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Utility of the dobutamine stress echocardiography in the evaluation of the effects of a surgical repair of aortic coarctation in children

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Abstract

Background: *Exercise-induced hypertension following repair of the coarctation of the aorta (CoA) is a well known phenomenon. The most important functional parameters in the assessment of the effects of a surgical repair of CoA are the maximal pressure gradient in the descending aorta (GRAD) and systolic blood pressure (SBP). Results of treadmill exercise test using the Bruce protocol (treadmill test) and dobutamine stress echocardiography (DSE) were compared to determine utility of the DSE in the evaluation of the effects of surgical treatment of CoA in children.*

Methods: *The study population comprised of 29 patients, including 20 males and 9 females (mean age 12 years) who underwent a surgical repair of CoA. Changes of the cardiovascular parameters including SBP, GRAD and heart rate (HR) during the treadmill test and DSE were compared.*

Results: *During the treadmill test, SBP at peak exercise ranged from 120 to 230 (mean 163.7) mm Hg, GRAD ranged from 29 to 109 (mean 59.8) mm Hg, and HR ranged from 140 to 188 (mean 169) bpm. At the end of DSE, SBP ranged from 123 to 215 (mean 164.7) mm Hg, GRAD ranged from 29 to 113 (mean 55.4) mm Hg, and HR ranged from 76 to 155 (mean 111) bpm. We found positive correlations of SBP ($r = 0.68$, $p < 0.001$) and GRAD ($r = 0.82$, $p < 0.001$) values during both tests but no significant correlation for HR ($r = 0.42$, $p = NS$).*

Conclusions: *Dobutamine stress echocardiography is useful in the evaluation of the effects of surgical repair of CoA in children.* (Cardiol J 2009; 16: 20–25)

Key words: coarctation of the aorta, dobutamine stress echocardiography, treadmill exercise stress test

Introduction

Coarctation of the aorta (CoA) comprises 4–7% of all congenital cardiovascular disease. Significant anatomic variance of CoA is seen, and its hemodynamic effects depend on the degree of stenosis and the presence of collateral circulation. Elective surgical repair of CoA is performed at the age of 6–12 months. If heart failure ensues, surgical treatment must be undertaken immediately following the diagnosis.

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The effects of surgical repair depend on local anatomical conditions, experience of the surgeon, and the age of the patient. Long-term follow-up studies after surgical repair showed that left ventricular function is impaired even after an apparently successful repair, with persistence of left ventricular hypertrophy and diastolic dysfunction, thus leading to shortened life expectancy compared to healthy control subjects [1, 2]. Patients who underwent surgical repair of CoA are at risk of typical complications of arterial hypertension including atherosclerosis, myocardial infarction, stroke, and premature death [1]. Data available in the literature suggest that resting hypertension is present in 10–30% of patients following surgical repair, and exercise may induce hypertension in 30–65% of such patients [2]. Patients with normal resting blood pressure but significant exercise-induced hypertension are a particular subset that may be identified by a stress testing, most commonly an exercise test. As the latter is not feasible in the youngest children, we aimed to determine the utility of a pharmacological stress testing such as dobutamine stress echocardiography (DSE) in the evaluation of the effects of surgical repair of CoA.

Methods

We studied 29 consecutive patients after a surgical repair of CoA who were seen at the Department of Congenital Heart Disease and Pediatric Cardiology in Zabrze, Poland. We included patients who were operated at least one year before the study entry, were less then 18 years old at the time of the study, and were able to cooperate adequately during the treadmill exercise test and DSE. Exclusion criteria included other coexisting congenital heart disease including bileaflet aortic valve.

The study protocol and a parent questionnaire were approved by a local Ethics Committee.

We studied 20 male and 9 female patients. Their age ranged from 4.5 to 17.1 years (mean 12 years).

The subjects underwent treadmill exercise test using the Bruce protocol. Blood pressure was measured on the right arm at rest, at the end of each 3-minute exercise stage, at the end of the exercise test, and every 3 minutes during a 12-minute recovery. At the same time, blood flow velocity in the descending aorta was determined using an echocardiographic system by placing an Doppler ultrasound probe in the suprasternal notch (Hewlett-Packard 2000 or Sonos 5500, CW Doppler 2.5MHz). Doppler tracings were recorded on a video cassette and reviewed following the termination of the exercise test. Maximal pressure gradient was calculated using the simplified Bernoulli equation as $4\ V^2$, where V is maximal flow velocity. The exercise test was terminated at submaximal exercise or if one of the following conditions was met: abnormal ECG, excessive blood pressure rise, or patient request due to fatigue, pain, or dyspnea.

Dobutamine stress echocardiography was subsequently performed in a supine position, with continuous dobutamine infusion initially at the dose of 5 μg/kg/min, increased every 5 minutes by 5 μg/ /kg/min to the maximum dose of 20 μg/kg/min. Blood pressure measurements and determination of blood velocity in the descending aorta and calculation of pressure gradient were performed in a manner similar to the exercise test, at the end of each 5-minute period of dobutamine infusion. The latter was terminated after 20 minutes and subsequently three more sets of measurements of blood pressure and blood velocity in the descending aorta were performed at 5-minute intervals. ECG was monitored throughout the DSE, and the stress test was terminated when the dobutamine dose reached 20 μg/kg/min or prior to administration of such a dose, in case of reaching submaximal heart rate, abnormal ECG, excessive blood pressure rise, or patient request.

Statistical analysis

Statistical analysis included determination of correlations between maximal systolic blood pressure (SBP), pressure gradient in the descending aorta (GRAD), and heart rate values at the end of exercise during the treadmill test and upon termination of dobutamine infusion during DSE. Calculations of the Pearson linear correlation coefficient were performed using Statistica 6.2 software, with $p < 0.05$ regarded as statistically significant.

Results

Figures 1 and 2 show maximal GRAD and SBP values during the exercise test and DSE, as well as Pearson linear correlations for these parameters.

Resting SBP values were as follows: maximal 150 mm Hg, minimal 91 mm Hg, and mean 118 mm Hg, and corresponding SBP values at peak exercise were 230, 120 and 163 mm Hg, respectively. SBP at peak exercise reached 180 mm Hg in 4 subjects, exceeded 180 mm Hg in 4 subjects, and exceeded 200 mm Hg in 5 subjects.

Resting GRAD determined using Doppler ultrasound did not exceed 25 mm Hg in 14 subjects, and overall it ranged from 14 to 67 mm Hg (mean

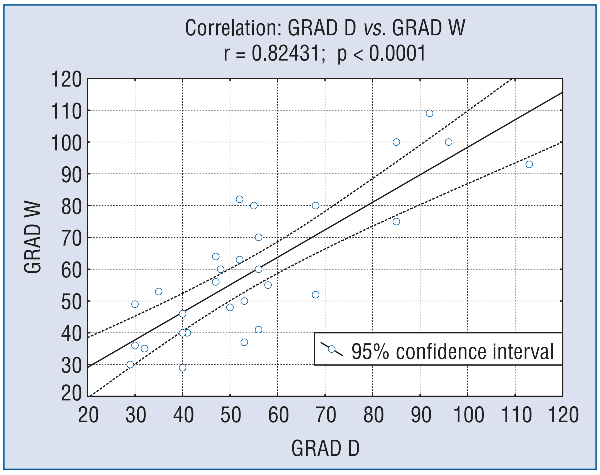

Figure 1. Correlation between the maximal pressure gradient in the descending aorta (GRAD) at peak exercise (GRAD W) and at the end of dobutamine infusion (GRAD D) in patients after surgical repair of coarctation of the aorta.

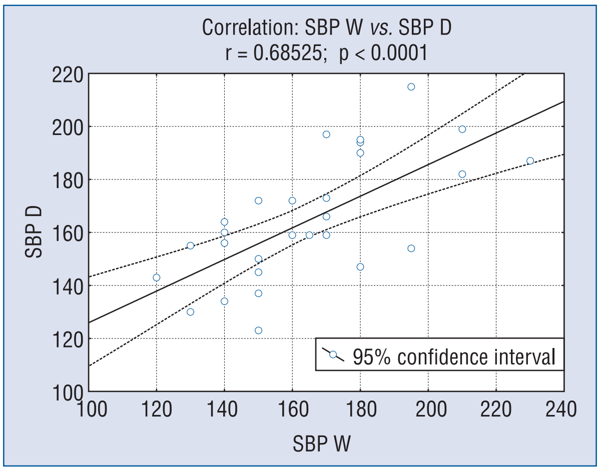

Figure 2. Correlation between systolic blood pressure (SBP) at peak exercise (SBP W) and at the end of dobutamine infusion (SBP D) in patients after surgical repair of coarctation of the aorta.

27.9 mm Hg). At peak exercise, maximal recorded GRAD was 109 mm Hg, minimal 29 mm Hg, and mean 59.7 mm Hg. SBP during infusion of a maximal dobutamine dose ranged from 123 to 215 mm Hg (mean 164.7 mm Hg). Heart rate (HR) was increased during dobutamine infusion, with maximal recorded value of 155 bpm, minimal 76 bpm, and mean 111 bpm. At peak exercise, maximal recorded HR was 188 bpm, minimal 144 bpm, and mean 169 bpm.

The exercise test was terminated due to reaching submaximal heart rate in 20 subjects, fatigue in 8 subjects, and an excessive blood pressure rise in one female patient. In two subjects, DSE was terminated at the dobutamine infusion rate of 10 μg/kg/min due to an excessive SBP rise to 197 and 199 mm Hg, respectively. No complications of DSE were noted. Five patients reported feeling of cold in limbs, one patient reported perioral numbness, one patient reported scalp itching and pressure in the suprasternal notch, one patient reported feeling of warmth in feet, and one patient reported marked palpitations. ECG showed supraventricular premature beats in 5 patients. All these symptoms and signs were not considered dangerous or severe enough as to necessitate termination of DSE testing. At the end of dobutamine infusion, maximal recorded GRAD was 113 mm Hg, minimal 29 mm Hg, and mean 55.4 mm Hg. Pearson linear correlation test showed significant correlation of both SBP and GRAD values at the end of treadmill exercise test and DSE. No such correlation was found for HR at the end of both tests. The correlation coefficients were as follows: $r = 0.6852$ ($p < 0.0001$) for maximal SBP during the exercise test versus DSE, $r = 0.8243$ ($p < 0.0001$) for maximal GRAD during the exercise test versus DSE, and $r = 0.4217$ ($p = 0.147$) for maximal HR during the exercise test versus DSE.

Discussion

Although the first surgical correction of CoA was performed 63 years ago, criteria of successful repair are still disputed, and in particular doubts are increasingly raised whether the achievement of normal aortic diameter really means cure of the defect. Currently, it is commonly thought that CoA should be viewed not only as a discrete aortic lesion but as a more generalized cardiovascular disorder with profound, long-term systemic effects. Outcomes of surgical treatment vary, and correcting the aortic anatomy does not guarantee blood pressure normalization. Postulated caused of persistent hypertension following the repair of CoA include differences in vascular receptor reactivity above and below the site of CoA, the shape of the aortic arch, and hypoplasia of the transverse arch. Thus, a diagnostic modality that would allow identification of patients at increased risk became desirable.

Residual coarctation or restenosis may be identified using various approaches. The simplest one is the physical examination, with significant findings including a systolic murmur at the left sternal border radiating to the interscapular area, difference in pulse volume between upper and lower limbs, and lower blood pressure in the lower limbs compared to the upper limbs. Chest X-ray and ECG are of no significant diagnostic value in patients after a surgical repair of CoA. More informative in regard to aortic anatomy and blood flow physiology is echocardiography combined with Doppler evaluation of the aortic flow. Indications for reintervention include significant aortic coarctation seen in imaging studies and the maximal aortic pressure gradient exceeding 30 mm Hg. Multidetector computed tomography is a particularly useful tool to imagine all structures relevant to CoA, including other arterial anomalies and collateral vessels. However, large radiation dose absorbed by the patient during imaging necessitates precise definition of indications for computed tomography scanning. Magnetic resonance imaging is also a precise diagnostic tool that allows delineation of coarctation anatomy and coexisting abnormalities. In addition, magnetic resonance imaging allows hemodynamic evaluations by determination of blood flow velocity. However, cardiac catheterization and conventional aortography remain gold standard modalities in the evaluation of CoA, although invasive nature of these studies, possible complications, need for general anesthesia in children, and radiation exposure limit indications for aortography only to patients who are candidates to reoperation or balloon angioplasty with or without stenting. Thus, attempts have been made to adopt diagnostic tools that are useful in the evaluation of cardiovascular disease risk in adults with hypertension, such as determination of intima-media thickness. It was shown that intima-media thickness may be useful as a marker of cardiovascular risk in children with repaired CoA [3]. However, these studies may guide decisions regarding preventive measures or even help determine the effectiveness of medical treatment, but give no data regarding such critical parameters of CoA as SBP or abnormal flow in the descending aorta.

Another widely used diagnostic tool is 24-hour blood pressure monitoring which has gained much acceptance and is successfully used in children, including those with repaired CoA [4]. However, 24-hour blood pressure monitoring also has some limitations, such as inability to evaluate younger children due to lack of appropriate reference values [5] or motion artifacts commonly seen in this subset of patients. In addition, some patients after a repair of CoA only show blood pressure rise during exercise, but limit their activity during 24-hour blood pressure recording due to such problems as device interference with active participation in sports. These problems make interpretation of ambulatory blood pressure data difficult.

Many publications described the utility of an exercise testing in the evaluation of abnormal cardiovascular parameters in patients with CoA. Clearly, this is a commonly used and useful tool, but it requires significant patient cooperation, including understanding of the purpose of the examination and adequate motivation to perform exercise. These conditions are hardly met in children, and exercise stress testing is virtually impossible in the youngest patients.

When evaluating patients treated due to CoA, Cyran et al. [6] noted a relation between increasing aortic pressure gradient and an excessive blood pressure rise during exercise. These authors were not able to give a clear explanation of this phenomenon but highlighted possible discrepancy between “anatomically” good procedural effect but insufficient physiologic improvement upon treatment.

This work prompted search for a modality that might be used to evaluate aortic flow during exercise. Echocardiography and Doppler evaluation during treadmill exercise test is technically demanding, requires significant operator experience, and the evaluation of abdominal aortic flow in these conditions is impossible. Cycloergometry, and in particular supine cycloergometry is a more convenient form of exercise for echocardiographic evaluation, but this form of exercise is more difficult for children, as cycling requires more coordinated, rhythmic effort compared to treadmill exercise. An ideal solution might be an echocardiographic evaluation of a supine patient undergoing pharmacological stress testing that results in a cardiovascular workload similar to conditions existing in an exercising subject. During such testing, increased aortic flow results not from exercise but from administration of a pharmacological stress agent, the dose of which may be precisely set and easily modified.

One commonly used and well-known tool fulfilling these conditions is DSE. Initial attempts of using dobutamine during echocardiographic examination were done already in 1970s [7]. Currently, DSE is a routine diagnostic modality in adult cardiology practice that allows evaluation of left ventricular function, myocardial perfusion, and valvular function. DSE is also a useful to estimate complication risk associated with vascular surgery [8, 9]. It has been used in pediatric populations as well, including evaluation of the left ventricle in Kawasaki disease, after anatomical correction of the transposition of great vessels, to evaluate pulmonary valve function following repair of the tetralogy of Fallot, to assess changes in ventricular inflow following the Mustard operation, and to evaluate the effect of chemiotherapy agents on the heart [10–15].

Similar cardiovascular response to dobutamine and exercise is supported by data published by Derric et al. [14] who found similar hemodynamic parameters during exercise and dobutamine infusion in patients after physiological correction of the transposition of great vessels. These authors showed significant correlation of stroke volume increase and other cardiac function parameters between these two tests.

In this regard, contrasting findings were published by Cnota et al. [16] who showed differences in the evaluated left ventricular function parameters between DSE and exercise testing. However, this study used supine cycloergometry and thus its findings may have been affected by an increase in venous return and cardiac preload in these conditions, complicating interpretation of the data as noted by the authors.

Utility of pharmacologic stress testing in patients after repair of CoA is suggested by a study by Miller et al. [17]. These authors selected patients for reintervention based on the results of pharmacologic stress using isoprenaline during a hemodynamic study. The patients were treated with repeated balloon angioplasty at the site of coarctation if aortic pressure gradient increased above 30 mm Hg during administration of isoprenaline. Following successful intervention, reduced aortic pressure gradient was seen both in rest and during isoprenaline administration, clearly indicating the value of such testing. However, pharmacologic characteristics of isoprenaline makes it unsuitable for routine pharmacologic stress testing. Isoprenaline has a positive chronotropic effect but also significantly reduces peripheral vascular resistance, thus leading to marked tachycardia. In addition, it increases myocardial oxygen demand and often provokes arrhythmia [18]. These properties prevented widespread adoption of isoprenaline as a diagnostic pharmacologic stress agent.

Although pharmacologic stress testing is routinely performed in current clinical practice, we are not aware of any previous study describing the use of DSE to evaluate the effect of CoA repair. We showed statistically significant correlation of GRAD and SBP values upon termination of exercise and dobutamine infusion. These data suggest the utility of DSE in the evaluation of the effects of surgical repair of CoA.

Some limitations of the current study should be noted. Statistical analysis showed significant correlations of aortic pressure gradient and SBP, but these evaluations would benefit from including a larger group of patients. We had no data on the anatomy of the transverse arch that is considered by some a risk factor for exercise-induced hypertension. Finally, our patients underwent different types of repaired procedures, were evaluated following a varying time that elapsed from the repair, and were of different age, with all these factors calling for more cautious interpretation of our data.

Finally, additional advantages of DSE should also be noted, such as lack of dependence of patient motivation to cooperate and exercise, as well standardization and reproducibility of cardiovascular workload by using strictly defined doses of the pharmacologic stress agent, thus facilitating both comparisons between different patients and serial evaluation of the same patient during a longer-term follow-up. The ability to monitor changes in the cardiovascular system that occur during many years following a surgical repair of CoA might prove very useful.

Conclusions

Our findings suggest that dobutamine stress echocardiography may be useful in the evaluation of the effects of surgical repair of CoA in children.

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