Correlation of Exercise Response in Repaired Coarctation of the Aorta to Left Ventricular Mass and Geometry

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The role of exercise testing to risk stratify patients with repaired coarctation of the aorta (CoA) is controversial. Concentric left ventricular (LV) hypertrophy, defined as an increase in the LV mass-to-volume ratio (MVR), is associated with a greater incidence of adverse cardiovascular events. The objective of the present study was to determine whether a hypertensive response to exercise (HRE) is associated with increased LVMVR in patients with repaired CoA. Adults with repaired CoA who had a symptom-limited exercise test and cardiac magnetic resonance imaging examination within 2 years were identified. A hypertensive response to exercise was defined as a peak systolic blood pressure >220 mm Hg during a symptom-limited exercise test. The LV mass and volume were measured using cardiac magnetic resonance by an investigator who was unaware of patient status. We included 47 patients (median age 27.3 years, interquartile range 19.8 to 37.3), who had undergone CoA repair at a median age of 4.6 years (interquartile range 0.4 to 15.7). Those with (n = 11) and without (n = 36) HRE did not differ in age, age at repair, body surface area, arm-to-leg systolic blood pressure gradient, gender, or peak oxygen uptake with exercise. Those with a HRE had a greater mean systolic blood pressure at rest (146 ± 18 vs 137 ± 18 mm Hg, p = 0.04) and greater median LVMVR (0.85, interquartile range 0.7 to 1, vs 0.66, interquartile range 0.6 to 0.7; p = 0.04) than those without HRE. Adjusting for systolic blood pressure at rest, age, age at repair, and gender, the relation between HRE and LVMVR remained significant (p = 0.001). In conclusion, HRE was associated with increased LVMVR, even after adjusting for multiple covariates. **(Am J Cardiol 2013;111:406−411)**

Despite anatomic repair, patients with coarctation of the aorta (CoA) remain at risk of systemic arterial hypertension, in part, because of abnormalities in vascular structure and function present at birth that persist throughout life.[1−3] Although many adults with repaired CoA are normotensive at rest, up to 1/3 of tested subjects have an exaggerated hypertensive response to exercise (HRE).[4−7] Since the 1970s, clinicians have used the blood pressure (BP) response during exercise testing to evaluate asymptomatic normotensive patients with repaired CoA.[6] Despite widespread use and inclusion of exercise testing in recently published guidelines for the care of patients with repaired CoA, scant data are available correlating an HRE to either adverse events or validated intermediate-risk markers for future cardiovascular events.[8,9] Concentric left ventricular (LV) hypertrophy is a physiologic response to increased afterload and contributes to hypertension through abnormalities in ventricular−arterial coupling.[10] Concentric LV hypertrophy is a well-validated risk marker for increased cardiovascular morbidity, including coronary artery disease and cerebral vascular accidents[11, 12] and is present in 8% to 12.5% of patients with repaired CoA.[13,14] The present investigation evaluated subjects with repaired CoA to determine whether HRE is associated with concentric LV hypertrophy.

Methods

The committee on clinical investigations at Boston Children's Hospital approved the study.

All subjects aged ≥16 years with either surgical or transcatheter repair of CoA who had had a symptom-limited exercise test and cardiac magnetic resonance imaging (CMR) examination within 2 years of each other from 1998 to 2008 were identified through a search of the Boston Children's Hospital cardiovascular database. The exercise tests and CMR were performed as clinically indicated studies as determined by the treating physicians.

Subjects were excluded if they had hemodynamically significant re-coarctation that was clinically determined to require either catheter or surgical reintervention or had collateral vessels identified on CMR. They were also excluded if they had associated complex congenital heart disease, an interrupted aortic arch, aortic valve dysfunction (valve area <1.5 cm^2, peak velocity by continuous wave Doppler echocardiography of ≥3 m/s, or moderate or

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See page 411 for disclosure information.

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Table 1
Baseline demographic, clinical variables, exercise, and cardiac magnetic resonance imaging (CMR) data

Variable	Hypertensive Response		p Value
	Yes (n = 11)	No (n = 36)	
Age (yrs)	22.5 (20.5−37.4)	28.5 (17.7−37.3)	0.26
Male subjects	7 (64%)	17 (47%)	0.49
Age at repair (yrs)	3.0 (0.2−9.4)	6.8 (0.5−16.9)	0.33
Weight (kg)	75 (67.0−92.4)	71 (64.2−79.4)	0.38
Body surface area (m^2)	1.9 (1.8−2.2)	1.8 (1.7−2.0)	0.19
Interventions (n)	1 (1−3)	1 (1−2)	0.43
Systolic blood pressure at rest (mm Hg)	146 ± 18	134 ± 17	0.04
Arm-to-leg systolic blood pressure gradient (mm Hg)	14 ± 19	3.9 ± 18	0.20
Antihypertensive medication	7 (64%)	20 (56%)	0.74
Bicommissural aortic valve	7 (64%)	23 (63%)	0.28
Exercise results			
Peak workload (W)	172 ± 26	180 ± 62	0.74
Peak oxygen consumption (ml/kg/min)	26 ± 5	32 ± 11	0.26
Peak oxygen consumption (% of predicted)	80 ± 16	88 ± 23	0.41
Peak oxygen pulse (ml/beat)	13 ± 4	13 ± 4	0.89
Peak oxygen pulse (% of predicted)	83 ± 14	96 ± 18	0.20
Peak systolic blood pressure (mm Hg)	235 ± 3	179 ± 4	<0.0001
Peak exercise arm-to-leg systolic blood pressure gradient (mm Hg)	68 (58−76)	50 (33−65)	0.04
Magnetic resonance imaging results			
Indexed left ventricular end-diastolic volume (ml/m^2)	73 (64−92)	91 (79−110)	0.03
Left ventricular ejection fraction (%)	67 ± 6	62 ± 9	0.10
Left ventricular mass (g)	128 (78−217)	113 (87−144)	0.35
Left ventricular mass-to-volume ratio (g/ml)	0.85 (0.71−1.0)	0.66 (0.55−0.77)	0.007

Data are presented as mean ± SD.

greater aortic regurgitation [regurgitation fraction ≥20%]), or other features that would predispose to increased LV mass. Subjects with known genetic syndromes (e.g., William or Turner syndrome) or inherited cardiomyopathy (e.g., Fabry or Gaucher disease) were also excluded.

Demographic data were extracted from the medical records and included age, age at initial repair, number and type of interventions, gender, race, use and type of antihypertensive medications, and bicommissural status of the aortic valve.

Baseline BP was measured with the subject supine, after ≥2 minutes of rest as a part of the standard clinical protocol for cardiopulmonary exercise testing. Arm and leg BP measurements were taken using an automated cuff (Dinamap, Milwaukee, Wisconsin) with the patient supine. Exercise BP was measured in the arm using a manual cuff at 3-minute intervals. The peak exercise systolic BP was defined as the greatest systolic BP measured either during exercise or in the immediate recovery period. Subjects who exhibited a peak systolic BP >220 mm Hg were defined as having a hypertensive response to exercise (HRE positive).[15] Exercise diastolic BP was not reported, because these measurements have been recognized to be less reliable. Patients were instructed to take their prescribed antihypertensive medications on the day of the exercise test.

Exercise testing was performed on either a progressive bicycle ergometer or a treadmill using the standard Bruce protocol. A subset of subjects also completed metabolic cart testing with baseline spirometry followed by breath-by-breath analysis of expiratory gases using a metabolic cart (Medical Graphics, St Paul, Minnesota) and continuous electrocardiographic monitoring. The subjects were excluded if they failed to reach a peak respiratory exchange ratio ≥1.1 (indicating submaximum effort) or if the reason for termination of the exercise test was other than fatigue.

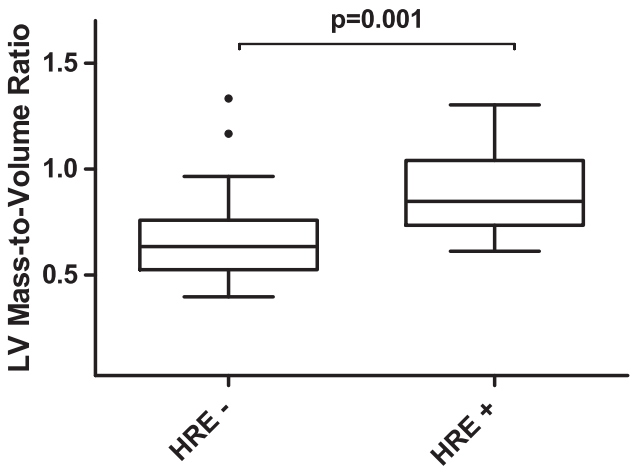

Figure 1. Box plot representing median and 25th to 75th percentiles, with *error bars* indicating 1.5 times interquartile range. *Dots* represent outliers outside the 1.5 times interquartile range. Patients with HRE had a greater LVMVR. p Values represent multivariate analysis adjusting for age, age at repair, gender, body surface area, and systolic blood pressure at rest. HRE+ = those with a hypertensive response to exercise; HRE− = those without a hypertensive response to exercise. Data on outliers in the HRE-negative group: patient 1, LV mass of 203.8 g, indexed LV end-diastolic volume 152.8 ml, and peak exercise BP 210 mm Hg; patient 2, LV mass of 179.2 g, indexed LV end-diastolic volume 153.5 ml, and peak exercise BP 188 mm Hg.