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The Role of Chronotropic Impairment During Exercise After the Mustard Operation

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To better understand the role of chronotropic impairment on exercise performance after the atrial switch (Mustard) operation, 20 patients who had undergone this operation for uncomplicated d-transposition of the great arteries exercised to maximal volition using a 1 min incremental treadmill protocol. Heart rate, oxygen consumption, carbon dioxide production and minute ventilation were monitored continuously. Two-dimensional echocardiograms were obtained before testing to calculate the right ventricular inflow volume indexed to body surface area.

All patients achieved maximal aerobic capacity based on their ventilatory patterns and respiratory exchange ratio. Maximal heart rate was reduced (175 beats/min; 87% of predicted for age) and maximal oxygen consumption was decreased (31 ml/kg per min; 75% of predicted for age and gender). There was no correlation between maximal oxygen consumption and maximal heart rate. Right ventricular volume index, however, had a significant inverse correlation with maximal heart rate ($r = -0.62$, $p < 0.005$). There was no correlation between right ventricular volume index and heart rate at rest.

These results suggest that decreased maximal oxygen consumption in patients after the Mustard procedure is not a result of chronotropic impairment. Right ventricular dilation may be a compensatory response to chronotropic impairment.

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Previous studies (1–6) of exercise performance in children and adolescents after the Mustard (atrial switch) operation have shown these patients to have varying degrees of exercise limitation and reduced aerobic capacity. Ventricular dysfunction, especially of the right ventricle, and an impaired chronotropic response to exercise have been cited as possible mechanisms for the observed exercise limitation. In previous studies, the large number of patients with additional defects, such as ventricular septal defect, residual ventricular outflow obstruction or atrial baffle obstruction, as well as those with significant atrial or ventricular arrhythmias have made the evaluation of the causes of exercise limitation difficult. The role that these additional defects play in determining exercise tolerance is not clear.

This study was undertaken to evaluate the relative importance of chronotropic impairment to exercise limitation in patients after the Mustard procedure by eliminating the potential confounding variables just listed and using complete metabolic measurements to accurately determine achieved maximal heart rate.

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Methods

Study patients. Between October 1987 and December 1989, 56 patients previously operated on for d-transposition of the great arteries using the Mustard operation underwent exercise testing at Children's Hospital of Michigan. Twenty patients were excluded from the study for having other anatomic defects, symptomatic arrhythmias or arrhythmias for which they were receiving medication. Thirteen patients were excluded when postexercise evaluation of their metabolic measurements indicated that they terminated exercise before achieving maximal aerobic capacity. Three patients were excluded because a two-dimensional echocardiogram had not been performed within 6 months of their exercise test.

The remaining 20 patients made up the study group. All had d-transposition of the great arteries as their sole congenital heart defect. Patients' gender and age at operation and testing are summarized in Table 1. All patients were in New York Heart Association functional class I and were taking no cardiac medication at the time of testing. Cardiac Rhythm at rest was either sinus ($n = 18$) or sinus with intermittent junctional escape ($n = 2$).

Echocardiography. Two-dimensional echocardiograms were performed on all patients within 6 months of exercise testing. The inflow portion of the right ventricle was visualized during diastole from the apical four chamber view using either a Hewlett-Packard Sonos 100, HP 7520A or an Acuson 128. The inflow area was determined by planimetry and the inflow volume calculated by Simpson's method with use

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Table 1. Exercise Data in 20 Patients

Pt No.	Gender	Age (yr)		Heart Rate (beats/min)		% Predicted Max HR	Work Rate (Watts)	% Predicted Work Rate	Max $\dot{V}O_2$ (ml/kg per min)	% Predicted Max $\dot{V}O_2$	$\dot{V}O_2$ at VAT (ml/kg per min)	% Max $\dot{V}O_2$ at VAT	RER
		Oper	Test	Rest	Max								
1	M	2.3	8	66	179	87	86	78	34	80	23	68	1.15
2	M	1.3	16	55	162	81	163	89	27	54	22	81	1.19
3	F	1.1	6	92	194	97	37	49	22	58	15	68	1.12
4	M	0.5	15	71	155	77	171	75	23	44	17	74	1.20
5	F	1.2	16	61	168	87	142	95	30	80	19	63	1.43
6	F	2.2	15	65	164	84	162	96	28	80	14	50	1.26
7	M	1.4	10	70	159	78	165	130	29	65	17	59	1.18
8	M	0.8	9	66	191	93	93	88	28	64	18	64	1.19
9	M	1.1	15	56	161	80	252	123	36	72	23	64	1.44
10	M	1.1	11	75	185	91	103	99	38	90	22	58	1.16
11	F	0.8	13	66	186	94	186	110	37	108	20	54	1.22
12	F	0.1	10	84	181	91	96	92	26	68	15	58	1.21
13	M	0.5	14	52	191	95	242	116	37	70	23	62	1.13
14	M	0.7	15	62	172	85	236	117	45	89	23	51	1.19
15	F	1.1	12	81	192	100	211	158	33	98	18	54	1.31
16	F	0.8	13	81	151	73	117	97	29	81	17	59	1.26
17	F	0.3	13	68	162	79	191	135	28	78	16	57	1.24
18	M	0.1	15	61	162	78	156	97	35	85	20	57	1.36
19	F	0.6	13	81	196	95	132	109	26	71	17	65	1.23
20	M	0.7	15	93	181	88	161	97	33	78	21	64	1.19
	F 9												
Mean	M 11	0.9	13	70	175	87	155	103	31	75	19	62	1.23

F = Female; HR = heart rate; M = male; Max = maximal; Oper = operation; Pt = patient; RER = respiratory exchange ratio; Rest = resting; Test = testing; VAT = ventilatory anaerobic threshold; $\dot{V}O_2$ = minute oxygen consumption; % Predicted = percent of predicted normal values.

of an offline digitizing pad measurement program. Volume was normalized to body surface area. Measurements were performed by one of the authors who did not know the results of the exercise testing.

Exercise testing protocol. All patients were exercised to maximal volition using a 1 min incremental treadmill protocol. This consisted of 3 min of initial walking at grade 0, followed by an increase in grade and speed each minute until maximal work rate was achieved.

Electrocardiographic measurements. A 15 lead electrocardiogram (ECG) obtained in the supine position during a clinic visit within 6 months of the exercise test was used to measure heart rate and rhythm at rest. During exercise testing, ECG leads II, aVF and V_5 were monitored continuously. A 12 lead ECG was obtained every minute during exercise testing and during the first 5 min of recovery.

Metabolic and pulmonary measurements. Minute oxygen consumption ($\dot{V}O_2$), minute carbon dioxide production ($\dot{V}CO_2$), minute ventilation ($\dot{V}E$) and respiratory exchange ratio were monitored continuously on a breath by breath basis. The ventilatory equivalents of oxygen ($\dot{V}E/\dot{V}O_2$) and carbon dioxide ($\dot{V}E/\dot{V}CO_2$) were monitored by continuous graphic display during testing.

Criteria for measurement of aerobic capacity. Patients were judged to have achieved maximal aerobic capacity at peak exercise if the following criteria were met: respiratory exchange ratio at maximal work rate >1.1 and a clearly defined ventilatory anaerobic threshold could be measured from the graphs of the ventilatory equivalents of oxygen and carbon dioxide (7). Patients who did not meet both of these criteria during the exercise test were judged to have stopped exercise before achieving maximal aerobic capacity regardless of their maximal heart rate and were excluded from further analysis.

Statistical analysis. Analysis was by linear regression. A p value <0.05 was considered significant.

Results

Work rate. Table 1 summarizes the results of the exercise testing for the 20 patients who achieved maximal aerobic capacity. Maximal work rate was normal for the entire study group.

Maximal heart rate. This was decreased for the entire study group at 87% of the predicted values for the group based on age. Maximal exercise and rest heart rate showed no correlation with either age at the time of operation or age at the time of exercise testing.

Oxygen consumption. Maximal $\dot{V}O_2$ also was decreased for the study group (mean 31 ml/kg per min). This was a more marked decrease than that of the maximal heart rate at 75% of predicted for age and gender. There was no correlation between age at operation or age exercise testing and the maximal $\dot{V}O_2$. Oxygen consumption for the study group at

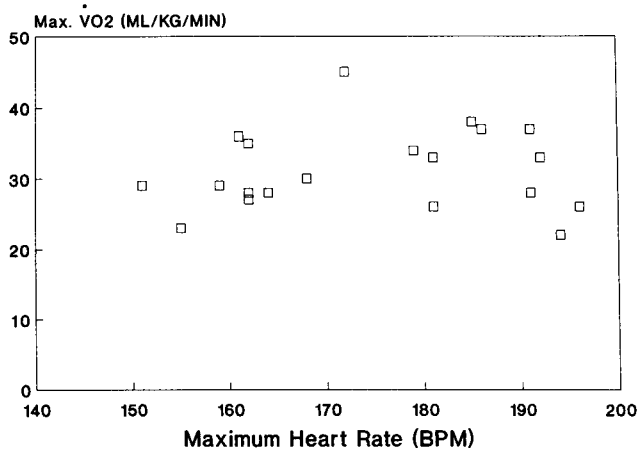

Figure 1. Maximal $\dot{V}O_2$ versus maximal (Max.) heart rate for each of the 20 patients. y = 0.36x −22.3; r = −0.24 (not significant). BPM = beats/min.

ventilatory anaerobic threshold was 19 ml/kg per min (Table 1). When $\dot{V}O_2$ at ventilatory aerobic threshold was expressed as a percent of the patient's maximal $\dot{V}O_2$, the mean for the patient group was 62%.

Maximal $\dot{V}O_2$ was compared with maximal heart rates for each of the patients (Fig. 1). There was no correlation between either the maximal or rest heart rate and maximal $\dot{V}O_2$. There was also no correlation between the maximal $\dot{V}O_2$ and the right ventricular volume index.

Right ventricular volume. Right ventricular volume index and rest and maximal heart rate are compared in Figure 2. There was no correlation between right ventricular volume index and rest heart rate. There was an inverse correlation (r = −0.62) between right ventricular volume index and maximal heart rate ($p < 0.005$). There was no correlation between right ventricular volume index and age of the patients at operation or during exercise testing.

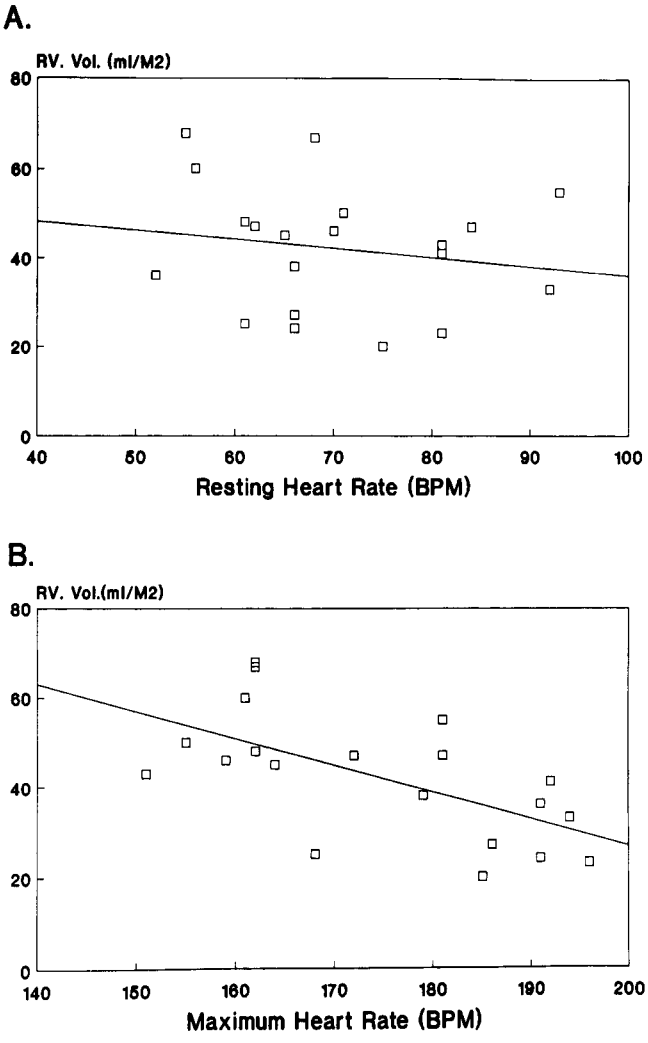

Figure 2. Right ventricular volume index (RV. Vol.) versus rest (**A**) and maximal (**B**) heart rate for each of the 20 patients. **A**, y = −0.12x +52; r = −0.11 (not significant); **B**, y = −0.60x +147; r = −0.62 ($p < 0.005$). BPM = beats/min.

Discussion

Comparison with previous studies. As in previous reports (1,2), we found decreased maximal $\dot{V}O_2$ for the patients compared with healthy individuals. The average maximal $\dot{V}O_2$ for patients in the study of Ensing et al. (1) was less (27 ml/kg per min) than the values in our study. Their patients' working capacity (1) as well as the working capacity of the older patients in the study of Mathews et al. (2) was also decreased compared with that of healthy subjects. The reason for these discrepancies may be due to patient selection in our present study, in which any associated cardiac defects were excluded. In previous studies, many patients had additional complicating cardiac defects and residual hemodynamic abnormalities, such as ventricular outflow obstruction. Of the seven patients listed as "very well" clinically in the study of Ensing et al. (1), four had additional associated cardiac lesions. Mathews et al. (4) reported similar numbers. Another possible factor may be the exercise mode used in the study of Ensing et al. (1). They (7) used cycle ergometry, which may have resulted in a somewhat lower maximal $\dot{V}O_2$ compared with treadmill testing.

Age at the time of surgical repair may also be a factor. The mean age for repair in previous studies (1–6) has ranged from 1.5 to 4 years. The mean age at repair in our study (11 months) was less. There was no correlation between maximal $\dot{V}O_2$ and age at operation in our study; however, the range of ages in our study is narrow. Only two of the patients underwent surgical repair after (approximately) 1 year of age. For these reasons, our patients may have performed somewhat better than previous patient groups, as assessed by both maximal work rate and maximal $\dot{V}O_2$.

Reasons for decreased maximal oxygen consumption. Maximal $\dot{V}O_2$ was decreased in our study patients (75% of predicted) despite their normal physical working capacity. Compared with the low maximal $\dot{V}O_2$, the normal working capacity might be due to some patients excessively holding the support bar on the treadmill. The respiratory exchange ratio was also high for this group of patients, suggesting that

a significant fraction of their work was performed anaerobically. Maximal $\dot{V}O_2$ at anaerobic threshold in this group was reduced compared with previous reported values of 30 to 35 ml/kg per min in children (8,9). When expressed as a percent of the maximal $\dot{V}O_2$ it was normal (62%) (8,9). This finding suggests that $\dot{V}O_2$ at anaerobic threshold is low because of the reduced maximal $\dot{V}O_2$.

Maximal $\dot{V}O_2$ was decreased even in our patients who had a normal or near normal maximal heart rate. There was no correlation between maximal $\dot{V}O_2$ and maximal heart rate. This observation suggests that aerobic capacity was diminished by a mechanism other than chronotropic impairment in these patients.

Several studies (4–6) have shown diminished right ventricular ejection fraction during exercise in patients after the Mustard operation. Murphy et al. (4) showed that the patients' age at testing and operation, as well as the presence of associated defects, correlated with decreased right ventricular function. Our study suggests that even in the absence of additional defects, diminished right ventricular function occurs and results in decreased aerobic capacity.

The diminished aerobic capacity reflected by the decreased maximal $\dot{V}O_2$ did not decrease further as chronotropic impairment increased over a wide range of maximal heart rates in our study. The inverse correlation between right ventricular volume index and maximal heart rate suggests that right ventricular dilation may be a compensatory mechanism to maintain cardiac output, and hence maximal oxygen consumption, as maximal heart rate decreases. This implies that ventricular dilation results in an increase in stroke volume.

No other factor, including heart rate at rest, maximal $\dot{V}O_2$ and age, had any correlation with right ventricular volume. Nevertheless, it seems unlikely that maximal heart rate is the major determinant of right ventricular volume. It is likely that both maximal heart rate and the underlying degree of ventricular dysfunction play a significant role in determining right ventricular volume.

Role of rate-responsive pacing. The long-term effects of right ventricular dilation in response to increasing chronotropic impairment are unclear from the current data. Sinus node dysfunction in our group of patients was not severe enough to result in symptomatic bradycardia at rest. The ability of the right ventricle to compensate for decreasing heart rate response as chronotropic impairment worsens may be limited. Preliminary studies (10) from our laboratory in patients with symptomatic bradycardia while at rest after the Mustard operation suggest that this may be the case. In these patients, maximal $\dot{V}O_2$ during exercise could be significantly increased by the use of rate-responsive pacing to improve chronotropic response (10). This implies that although chronotropic impairment may be less important than intrinsic ventricular function in determining maximal $\dot{V}O_2$ in asymptomatic patients, this may not be the case in those patients with symptoms or arrhythmias at rest.

The data from the current study also raised the question as to the use and timing of a rate-responsive pacemaker in this group of patients. The correlation between right ventricular volume was significant with maximal heart rate but not with heart rate at rest. Neither condition, however, is the state most patients are in throughout the day; rather, they are performing some level of submaximal activity. It is possible that their limited ability to increase heart rate with this level of activity may be a more important determinant of right ventricular volume than their actual maximal heart rate. It is not possible to confirm this hypothesis from the data in this study. If this were the case, however, rate-responsive pacing might mitigate ventricular dilation. Continued study, perhaps using Holter ECG monitoring to assess heart rate and submaximal activity levels, may be useful in answering this question.

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