systolic pressures were also measured using a transcutaneous Doppler probe before exercise and within 1 min of completing each work load. Heart rate was obtained from a continuous ECG recording.

Blood flow kinetics. Transcutaneous arterial blood flow was evaluated by a well trained investigator using a Hewlett-Packard Sonos 100 transcutaneous Doppler ultrasound, which allows determination of vessel diameter as well as instantaneous and mean blood flow velocities (18,19). A 3.5-MHz scanhead transducer was used for Doppler and two-dimensional echocardiographic imaging of the renal artery. A 5.0-MHz transducer was used for the humeral and femoral arteries. Velocity waveform information was videotaped for later analyses. All measurements were made over three successive cardiac cycles and averaged to provide a single value for each observation period. Coefficients of intraobserver and interobserver variability were obtained from two observers for six different subjects under all conditions. For peak systolic and end-diastolic velocities, these ranged from 1.5% to 4% under both rest and exercise conditions.

Figure 1 illustrates a Doppler femoral recording at rest with its corresponding two-dimensional echocardiographic image. Peak systolic velocity was taken as the maximal positive incursion of the velocity waveform. Protodiastole was taken as the maximal negative incursion of the velocity waveform. End-diastolic velocity was taken as the difference between protodiastole and the minimal positive incursion of the velocity waveform. In the absence of a negative protodiastolic velocity, such as found in response to exercise, end-diastolic velocity was taken as the minimal positive incursion. The velocity–time integral was calculated automatically as the area under the entire defined waveform curve. Mean flow velocity (cm/s) was calculated as the velocity–time integral corrected for the corresponding RR interval, multiplied by 1/cos θ, where θ is the angle between the Doppler probe and the vessel. Electromechanical delay was calculated as the time (ms) between the Q wave of the ECG and the onset of the Doppler waveform.
Femoral diameter measurements were obtained from the longitudinal two-dimensional ultrasound image as the distance between the anterior and posterior “m” lines (the interface between media and adventitia) at end-diastole, incident with the R wave on the ECG. Great care was taken in obtaining the longitudinal view with the maximal possible diameter. The average of three diameter measurements was obtained with a coefficient of variation <5% along a segment measuring at least 1 cm. Femoral diameter measurements were obtained simultaneously with each measurement of velocity. The coefficients of interassay and intraassay variability were, respectively, 2.3% and 3.0% for rest femoral diameter and 2.4% and 3.5% for exercise femoral diameter. After the determination of femoral diameter and mean flow velocity (mVel), femoral blood flow (ml/min) was calculated as \( \frac{\pi D^2}{4} \times mVel \times 60 \) s, where \( D \) is the diameter of the femoral artery. Resistance index was calculated by subtracting end-diastolic velocity from peak systolic velocity, corrected for peak systolic velocity (20).

### Statistical analyses
All dependent variables are expressed as mean value ± SE. The Student t test was used for comparison of mean values of electromechanical delay, mean velocity, resistance indexes, blood flow and arterial blood pressure between control and patient groups. Comparison for these variables between rest and sequential exercise intensities or arteries were achieved through multivariate analysis of variance followed by simple main-effects analysis of variance when a significant interaction between group, exercise level or arteries was found. Post hoc analyses (Scheffé multiple-range test) were carried out to isolate specific differences related to arteries, groups or exercise intensity. All statistical analyses were performed using the SAS (Statistical Analysis System) statistical package (SAS Institute). Statistical significance was set at \( p < 0.05 \).

### Results
Similar maximal work loads were achieved in patients (162 ± 19 W) and control subjects (156 ± 12 W). Similar absolute submaximal work loads were also achieved in both groups for mild (patients 57 ± 6 W, control subjects 64 ± 4 W) and moderate exercise intensity (patients 93 ± 10 W, control subjects 114 ± 8 W).

### Heart rate and blood pressure responses
Individual heart rate and blood pressure responses to exercise are shown in Table 1. Rest systolic and diastolic blood pressures, measured by sphygmomanometry, were not significantly different between groups (patients 125 ± 3/71 ± 4 vs. control subjects 121 ± 4/73 ± 3 mm Hg). Exercise significantly increased

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Table 1. Doppler Systolic Blood Pressure and Heart Rate Measurements at Rest and During Exercise

<table>
<thead>
<tr>
<th>No./Gender</th>
<th>Age (yr)</th>
<th>Humeral Artery (mm Hg)</th>
<th>Tibial Artery (mm Hg)</th>
<th>Humeral/Tibial Ratio</th>
<th>Heart Rate (bpm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Rest Mild Mod Max</td>
<td>Rest Mild Mod Max</td>
<td>Rest Mild Mod Max</td>
<td>Rest Mild Mod Max</td>
</tr>
<tr>
<td>1/M</td>
<td>12</td>
<td>110 120 120 130</td>
<td>115 130 120 130</td>
<td>1.18 1.25 1.21 1.12</td>
<td>72 122 144 192</td>
</tr>
<tr>
<td>2/M</td>
<td>15</td>
<td>115 130 120 130</td>
<td>130 140 160 135</td>
<td>1.13 1.08 1.33 1.04</td>
<td>72 109 126 177</td>
</tr>
<tr>
<td>3/F</td>
<td>14</td>
<td>110 125 130 130</td>
<td>120 130 115 85</td>
<td>1.09 1.04 0.88 0.65</td>
<td>68 100 130 176</td>
</tr>
<tr>
<td>4/F</td>
<td>11</td>
<td>130 140 120 135</td>
<td>140 125 105 110</td>
<td>1.08 0.89 0.88 0.81</td>
<td>96 152 189 179</td>
</tr>
<tr>
<td>5/F</td>
<td>14</td>
<td>125 130 140 145</td>
<td>130 140 135 125</td>
<td>1.04 1.08 0.96 0.78</td>
<td>61 125 143 182</td>
</tr>
<tr>
<td>6/M</td>
<td>16</td>
<td>150 135 135 190</td>
<td>120 130 132 85</td>
<td>0.80 0.96 0.97 0.45</td>
<td>55 123 150 194</td>
</tr>
<tr>
<td>7/M</td>
<td>21</td>
<td>115 130 140 145</td>
<td>125 130 115 110</td>
<td>1.09 1.00 0.82 0.76</td>
<td>80 119 145 169</td>
</tr>
<tr>
<td>8/M</td>
<td>8</td>
<td>125 130 130 164</td>
<td>130 140 120 125</td>
<td>1.04 1.08 0.92 0.76</td>
<td>91 137 192 163</td>
</tr>
<tr>
<td>9/M</td>
<td>22</td>
<td>115 130 140 150</td>
<td>140 155 150 145</td>
<td>1.22 1.15 1.07 0.97</td>
<td>49 94 128 167</td>
</tr>
<tr>
<td>10/M</td>
<td>21</td>
<td>135 140 155 130</td>
<td>140 140 115 115</td>
<td>1.04 1.00 0.74 0.88</td>
<td>87 142 186 197</td>
</tr>
<tr>
<td>Mean</td>
<td>15</td>
<td>125* 132* 133* 146*</td>
<td>131* 138 129 118*</td>
<td>1.07* 1.05* 0.98* 0.82*</td>
<td>75 121† 154† 178†</td>
</tr>
<tr>
<td>SEM</td>
<td>1.4</td>
<td>4.0 2.0 3.6 6.3</td>
<td>2.4 3.0 5.7 6.8</td>
<td>0.04 0.03 0.06 0.06*</td>
<td>5.0 6.5 9.2 3.7</td>
</tr>
</tbody>
</table>

* p ≤ 0.05 versus control subjects (Ctrls); † p ≤ 0.05 versus rest value. F = female; M = male; Max = maximal exercise; Mild = mild exercise; Mod = moderate exercise; Pts = patients.
systolic blood pressure from rest in both patients and control subjects. Doppler humeral systolic pressure values were higher in patients at rest as well as for any given level of exercise, but statistical significance between groups was reached only at mild exercise intensity. However, rest tibial systolic pressure was significantly lower in patients than control subjects. Exercise tended to decrease tibial systolic pressure in patients but not in control subjects, leading to a significant difference between groups. The tibial/humeral systolic pressure ratio remained >1.0 for all exercising conditions in control subjects but decreased significantly in patients. Heart rate values were similar in both groups under all conditions.

**Blood flow kinetics.** As expected, electromechanical delay was significantly less in proximal than in distal arteries and was significantly reduced by exercise.

A significant increase in femoral peak systolic velocity was found in both groups in response to exercise (data not shown). However, at maximal exercise, patients had lower values than control subjects (124.1 ± 9.4 vs. 157.7 ± 9.8, respectively, p < 0.05). Similarly, significant increases were found for humeral but not for renal peak systolic velocities in response to exercise. Renal systolic peak velocity was significantly lower in patients than in control subjects at rest as well as in response to mild and moderate exercise intensities (p < 0.05).

Figure 2 illustrates the relation between exercise work load and mean flow velocity of the femoral artery. A linear progressive increase in mean flow velocity with increasing exercise intensity was found in both groups. However, the slope, m, of the work load–velocity relation was significantly steeper in control subjects (m = 0.56) than in patients (m = 0.38, p < 0.01). Similarly, the magnitude of change in humeral mean flow velocity with increasing exercise intensity was slightly lower in patients than in control subjects (m = 0.06 vs. 0.11, p < 0.05). Values of mean flow velocity for the renal artery remained unchanged in response to exercise, and differences between groups were not observed.

A significant increase in femoral blood mean flow velocity was observed in response to mild and moderate exercise in both patients and control subjects (Fig. 3), reaching a sixfold increase in patients and a ninefold increase after maximal exercise. However, although values increased continuously from rest to maximal exercise in control subjects, a plateau was reached at moderate exercise in patients, leading to a significant difference between groups at maximal exercise intensity.

Femoral resistance sharply decreased from rest to mild exercise intensity in both groups (patients 1.4 ± 0.04 vs. 0.69 ± 0.03; control subjects 1.4 ± 0.04 vs. 0.72 ± 0.03). In control subjects, no further decrease was observed for higher exercise intensities, but in patients, a slight continuous decrease was found with increasing work load (0.60 ± 0.04), leading to a significant difference between groups after moderate and maximal exercise.

The resistance index of the humeral and renal arteries was not significantly different between groups at rest or during exercise, although values appeared to be systematically lower in patients. Resistance index was not modified in response to exercise for the humeral artery, but for the renal artery it increased significantly in both groups (patients 0.54 ± 0.01 vs. 0.68 ± 0.04, respectively, p < 0.05).
[humeral artery] vs. 0.59 ± 0.01 [renal artery]; control subjects 0.58 ± 0.02 [humeral artery] vs. 0.63 ± 0.02 [renal artery]).

Discussion

Blood flow impairment in patients with successful correction of coarctation of the aorta. Results from the present investigation demonstrate an impairment in femoral blood flow to a short session of strenuous exercise in patients with successful correction of coarctation of the aorta in childhood, resulting in a decrease in tibial artery pressure and a significant decrease in the tibial/brachial systolic pressure ratio. A decrease in the arm–leg systolic blood pressure gradient has commonly been reported (1,4,9,10) during dynamic exercise after complete repair of coarctation of the aorta. Potential explanations for this observation include restenosis of the descending aorta or abnormalities in lower limb blood flow distribution. In the present study, patients at rest did not show a significant gradient across the isthmus or a significant arm–leg systolic pressure gradient, suggesting that recoarctation of the aorta was not a predominant factor. A reduction in lower limb blood flow during cycling exercise has previously been suggested (17) in patients with successful correction of coarctation of the aorta on the basis of higher intramuscular lactate concentrations in the exercising leg of these patients despite a similar glycogen depletion pattern in both patients and control subjects. However, in the latter study, blood flow to the limbs was not measured, and the presence of aortic restenosis was not verified.

The present investigation confirms that blood flow distribution to the limbs is impaired during exercise in patients, as reflected by the lower slope of the femoral mean velocity–work load relation. In the absence of restenosis, the reason for this impairment could be related to hypoplasia of the transverse aortic arch, which has been reported (3,21,22) in some postoperative patients. However, such an abnormality was not detected in the present study.

This impairment could also be related to structural alterations of the descending aorta. A decrease in vascular reactivity of the aorta and an increase in the rigidity of the preocclusive aortic arch have been reported in patients undergoing correction of coarctation of the aorta (23). These findings were associated with an increase in collagen content and a reduction of the smooth muscle content of the aortic media proximal to the coarctation. Using echocardiography, Ong et al. (24) similarly reported a higher stiffness index of the transverse aortic arch up to 6 years after repair of coarctation.

Although under conditions of high blood flow velocity, such as during strenuous exercise, an increase in bloodstream turbulence is to be expected, a decrease in aortic wall elasticity at the site of the resection of the coarcted segment could create exaggerated flow turbulence, resulting in reduced distal flow velocity and lower limb blood flow. This result could explain the significantly lower femoral and renal peak systolic velocity and the lower femoral mean velocity presently observed in our patients.

In the present study, the slope of the increase in humeral mean velocity in response to increasing work load was also lower in patients. This finding is compatible with those reported by Samanez et al. (11) using Xenon-133 clearance showing maximal ischemic exercise blood flows to be lower and vascular resistance to be higher in the upper limbs of patients after successful surgical repair of aortic coarctation. These observations could be accounted for by the prolonged exposure of the precoarctation area to sustained hypertension before operation, leading to alterations in the structure of the media of the arterioles and a subsequent pathologic increase in vascular resistance (25,26).

Exercise-induced hypertension is a common finding after surgical repair of coarctation of the aorta (3,4,8–10,13,27–29). In the present study, no significant differences in brachial systolic or diastolic pressures could be observed between groups, although patients systematically exhibited slightly higher brachial systolic pressures. Balderston et al. (30) reported similar findings in patients with comparable characteristics (age at evaluation and operation as well as mean follow-up). The absence of exercise hypertension could be due to the relatively short postoperative period (9 years), an increase in the prevalence of hypertension being reported with a longer postoperative period (≥13 years) (31,32). Moreover, in the present study, great care was taken to include only patients with a perfect or near-perfect surgical result and residual acceptable gradients smaller than those in other studies (1,33).

Blood flow redistribution during dynamic exercise. Although the redistribution of cardiac output to working muscles during dynamic exercise is a well-documented phenomenon, there is still little information concerning the kinetics of blood flow distribution to working muscles and nonexercising limbs and the ensuing decrease in total peripheral resistance. Whereas femoral blood flow increased gradually in response to the progressively increasing work output, femoral resistance decreased immediately on initiation of exercise. This result is in agreement with recent determinations (34) of active leg blood flow kinetics during progressive dynamic cycling using exercise thallium-201 activity showing that the increase in leg blood flow occurred rapidly in response to progressive maximal exercise. This observation suggests that the regulation of vasmotor tone on initiation of exercise is not dependent on muscle chemoreflex activation related to the metabolic rate of active muscles. However, a chemoreflex response may be responsible for the subsequent progressive vasodilation found in patients in light of the reduced muscle perfusion and the ensuing accumulation of intramuscular metabolic factors.

Conclusions. The results of the present study suggest that despite greater exercise-induced femoral vasodilation, patients with successful correction of coarctation of the aorta demonstrate impaired lower limb blood flow after short intense supine dynamic exercise. In the absence of aortic stenosis at rest, this alteration could result from exaggerated flow turbulence in the descending aorta distal to the site of correction caused by aortic wall stiffness. These observations may have
practical implications for patients with successful correction of coarctation of the aorta, suggesting a potential limitation to exercise performance during activities of longer duration when additional circulatory demands are important for thermoregulatory purposes.

References


24. Ong CM, Canter CE, Gutierrez FR, Sekarski DR, Goldring DR. Increased stiffness and persistent narrowing of the aorta after successful repair of coarctation of the aorta: Relationship to left ventricular mass and blood pressure at rest and with exercise. Am Heart J 1992;123:1594-600.


