

Exercise Testing in Adults after Repair of Aortic Coarctation

Evaluation of Cardiopulmonary Exercise Capacity and B-Type Natriuretic Protein Levels

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The aim of the study was to investigate, in adult patients after successful repair of aortic coarctation, potential relationships between B-type natriuretic peptide levels and exercise capacity and the following factors: arterial hypertension, residual stenosis of the ascending aorta, and age at the time of surgery.

The study group comprised 74 patients (45 men) aged 19 to 61 years (mean, 31.2 ± 9.8 yr), who had undergone surgery at the age of 0.5 to 34 years (mean, 10.4 ± 6.8 yr). The surgery was performed between 5 and 34 years earlier (mean, 21.4 ± 6.2 yr). A subgroup with residual aortic stenosis (significant when ≥ 25 mmHg) comprised 32 patients; a subgroup without residual stenosis comprised 42 patients. Patients were also divided into subgroups without arterial hypertension ($n=32$), with exercise-induced arterial hypertension ($n=10$), and with persistent arterial hypertension ($n=32$). All patients were in New York Heart Association functional class I. The control group comprised 30 healthy subjects (18 men) aged 26 to 46 years (mean, 32.2 ± 6.6 yr).

After testing exercise capacity in accordance with a modified Bruce protocol, we concluded that the exercise capacity of adults is reduced after surgical repair of aortic coarctation. This reduction is more pronounced in patients who have arterial hypertension, but it is unaffected by residual stenosis of the descending aorta. Serum B-natriuretic peptide concentrations, as determined by immunoradiometric assay, are significantly elevated, which may result from pressure overload of the left ventricle or from residual myocardial lesions due to coarctation repair at an older age. (*Tex Heart Inst J* 2007;34:412-9)

Surgical repair of coarctation of the aorta has been performed with satisfactory results for over half a century.¹⁻⁴ Long-term follow-up data show that the results of the surgery are better in patients who undergo operation in early childhood,^{2,3,5} although neonatal patients experience a higher incidence of residual stenosis of the ascending aorta.⁶⁻¹¹ Life expectancy is reduced, even after successful repair.^{4,8,10} After repair of coarctation of the aorta, a considerable number of adults present with arterial hypertension and premature coronary artery disease, and hence develop heart failure that is one of the causes of early death in this population.^{2,3} Although most post-coarctation-repair patients find their exercise capacity satisfactory, subjective appraisal of exercise performance does not necessarily reflect the actual clinical condition of the patient.^{2,3,11} Therefore, it may be essential to evaluate oxygen uptake (peak VO_2) with the maximum stress test combined with spirometry—cardiopulmonary exercise testing, which is the objective tool for measuring exercise tolerance. The results of cardiopulmonary stress testing are recognized predictors of prognosis in patients with heart failure.¹² B-Type natriuretic peptide (BNP) concentration is another acknowledged diagnostic and prognostic factor in heart failure.¹³⁻¹⁶ The value of this hormone has been documented in evaluating acute, chronic, and subclinical left ventricular heart failure.^{13,16} Indeed, the elevation of BNP level is a risk factor for sudden cardiac death in heart failure patients.¹⁷ The importance of BNP has also been shown in evaluating selected populations of patients who have congenital heart diseases,^{14,18-23} arterial hypertension,^{24,25} and left ventricular outflow tract obstruction.²⁶⁻²⁹ To our knowledge, there are no studies to date concerning BNP levels in patients who have undergone successful repair of coarctation of the aorta.

The aim of the study was to investigate, in adult patients after successful repair of coarctation of the aorta, any potential relationships between BNP levels and exercise

capacity (this last measured by cardiopulmonary stress testing) and the following factors: arterial hypertension, residual stenosis of the ascending aorta, and age at the time of surgery.

Patients and Methods

The study population was selected from 107 successful coarctation-repair patients of our congenital heart disease outpatient clinic. To be eligible for inclusion, patients had to display normal left ventricular systolic function, to be able to complete a cardiopulmonary exercise test, and to show no evidence of ischemic heart disease, respiratory disorder, or significant aortic regurgitation. Ultimately, the study enrolled 74 patients (29 women and 45 men) aged 19 to 61 years (mean, 31.2 ± 9.8 yr), who had undergone operation at the age of 0.5 to 34 years (mean, 10.4 ± 6.8 yr). The control group consisted of 30 healthy individuals (12 women, 18 men) aged 26 to 46 years (mean, 32.2 ± 6.6 yr). Most patients in the study group ($n=65$, 88%) had undergone synthetic patch repair by the same cardiac surgeon; 3 (4%) had undergone subclavian flap aortoplasty, 6 (8%) had undergone end-to-end anastomosis, and 1 had received a St. Jude 24-mm mechanical prosthetic valve (St. Jude Medical; St. Paul, Minn). Eight study patients had undergone reoperation due to stenosis of the ascending aorta; 1 patient had received noninvasive treatment of recoarctation; and another had undergone stent-graft implantation in the ascending aorta, due to aneurysm. The following congenital heart diseases were additionally diagnosed: ventricular septal defect, surgically repaired ($n=6$); occluded persistent arterial duct ($n=5$); and trivial mitral insufficiency ($n=19$). All participants in the study and control groups were classified in New York Heart Association functional class I, and all displayed sinus rhythm. Creatinine serum concentrations did not exceed $140 \mu\text{mol/L}$, and aspartate aminotransferase levels did not exceed double the normal values.

Echocardiographic examination was performed using Vivid 7 Dimension '06 (GE Healthcare; Chalfont-on-Giles, UK) with a 2.5-MHz probe in 2-D, M, and Doppler modes. Our investigator evaluated cardiac anatomy and left ventricular systolic function by means of the Simpson biplane method (normal systolic function was a criterion for inclusion in the study). The peak aortic valve pressure gradient was determined by means of continuous-wave Doppler echocardiography. The severity of residual stenosis of the ascending aorta was determined by evaluating the suprasternal notch. Restenosis was diagnosed when the ascending aorta pressure gradient was equal to or greater than 25 mmHg .² This measurement was used to divide the study population into subgroups with (AoD+) and without (AoD-) residual stenosis of the descending aorta. All echocardiography was performed by a single investigator.

All patients in the study group underwent maximum, symptom-limited (fatigue, dyspnea, or both) treadmill exercise testing in accordance with a modified Bruce protocol (added to the standard protocol was a 0–3-min stage at 1.7 km/hr and 5% inclination). The control subjects, however, followed the standard Bruce protocol. Patients were encouraged to continue the test for as long as their respiratory quotients (RQ) exceeded 1. The maximum oxygen uptake (peak VO_2), carbon dioxide production (VCO_2), and respiratory minute volume (VE) were measured using breath-to-breath gas analysis (Vmax29®, SensorMedics Corporation, part of VIASYS Respiratory Care, a unit of Cardinal Health; Dublin, Ohio). The system was calibrated with a standard gas mixture of known concentration before each test. A standard 12-lead electrocardiogram was continuously recorded. Blood pressure was recorded every 2nd minute using a cuff sphygmomanometer. Peak VO_2 was determined as an average value within the last 20 sec of exercise, and was expressed both as $\text{mL}/(\text{kg}\cdot\text{min})$ and as the percentage of predicted peak oxygen uptake. The VE/ VCO_2 slope—which indicates the increase of ventilation relative to carbon dioxide production—was calculated automatically by the Vmax29 software. Spirometry, including the measurement of forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV_1), was performed in all subjects before the cardiopulmonary exercise test, and the resulting values were then calculated as percentages of predicted values, taking into account age, sex, and body weight. For analysis, we selected the best achieved results from 3 to 4 spirometry cycles. The evaluation of the cardiopulmonary exercise test was performed by investigators who were blinded to the results of BNP levels.

In all patients, the blood samples were drawn from an antecubital vein after 15 minutes of rest in the supine position, before exercise testing. The concentrations of BNP in human plasma were determined with the use of an immunoradiometric assay kit (Shionoria BNP; CIS Bio International Diagnostic, part of Bayer Schering Pharma AG; Berlin, Germany). The radioactivity was measured for 1 minute with an NZ 335 gamma scintillation counter.

A cuff sphygmomanometer was used to measure blood pressure in all participants, both at rest and immediately after exercise. Exercise-induced arterial hypertension was diagnosed if systolic blood pressure at peak exercise exceeded 200 mmHg in patients whose baseline blood pressure was normal.⁹ Blood pressure exceeding $140/90 \text{ mmHg}$ was called arterial hypertension in accordance with guidelines established in 2003 by the European Society of Hypertension and the European Society of Cardiology.³⁰ The study involved both hypotensive-agent naïve patients and patients from whom antihypertensive therapy was withdrawn for at least 2 weeks before the treadmill test.

For variables following normal distribution, statistical analysis was performed with the Student *t* test for unpaired samples. For variables not following normal distribution, the Mann-Whitney U test was used. To determine the relationships between variables, the Spearman rank-order correlations were analyzed. Results of *P* < 0.05 were considered statistically significant.

Informed consent was obtained from each patient, and our study protocol, as approved a priori by our institution's human research committee, conformed to the ethical guidelines set forth by the 1975 Declaration of Helsinki.

Results

Table I shows the results of cardiopulmonary testing, which revealed that the exercise performance of adults after the repair of coarctation was significantly reduced: peak oxygen uptake (VO_2max) in study patients was lower than in healthy individuals (26.77 ± 6.75 vs 35.27 ± 7.6 mL/([kg·min]); *P*=0.0001), and similarly when expressed as percentages ($\text{VO}_2\text{max}\%$, 70.09

± 13.39 vs 90.3 ± 15.35 ; *P*=0.0001). The ventilation/carbon dioxide slope (VE/VCO_2) was higher in the study group than in the control (33.14 ± 5.33 vs 29.73 ± 3.32 ; *P*=0.001). The heart rate at maximum workload in the study group was reduced in comparison with the control (167.91 ± 21.25 vs 180.83 ± 12.93 beats/min; *P*=0.0001); and the same was observed for HRmax% (88.25 ± 10.17 vs 100.33 ± 7.11 ; *P*=0.0001). The RQ in patients after surgery was lower than in members of the control group (1.06 ± 0.07 vs 1.13 ± 0.09 ; *P*=0.001). Diastolic blood pressure at rest and during physical exertion did not differ between the groups, whereas systolic blood pressures, both resting (136.58 ± 18.92 vs 126.66 ± 11.87 mmHg; *P*=0.004) and during exercise (198.25 ± 25.29 vs 167.94 ± 15.67 mmHg; *P*=0.001), were higher in the study patients. The measurements of pulmonary elasticity, including FVC and FVC% (percent of forced vital capacity), were lower in the study patients than in the controls: 4.12 ± 0.95 L vs 8.03 ± 0.53 L (*P*=0.02) and $93.19\% \pm 16.49\%$ vs $103.2\% \pm 9.3\%$, respectively (*P*=0.001). Moreover, the parameters used to identify airway obstruction, including a FEV₁ of 3.30

TABLE I. Characteristics and Comparison of Serum BNP Levels and Cardiopulmonary Values in Study and Control Groups

Characteristic	Study Group (n=74)	Control Group (n=30)	P Value
Current age (yr)	31.2 ± 9.8	32.2 ± 6.6	NS
Age at surgery (yr)	10.4 ± 6.8	—	NS
BMI (kg/m ²)	29.4 ± 2.21	30.2 ± 3.12	NS
BNP (pg/mL)	31.05 ± 33.68	10.61 ± 6.3	0.0001
VO_2max (mL/[kg·min])	26.77 ± 6.75	35.27 ± 7.6	0.0001
$\text{VO}_2\text{max}\%$	70.09 ± 13.39	90.3 ± 15.35	0.0001
VE/VCO_2	33.14 ± 5.33	29.73 ± 3.32	0.001
HRmax (beats/min)	167.91 ± 21.25	180.83 ± 12.93	0.0001
HRmax%	88.25 ± 10.17	100.33 ± 7.11	0.0001
FVC (l)	4.12 ± 0.95	8.03 ± 0.53	0.02
FVC%	93.19 ± 6.49	103.2 ± 9.3	0.001
FEV ₁ (l)	3.30 ± 0.80	3.76 ± 0.86	0.02
FEV ₁ %	87.86 ± 14.4	98.37 ± 10.65	0.0004
RQ	1.06 ± 0.07	1.13 ± 0.09	0.001
SBP at rest (mmHg)	136.56 ± 18.92	126.66 ± 11.87	0.004
DBP at rest (mmHg)	85.76 ± 8.61	83.33 ± 8.23	NS
SBP ex (mmHg)	198.25 ± 25.29	167.93 ± 15.67	0.001
DBP ex (mmHg)	88.82 ± 1.40	86.50 ± 9.94	NS

BMI = body mass index; BNP = brain natriuretic peptide; DBP = diastolic blood pressure; ex = exercise; FEV₁ = forced expiratory volume in 1 sec; FVC = forced vital capacity; HRmax = peak exercise heart rate; NS = not significant; RQ = respiratory quotient; SBP = systolic blood pressure; VE/VCO_2 = ventilatory equivalent for carbon dioxide; VO_2max = maximum oxygen uptake

± 0.80 L and FEV₁% of 87.86 ± 14.41 , were significantly lower in postsurgical patients: FEV₁, 3.76 ± 0.86 L and FEV₁%, 98.37 ± 10.65 ($P=0.02$ and $P=0.0004$, respectively).

Maximum aortic valve pressure gradients ranged from 4.11 to 28.53 mmHg (mean, 11.75 ± 6.19 mmHg). In 32 patients, in whom residual stenosis of the descending aorta was found (AoD+), the pressure gradient ranged from 25.0 to 60.2 mmHg (mean, 36.66 ± 9.81 mmHg); in the remaining 42 patients, in whom no residual stenosis of the descending aorta was found (AoD-), the pressure gradient ranged from 5.51 to 24.0 mmHg (mean, 15.91 ± 5.08 mmHg). The comparison of cardiopulmonary parameters between AoD+ and AoD- groups set forth in Table II reveals no significant differences. It should be observed that AoD+ patients were operated on at an older age (12.45 ± 7.49 yr) than were AoD- patients (8.98 ± 5.94 yr; $P=0.03$).

Thirty-three patients had normal resting blood pressure (AH-), and 10 had arterial hypertension induced by exercise (AH_{ex}); the remaining group of 31 patients (AH+) had persistent arterial hypertension (Table III). Study of AH- and AH_{ex} showed that patients with ex-

ertional arterial hypertension had higher ventilation-to-perfusion ratios—VE/VCO₂ (28.31 ± 4.56 vs 33.89 ± 5.02 ; $P=0.01$)—but reached lower heart rates at peak exercise (181.00 ± 13.05 vs 171.24 ± 15.76 beats/min; $P=0.001$). The comparison between the AH- and AH+ subgroups showed that persistently hypertensive patients had the following values reduced: VO₂max (26.30 ± 15.08 vs 28.05 ± 7.9 mL/[kg·min]; $P=0.01$), VO₂max% (66.17 ± 14.58 vs 74.75 ± 12.16 ; $P=0.02$), HRmax (162.46 ± 21.76 vs 181.00 ± 13.05 beats/min; $P=0.0001$), HR% (84.46 ± 10.58 vs 94.31 ± 7.91 ; $P=0.0004$), and RQ (1.04 ± 0.5 vs 1.08 ± 0.09 ; $P=0.03$). However, VE/VCO₂ was higher (28.31 ± 4.56 vs 34.06 ± 4.78 ; $P=0.003$). The comparison between the AH_{ex} and AH+ subgroups proved that patients with persistent arterial hypertension had lower HRmax (162.42 ± 21.13 vs 171.24 ± 15.76 beats/min; $P=0.001$), HR% (92.30 ± 6.11 vs 84.46 ± 10.58 ; $P=0.01$), and RQ (1.09 ± 0.07 vs 1.04 ± 0.05 ; $P=0.02$). Between all groups, we observed no significant differences in spirometric measurements.

Patients with AH+ were older than those with AH- (35.59 ± 11.02 vs 28.62 ± 7.78 yr; $P=0.004$) and those with AH_{ex} (35.59 ± 11.02 vs 25.20 ± 5.07 yr; $P=0.006$).

TABLE II. Characteristics and Comparison of Serum BNP Levels and Cardiopulmonary Values in Patients with Respect to the Presence of Recoarctation

Characteristic	Study Group AoD- (n=42)	Study Group AoD+ (n=32)	P Value
Current age (yr)	29.47 ± 9.13	33.45 ± 10.58	NS
Age at surgery (yr)	8.98 ± 5.94	12.45 ± 7.49	0.03
BNP (pg/mL)	23.66 ± 20.88	41.17 ± 43.82	0.03
Vo ₂ max (mL/[kg·min])	27.04 ± 6.33	26.61 ± 7.48	NS
Vo ₂ max%	71.96 ± 12.79	68.78 ± 12.52	NS
VE/Vco ₂	26.13 ± 5.50	33.72 ± 5.40	NS
HRmax (beats/min)	167.18 ± 21.74	163.82 ± 20.93	NS
HRmax%	87.29 ± 10.66	91.75 ± 10.38	NS
RQ	1.07 ± 0.09	1.05 ± 0.07	NS
FVC (l)	4.25 ± 1.00	3.97 ± 0.88	NS
FVC%	92.73 ± 12.83	96.14 ± 16.48	NS
FEV ₁ (l)	3.40 ± 0.80	3.16 ± 0.82	NS
FEV ₁ %	86.38 ± 13.27	88.45 ± 15.34	NS
SBP at rest (mmHg)	136.31 ± 19.99	138.39 ± 18.31	NS
DBP at rest (mmHg)	85.57 ± 0.06	84.64 ± 9.32	NS
SBP ex (mmHg)	201.63 ± 27.15	196.89 ± 21.94	NS
DBP ex (mmHg)	87.36 ± 12.12	88.50 ± 10.75	NS

AoD+ = patients with residual stenosis; AoD- = patients without residual stenosis; BNP = brain natriuretic peptide; DBP = diastolic blood pressure; ex = exercise; FEV₁ = forced expiratory volume in 1 sec; FVC = forced vital capacity; HRmax = peak exercise heart rate; NS = not significant; RQ = respiratory quotient; SBP = systolic blood pressure; VE/Vco₂ = ventilatory equivalent for carbon dioxide; Vo₂max = maximum oxygen uptake

TABLE III. Characteristics and Comparison of Serum BNP Levels and Cardiopulmonary Values in Patients with Respect to Arterial Hypertension Presence

Characteristic	Study Group AH- (n=33)	Study Group AH _{ex} (n=10)	Study Group AH+ (n=31)	P Value, AH- and AH _{ex}	P Value, AH- and AH+	P Value, AH+ and AH _{ex}
Current age (yr)	28.62 ± 7.78	25.20 ± 5.07	35.59 ± 11.02	NS	0.004	0.006
Age at surgery (yr)	9.12 ± 5.83	6.50 ± 3.71	12.95 ± 7.53	NS	0.02	0.01
BNP (pg/mL)	24.62 ± 19.98	28.97 ± 23.36	38.14 ± 44.92	NS	NS	NS
VO ₂ max (mL/[kg·min])	28.05 ± 7.9	27.97 ± 6.68	26.30 ± 15.08	NS	0.01	NS
VO ₂ max%	74.75 ± 12.16	71.00 ± 13.49	66.17 ± 14.58	NS	0.02	NS
VE/VCO ₂	28.31 ± 4.56	33.89 ± 5.02	34.06 ± 4.78	0.01	0.003	NS
HRmax (beats/min)	181.00 ± 13.05	171.24 ± 15.76	162.46 ± 21.73	0.001	0.0001	0.001
HRmax%	94.31 ± 7.91	92.30 ± 6.11	84.46 ± 10.58	NS	0.0004	0.001
RQ	1.08 ± 0.9	1.09 ± 0.07	1.04 ± 0.05	NS	0.03	0.02
FVC (l)	4.72 ± 0.75	4.42 ± 0.77	4.07 ± 1.12	NS	NS	NS
FVC%	92.79 ± 19.10	91.50 ± 9.61	94.21 ± 15.9	NS	NS	NS
FEV1 (l)	3.22 ± 0.65	3.38 ± 0.65	3.21 ± 0.95	NS	NS	NS
FEV1%	89.89 ± 14.71	86.40 ± 8.34	86.28 ± 15.98	NS	NS	NS
SBP at rest (mmHg)	126.20 ± 15.50	132.00 ± 8.21	149.71 ± 8.98	NS	0.0001	0.01
DBP at rest (mmHg)	80.51 ± 8.48	82.50 ± 3.53	91.17 ± 2.74	NS	0.0001	0.001
SBP ex (mmHg)	169.48 ± 19.88	212.00 ± 11.98	210.23 ± 23.21	0.0001	0.0001	NS
DBP ex (mmHg)	85.17 ± 9.77	87.00 ± 14.18	95.46 ± 7.09	NS	0.0001	0.003
BNP (pg/mL)	28.62 ± 7.78	25.20 ± 5.07	35.59 ± 11.02	NS	0.004	0.006

AH+ = patients with persistent arterial hypertension; AH- = patients with normal resting blood pressure; AH_{ex} = arterial hypertension induced by exercise; BNP = brain natriuretic peptide; DBP = diastolic blood pressure; ex = exercise; FEV₁ = forced expiratory volume in 1 sec; FVC = forced vital capacity; HRmax = peak exercise heart rate; NS = not significant; RQ = respiratory quotient; SBP = systolic blood pressure; VE/VCO₂ = ventilatory equivalent for carbon dioxide; VO₂max = maximum oxygen uptake

The age of AH+ patients at the time of the surgery was higher than the age of both the AH- (12.95 ± 7.53 vs 9.12 ± 5.83 yr; $P=0.02$) and AH_{ex} subgroups (12.95 ± 7.53 vs 6.50 ± 3.71 yr; $P=0.01$). At the same time, the mean pressure gradient through the descending aorta did not differ among groups (HT-, 25.52 ± 14.02 mmHg; AH_{ex}, 30.69 ± 15.3 mmHg; and AH+, 24.68 ± 13.4 mmHg).

Linear correlation analysis of results for the entire study group—including current age, age at operation, time after operation, blood pressure, and cardiopulmonary values—showed significant negative correlation between current age of patient and VO₂max ($r= -0.0432$, $P=0.0003$) and significant positive correlation between current age and VE/VCO₂ ($r=0.342$, $P=0.004$); significant negative correlations were found between the age at surgical repair and VO₂max ($r= -0.360$, $P=0.003$) and between the age at surgical repair and VE/VCO₂ ($r=0.369$, $P=0.002$). No significant correlations were seen between exercise-capacity parameters and blood pressure.

Serum BNP levels in the study group were higher than in the control group (31.06 ± 33.68 vs 10.61 ± 6.3 pg/mL, respectively; $P=0.0001$); and serum BNP levels were higher in the subgroup with residual stenosis of the descending aorta (AoD+) than in the gradient-negative (AoD-) group (41.17 ± 43.82 vs 23.66 ± 20.84; $P=0.03$) but did not reach statistical significance. Differences in serum BNP concentrations with respect to the diagnosis of arterial hypertension were insignificant. It was observed that BNP level positively correlated with age at surgery ($r=0.275$, $P=0.02$) (Fig. 1) and with aortic valve pressure gradients ($r=0.233$, $P=0.04$) (Fig. 2). The BNP level did not correlate significantly with the descending aorta pressure gradient or with any of the cardiopulmonary parameters tested.

Discussion

According to a large number of investigators,^{2,3,11} adult patients, after repair of coarctation of the aorta, tend to think that their exercise capacity is satisfactory; however,

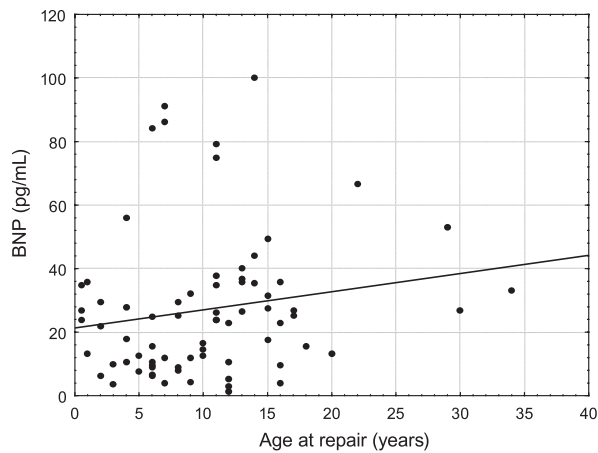


Fig. 1 B-Type natriuretic peptide levels (BNP) and age at repair.

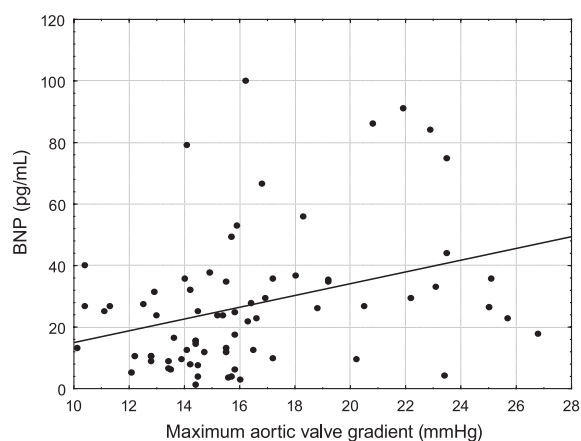


Fig. 2 B-Type natriuretic peptide levels (BNP) and maximum aortic valve gradient.

our objective evaluation by means of cardiopulmonary exercise testing showed its considerable impairment. In children and adolescents, diverse observations have been made, respectively, by Balderston and colleagues³¹ and Markham and associates.⁸ Our findings are consistent with those of Rhodes and coworkers³² and with the results of a comprehensive analysis of a population of adults with congenital heart disease (including patients who had undergone surgical repair of coarctation of the aorta) that was carried out by investigators from Royal Brompton Hospital in London.¹¹ These authors showed that $\text{VO}_2\text{max} \leq 15.5 \text{ mL}/(\text{kg}\cdot\text{min})$ was an independent predictor of hospitalization and death in patients with congenital heart disease. All of the patients in our study group reached at least this low point in peak oxygen uptake. Chronotropic reaction was compromised in our study patients, as others have observed in adults with various congenital heart diseases.^{8,11,33} Swan⁶ and Balderston³¹ and their associates did not make such an observation, but their populations included only children.

Our study patients exhibited restrictive and obstructive respiratory disorders. Because the pathomechanisms that lead to these abnormalities reduce pulmonary compliance, physicians should investigate the possibility of heart enlargement, pulmonary fibrosis secondary to chronic fluid retention in the pulmonary circulation, and respiratory myopathy.^{11,34} The degree of impairment of pulmonary function did not differ, however, between subgroups of the study group in regard to recoarctation, persistent arterial hypertension, or exercise-induced arterial hypertension.

Clearly, exercise-capacity impairment worsened as the age of the patient increased,¹² but at the same time it was inversely related to age at the time of coarctation repair (improving with younger age). A similar relationship between exercise capacity and age at operation was observed by the Royal Brompton Hospital investigators in 335 adults with congenital heart diseases.¹¹ This finding supports early repair of this anatomical defect.^{2-4,9}

Exercise-capacity impairment was similar in patients with recoarctation and those without residual stenosis of the descending aorta. However, it is worth emphasizing that our patients with residual stenosis of the descending aorta did not manifest higher blood pressures than did our patients who were free of recoarctation; this finding is in accord with the results of some studies,^{35,36} but not others.^{1,6-9} Isolated arterial hypertension was associated with exercise capacity. Significantly worse cardiopulmonary values (peak oxygen uptake and ventilation-perfusion ratio) were observed in hypertensive than in normotensive patients. In addition, patients with exercise-induced arterial hypertension showed higher ventilation-perfusion ratios than did normotensive patients.

The severity of chronotropic impairment was also significantly different among subgroups of our study group. Among patients with persistent arterial hypertension (in comparison with normotensive patients), our findings might well have been affected by the patients' older age, both at present and at the time of repair. Normotensive patients did not differ from patients with exercise-induced arterial hypertension in regard to current age and age at operation; however, the exercise capacity of the hypertensive group was worse. This suggests that—contrary to the theory of Swan⁶ and Leandro³⁷ and their colleagues, who challenge the need for identifying patients with “latent hypertension” after repair of coarctation of the aorta—patients with exercise-induced arterial hypertension should receive special clinical surveillance^{1-3,7} and, if we follow the judgment of some investigators,⁴ earlier implementation of antihypertensive therapy.

We found that the level of B-type natriuretic hormone was significantly increased in adults after surgical repair of coarctation of the aorta. As we have said above, the elevation of BNP is also observed in adults with other

congenital heart diseases.¹⁸⁻²³ Mair and coworkers²⁴ and Bolger's group¹⁴ have noted that an increase of BNP level in these populations depends specifically upon cardiac dysfunction, rather than the variant anatomic substrate. Law and colleagues¹⁸ have largely associated the elevation of serum BNP levels in this anatomically heterogeneous population with increased strain upon the left ventricular walls. In common with Westerlind and associates,³⁸ we observed that B-type natriuretic hormone levels correlated with left ventricular outflow tract pressure gradients, after surgical repair of coarctation. Our calculations showed that BNP concentrations were significantly higher in subjects who had substantial pressure gradients through the descending aorta. Therefore, we infer that BNP secretion is activated by increased strain on the left ventricular walls.^{19,26,27,29} Holmgren's group²⁰ documented that left ventricular volume overload (rather than pressure overload) was responsible for stimulating the production of BNP, but their observation was restricted to children. Analysis of the pathogenesis of the decreased exercise capacity of adult coarctation-repair survivors should take into consideration the fact that arteries arising from the aorta proximal to the stenosis are characterized by increased stiffness. Although early coarctation repair appears to help preserve the elastic properties of these arteries, their vascular reactivity remains reduced.¹⁰ Coronary artery lesions have been observed in 25% to 37% of this population.^{1,2,4,9} Because BNP levels are known to increase in coronary artery disease,^{24,40} such a cause of natriuretic hormone level elevation cannot be excluded. Moreover, an association has been shown between BNP concentration and age at the time of repair, which may indirectly indicate the severity of myocardial damage before surgery and (once again) weigh in favor of early repair.^{2-4,9}

Conclusions

Our most important conclusions are these:

1. The exercise capacity of adults, after surgical repair of coarctation of the aorta, is reduced.
2. This reduction is more pronounced in patients who have arterial hypertension, and it is unaffected by residual stenosis of the descending aorta.
3. Serum BNP concentration is significantly increased in patients who have substantial residual pressure gradients through the descending aorta, which may result from pressure overload of the left ventricle or from residual myocardial lesions due to repair at an older age.

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