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Exercise-Induced Hypertension After Repair of Coarctation of the Aorta: Arm Versus Leg Exercise

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The etiology of exercise-induced upper limb hypertension after repair of coarctation of the aorta is unknown. We hypothesized that blood flow across the coarctation repair site is a major determinant of such exercise-induced hypertension. Because arm ergometry should produce a smaller increase in descending aortic blood flow than treadmill exercise, we compared the changes in upper limb pressure and the coarctation gradient produced by each type of exercise at equivalent levels of heart rate and peak oxygen consumption in 28 children with repaired coarctation of the aorta. The children were classified into three groups: Group I, resting gradient less than 15 mm Hg and treadmill gradient less than 20 mm Hg; Group II, resting gradient less than 15 mm Hg and treadmill gradient greater than 20 mm Hg; and Group III, resting gradient greater than or equal to 15 mm Hg. Twelve children with no heart disease served as control subjects. All children were exercised to exhaustion with 45 minutes' rest between the two exercise protocols. There were no differences in maximal heart rate and oxygen consumption between the two types of exercise.

In all groups, treadmill exercise produced a larger increase in arm systolic blood pressure and arm-leg gradient than did arm exercise. With treadmill exercise coarctation Groups II and III developed a greater rise in both arm-leg gradient and arm systolic pressure than was observed in the control subjects ($p < 0.05$). However, with arm exercise, Group III developed a significantly greater rise in both arm pressure and arm-leg gradient ($p < 0.05$) than was observed in the control subjects. Angiography was performed in six patients from Group II and seven patients from Group III and disclosed that patients in Group III had a significantly smaller ratio of the coarctation repair site to the abdominal descending aorta (0.80 ± 0.08 [Group II] versus 0.39 ± 0.08 [Group III]) ($p < 0.05$). Our data, therefore, suggest that upper limb hypertension with treadmill exercise is due to a marked increase in descending aortic blood flow across a mild to moderately narrowed coarctation repair site.

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Upper limb hypertension during exercise has been well documented in children with repaired coarctation of the aorta (1–4). In some patients, the hypertension is clearly related to residual or recurrent coarctation. In others, however, the cause of the postoperative upper limb hypertension is less clear. Because the pressure gradient across an anatomic stenosis is determined by both the cross-sectional area and the flow across the stenosis, the regulation of descending aortic blood flow during exercise must be critical to the pathogenesis of exercise-induced upper limb hypertension.

The circulatory response to exercise varies with the type of work and the muscle group involved. In particular, maximal cardiac output has been reported to be lower during arm work when compared with leg work, whereas the maximal heart rate, systolic blood pressure and rate-pressure product are similar or only slightly lower during arm exercise (5–7). Bevegard et al. (7) also demonstrated that peripheral vascular resistance is significantly higher during arm work than during leg work. On the basis of these observations, and because with exercise the resistance vessels dilate in the active muscles and constrict in the inactive muscles (8–10), it seems likely that descending aortic blood flow should be less with arm exercise than with leg exercise. The present study was, therefore, designed to compare the cardiovascular responses to arm ergometry with treadmill

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exercise in a group of children with repaired coarctation of the aorta. In particular, we were interested in comparing the magnitude of both upper limb hypertension and arm-leg pressure gradient induced by these two types of exercise.

Methods

Patients. The study population for this investiation consisted of 28 children, 21 male and 7 female, with surgical repair of coarctation of the aorta. They ranged in age from 8 to 20 years (mean 13.8 ± 2.8) and had undergone repair of their coarctation 1 to 12 years (mean 4.1 ± 3.7) earlier. Repair of the coarctation was performed at age 5 days to 14 years (median 6 years) and consisted of excision and end to end anastomosis in 14 and patch angioplasty in 14. All of the patients had thoracic coarctation without significant associated cardiac anomalies. No patient had symptoms referrable to the cardiovascular system and none were receiving any antihypertensive medication at the time of this study.

The children were classified into the following three groups depending on the peak systolic gradient at rest and maximal treadmill exercise gradient: Group I, seven children with a good surgical repair (rest arm-leg systolic gradient of <15 mm Hg) and little change in gradient with treadmill exercise (peak systolic gradient of <20 mm Hg); Group II, nine children with a good surgical repair (rest arm-leg systolic gradient of <15 mm Hg) and a large change in gradient with treadmill exercise (peak systolic gradient ≥20 mm Hg); and Group III, 12 children with a poor surgical repair (rest arm-leg systolic gradient of ≥15 mm Hg). There were no significant differences among the groups with regard to age at surgery, years postoperative or type of surgery performed. Because in our institution children are not catheterized after repair of coarctation unless reoperation is thought to be necessary, only 13 of the 28 patients (6 of 9 in Group II and 7 of 12 in Group III) have undergone postoperative cardiac catheterization.

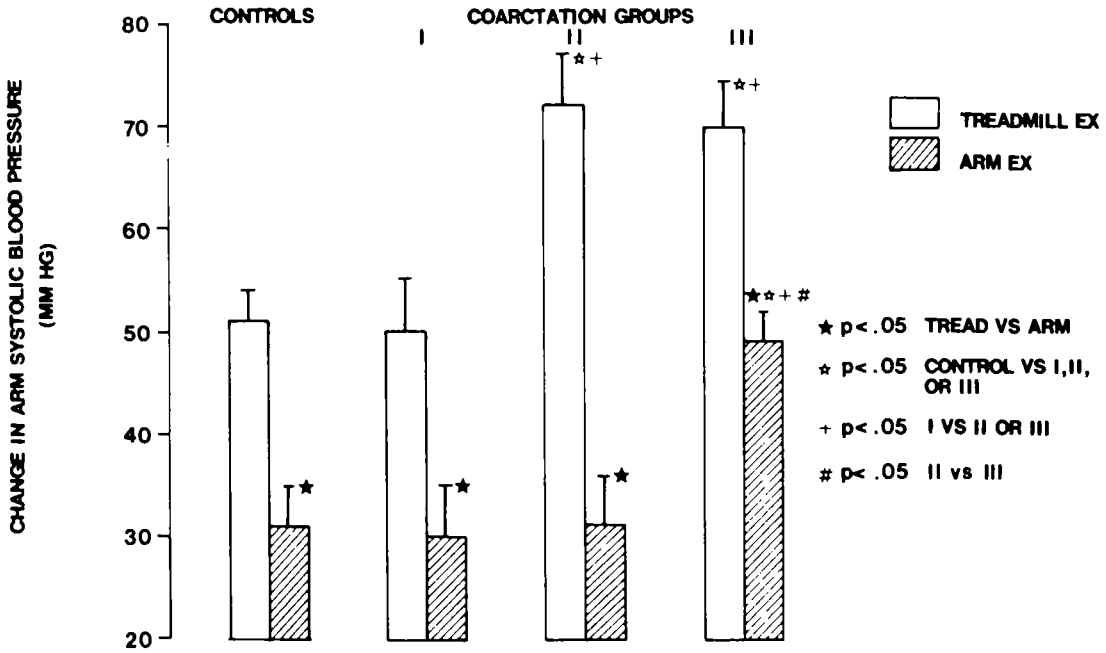
The control group consisted of 12 asymptomatic children (9 male and 3 female) with no hemodynamically significant heart disease. The control children ranged in age from 9 to 17 years (mean 14.0 ± 2.9).

Exercise testing. After informed consent was obtained, all children underwent both treadmill exercise and arm exercise in a random sequence. Between each exercise study the children rested in the sitting position for 45 minutes. All children were exercised to exhaustion on a motorized treadmill (Quinton) using the Bruce protocol (11). Arm exercise was performed using an electronically braked bicycle ergometer (Quinton). The arm ergometer was positioned so that the subject could arm pedal while seated upright with the feet flat on the floor. The ergometer height was adjusted so that the midpoint of the sprocket wheel was at shoulder height. All children were arm-exercised to exhaustion using the Fardy protocol (12) with discontinuous

Table 1. Rest and Exercise Data in Control and Coarctation Patients

	Control Patients	Coarctation Patients		
		Group I	Group II	Group III
No. of patients	12	7	9	12
Rest data				
HR	72 ± 8	78 ± 7	72 ± 11	75 ± 15
BP arm (syst/diast)	109 ± 12 / 60 ± 7	102 ± 15 / 64 ± 7	124 ± 18*† / 61 ± 11	126 ± 15*† / 63 ± 9
A-L	−9 ± 10.3	−9 ± 10	0 ± 11	24 ± 7*†‡
VO_2	5.9 ± 1.5	5.2 ± 0.8	5.1 ± 0.7	5.3 ± 1.1
Treadmill exercise				
Max HR	187 ± 8	194 ± 8	187 ± 17	176 ± 53
Max BP (syst/diast)	166 ± 20 / 58 ± 9	152 ± 19 / 61 ± 7	194 ± 28*† / 58 ± 12	196 ± 19*† / 59 ± 4
Max A-L	7 ± 7	10 ± 5	58 ± 12*†	59 ± 15*†
Max VO_2	42.6 ± 10	39.8 ± 4	42.9 ± 8.4	42.4 ± 9
Duration (min)	14.9 ± 2.2	13.6 ± 1.7	13.6 ± 4	14.0 ± 2.9
Arm exercise				
Max HR	173 ± 13	179 ± 8.6	174 ± 11	179 ± 8
Max BP (syst/diast)	146 ± 13 / 66 ± 10	139 ± 10 / 72 ± 11	159 ± 12*† / 72 ± 12	172 ± 11*‡ / 67 ± 8
Max A-L	−2 ± 12.4	−4 ± 14	11 ± 9‡	47 ± 8*†‡
Max VO_2	34.7 ± 10	34 ± 4.7	35 ± 6	36.6 ± 8
Duration (min)	17.8 ± 7.5	12.5 ± 4.0	14.9 ± 7.2	15.2 ± 6.3

* $p < 0.05$, control versus Group I, II or III; † $p < 0.05$, Group I versus II or III; ‡ $p < 0.05$, Group III versus II. A-L = systolic arm-leg pressure gradient (mm Hg); BP = blood pressure; BP arm = right arm blood pressure (mm Hg); diast = diastolic; HR = heart rate (beats/min); Max = values at maximal exercise; syst = systolic; VO_2 = oxygen consumption ($ml \cdot min^{-1} \cdot kg^{-1}$). Values are expressed as mean ± SD.



4 minute stages of increasing work load. The initial work load was 200 kp·m·min $^{-1}$ and each stage was increased 150 kp·m·min^{-1} with a 1 minute rest period between stages. A constant pedal speed of 60 rpm was maintained throughout the study.

Simultaneous supine blood pressures in the arm and leg were obtained at rest and within 1 minute of concluding both arm exercise and treadmill exercise. Blood pressure was measured over the right brachial artery with a Critikon Exercise Monitor (model 1165) using a cuff that occluded approximately two-thirds of the upper arm (13). Systolic pressure in the leg was obtained from the right posterior tibial artery with a Doppler flow probe, using a cuff that

Figure 1. Changes in arm systolic blood pressure with treadmill (TREAD) and arm exercise (EX). Treadmill exercise resulted in a larger increase in arm systolic blood pressure in all groups of children. When compared with the control group, coarctation Groups II and III developed a significantly larger increase in arm pressure with treadmill exercise, whereas with arm exercise only coarctation Group III developed a significantly larger increase in arm systolic pressure.

Figure 2. Changes in arm-leg systolic pressure gradient with exercise. When compared with the control group, coarctation Groups II and III developed a significantly greater increase in arm-leg systolic gradient with treadmill exercise, whereas only Group III developed a significantly larger increase in arm-leg pressure gradient. Abbreviations as in Figure 1.

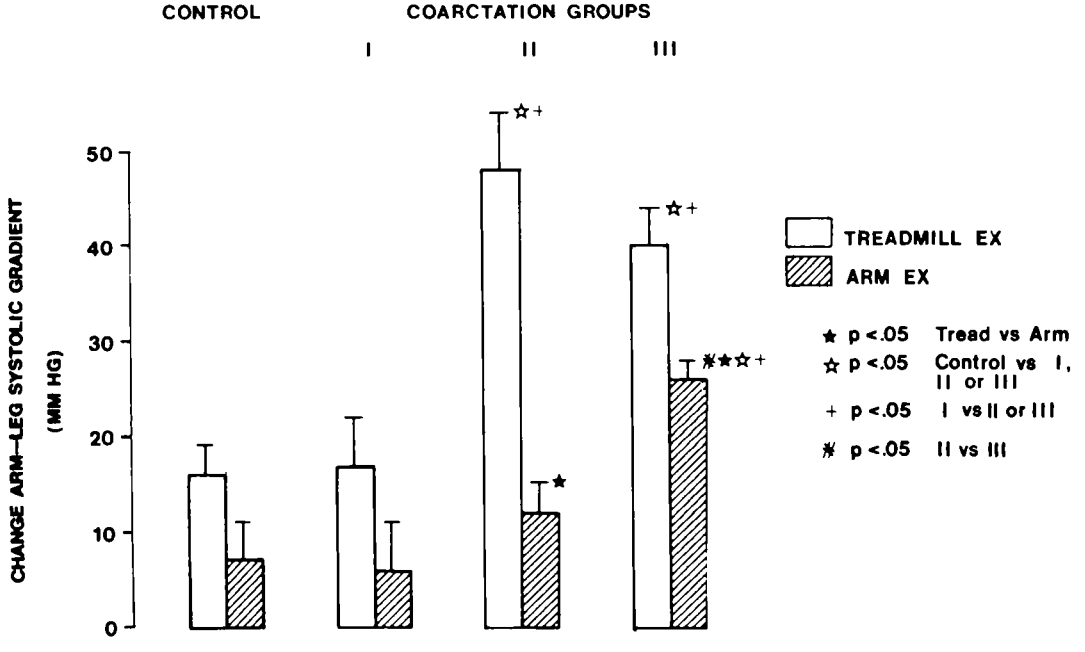


Table 2. Comparison of Hemodynamic and Angiographic Data With the Noninvasive Exercise Data in 13 Patients Who Underwent Cardiac Catheterization

	Noninvasive Exercise Data			Catheterization Data				
	ΔA-L Gradient (mm Hg)			At Rest			Supine Ex.	
Case	At Rest	Treadmill	Arm Ex.	BP AoAs (mm Hg)	ΔA-L (mm Hg)	CO (liters/min)	BP AoAs (mm Hg)	ΔA-L (mm Hg)
Group II								
1	14	77	10	130/72	2	4.6	194/95	52
2	12	38	16	142/78	13	6.9	190/100	48
3	10	45	16	158/78	14	6.8	212/110	60
4	7	90	22	148/82	10	7.5	195/110	58
5	6	86	15	128/83	5	9.4	175/100	55
6	8	52	10	153/101	3	4.4	199/102	45
Mean ± SD	10 ± 3	65 ± 22		143 ± 12 82 ± 9	8 ± 5	6.6 ± 1.9	194 ± 12 103 ± 6	53 ± 6
Group III								
7	24	73	58	140/90	33	5.7	210/100	60
8	45	74	56	130/72	32	5.5	165/120	40
9	35	64	45	133/78	29	4.7	192/110	54
10	22	60	36	140/59	20	6.2	—	—
11	28	65	48	138/75	25	5.8	—	—
12	20	58	54	123/70	22	7.2	—	—
13	24	71	55	128/60	25	5.7	—	—
Mean ± SD	28 ± 9*	66 ± 6	50 ± 8*	133 ± 6 74 ± 8	27 ± 5*	5.8 ± 0.8	189 ± 23 110 ± 10	51 ± 10

*$p < 0.05$, Group II versus III. A-L = arm to leg systolic pressure gradient; BP AoAs = ascending aortic blood pressure; CO = cardiac output; Ex. = exercise; Isuprel = isoproterenol; Repair Site DsAo = diameter of descending aorta at the coarctation repair site.

covered at least two-thirds of the calf (3). During treadmill exercise blood pressure in the arm was monitored during the third minute of each stage, while during arm exercise blood pressure in the arm was monitored immediately at the end of each stage. Leg blood pressure was measured only at the end of each type of exercise. Oxygen consumption was measured at rest and during the last 30 seconds of each form of exercise using a Douglas bag collection of expired air. Electrocardiographic leads II, aVF and V_5 were monitored at rest continuously during exercise and for 10 minutes after exercise.

Cardiac catheterization data. Thirteen patients underwent right and left heart catheterization under light sedation consisting of morphine sulfate (0.1 mg/kg, maximum 5 mg) and diphenhydramine (1 mg/kg, maximum 50 mg). Three catheters were placed percutaneously for pressure monitoring: a 7F thermodilution catheter in the right pulmonary artery, a 7F or 8F pigtail catheter in the ascending aorta and a 6F pigtail catheter in the descending thoracic aorta. After placement of all catheters, the patient was heparinized (100 U/kg, maximum 2,000 U). Nine of the patients then underwent supine bicycle ergometry exercise with simultaneous measurement of ascending and descending aortic pressures. The exercise protocol consisted of 4 minute stages with an initial work load of 200 kp·m·min^{-1} increasing by 200 kp·m·min^{-1} increments until exhaustion (14).

The following hemodynamic measurements were made between the third and fourth minute of each stage: heart rate; pulmonary artery, ascending and descending aortic pressures; cardiac index; and pulmonary artery saturation. Isometric handgrip exercise was performed in 8 of the 13 patients using a hand dynamometer at 50% of maximal voluntary capacity.

Aortography was performed in all 13 patients using biplane cineangiography at rest and in 9 also during an infusion of isoproterenol that increased the heart rate to approximately 140 beats/min. The descending thoracic aorta at the coarctation repair site and at the level of the diaphragm were measured using calibrated grids.

Statistical analysis. Statistical analysis was performed using the repeated measures analysis of variance and the Scheffe procedure for multiple comparisons. Group values are reported as mean ± SD.

Results

Data at rest (Table 1). At rest, patients in Group II and III (coarctectomy patients who developed an arm-leg systolic pressure gradient of ≥20 mm Hg with treadmill exercise) had a significantly higher ($p < 0.05$) systolic arm pressure than either the control group or the patients in Group I. Only patients in Group III had a significantly larger rest arm-leg systolic gradient than was observed in the control group of children (Table 1). No significant differences

Table 2. (*continued*)

	Catheterization Data			Angiographic Data			
	Supine Ex.	Isometric Ex.		Isuprel		Rest	Isuprel
Case	CO (liters/min)	BP AoAs (mm Hg)	Δ A-L (mm Hg)	BP AoAs (mm Hg)	ΔA-L (mm Hg)	Repair Site DsAo	Repair Site DsAo
Group II							
1	15.4	155/105	8	175/48	41	0.84	0.85
2	16.5	152/88	11	172/55	35	0.70	0.69
3	16.3	—	—	180/50	40	0.85	0.86
4	15.2	150/100	8	178/75	45	0.75	0.72
5	26.8	135/90	3	150/83	32	0.79	0.75
6	9.9	158/106	4	182/72	50	0.92	0.88
Mean ± SD	16.7 ± 5.5	150 ± 9 98 ± 8	7 ± 3	173 ± 11 64 ± 15	40 ± 6	0.81 ± 0.08	0.80 ± 0.08
Group III							
7	14.2	190/105	36	190/60	60	0.32	0.33
8	10.2	170/95	22	180/65	48	0.52	0.48
9	16.5	185/121	20	161/52	43	0.38	0.31
10	—	—	—	—	—	0.42	—
11	—	—	—	—	—	0.35	—
12	—	—	—	—	—	0.44	—
13	—	—	—	—	—	0.28	—
Mean ± SD	10.3 ± 3.8	182 ± 11* 107 ± 13	26 ± 8*	177 ± 15 56 ± 4	50 ± 8	0.39 ± 0.08*	0.37 ± 0.09*

were observed between the control subjects and any of the three coarctation groups of children with regard to sex, age at exercise testing, heart rate at rest, oxygen consumption and diastolic arm blood pressure.

Exercise data (Table 1). Compared with treadmill exercise, arm exercise produced a somewhat lower maximal heart rate and oxygen consumption although the differences were not statistically different. In addition, because there were no significant differences in maximal heart rate and oxygen consumption among the four groups of patients for either type of exercise, it can be assumed that the groups performed comparable degrees of exercise. A significant difference in arm systolic pressure was observed with treadmill exercise, producing a larger increase than arm exercise in all three groups (Table 1, Fig. 1). There were also important differences among groups. With treadmill exercise, patients in Groups II and III generated a larger increase in systolic arm blood pressure than either Group I or control children. With arm exercise only children in Group III (the children with a large rest arm-leg gradient) developed a significantly greater increase in arm blood pressure. Thus, in children in Group II, the abnormal increase in right arm systolic blood pressure with treadmill exercise was not observed when the exercise was performed with the arms.

The exercise-induced changes in arm to leg systolic pressure gradient are depicted in Figure 2. By design, compared with either control or Group I patients, Group II and III children generated significantly larger increases in arm-leg gradients with treadmill exercise. However, with arm exercise only Group III children developed a significantly greater rise in arm-leg gradient ($p < 0.05$) when compared with control children (Fig. 2). Thus, like blood pressure, the abnormal increase in pressure gradient with treadmill exercise was not observed in children in Group II when the exercise was performed with the arms. There were no differences noted between the control and Group I children for any of the measured variables either at rest or during arm and leg exercise.

Catheterization data (Table 2). Because of upper limb hypertension and the development of a large systolic pressure gradient from arms to legs with treadmill exercise, 13 of the 28 children underwent cardiac catheterization. The rest and supine exercise hemodynamic measurements in nine children were not significantly different from their noninvasively determined measurements (rest systolic arm-leg gradient 20 ± 11 mm Hg at catheterization versus 18 ± 11 mm Hg noninvasively determined; maximal supine exercise systolic arm-leg gradient 52 ± 7 versus 67 ± 18 mm Hg during treadmill exercise). In addition isometric exercise, such as arm exercise, produced smaller arm-leg systolic gradients in Group II than were observed in Group III (7 ± 3 versus 26 ± 9 mm Hg, $p < 0.05$). All 13 patients demonstrated a residual indentation of the descending aorta at the site of the coarctation repair; however, only the seven children in Group III had evidence of significant anatomic narrowing. The diameter of the coarctation repair site was 39% of the descending aorta diameter in Group III compared with 81% in Group II ($p < 0.05$) (Table 2). In an attempt

JACC Vol. 8, No. 1
July 1986:165–71

to assess the effect of exercise on the size of coarctation repair site nine patients had aortography performed while receiving an isoproterenol infusion. Isoproterenol did not significantly change the ratio of the diameter of the coarctectomy repair site to the diameter of the descending aorta at the level of the diaphragm in the nine patients (0.67 ± 0.21 versus 0.65 ± 0.22; rest versus isoproterenol).

Discussion

Mechanism of systolic arm hypertension after coarctation repair. Although many investigators have demonstrated that systolic hypertension in the arm is common during treadmill or bicycle exercise after repair of coarctation of the aorta, the mechanism of the systolic upper limb hypertension is less clear (1–4). Data from the present study suggest that treadmill exercise-induced upper limb hypertension is due to the combined effects of both the cross-sectional area of the residual stenosis and the blood flow across the stenosis. In Group III (patients with a large rest arm-leg systolic pressure gradient), the cross-sectional area of the residual stenosis is probably the most important determinant of the exercise-induced hypertension because these patients develop a significant arm-leg gradient regardless of the type of exercise (treadmill, arm ergometry or supine bicycle exercise). In Group II (patients with a small arm-leg gradient at rest but a large gradient with treadmill exercise), treadmill exercise-induced upper limb hypertension is probably due to a marked increase in descending aortic blood flow across a mildly narrowed coarctation site.

We base this conclusion on the following two observations: 1) an abnormal increase in arm systolic blood pressure or arm-leg gradient was not observed when these children performed exercise with the arms, and 2) aortic angiograms in six of these children demonstrated only minimal angiographic evidence of residual stenosis. Although we did not directly measure descending aortic blood flow, because others have demonstrated that maximal cardiac output is lower with arm exercise (5–10) we believe it is reasonable to assume that descending aortic blood flow is less with arm exercise than with leg exercise.

Differences in descending aortic blood flow. Although changes in descending aortic blood flow may explain why Group II children (rest gradient <15 mm Hg) develop upper limb hypertension with treadmill exercise, why do Group I children (rest gradient <15 mm Hg) not develop exercise-induced hypertension? An obvious answer to this question is that children in Group I may have a larger cross-sectional area of the site of previous coarctation repair. Although we have not angiographically assessed the size of the coarctation repair in any of the patients in Group I, it is possible that this area may be slightly larger in Group I than in Group II patients. However, because patients in Group II had angiographic evidence of only mild residual narrowing, there must be other explanations for the difference in excercise response between patients in Groups I and II. An alternative explanation for the large arm-leg gradient observed with treadmill exercise in Group II may be an increased vascular reactivity of the arterial vessels proximal to the coarctation repair site. Patients in Group II had significantly increased rest arm and leg blood pressure when compared with both control and Group I children (Table 1). We have previously demonstrated that after repair of coractation patients with upper limb hypertension at rest have increased vascular reactivity to exogenous norepinephrine in the right arm and normal reactivity in the legs (15). Four of the nine children in Group II (Cases 2, 4, 5 and 6; Table 2) participated in the vascular reactivity study. Therefore, we speculate that during treadmill exercise in patients in Group II the resistance vessels dilate in the active muscles of the legs and markedly constrict in the inactive and highly catecholamine-sensitive arm vessels, thereby directing a greater proportion of the increase in cardiac output across the coarctation site to the descending aorta. In contrast, with arm exercise the vessels in the active muscles of the arms dilate and the vessels in the legs constrict, resulting in a smaller increase in flow to the descending aorta.

Clinical implications. On the basis of our data, we conclude that children with a rest arm-leg pressure gradient of greater than 15 mm Hg who develop a large arm-leg gradient with treadmill exercise are likely to have significant anatomic narrowing at the coarctation repair site. Cardiac catheterization and angiography are indicated in these patients because reoperation or balloon angioplasty will probably be required. However, in children with a minimal rest arm-leg gradient who develop upper limb systolic hypertension with treadmill exercise (even ≥200 mm Hg), significant anatomic narrowing of the repair site is unlikely. In these children, cardiac catheterization is probably not necessary and antihypertensive medication or limitation of strenuous physical activity should be considered.

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