Hemodynamic effects of dynamic exercise in children and adolescents with moderate-to-small ventricular septal defects

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ABSTRACT We studied the hemodynamic effects of dynamic exercise during cardiac catheterization in 35 children and adolescents with small-to-moderate ventricular septal defects. Eighteen of them exercised at 25% and 50% of their maximum workload and 17 exercised at 60%. There was no significant difference between the two groups with respect to age and body mass, height, and surface area. The changes evoked by exercise showed the same pattern at the different workloads, although they were more marked at the higher than at the lower percentage of maximum workload. During exercise the pulmonary vascular resistance did not change, in contrast to the systemic vascular resistance, which decreased. The pulmonary and systemic blood flows both increased, while the left-to-right shunt flow did not change, which led to a decrease of the left-to-right shunt fraction. As the heart rate increased and the shunt flow did not change, the shunt volume per beat decreased during exercise. We conclude that in patients with small-to-moderate ventricular septal defects the hemodynamic effects of dynamic exercise are favorable because the normal rise in systemic blood flow occurs without a corresponding increase in left-to-right shunt flow. Consequently, children and adolescents with such defects should not be restricted in their dynamic exercise activities.

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ISOLATED ventricular septal defects are present in 20% to 25% of children with a congenital heart disease.1,2 In most cases these defects are located high and anterior in the membranous septum.2 The size of the defect and, consequently, the clinical picture of these patients can vary widely. When the left-to-right shunt through the defect is smaller than 50% of the left ventricular output and the pulmonary vascular resistance is normal, surgical treatment at a young age is usually not advocated. This is because in 17% to 20% of the cases the shunt percentage decreases with advancing age,3,4 while it is even possible that the entire defect will close spontaneously.1,4 Moreover, the life expectancy of patients with small-to-moderate ventricular septal defects is almost normal.3,5 The major risk for these patients is bacterial endocarditis.1,3 Because this risk is very small with good antibiotic prophylaxis, it does not seem justified to operate on these children when they are asymptomatic and when their chest roentgenograms and electrocardiograms are normal.6

When these children are not operated on they are usually not restricted in their physical activities.7 However, it is not quite clear what the hemodynamic effects of exercise are in these patients. Available studies show no uniformity in the behavior of the left-to-right shunt through the defect during exercise.8-10 To define more carefully the response to exercise, as well as to answer the question of whether the policy not to restrict patients who are not operated on is justified, we studied a representative group of patients with ventricular septal defects, moderate-to-small left-to-right shunts, and normal values for pulmonary vascular resistance.

We designed our study with two main objectives. First, we studied children at two workloads to assess whether there was a progressive change with increasing exercise. Second, we assessed the effects of maximal exercise achievable under the conditions of cardiac catheterization.

Methods

Patients. We studied 35 patients with moderate-to-small ventricular septal defects, i.e., defects with left-to-right shunt...
between 35% to 50% and less than 35% of pulmonary blood flow, respectively, and normal pulmonary arterial pressures. There were 20 boys and 15 girls. Only patients over 9 years of age were selected for this study because we did not expect to achieve adequate cooperation in younger children. The patients had no complaints at rest or during exercise. They all had normal body weight and mass and normal electrocardiograms. In 23 patients the chest roentgenograms were normal, while in the other 12 the hearts were slightly enlarged; nine patients showed signs of pulmonary engorgement. The study was approved by the institution’s committee on clinical investigation, and informed consent was obtained from the patients’ parents. There were no complications in patients as a result of this study.

Protocol. The maximum workload of each patient was determined the day before cardiac catheterization by means of a progressive upright bicycle exercise test as described by Godfrey et al.11 One hour before cardiac catheterization each patient received 5 mg of diazepam orally. After local anesthesia with 1% lidocaine and an arterial and venous cut-down in the right arm, No. 6F NIH and No. 6F Lehman catheters were introduced, respectively. A thermistor was placed in front of the nostrils, which was used to record the respiration. After completion of the diagnostic right and left heart catheterization, the patient’s feet were placed on the pedals of the ergometer (Lode Instruments, type Angio), after which resting measurements were made. Then exercise studies were performed by 18 patients at 25% and 50% (group I) and by 17 patients at 60% of their maximum workload (group II). In group I we studied whether there was a progressive change in the hemodynamics with increasing exercise; in group II we assessed the hemodynamic effects of maximal exercise achievable under the conditions of cardiac catheterization. When 25%, 50%, or 60% of the maximum workload had been reached, we waited 3 min to allow a steady state to be attained before starting the measurements again. The patients of group I were allowed to rest for about 20 min after completing the first phase of the exercise. The following data were collected: blood pressures in aorta, pulmonary artery, right atrium, and wedge pulmonary arterial position; right and left ventricular pressures simultaneously; dye-dilution curves; oxygen saturations in aorta and distal right or left pulmonary artery; and hemoglobin and lactic acid concentrations in the aorta.

After catheterization, left ventricular cineangiographic studies were performed with patients in a left oblique projection of 65 degrees and a cranial angulation of 25 degrees.

Measurements and calculations. Pressures were measured at end-expiration through fluid-filled catheters. In 20 patients the pressure difference between the right and left ventricles was measured with a Statham P23 H differential transducer. The dye-dilution curves were obtained by injecting 2.5 mg of indocyanine green into the pulmonary artery and withdrawing blood through the No. 6F NIH catheter and a Waters-410 cuvette densitometer. Pressures, dye-dilution curves, respiration, and electrocardiograms were recorded on a Siemens-Elema EMT 169 recorder and on a Philips EL 1016 magnetic tape recorder.

Oxygen saturation and hemoglobin were determined by standard photometric techniques, and the lactic acid concentration was measured by means of an enzymatic ultraviolet method12 (Boehringer, Monotest Lactate).

In the 20 patients in whom the pressure difference between the right and left ventricles was measured with a differential pressure transducer, the mean pressure difference was obtained by planimetric integration of the tracings of six cardiac cycles. In the other 15 patients the signals of the right and left ventricular pressure measurements were played back from the magnetic tape and fed into a differential amplifier. The output of the differential amplifier was then treated in the same way as the output of the differential pressure transducer. The blood flows and shunt fractions were calculated from the dye-dilution curves as described by Mook and Zijlstra13 (figure 1). Pulmonary and systemic vascular resistances were calculated according to standard equations. Left ventricular stroke volume was calculated as the quotient of pulmonary blood flow and heart rate, and effective left ventricular stroke volume as the quotient of systemic blood flow and heart rate.

Statistical analysis. The rest and exercise values were compared by the paired Student’s t test. Comparisons between the groups were analyzed by the unpaired Student’s t test. Differences were considered to be statistically significant if p < .01. Results are expressed as mean ± SD.

Results

There was no significant difference between the two groups with respect to age and body mass, height, and surface area (table 1). In group I the maximum workloads assessed the day before cardiac catheterization were slightly higher (.01 < p < .05) than could be expected from the data of Godfrey et al.,11 while the maximum workloads in group II were about the same (table 2). The highest heart rates achieved during the maximum workloads in the upright bicycle exercise exercise.
test by our patients were comparable with those of normal children. When the children were at rest the pulmonary arterial oxygen saturation in group II was significantly lower than that in group I because of the smaller left-to-right shunts of the children in group II (table 3 and 4). There were no other significant hemodynamic and biochemical differences between the two groups at rest, except for the total left ventricular stroke volume, which was significantly lower in group II than in group I (p < .001). Pulmonary arterial pressures and vascular resistances were normal in both groups as expected with small-to-moderate ventricular septal defects and left-to-right shunts. Systemic blood flows were in the high-normal range.

The changes in measured and calculated data during exercise are given in table 3 and figures 2 and 4 for group I and in table 4 and figures 3 and 4 for group II. The changes evoked by exercise showed the same pattern at the different workloads, although as expected, they were usually more marked at the higher than at the lower percentage of maximum workload. The mean pressure differences between the left and right ventricles and the mean pulmonary arterial and aortic pressures in both groups increased significantly, except for the mean aortic pressure at 25% of the maximum workload. Although the mean pulmonary arterial wedge pressure was slightly higher during exercise, this increase was not statistically significant. The mean right atrial pressure on the other hand showed a significant decrease in group I. The pulmonary and systemic blood flows in the two groups increased from rest to exercise at the different workloads (p < .001). The left-to-right shunt flow, however, did not change significantly. Because pulmonary blood flow increased with the increase in workload and shunt flow did not change, the shunt fraction decreased.

The increase in systemic blood flow and heart rate during exercise at the different workloads was such that the left ventricular effective stroke volume, i.e., the total left ventricular stroke volume minus the shunt volume, hardly changed. This was in contrast to the total left ventricular stroke volume, which decreased as a result of the unaltered shunt flow at the different workloads.

The pulmonary vascular resistance (7 ± 2 and 8 ± 2 MN-sec-m⁻³) in groups I and II, respectively did not change significantly during exercise in both groups. This was in contrast to the systemic vascular resistance, which decreased (p < .001; tables 3 and 4). Only one patient showed little change in systemic vascular resistance at 25% of the maximum workload (72 to 76 MN-sec-m⁻³), probably as a result of his already low systemic vascular resistance at rest.
TABLE 4
Hemodynamic and biochemical data of the patients of group II at rest and during exercise

<table>
<thead>
<tr>
<th></th>
<th>Rest</th>
<th>60% max workload</th>
</tr>
</thead>
<tbody>
<tr>
<td>Workload (W/m²)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>90 ± 12</td>
<td>168 ± 10.3°F</td>
</tr>
<tr>
<td>Mean pressures (mm Hg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aortic</td>
<td>95 ± 9</td>
<td>111 ± 10.3°F</td>
</tr>
<tr>
<td>Pulmonary arterial</td>
<td>17 ± 3</td>
<td>24 ± 5°F</td>
</tr>
<tr>
<td>Right atrial</td>
<td>4 ± 2</td>
<td>4 ± 3</td>
</tr>
<tr>
<td>Pulmonary arterial wedge</td>
<td>10 ± 3</td>
<td>12 ± 4</td>
</tr>
<tr>
<td>Left ventricle–right ventricle</td>
<td>40 ± 4</td>
<td>53 ± 6°F</td>
</tr>
<tr>
<td>Blood flows (l/min/m²)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systemic</td>
<td>3.8 ± 0.7</td>
<td>6.9 ± 0.9</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>5.0 ± 0.5</td>
<td>8.2 ± 1.0</td>
</tr>
<tr>
<td>Left ventricular stroke volumes (ml/m²)</td>
<td>56 ± 6°</td>
<td>50 ± 6°</td>
</tr>
<tr>
<td>Total</td>
<td>43 ± 7</td>
<td>42 ± 5</td>
</tr>
<tr>
<td>Effective</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systemic vascular resistance (MN-sec-m⁻¹)</td>
<td>140 ± 35</td>
<td>97 ± 30°</td>
</tr>
<tr>
<td>Oxygen saturations (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aortic</td>
<td>99 ± 1</td>
<td>98 ± 1</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>82 ± 2ª</td>
<td>49 ± 4°</td>
</tr>
<tr>
<td>Hemoglobin concentration (g/l)</td>
<td>129 ± 8</td>
<td>135 ± 8°</td>
</tr>
<tr>
<td>Lactic acid concentration (mM)</td>
<td>1.0 ± 0.5</td>
<td>2.9 ± 1.6°</td>
</tr>
</tbody>
</table>

Data are mean ± SD (n = 17).
Paired t test vs control: *p < .001.
Unpaired t test vs rest in group I: †p < .005, ‡p < .001; vs 50% maximum workload in group I: §p < .005, ¶p < .002, ‡p < .001.

The pulmonary arterial oxygen saturation decreased and the arterial hemoglobin and lactic acid concentrations increased significantly with exercise in both groups, while the aortic oxygen saturation did not change. Although the workloads of the patients exercising at 50% and 60% of their maximum workload were not significantly different, heart rate (p < .001) and mean aortic pressure (p < .001) were significantly higher while pulmonary arterial oxygen saturation (p < .002) was lower in the patients exercising at 60% of their maximum workload than in those exercising at 50%. This lower pulmonary arterial oxygen saturation at 60% was probably due not only to the higher workload but also to the smaller left-to-right shunt flow of the patients in group II.

Discussion

This study was designed to assess the influence of dynamic exercise on the hemodynamics and especially on the left ventricular output and systemic blood flow in patients with small-to-moderate ventricular septal defects and normal pulmonary vascular resistance. The hemodynamic effects of exercise in normal adults have been studied extensively.14,15 Few reports, however, have been published about hemodynamic effects of exercise in normal children or in children with congenital heart disease.17-21 Cumming18 and Lock et al.20 showed in normal children and children with a mild isolated pulmonary or aortic valve stenosis that there

FIGURE 2. Pulmonary (qp), systemic (qs), and left-to-right shunt flows (qy) with patients at rest and during 25% and 50% of the maximum workload (Wmax). Data are mean ± SD. *p < .001 vs rest.

FIGURE 3. Pulmonary (qp), systemic (qs), and left-to-right shunt flows (qy) with patients at rest and during 60% of the maximum workload (Wmax). Data are mean ± SD. *p < .001.
was no essential difference between the hemodynamic response in children and adults.

Exercise performance during cardiac catheterization is usually expressed as a percentage of the maximum workload. This maximum workload can be assessed by using the simple progressive upright bicycle test or the treadmill test. Although it is questionable whether children who perform the simple progressive upright bicycle test reach their maximum exercise level, we gave preference to this test because we use the bicycle ergometer in the catheterization laboratory and because we were not primarily interested in the maximum exercise level but in comparable workloads for our patients during cardiac catheterization.

The maximum workload achieved by our patients with the simple progressive upright bicycle exercise test was in agreement with the values obtained by Godfrey et al.\textsuperscript{11} in normal children. Goldberg et al.\textsuperscript{22} and Cumming,\textsuperscript{19} however, stated that patients with ventricular septal defects and left-to-right shunts comparable to those of our patients have lower exercise capacities than normal children. This discrepancy between our findings and those of Goldberg et al.\textsuperscript{22} may be explained by their higher increments in workload and by the 2 min per workload that their patients cycled compared with the 1 min per workload cycled by our patients. Cumming\textsuperscript{19} used a maximal treadmill test, which leads to a higher mean value for maximum oxygen uptake than the maximal progressive upright bicycle test.\textsuperscript{14} This could explain why 18\% of his patients with ventricular septal defects and moderate left-to-right shunts had values below the 10th percentile of his "normal" clinical group.

Systemic and pulmonary blood flows in cases of left-to-right shunt at the ventricular level can be determined by the dye-dilution technique or by the Fick method. For exercise studies, however, the Fick method is not reliable because in these individuals mixed venous oxygen saturation measured under conditions of exercise is not accurate.\textsuperscript{5, 23} Therefore we used the dye-dilution method, although this also has potential for errors. When the left-to-right shunt is substantially larger than 50\% of the pulmonary blood flow or when the sampling rate is too small, it may be difficult to separate the area of the left-to-right shunt from both the normal part and the recirculation part of the curve. However, we did not encounter these difficulties, either at rest or during exercise, because we used a sampling rate of 0.63 ml/sec and because the highest shunt percentage was slightly larger than 50\% in only three of our patients. Besides these difficulties, the calculated left-to-right shunt fraction from a dye-dilution curve might be overestimated when the method of Mook and Zijlstra\textsuperscript{13} is applied (figure 1) because part of the area of the left-to-right shunt may originate from early normal recirculation. However, a good agreement between calculated left-to-right shunt fractions from oximetric data and from dye-dilution curves has been obtained with this method.

In our patients the pulmonary vascular resistance did not change significantly from rest to exercise, while the systemic vascular resistance decreased substantially. Since the pulmonary and systemic blood flows increased equally, the relative change in mean pulmonary arterial pressure during exercise was twice as high as that in mean aortic pressure. However, the absolute increase in mean aortic pressure was larger than that in mean pulmonary arterial pressure, which resulted in an increase in the mean pressure difference between the left and right ventricle. This pressure difference, along with the size of the ventricular septal defect, is the factor responsible for the rate of flow through the defect. The diameter of the defect in patients with small-to-moderate left-to-right shunts varies between 0.5 and 1.0 cm.\textsuperscript{1, 2, 24} In defects of this size, the mean resistance to left-to-right shunting is at the site of the defect. Because all but one of our patients had defects of the membranous septum, a change in the size of the defect by contraction during systole was not likely to occur. So with the unchanged size of the defect during exercise and the increase in mean pres-
sure difference between the left and right ventricles, one would expect an increase in the shunt flow; however, this did not take place. This may be due to the possibility that our assumption of stable size of the membranous ventricular septal defect is not correct or that the resistance to the shunt flow across the defect increases during exercise as a result of an increased flow disturbance caused by the increase of the blood flow rate in the ventricles.

The fact that the shunt flow does not change during exercise indicates, first, that as heart rate increased, shunt volume per beat decreased proportionally, and second, that the shunt fraction decreased in proportion to the increase in systemic blood flow (figure 4). Thus it appears that exercise improves the hemodynamic adaptation to a ventricular septal defect by decreasing the shunt volume per beat. This decrease in shunt volume per beat was not concomitant with an increase in effective stroke volume, contrary to expectations, since in normal individuals the total stroke volume of the left ventricle usually increases or at least stays the same during exercise.25,26 In our patients, however, total left ventricular stroke volume decreased significantly at 50% and 60% of the maximum workload. It is possible that this decrease is the consequence of the chronic volume overload of the left ventricle by the left-to-right shunt flow. The unchanged left-to-right shunt flow and significant decrease of the shunt fraction from rest to exercise in our patients shows the importance of assessing the left-to-right shunt by measuring actual blood flows instead of calculating shunt fractions.

Other dynamic exercises, such as running and free cycling, probably result in hemodynamic changes similar to those seen in this study. We therefore conclude that the policy not to restrict patients with moderate-to-small ventricular septal defects and normal pulmonary vascular resistance in dynamic exercise is justified because the normal rise in their systemic blood flow during dynamic exercise occurs without a corresponding increase in left-to-right shunt flow. Whether this is also true for static exercise is questionable, since the increase in pressure difference between the left and right ventricles may be substantially larger than that during dynamic exercise and may consequently increase the left-to-right shunt flow.

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CIRCULATION
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