Assessment of Right Ventricular Function During Supine Bicycle Exercise After Mustard’s Operation

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SUMMARY Right ventricular (RV) performance during supine bicycle exercise was evaluated by gated equilibrium nuclear angiography in 19 clinically well children with d-transposition of the great arteries (d-TGA), 6.4 ± 2.7 years after Mustard’s operation. Comparisons were made between rest and peak exercise. The mean resting ejection fraction was 44 ± 12% (range 30–75%) and was unchanged at peak exercise. Eight children had a normal ejection fraction response, whereas 11 children had either no increase or a decrease in ejection fraction. Relative end-diastolic volumes decreased from resting values in all patients who had an abnormal ejection fraction response. Among patients whose ejection fraction increased, the end-diastolic volume increased in three, decreased in four and was unchanged in one at peak exercise. Heart rate increased 84% (range 52–135%) and systolic blood pressure increased 16% (range 0–28%) at peak exercise. There was no correlation between exercise response and age at surgery or interval since surgery. These data indicate that clinically well children after Mustard’s procedure may have abnormal right ventricular function under stress, raising concerns about the ability of the right ventricle to function as the systemic ventricle.

HEMODYNAMIC and electrocardiographic abnormalities have been reported in asymptomatic as well as asymptomatic patients after Mustard’s operation for d-transposition of the great arteries (d-TGA).

Because the long-term success of the procedure depends on the ability of the right ventricle to perform as the systemic pump, numerous investigators have evaluated right ventricular (RV) performance at rest using angiographic and echocardiographic methods both pre- and postoperatively. Because pump function during resting conditions does not necessarily reflect function during stress, methods have been devised to measure dynamic reserve during acute interventions. In this study, we assessed the RV reserve in response to supine bicycle exercise using gated equilibrium blood pool radionuclide angiography in a group of clinically well children who had undergone Mustard’s procedure.

Materials and Methods

Patient Selection

From May 1963 to November 1977, 925 children underwent Mustard’s procedure, using a pericardial intraatrial baffle for correction of d-TGA, at the Hospital for Sick Children, Toronto, Ontario. We reviewed all patient records and contacted children who were 6 years of age or older and considered clinically well. Thirty-four sets of parents and children consented to an exercise nuclear angiogram.

Patient Data

Clinical data on 19 patients with d-TGA who had complete studies with good separation of left ventricular (LV) and RV chambers and satisfactory radionuclide activity over the RV region of interest are reported in Table 1. Fifteen studies could not be included in the final data analysis because radioactivity over the region of interest was too low for analysis or because computer malfunction resulted in lost data. In the first few studies, the dose of technetium was adjusted for weight, but systole became too short during exercise to obtain sufficient counts; in the remaining studies we used a full adult dose to overcome this problem. The protocol was approved by the Human Experimentation Committee of the University of Toronto. Ten children underwent postoperative catherization 1–8 years before this study. All patients had normal pulmonary pressures, normal right and left ventricular end-diastolic pressures, and no evidence of pulmonary or systemic venous baffle obstruction. Three patients’ studies were entirely normal, two had mild tricuspid regurgitation, three had trivial or mild pulmonic stenosis (gradient 30 mm Hg), two had baffle leaks too small to quantitate, and one patient (no. 11) had mild aortic regurgitation and a residual muscular ventricular septal defect (Qp/Qs < 2:1). The d-TGA group had 10 males and nine females, mean age 8.3 ± 2.5 years (± sd) (range 6–16.5 years). The mean age at surgery was 2.0 ± 1.0 years (range 0.5–4.5 years) and the average follow-up interval was 6.4 ± 2.7 years (table 1). The mean cardiothoracic ratio (CTR) was 52 ± 3%. Sixteen patients were in sinus rhythm, two had a junctional rhythm and one had a wandering atrial
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pacemaker. Three children had right bundle branch block and two had first-degree atrioventricular block.

Study Protocol

Before exercise testing, each patient had a complete physical examination, a resting 12-lead ECG and a chest roentgenogram. Two-dimensional echocardiography was performed to determine septal obliquity so that the scintillation camera could be positioned to obtain maximal separation of RV and LV chambers. The procedure was carefully explained to all children, as full cooperation was necessary. A 19-gauge needle was secured in an antecubital vein and flushed periodically with a sterile saline solution. The children were positioned supine with their feet in the pedals of a Elema electric ergometer (type AM 368) with the pedal axle 32 cm above the table plane. An odometer was visible to the child. In all patients, heart rate (HR) from ECG lead II and systolic blood pressure (SBP) measured by sphygomomanometry were recorded at 2-minute intervals during rest and exercise. After aligning the camera with the child comfortable, a resting equilibrium angiogram was imaged for 300 heart beats. The patients then pedaled for 3 minutes at a cycle rate of 60 rpm, with the ergometer set at 50 kilopond-meters per minute (kpm). The work load was then increased, by 50–100 kpm every 3 minutes until exhaustion. Leg fatigue was the reason for stopping in all subjects. Imaging was performed during the final 2 minutes of each work period, when HR and blood pressure changes had reached a plateau. Two minutes after peak exercise, with the patient’s feet remaining in the pedals, a postexercise angiogram was obtained. The average length of each study was 15–25 minutes. The average workload for the d-TGA group was 8.4 ± 2.5 kpm/kg per minute (range 3.4–12.0 kpm/kg per minute).

Radionuclide Technique

Imaging was performed with the in vivo labeled red blood cell technique. An i.v. injection of 5 mg of cold stannous pyrophosphate dissolved in 3 ml of normal saline was given, followed in 15–20 minutes by 20 mCi of technetium-99m pertechnate. A mobile single-crystal scintillation camera equipped with a high-resolution, parallel-hole collimator (Ohio Nuclear) and a Digital Equipment Corporation 11/40 computer system using gamma-11 software were used for data acquisition and analyses. The multiple-gated studies were acquired with the patient supine and the camera head in the 70–80° left anterior oblique position. After injection of the radionuclide, the camera was repositioned to obtain maximal separation of RV and LV chambers. Scintillation data were accumulated in list mode and stored in histogram form in the computer memory; the R wave of the ECG served as the synchronizing impulse. After each cardiac cycle, the RR interval was examined automatically to determine whether it fell into a predetermined window. Cycles that fell outside this window were eliminated to avoid distortion of the time-activity curve. The cardiac cycle was divided into 20 frames/cycle at rest and data were collected for 300 cycles; exercise cycles were divided into 16 frames/cycle and accumulated for 2 minutes. Statistically reliable information was obtained by summing the radioactivity in the ventricle during many beats; in most studies, 200–400 beats were accumulated and summed.

Processing

Each gated study was displayed as an endless-loop movie on a color video-display to visualize the right ventricle and outflow tract. A region of interest was outlined over the right ventricle and a time-activity curve obtained. The end-systolic (ES) and end-diastolic (ED) frames were identified, and a region of interest outlining each ventricle was manually obtained; activity over the aorta was excluded. Background activity was determined as a lateral line one cell wide and two to three cells from the blood pool and subtracted from the total counts at ED and ES. The RV ejection fraction was calculated as ED
counts minus ES counts divided by ED counts times 100. Based on 10 transposition patients, the intraobserver error for right ventricular estimations with two observations per film was 3.0 ± 2.2 ejection fraction (EF) units. The interobserver error, based on a comparison of two observations by one person and a third observation by a second person, was 2.5 ± 1.7 EF units.

Relative RV Volumes

After correction for background, the number of radioactive emissions from the right ventricle is proportional to the amount of blood in the right ventricle. The method used during this study did not allow estimation of absolute volumes, but defined "relative" volumes ("EDV" and "ESV"). The change in RV volume from rest to exercise was determined by comparing background and frame-duration-corrected ED counts at rest and peak exercise. The number of emissions collected during exercise was not corrected for loss by physical decay or biologic excretion.

Statistical Analysis

Data are presented as mean ± SD. The significance of group differences was assessed by two-tailed, paired t tests. A p value < 0.05 was considered significant. Each patient was compared in terms of percent change from their resting values.

Results

The mean EF at rest was 44 ± 12% (range 30-75%) and 46 ± 11% (range 32-67%) at peak exercise (fig. 1)(NS). An increase of 5% or greater between resting and exercise EF was considered normal. The groups were divided into three subsets (table 2).

Group A consisted of eight patients who increased their EF from a mean of 40 ± 9% (range 30-47%) to 52 ± 12% (range 36-60%) (p < 0.01). There was an 86 ± 25% (range 55-135%) increase in HR and 17 ± 9% (range 0-28%) increase in SBP (fig. 2). "EDV" decreased from rest to peak exercise in four patients (p < 0.05), was unchanged in one patient and increased in three (fig. 3).

Group B consisted of five patients in whom the EF showed less than a 5% relative change between rest (40 ± 10%) and exercise (40 ± 9%) (NS). The HR increased 60 ± 19% (range 42-86%) and SBP increased 19 ± 8% at peak exercise (range 10-28%) (fig. 2). In four of these children, "EDV" and "ESV" decreased during exercise (p < 0.01) (fig. 4A); in patient 13, "EDV" and "ESV" increased.

Group C consisted of six children in whom EF decreased to a mean of 19 ± 9% (range 11 to 38%) during exercise. HR increased 92 ± 31% (range 52-127%) and SBP increased 15 ± 2% (range 11-18%) (fig. 2). Their mean resting EF was 55 ± 11% (range 45-75%) and at peak exercise 44 ± 12% (range 39-67%) (p < 0.01); "EDV" decreased to the same extent as "ESV" (fig. 4B). Two patients had a small (< 5%) increase in "ESV" and little change in "EDV" at peak exercise, accounting for a decrease in EF.

There was no significant difference between groups in peak exercise work load, HR or blood pressure elevation, resting ECG pattern (T wave in V1, QRS-T angle) or CTR. No correlation could be found between resting or exercise EF response, and age at surgery, follow-up interval, associated lesions, events at surgery (time of ischemic arrest and temperature, or immediate postoperative course), and findings at postoperative catheterization.

Discussion

Mustard’s operation to correct d-TGA leaves the right ventricle as the systemic pump. Its ability to sustain this function over a long period and to respond normally to increased work loads is vital to the well-being of these patients. RV myocardial fiber array differs from that of the left ventricle and may render the right ventricle less able to function systemically. Echocardiographic studies and measurements of circumferential (LV-like) fiber shortening suggest that the right ventricle cannot benefit from the septal component of ejection, because of the bellows-like action of the RV free wall. This configuration is better suited to the ejection of large volumes of blood with minimal shortening. In patients with d-TGA, the right ventricle, with its larger EDV and systemic pressure, must accept higher wall tensions throughout contraction and therefore have a higher oxygen consumption than a normal right ventricle or a systemic left ventricle, and the increased RV pressure existing from birth induces a proliferation of both myocytes and fibroblasts. These features may create a mismatch between RV blood supply and demand, especially because the right ventricle is primarily dependent on a single major coronary arterial supply.

The assessment of ventricular function during exercise is useful in diagnosing abnormal cardiac function...
Table 2. Exercise Data

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<td>Mean ± SD</td>
<td>7.9 ± 3</td>
<td>40 ± 9</td>
<td>52 ± 12</td>
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Group B

|    | 5.0           | 30     | 32                                 | 6  | −7    | −10   | 12  | 42 |
| 10 | 10.0          | 37     | 37                                 | 0  | −13   | −16   | 22  | 80 |
| 11 | 9.6           | 31     | 34                                 | 9  | −14   | −19   | 28  | 82 |
| 12 | 7.7           | 49     | 47                                 | −5 | −40   | −38   | 10  | 57 |
| 13 | 10.6          | 53     | 53                                 | 0  | 77    | 39    | 22  | 86 |
| Mean ± SD | 8.6 ± 2.0     | 40 ± 10 | 40 ± 9                           | 2 ± 5 | 0.6 ± 44 | −9 ± 29 | 19 ± 8 | 69 ± 19 |

Group C

|    | 9.0           | 49     | 39                                 | −21 | −5    | 8     | 15  | 124|
| 15 | 10.0          | 54     | 34                                 | −38 | −54   | −32   | 15  | 72 |
| 16 | 13.0          | 49     | 40                                 | −19 | −25   | −15   | 18  | 107|
| 17 | 9.4           | 74     | 67                                 | −11 | 35    | −18   | 11  | 72 |
| 18 | 12.0          | 58     | 50                                 | −14 | 6     | 9     | 14  | 127|
| 19 | 5.7           | 43     | 37                                 | −14 | −32   | −28   | 15  | 52 |
| Mean ± SD | 10.0 ± 2.3    | 55 ± 11 | 44 ± 12                           | −19 ± 9 | −13 ± 31 | −15 ± 17 | 15 ± 2 | 92 ± 31 |

Overall mean ± SD

|    | 44 ± 11       | 46 ± 11 | 46 ± 12                           | 7 ± 26 | −2 ± 39 | −14 ± 29 | 17 ± 8 | 84 ± 26 |

Abbreviations: EF = ejection fraction; "EDV" and "ESV" = relative end-systolic and end-diastolic volumes; SBP = systolic blood pressure; HR = heart rate.

not apparent at rest.11-14, 17, 26 M-mode and two-dimensional echocardiography are helpful in assessing left ventricular function, but are less well suited to exercise studies or functional studies of the normally positioned right ventricle. Investigators have therefore relied upon contrast dye cineangiography during cardiac catheterization to evaluate RV morphology and performance,1-3, 5-10 although these methods depend on geometric approximations of the complex, highly trabeculated right ventricle27 and are usually limited to single observations at rest because of dose constraints and adverse effects of contrast media on volume and contractility.

Gated equilibrium blood pool imaging allows a

Figure 2. Heart rate and systolic blood pressure at rest (open column) and peak exercise (hatched column). Bars indicate mean ± sd d-TGA = d-transposition of the great arteries.
continuous noninvasive measurement of cardiac performance during exercise, is free from geometric assumptions of ventricular shape and correlates well with first-pass RVEF by nuclear angiography. Nevertheless, the contribution of atrial counts to RV activity may interfere with the EF determination. The manual method of excluding the atrial region from the RV region of interest only slightly corrects the EF calculation. Because data analysis was performed using each patient as his own control, the percent contribution of right atrial counts to the EF was assumed to be constant.

Normal values for RVEF when the RV is functioning systemically as it does in d-TGA do not exist. Accordingly, different centers have reported good to poor function both pre- and postoperatively, depending on a predefined normal RVEF. There have been few studies of the hemodynamic response to exercise after Mustard's procedure. Those patients so studied are a small, heterogeneous group and therefore general conclusions are difficult to make. We studied a group of children, 6 years of age or older, who appeared clinically to have a good result from the Mustard operation.

RVEF and LVEF at rest and in response to exercise have been assessed by radionuclide techniques in the normal adults and have consistently shown a relative increase of more than 5% in EF at peak exercise for both ventricles. This degree of response was chosen a priori to separate normal from abnormal function. In the adult studies, resting supine LVEF averaged 66 ± 7% and increased to 79 ± 7% at maximal exercise. The average normal RVEF was 46 ± 7% at rest and increased to an average of 57 ± 6%. Thus, because of a larger diastolic volume, the normal right ventricle had a lower resting EF than a normal left ventricle, allowing minute-to-minute equality of pulmonary and systolic stroke volumes. One should not, therefore, expect a normally functioning systemic right ventricle, because of morphologic considerations, to have the same EF as a resting systemic left ventricle.

The resting RVEF in the d-TGA patients was 44 ± 11% (with only five children above 50%), similar to previously reported resting RVEF by cineangiography. Because we lack "normal" resting values, the response to exercise should provide greater insight into ventricular function and reserve than a single resting value.

The EF response to exercise is modulated by the in-

![Figure 3](http://circ.ahajournals.org/)

**Figure 3.** Percent change from rest (R) to peak exercise (PE). (A) Patients whose "EDV" decreased with exercise. (B) Patients whose "EDV" remained unchanged or increased with exercise. EF = ejection fraction; "EDV" = relative end-diastolic volume; "ESV" = relative end-systolic volume.

![Figure 4](http://circ.ahajournals.org/)

**Figure 4.** Percent change from rest to peak exercise. (A) Volume changes in patients whose ejection fraction (EF) did not change. (B) Volume changes in patients whose EF decreased. Abbreviations as in figure 3.
terrelation of preload, afterload and contractility. Therefore, an abnormal response may not reflect impaired myocardial function but a mismatch between pre- and afterload conditions. A diminished preload contributes to an abnormal EF response by reducing stroke volume at rapid HRs. After the Mustard operation, obstruction at the inferior limb of the atrial baffle could contribute to a diminished preload during supine exertion, as could pulmonary venous obstruction, and may underlie an abnormal EF response independent of the adequacy of myocardial contractility. At postoperative catheterization, however, no patient had angiographic or hemodynamic evidence of baffle obstruction or clinical evidence of systemic venous congestion (hepatomegaly or venous engorgement). It is unlikely that abnormal preload conditions contributed to an abnormal response in this selected group.

Changes in peak SBP at peak exercise were inappropriately low for the degree of exertion. Although maximal exercise may not be identical to peak exercise in our patient group, steadily increasing HR during increasing work load suggests that oxygen consumption was increasing. Cummings found during catheterization in “normal” children that brachial artery systolic pressure increased during supine exercise to at least 161 mm Hg, compared with a peak average of 110 ± 11 mm Hg (17% increase) in our d-TGA patients (fig. 2). In our laboratory, peak systolic blood pressure during supine exercise exceeds 180 mm Hg in normal adolescents and young adults.

Because systolic wall tension (i.e., afterload) is linearly related to pressure and the square of the radius, directional changes can be estimated between rest and exercise wall tension in our patients. In the children in groups B and C (fig. 3), “EDV” decreased, associated with no change or a decrease in EF. Because blood pressure did not increase significantly and the ventricular radius was smaller, the afterload at peak exercise was not significantly elevated. Thus, depressed function due to an inappropriate level of contractility probably caused the abnormal EF response.

In group A (increased EF), two subgroups could be identified depending on their “EDV” response. Four patients had a relative decrease in “EDV” (fig. 3A) associated with an inadequate increase in blood pressure, which suggests an inappropriately low afterload for that degree of exertion. As the “ESV” decreased considerably, EF increased, perhaps representing a compensatory response to exertion. The four remaining children (fig. 3B), had an elevation or no change in “EDV.” The EDV response to supine exercise in normal subjects is not clear. Some investigators have found no change and others an increase in EDV, but this depends largely on the level of exertion. Consequently, this remaining subgroup may represent a normal response to exercise. The work loads achieved by all three subgroups were well below published values for supine bicycle exercise in children (233 ± 71 kpm/m² for the d-TGA group and 316 kpm/m² in normal children) and adults (13.7 kpm/kg · min⁻¹). Whether this is an abnormal response will depend on future follow-up studies.

The causes for the obvious RV dysfunction in groups B and C and compensated or questionably normal function in group A are not apparent from our data. The type of response did not correlate with age at surgery or length of follow-up. No clinical variable (e.g., ECG or chest roentgenogram) could predict the response. Attempts to correlate these findings with the potential for myocardial damage during surgery were unsuccessful when patients were grouped according to ischemic arrest time and degree of hypothermia. Nevertheless, the effects of surgical methods for myocardial preservation on myocardial function need further evaluation.

These data indicate that RV function is compromised during exercise stress in many clinically well patients after Mustard’s procedure. Long-term cardiac function remains to be evaluated at rest and during stress. Alternatives to the intraatrial baffle operation, such as the Jatene procedure, carry a high mortality.

Acknowledgment

The authors thank Cathy Heteniak for editing and typing this manuscript.

References

Assessment of right ventricular function during supine bicycle exercise after Mustard's operation.
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_Circulation_. 1982;65:1052-1059
doi: 10.1161/01.CIR.65.6.1052
_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/65/6/1052

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