Exercise blood pressure response, cardiac output and 24-hour ambulatory blood pressure monitoring in children after aortic coarctation repair

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Key words:
Ambulatory blood pressure monitoring; Cardiac output; Coarctation of the aorta; Exercise.

Background. **The aim of this study was to assess blood pressure at rest, the response to exercise and the 24-hour ambulatory blood pressure monitoring (ABPM) profile in children operated for aortic coarctation.**

Methods. **Twenty children were operated upon for aortic coarctation. The patients' data were compared with those obtained from 19 healthy controls of the same age. Treadmill exercise testing was performed and cardiac output was determined using the acetylene-rebreathing method and indexed for the body surface area; ABPM was performed only in the patients group. The main outcome measures were the time of exercise, systolic (SBP) and diastolic (DBP) blood pressure both at rest and at peak exercise, maximal heart rate, total peripheral vascular resistance at rest and at peak exercise, and the pulse pressure (PP = SBP - DBP) at rest, at peak exercise and at ABPM. The Mann-Whitney test (non-parametric) and linear regression analysis were used when appropriate.**

Results. **Patients compared with healthy controls showed significant differences in SBP and PP at rest, and in DBP, cardiac index, total peripheral vascular resistance and PP at peak exercise. In the patients group only, linear regression analysis showed a significant correlation between PP and cardiac output, both at rest and at peak exercise, and between the arm-leg gradient at rest and PP at ABPM.**

Conclusions. **These findings suggest that blood pressure abnormalities could be due both to the altered baroceptor reflex control mechanism, resulting in cardiac output and total peripheral vascular resistance abnormalities, and to the progressive increase in resistance during exercise at the site of the repair, resulting in the higher PP, that may be related to a local loss of the natural aortic elasticity.**

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Introduction

Surgical repair and balloon angioplasty have radically changed the natural history of aortic coarctation, even though long-term follow-up studies still show a limited life expectancy in aortic coarctation compared to the general population[1]. The most important complication arising during follow-up is systolic hypertension, sometimes associated with post-surgical recoarctation. Studies investigating aortic coarctation have underlined the advisability of surgical correction before the age of 1.5 to 3 years to prevent the development of systolic hypertension consequent to mechanisms including the baroceptor reflex, left ventricular hypertrophy and/or kidney and blood vessel damage[1-3]. In the follow-up of patients operated upon for aortic coarctation, blood pressure abnormalities have been found. In a previous study[4] we have evaluated the 24-hour ambulatory blood pressure monitoring (ABPM) profiles in these patients; as other authors have later confirmed[5], ABPM was able to detect abnormalities in blood pressure behavior more often than office blood pressure measurements. Moreover, numerous studies have stressed the occurrence of recoarctation at the site of operation, with a residual arm-leg blood pressure gradient that leads to alterations in blood pressure both at rest and during exercise[6-9]. The aims of our study were to assess blood pressure and cardiac output at rest and during exercise, to determine the peripheral vascular tone and to investigate the possible relationships between these parameters and the ABPM values.

Methods

Twenty patients (12 males, 8 females) with a mean age of 13.7 ± 4.2 years, not on antihypertensive therapy, and 19 healthy controls (13 males, 6 females) aged 12.4 ± 2.1 years (p = NS) were enrolled in the study. All subjects (or their guardians) gave their informed consent to the study which was approved by our Research Institute Ethics Committee. Surgical repair was performed at a mean age of 46 ± 62 months. There were 3 end-to-end anastomoses, 10 patch angioplasties, and 7 left subclavian flap repairs. The healthy controls had no history of heart disease or hypertension, were taking no medications, described themselves as healthy and were not involved in competitive sports.

Blood pressure at rest. All subjects underwent a physical examination with the measurement of blood pressure at rest using a calibrated Tycos aneroid sphygmomanometer; the systolic (SBP) and diastolic (DBP) blood pressures were measured in the right arm with the subjects seated and the pulse pressure (PP) was calculated (i.e. PP = SBP - DBP). The cuff size complied with the criteria of the Task Force on High Blood Pressure in Children and Adolescents[10]. The blood pressure used for analysis was the mean of three separate measurements taken at 3-5 min intervals. In the patients group the blood pressure was also measured in the supine position to determine the arm-leg gradient. The patients were included only if both the arm-leg blood pressure gradient and the echo-Doppler gradient were < 20 mmHg without evidence of recoarctation. The arm-leg gradient was measured only at rest, because at peak exercise the patients were left standing on the treadmill in order to determine the cardiac output.

Treadmill exercise test. All subjects performed a treadmill exercise test (Bruce protocol) recording the time of exercise in minutes, the maximal heart rate in b/min, and the peak SBP and DBP in mmHg; these measurements were taken in all subjects while they were standing on the treadmill to determine the cardiac output. They were stopped at peak exercise to obtain an accurate value of DBP and to help them while performing the cardiac output technique. At rest and at peak exercise the blood pressure values, used to calculate the total peripheral vascular resistance (TPVR), were measured in all subjects while they were standing on the treadmill and performing the rebreathing technique. We determined the cardiac output with the rebreathing technique (acetylene-helium) in l/min using a mass spectrometer which was calibrated daily (AMIS 2000, Innovision, Odense, Denmark). We then calculated the TPVR using the formula: TPVR = mean arterial pressure (MAP)/cardiac output $\times$ 80 dyne/cm/s^{-5}. The MAP was calculated using the following formula: MAP = (SBP + 2DBP)/3. To evaluate the differences in cardiac output we indexed it for the body surface area (cardiac output/m^2 = cardiac index). The patients' data were analyzed and then compared to those of the healthy controls.

Twenty-four-hour ambulatory blood pressure monitoring. The 24-hour blood pressure was measured using a Spacelab 90207 ABP Recorder (Spacelab Inc., Redmond, WA, USA) (oscillatory method); the readings were modulated every 15 min during the day (7.00 a.m.-11.00 p.m.) and every 30 min during the night (11.00 p.m.-7.00 a.m.). The mean 24-hour daytime and night-time SBP and DBP and the mean 24-hour PP were calculated. Reference values were obtained from previous reports[11].

Statistical analysis. The Mann-Whitney test (nonparametric) was used to compare data; statistical significance was set at 0.05 and linear regression analysis was used to investigate the possible relationships between PP and cardiac output, at rest and at peak exercise, and between the mean 24-hour PP and the arm-leg gradient at rest.

Results

At rest. Significant differences were found for SBP and PP; no significant differences were found for DBP, cardiac index and TPVR (Table I). Only in the patients group did linear regression analysis show a significant correlation between PP and cardiac output (p = 0.028, r = 0.490) (Fig. 1).

At peak exercise. Significant differences were found for PP and DBP, while no significant differences were found for the time of exercise, maximal heart rate, TPVR, cardiac index and SBP at peak exercise (Table II); however, the patients group showed, at the same workload, a significant difference for SBP and DBP, implying an exaggerated blood pressure response to exercise (Table III); only in the patients group did linear regression analysis still show a significant correlation between PP and cardiac output (p = 0.005, r = 0.602) (Fig. 2).

Table I. Anthropometric and rest data.

	Patients (n = 20)	Controls (n = 19)	p
Age (years)	13.3	12	NS
Height (cm)	150	157	NS
Weight (kg)	48.5	48	NS
SBP (mmHg)	115.5	112	0.05
DBP (mmHg)	59.5	70	NS
CI (l/min/m^2)	3.9	3.8	NS
TPVR (dyne/cm/s^{-5})	1273	1172	NS
PP (mmHg)	55.5	40	0.0001

Values are expressed as median. CI = cardiac index; DBP = diastolic blood pressure; PP = pulse pressure; SBP = systolic blood pressure; TPVR = total peripheral vascular resistance.

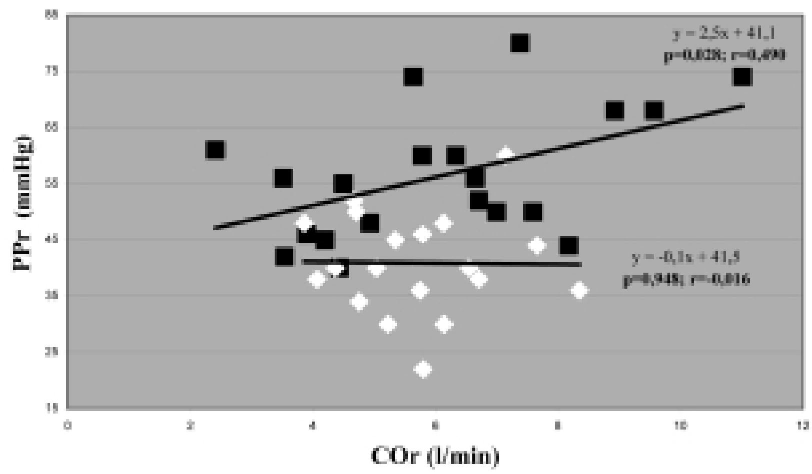

Figure 1. *Linear regression analysis between pulse pressure (PPr) and cardiac output (COr) at rest. ■ = patients; ◆ = controls.*

Table II. Exercise testing data.

	Patients (n = 20)	Controls (n = 19)	p
Time of exercise (min)	11	12	NS
SBP (mmHg)	153	140	NS
DBP (mmHg)	65	70	0.01
HR (b/min)	166	180	NS
CI (l/min/m^2)	6.8	6.98	NS
TPVR (dyne/cm/s^{-5})	818	781	NS
PP (mmHg)	95	70	0.01

Values are expressed as median. CI = cardiac index; DBP = diastolic blood pressure; HR = heart rate; PP = pulse pressure; SBP = systolic blood pressure; TPVR = total peripheral vascular resistance.

Table III. Exercise data at the same workload.

	Patients (n = 20)	Controls (n = 19)	p
Time of exercise (min)	10.5 ± 2	10.5 ± 2.3	NS
HR (b/min)	171 ± 17	167 ± 10	NS
SBP (mmHg)	152 ± 26	136 ± 18	0.03
DBP (mmHg)	59 ± 10	69 ± 5	< 0.001

Values are expressed as mean ± SD (Student's t-test). DBP = diastolic blood pressure; HR = heart rate; SBP = systolic blood pressure.

Twenty-four-hour ambulatory blood pressure monitoring. Nine/20 (45%) patients had abnormalities in the 24-hour ABPM profile; in particular, in 8/9 there was no nocturnal decrease in blood pressure (7 for SBP and 1 for DBP), 5/9 presented with an increased daytime SBP, one of them even with an increased daytime DBP, and 8/9 were hypertensive for the night-time SBP. We calculated PP during 24 hours, which was closely related to the arm-leg gradient at rest ($p = 0.003$, $r = 0.650$) (Fig. 3).

When analyzed for the type of surgical repair, all the blood pressure values considered (rest, exercise, ABPM) were found to be better in the group of the end-to-end anastomoses, but the low number of patients (only 3) did not allow significant conclusions.

Discussion

Several studies have defined a higher incidence of hypertension in patients operated upon for aortic coarctation with a blood pressure found to be elevated during routine activities[1-3] and during exercise[12,13]. Leandro et al.[3] reported an elevated ambulatory blood pressure in postoperative aortic coarctation patients who were normotensive at rest and had a greater left ventricular mass and an enhanced contractility of the left ventricle. Johnson et al.[14] evaluated ABPM data of aortic coarctation in two groups, more than and less than 10 years following surgical repair. They found an exaggerated SBP and DBP reactivity and that the prevalence of systolic hypertension doubled 10 years after surgery.

Hypotheses have been proposed but the exact mechanism(s) is/are not clear. Hauser et al.[15] have argued that since blood pressure abnormalities occurred independently of significant mechanical obstructive factors such as the shape of the aortic arch, a reduced sensitivity of the baroceptor reflexes and neurohumoral factors may both contribute to the development of hypertension. The alterations in the aortic root after aortic coarctation repair were also described by Sehested et al.[16] who found evidence of an excessive rigidity and of collagen deposition within the aortic wall specimens obtained at the time of repair, and by Ong et al.[17] who found the transverse aorta of patients with successful aortic coarctation repairs to be stiffer than the one of normal subjects. Moreover, Daniels[18] in his review has underlined the importance of the early detection and treatment of aortic coarctation that are associated with

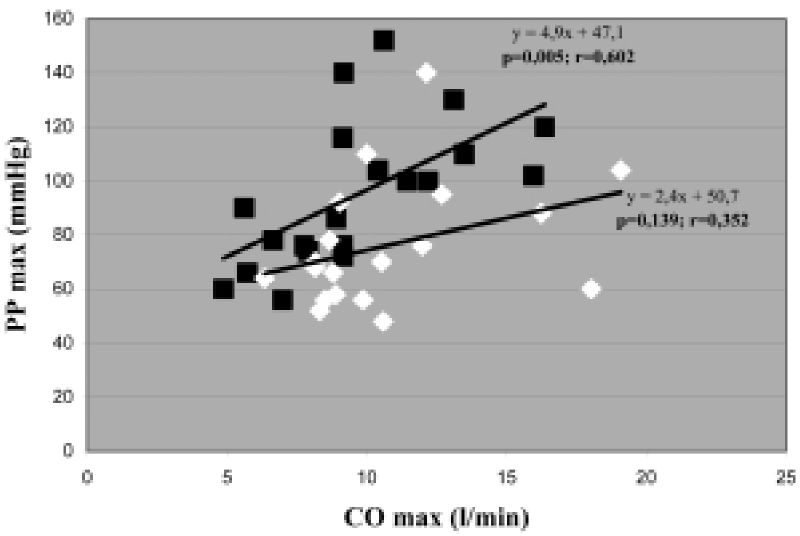

Figure 2. *Linear regression analysis between pulse pressure (PP) and cardiac output (CO) at peak exercise. ■ = patients; ◆ = controls.*

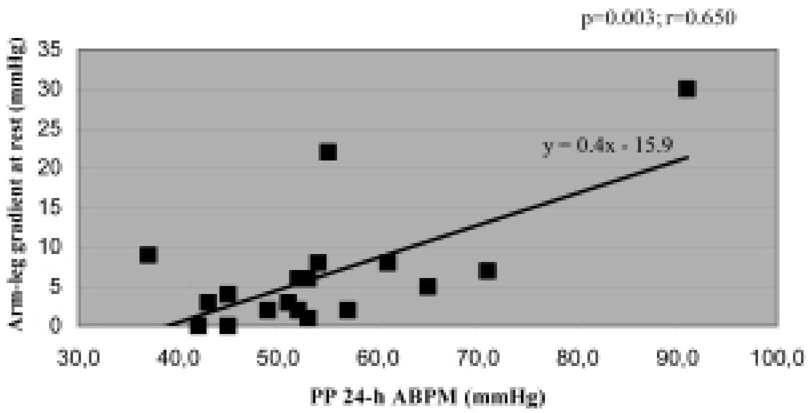

Figure 3. *Linear regression analysis between the arm-leg gradient at rest and the pulse pressure (PP) during 24-hour ambulatory blood pressure monitoring (ABPM).*

the best outcomes. Aortic coarctation repair is the best available option, despite the age at which it is detected. Besides, surgical repair is safe even in adults and, as Bhat et al.[19] have confirmed, improves systemic hypertension.

As far as we are concerned, no data exist about cardiac output and TPVR in patients after aortic coarctation repair. In these patients we have observed an anomalous behavior of TPVR during exercise, in particular a less marked decrease. After aortic coarctation repair children have an altered peripheral vascular tone with a lesser increment in the cardiac index. We may postulate that TPVR does not decrease because the persistent preoperative hypertension in the "upper compartment" vessels and/or the loss of elasticity in the aortic segment could contribute to maintain the high level of resistance. This mechanism may be enhanced during exercise when cardiac output increases. The demonstration of a higher PP, an important parameter to consider in hypertensive patients[20,21], both at rest and at peak exercise and during 24-hour ABPM, means that the site of repair is not compliant to the increment in cardiac output as has been shown to occur in healthy controls, especially during exercise. As other authors have demonstrated[3], this contributes to the early development of cardiac abnormalities in these patients. Moreover, the behavior of blood pressure in these patients is similar to that observed in patients with aortic valve insufficiency[22]; this could imply abnormalities of the elasticity of the aortic wall that result in lower DBP values in the patients group. This could also be supported by the close relationship of the 24-hour PP and the arm-leg gradient (Fig. 3).

In conclusion, the lesser decrease in TPVR during exercise in patients could mask abnormalities of the baroceptor reflex control. Our approach using hemodynamic data during both rest and exercise confirms that cardiac output and TPVR appear to be parameters that could be helpful when assessing the clinical conditions of these patients while ABPM is useful to evaluate the 24-hour blood pressure profile and to choose the best possible pharmacologic agent when therapy is needed.

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