Exercise Hemodynamics of Pulmonary Valvular Stenosis

Study of 64 Children

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SUMMARY

Sixty-four children with pulmonary stenosis were studied by cardiac catheterization both at rest and on exercise. Whereas milder degrees of stenosis were associated with normal right ventricular function, more severe stenosis was associated with fixed stroke index and elevated RVEDP, and suboptimal response of cardiac index. These changes result from altered right ventricular compliance. In several the compliance abnormality was related to myocardial hypertrophy, whereas in four patients it was most likely caused by myocardial fibrosis.

Additional Indexing Words:
Right ventricular function    Myocardial hypertrophy    Stroke index
Right ventricular end-diastolic pressure    Myocardial fibrosis

PULMONARY valvular stenosis is a progressive condition in some patients. Progression might be explained by growth of the child without a corresponding increase in the orifice of the stenotic pulmonary valve. Serial cardiac catheterization data, however, demonstrate an increase in pulmonary valve area congruent to increase in body size. Furthermore, deterioration in clinical condition is unusual during the rapid growth years of childhood and more frequently occurs in adults. Hemodynamic studies performed in adult patients following pulmonary valvotomy have shown impairment of myocardial function. Such studies suggest the development of myocardial fibrosis underlies the clinical deterioration observed in patients with pulmonary stenosis.

Little data are available to indicate if limitations of myocardial function exist in children with pulmonary stenosis. Assessment of right ventricular pump function requires the measurement of hemodynamic parameters during exercise, since in this physiologic state abnormalities may be unmasked.

We have studied 64 children with isolated pulmonary valvular stenosis both at rest and during exercise. These studies were useful in defining limitations of right ventricular function in children with severe stenosis. These limitations were related to altered compliance usually from myocardial hypertrophy, but in four the altered right ventricular filling was related to myocardial fibrosis.

Materials and Methods

Sixty-four children with isolated pulmonary valvular stenosis were studied. Thirty-six of these patients were between 4 and 10 years of age, and 28 patients were between 11 and 16 years of age. In each the clinical, electrocardiographic, and roentgenographic data indicated the presence of...
isolated pulmonary stenosis. Selective injection of contrast material into the right ventricle revealed the pulmonary valve to be the site of obstruction. Fixed infundibular stenosis was not considered present. In several patients, the infundibular area narrowed during systole but was normal in diastole. In no patient was infundibular stenosis found on pressure tracings. Other cardiac malformations were not present.

Each patient was studied in a resting, fasting state and in the supine position. Premedication consisted of morphine and phenobarbital. A Goodale-Lubin catheter was utilized to measure right-sided cardiac pressures, and a Teflon arterial cannula, inserted into the brachial artery, was used to measure systemic arterial pressure. These were connected to 223d Statham strain gauges, and the pressure recorded on an Electronics for Medicine DR-12 optical recorder. In each patient the resting cardiac output was measured utilizing the Fick principle. For a 6-min period the patient’s expired air was collected in a Collins chain-driven tank and analyzed by the Tissot-Schonander method to determine the patient’s rate of oxygen consumption. Midway through the collection, blood was withdrawn simultaneously from the brachial and pulmonary arteries for Van Slyke oxygen analysis. With continuous pressure recording, the venous catheter was then withdrawn from the pulmonary artery through the right ventricle to the right atrium. The right ventricular end-diastolic pressure (RVEDP) and right atrial pressures were recorded at a low attenuation. The patient was then exercised in the supine position utilizing a variable resistance bicycle ergometer at a work load designed to raise the heart rate to between 140 and 160 beats/min. The duration of exercise was from 10 to 15 minutes and hemodynamic parameters were measured after a steady state of exercise had been achieved for 4 min. The cardiac output was again measured as outlined previously. During the oxygen consumption the catheter was withdrawn from the pulmonary artery through the right-sided cardiac chambers, while pressures were recorded.

The recording was analyzed for heart rate and systolic and diastolic pressures. RVEDP was measured after the “a” wave. The pulmonary valve area was calculated utilizing a modification of Gorlin’s formula.4 The patients were divided into three groups on the basis of the indexed pulmonary valve area. We grouped the patients according to valve area rather than peak systolic gradient since the latter value varies with cardiac output, while the former considers cardiac output in its calculation.

In each patient the measured and derived data for rest and exercise were compared. For each group the mean value for each hemodynamic parameter was calculated and the groups were compared by standard statistical methods (table 1).

Results

The 64 patients were divided into groups as follows: group I, PVA > 1.0 cm²/m², 14 patients; group II, PVA 0.5–1.0 cm²/m², 28 patients; and group III, PVA < 0.5 cm²/m², 22 patients. The mean ages of the groups were 10.7 years, 9.5 years, and 9.3 years, respectively. No significant difference was present between the groups in regard to heart rate or oxygen consumption, either at rest or in the exercise state (table 1). Thus, the resting and exercise states were comparable among the three groups.

The resting cardiac index was greater than 3.0 liters/min/m² in 60 of the patients. In four patients with severe pulmonary stenosis (PVA < 0.2 cm²/m²) the cardiac indices were 2.6, 2.7, 2.7, and 2.9 liters/min/m², respectively. Comparing the mean cardiac indices at rest (table 1), patients in group I had a greater cardiac index (4.5 ± 0.8 liters/min/m², \( P < 0.05 \)) than either of the groups with more severe stenosis. The cardiac index on exercise was significantly smaller (6.4 ± 1.2 liters/min/m²) in the group with the most stenotic valves (group III) than either group I or II (7.4 liters/min/m²).

The relationship between oxygen consumption and cardiac index on exercise was normal in 60 patients (fig. 1). In the remaining four patients, each with severe stenosis, the cardiac index was lower than anticipated for the amount of oxygen consumed.

The arteriovenous oxygen difference at rest was smaller in the patients of group I and significantly greater in both groups II and III (\( P < 0.05 \)). No significant statistical difference of the arteriovenous oxygen difference during exercise was found, although it was larger in group III. Since the cardiac output was lower in this group, the widened A-V oxygen difference is more important.

The stroke index was largest in patients with milder stenosis (group I, 51 ± 8 cc/beat/m²), and the smallest in group III (46 ± 6 cc/beat/m²). The difference was significant.
Table 1

Hemodynamic Variables in Children with Pulmonary Stenosis of Three Levels of Severity

<table>
<thead>
<tr>
<th>Hemodynamic parameter</th>
<th>Physiologic state</th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>1 vs II</th>
<th>1 vs III</th>
<th>II vs III</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PVA &gt; 1.0 cm²/m²</td>
<td>PVA 0.5–1.0 cm²/m²</td>
<td>PVA &lt;0.5 cm²/m²</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oxygen consumption (cc O₂/min/m²)</td>
<td>Rest</td>
<td>169 ± 15</td>
<td>162 ± 26</td>
<td>165 ± 30</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>Exercise</td>
<td>621 ± 160</td>
<td>654 ± 180</td>
<td>548 ± 136</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>A-V oxygen difference (vol %)</td>
<td>Rest</td>
<td>3.75 ± 0.3</td>
<td>4.0 ± 0.4</td>
<td>4.3 ± 0.77</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td></td>
<td>Exercise</td>
<td>8.5 ± 1.7</td>
<td>8.9 ± 1.7</td>
<td>9.5 ± 1.5</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Cardiac index (liters/min/m²)</td>
<td>Rest</td>
<td>4.5 ± 0.8</td>
<td>4.1 ± 0.6</td>
<td>3.9 ± 0.7</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>Exercise</td>
<td>7.4 ± 0.7</td>
<td>7.4 ± 1.4</td>
<td>6.4 ± 1.2</td>
<td>NS</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>Rest</td>
<td>90 ± 15</td>
<td>87 ± 16</td>
<td>89 ± 16</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>Exercise</td>
<td>138 ± 26</td>
<td>148 ± 21</td>
<td>146 ± 20</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Stroke index (cc/beat/m²)</td>
<td>Rest</td>
<td>51 ± 8</td>
<td>48 ± 8</td>
<td>46 ± 6.0</td>
<td>NS</td>
<td>&lt;0.01</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>Exercise</td>
<td>56 ± 9</td>
<td>50 ± 9</td>
<td>45 ± 8.0</td>
<td>&lt;0.05</td>
<td>&lt;0.001</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>RV systolic pressure (mm Hg)</td>
<td>Rest</td>
<td>35 ± 9</td>
<td>62 ± 13</td>
<td>127 ± 39</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>Exercise</td>
<td>53 ± 10</td>
<td>107 ± 22</td>
<td>184 ± 46</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>RVEDP (mm Hg)</td>
<td>Rest</td>
<td>6.6 ± 1.8</td>
<td>8.0 ± 2.7</td>
<td>10.3 ± 2.6</td>
<td>&lt;0.05</td>
<td>&lt;0.001</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td></td>
<td>Exercise</td>
<td>4.8 ± 1.4</td>
<td>7.8 ± 3.1</td>
<td>13.9 ± 4.4</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pulmonary valve area (cm²/m²)</td>
<td>Rest</td>
<td>1.6 ± 0.4</td>
<td>0.65 ± 0.15</td>
<td>0.31 ± 0.10</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>Exercise</td>
<td>1.7 ± 0.3</td>
<td>0.6 ± 0.15</td>
<td>0.32 ± 0.12</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>
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Figure 1

Relationship between oxygen consumption and cardiac index during exercise in 64 children with pulmonary stenosis. Shaded area represents normal range. Four patients with severe stenosis are distinctly below normal range.

between groups I and III ($P < 0.01$). Significant differences were present between the stroke indices of each of the three groups on exercise (table 1). The pattern of change of stroke index was also different in each of the three groups. In patients with milder stenosis the stroke index rose during exercise, in group II it increased only slightly, and in group III it decreased slightly.

On exercise the right ventricular systolic pressure increased in 63 patients, and decreased in only one patient (PVA 0.2 cm$^2$/m$^2$) (fig. 2). As expected the greatest increase in systolic pressure occurred in patients with more severe pulmonary stenosis.

Both at rest and exercise, significant differences in RVEDP were found in the three groups (table 1). RVEDP was higher both at rest and exercise in patients with more severe pulmonary stenosis. Among patients in group I, the RVEDP tended to fall on exercise (fig. 3), among those in group II it was variable but tended to rise (fig. 4), and in most patients with PVA $< 0.5$ cm$^2$/m$^2$ (group III) RVEDP rose on exercise (fig. 5).

When the changes from rest to exercise of both the stroke index and RVEDP were compared, differences between the groups were apparent. In group I patients, the stroke index usually increased on exercise while RVEDP fell. This pattern indicates a normal myocardial response (fig. 6). Patients in group II showed a more variable response, but in each the response could be considered normal (fig. 7). In contrast, the response in patients of group III was often abnormal (fig.
Several of these patients showed major increases in RVEDP, but only small changes in stroke index. This suggests abnormal myocardial compliance related to myocardial hypertrophy, rather than myocardial damage. On the other hand, in three other patients in this group, RVEDP rose on exercise, but the stroke index showed a major fall. Such a response can be considered an indication of myocardial damage. The patients showing the latter response to exercise were among the four who showed an abnormal relationship between cardiac index and oxygen consumption (fig. 1).

Figure 2

Relationship between peak right ventricular systolic pressure and cardiac index in 64 patients with pulmonary stenosis. Connected dots represent values obtained at rest and during exercise. Only one patient showed a fall in peak pressure on exercise. In general, the greater the resting right ventricular pressure the greater the rate of rise during exercise.
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Figure 3

Relationship between right ventricular end-diastolic pressure and cardiac index in 14 patients of group I (PVA > 1.0 cm²/M²) during rest (open dot) and exercise (closed dot). Exercise tended to increase cardiac index and decrease RVEDP.

Discussion

At cardiac catheterization ventricular function can be analyzed by the measurement of various parameters, some reflecting primarily pump function, others determining principally myocardial muscle function. By analyzing specific aspects of cardiac output and right ventricular pressure we investigated factors defining pump function in pulmonary stenosis.

Cardiac pump function has been studied by measurement of cardiac output either at rest or exercise, by comparison of cardiac index to oxygen consumption, and by observation of changes in end-diastolic pressure which occur with changes in cardiac output. Utilizing such parameters, we found limitations in cardiac function in few of the 64 children with pulmonary stenosis studied.

A lower than normal resting cardiac output may be an indication of depressed myocardial function. Among our patients, the group with the most severe stenosis showed the lowest resting cardiac indices. In four of the 22 patients in this group (III), the resting cardiac index was less than 3.0 liters/min/m².

Deficiencies in cardiac pump function may be accentuated by studying exercise cardiac output. More significant differences were found between the groups when our exercise data were analyzed. On exercise, the patients with severe stenosis showed a significantly lower cardiac index. An expression of limited cardiac pump function may be obtained by comparing the exercise cardiac index and corresponding oxygen consumption with normal values. During exercise four of our patients with severe stenosis showed a lower than anticipated cardiac index for the amount of oxygen consumed.

Figure 4

Relationship between right ventricular end-diastolic pressure and cardiac index in 28 children of group II (PVA 0.5-1.0 cm²/M²) during rest (open dot) and exercise (closed dot). Exercise increased cardiac index, but the RVEDP change was variable.

Figure 5

Relationship between right ventricular end-diastolic pressure and cardiac index in 22 children of group III (PVA < 0.5 cm²/M²) during rest (open dot) and exercise (closed dot). The rise of cardiac index during exercise was less than in the severe pulmonary stenosis, and the RVEDP increased in the majority.
Observing changes in stroke index affords another means of studying pump function. Normally, during supine exercise stroke index increases slightly and such a pattern was found in those patients with milder stenosis. The stroke index, however, did not show such changes in the groups with more severe stenosis. In these patients it remained constant on exercise, indicating a limitation of pump function. In fact, even at rest, patients with the greatest degrees of stenosis consistently showed a lower stroke index.

Measurement of RVEDP may be used as an indicator of myocardial function, particularly by determining its change on exercise. Normally, RVEDP falls on exercise. If it remains constant or rises, an abnormality of ventricular compliance is indicated. Factors such as myocardial hypertrophy, fibrosis, and increased right ventricular volume can elevate RVEDP. Our data in patients with pulmonary stenosis reveal several abnormalities in...
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RVEDP. Patients with more severe stenosis showed higher resting RVEDP than normal. Secondly, in patients with mild stenosis RVEDP fell, with moderate stenosis it changed little, and with severe stenosis it rose. Since the cardiac size was normal in our patients, the alterations in RVEDP most likely represent changes in ventricular compliance rather than changes in ventricular volume.

Patients with altered myocardial compliance related to isolated myocardial hypertrophy show an increase in RVEDP but little change in stroke index. Patients with altered compliance resulting from myocardial fibrosis also show an increase in RVEDP, but usually a major fall in stroke index. Whereas several of our patients with severe stenosis revealed the first pattern, three followed the second pattern.

Therefore, the indications of abnormal right ventricular pump function in children with more severe pulmonary stenosis appear to be related to right ventricular hypertrophy in the majority. Only four patients gave indication of myocardial fibrosis. This finding is in contrast to the studies of others who have shown abnormal cardiac function in pulmonary stenosis, either preoperatively2,3 or postoperatively.5-8 Dealing primarily with adult patients, these authors have found a low resting cardiac index particularly in relation to the oxygen consumption. Similarly, postoperative studies in adult patients have shown an inability to increase cardiac output on exercise.2,3 These studies suggest an abnormal exercise response related to myocardial fibrosis in adult patients with pulmonary stenosis. Utilizing similar hemodynamic parameters we were unable to uncover similar changes in most of the children studied.

The comparison of our experience with children and the reported data of adults correlates with longitudinal clinical experience in some patients with pulmonary stenosis. Typically, some patients with pulmonary stenosis have a period of well being, without symptoms and with normal growth and development. Subsequently, symptoms of fatigue on exercise develop, and finally congestive cardiac failure appears. Serial cardiac catheterization studies indicate that in most patients the level of peak right ventricular systolic pressure remains constant. Thus, the clinical deterioration appears to result from factors other than a fixed-sized pulmonary valvular orifice.

On the other hand, there is evidence that the development of right ventricular myocardial fibrosis may be an important factor in the natural history of pulmonary stenosis.9 Supportive data is found in the studies indicating that adult patients following pulmonary valvotomy often are unable to increase their cardiac output on exercise.2,3 Further, the right ventricle of patients with severe pulmonary stenosis shows greater amounts of fibrosis than normal.

The difference between our children and the reports of adult patients with pulmonary stenosis yields some insight into the natural history of pulmonary stenosis. The chronic effect of elevated right ventricular afterload leads to alterations in the myocardium. With age, the myocardial factor eventually becomes the limiting factor in the disease.

If the myocardial factor is important in the natural history and is affecting the results of pulmonary valvotomy, then operation should precede the impairment of right ventricular function. Hemodynamic assessment of the pump function of the right ventricle should thus prove useful in the management of patients with pulmonary stenosis. Studies performed during exercise serve to more clearly define hemodynamic abnormalities than those done at rest alone.

In the present study relatively simple indicators of myocardial function were used to assess pump function but not the muscle function of the right ventricle. More detailed studies are needed to investigate the right ventricle. Because of its geometric shape, determination of right ventricular volume is difficult and can be done currently only by indicator-dilution methods. To our knowledge, studies of \( V_{max} \) and other indicators of velocity of myocardial contractility have not been performed on the right ventricle, so
experience with these parameters is not available.

While we await the development of the more sophisticated hemodynamic measurements to define the optimal time for operative intervention, it is our current practice to operate on children with pulmonary valve areas of less than 0.5 cm²/m² and in the few among those with larger valve areas who demonstrate abnormal exercise hemodynamics.

References
Exercise Hemodynamics of Pulmonary Valvular Stenosis: Study of 64 Children
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