Pre- and postoperative exercise capacity associated with hemodynamics in adult patients with atrial septal defect: A retrospective study

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Abstract

Objective: This study evaluated the pre- and postoperative exercise capacity in adult patients with atrial septal defect (ASD) associated with hemodynamic variables. Methods: Adults (70) with ASD underwent symptom-limited exercise tests. Peak O₂ uptake (Peak VO₂) and % peak VO₂, that is the percentage of predicted value, were measured. These patients were divided into three groups according to pulmonary-to-systemic flow ratio (Qp/Qs) and systolic pulmonary arterial pressure (PAs); Group A: Qp/Qs ≤ 3, PAs ≤ 50 mm Hg, Group B: Qp/Qs > 3, any PAs, Group C: Qp/Qs ≤ 3, PAs > 50 mm Hg. Exercise test was repeated in 22 patients after surgical closure of ASD (mean 4.6 ± 2.0 months). Results: Peak VO₂ was significantly lower in group B (P < 0.01) and group C (P < 0.01) than in group A (19.3 ± 5.7, 17.6 ± 3.6, 27.6 ± 6.3 ml/min/kg, respectively). In patients except those in group C, there were a weak negative correlation between PAs and % peak VO₂ (r = 0.61) and a significant negative correlation between Qp/Qs and % peak VO₂ (r = 0.86). Postoperative peak VO₂ increased significantly in group A (27.2 ± 5.1–31.1 ± 5.1 ml/min/kg, P < 0.05) and group B (16.7 ± 3.3–21.5 ± 2.1 ml/min/kg, P < 0.01). However, there was no significant difference between pre- and postoperative peak VO₂ in group C (16.8 ± 1.3–17.8 ± 2.8 ml/min/kg, NS). Conclusions: In ASD patients except those with small or moderate left-to-right shunt and high pulmonary arterial pressure, there was a significant negative correlation between Qp/Qs and peak VO₂ corrected by age and gender. Patients with large left-to-right shunt and/or high pulmonary arterial pressure had reduced exercise capacity. However, exercise capacity in patients with large left-to-right shunt increased after closure of ASD regardless of whether they had high pulmonary arterial pressure. © 1997 Elsevier Science B.V.

Keywords: Atrial septal defect; Exercise test; Operation

1. Introduction

Several studies have shown reduced pre- and postoperative exercise capacity in patients with atrial septal defect (ASD) [4,6,10,16,18]. However, there are few available studies of factors influencing pre- and postoperative exercise capacity. Lifelong right ventricular and pulmonary artery volume overload is the main characteristic of patients with ASD and some of those patients develop pulmonary hypertension. Although several studies showed the relation between hemodynamic variables and cardiac disability [5,9], the relation between hemodynamic variables and exercise capacity has not been fully evaluated by objective and quantitative methods [4,8,15]. Although several follow-up reports have shown that surgical correction of ASD usually produced considerable symptomatic and hemodynamic improvement, there is little information about the relation between preoperative hemodynamic variables and improvement of exercise capacity. The present study evaluated the relation between pre- and postoperative exercise capacity and hemodynamic variables in adult patients with ASD.

Table 1
Clinical background

<table>
<thead>
<tr>
<th></th>
<th>Group A (n = 28)</th>
<th>Group B (n = 28)</th>
<th>Group C (n = 14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>42.3 ± 15.9</td>
<td>47.3 ± 97</td>
<td>46.3 ± 12.3</td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>11/17</td>
<td>8/20</td>
<td>6/8</td>
</tr>
<tr>
<td>Atrial fibrillation(%)</td>
<td>7</td>
<td>18</td>
<td>7</td>
</tr>
<tr>
<td>Hemoglobin (g/dl)</td>
<td>138 ± 2.0</td>
<td>142 ± 1.5</td>
<td>15.1 ± 2.0</td>
</tr>
<tr>
<td>Qp/Qs</td>
<td>2.5 ± 0.4</td>
<td>3.9 ± 0.8b</td>
<td>1.7 ± 0.4b,c</td>
</tr>
<tr>
<td>L-R shunt volume (l/min)</td>
<td>5.3 ± 1.4</td>
<td>10.2 ± 2.7b</td>
<td>2.5 ± 1.0b,c</td>
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<tr>
<td>R-L shunt volume (l/min)</td>
<td>—</td>
<td>—</td>
<td>0.2 ± 0.2</td>
</tr>
<tr>
<td>PAs (mm Hg)</td>
<td>26.8 ± 6.1</td>
<td>35.9 ± 11.7b</td>
<td>74.8 ± 14.6b,c</td>
</tr>
<tr>
<td>PVR (dynes s/cm²)</td>
<td>86 ± 30</td>
<td>79 ± 28</td>
<td>506 ± 192b,c</td>
</tr>
<tr>
<td>SVR (dynes s/cm²)</td>
<td>1741 ± 283</td>
<td>1721 ± 228</td>
<td>1666 ± 302</td>
</tr>
<tr>
<td>Preoperative NYHA (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>class I</td>
<td>57</td>
<td>39</td>
<td>7</td>
</tr>
<tr>
<td>class II</td>
<td>43</td>
<td>61</td>
<td>86</td>
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<tr>
<td>class III</td>
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<td>0</td>
<td>7</td>
</tr>
<tr>
<td>Postoperative NYHA (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>class I</td>
<td>93</td>
<td>100</td>
<td>11</td>
</tr>
<tr>
<td>class II</td>
<td>7</td>
<td>0</td>
<td>89</td>
</tr>
<tr>
<td>class III</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Postoperative pressure gradient across TV by Doppler (mm Hg)</td>
<td>19.4 ± 43</td>
<td>20.2 ± 56</td>
<td>63.7 ± 11.8b,c</td>
</tr>
<tr>
<td>Ex. test after operation (Mo)</td>
<td>3.7 ± 1.4</td>
<td>4.4 ± 2.0</td>
<td>5.6 ± 2.3</td>
</tr>
</tbody>
</table>

Qp/Qs, pulmonary-to-systemic flow ratio; L-R, left-to-right; R-L, right-to-left; PAs, systolic pulmonary arterial pressure; PVR, pulmonary vascular resistance; SVR, systemic vascular resistance; NYHA, New York Heart Association functional classification; TV, tricuspid valve; Doppler Doppler echocardiography; Ex, exercise; Mo, months.

*P < 0.05 vs. Group A.

**P < 0.01 vs. Group A.

***P < 0.01 vs. Group B.

### 1.1. Material and methods

#### 1.1.1. Study patients

A total of 70 adult patients with ASD who did not have other cardiac disease underwent symptom-limited exercise tests and cardiac catheterization. All patients had a secundum type ASD. None of the patients had pulmonary stenosis, serious ventricular arrhythmia, moderate or severe intral regurgitation, or respiratory dysfunction. Patients were divided into three groups according to their pulmonary-to-systemic flow ratio (Qp/Qs) and systolic pulmonary arterial pressure (PAs) at rest; Group A: Qp/Qs ≤ 3, PAs ≤ 50 mm Hg, Group B: Qp/Qs > 3, any PAs, Group C: Qp/Qs ≤ 3 PAs > 50 mm Hg. The clinical background of these three groups are presented in Table 1. There were no significant differences in age, gender, or incidence of atrial fibrillation among the three groups. The hemoglobin concentration was higher in group C than in group A or group B.

Of 70 patients, 47 underwent surgical closure of ASD, 15 are currently waiting operation, and 8 are being followed without operation. There were no death and events before and after operation. Postoperative New York Heart Association (NYHA) functional classification became class I in most of the patients of Group A and Group B, however, that was class II in most of those of group C. In 26 of the 47 patients who underwent operation, tricuspid regurgitation was shown and the pressure gradient across tricuspid valve was estimated by Doppler echocardiography using the modified Bernoulli equation. The high pressure gradient that meant high pulmonary arterial pressure after operation was shown in group C.

#### 1.2. Exercise protocol

A symptom-limited exercise test was performed on an upright, electromagnetically braked cycle ergometer (Minato 232C, Minato Medical Science, Tokyo). The work rate of the cycle ergometer was increased continuously at a rate of 15 W/min (ramp protocol) after 1 min of unloaded pedaling (OW). The and heart rate were monitored throughout the testing by the
Stress Test System (ML-5000, Fukuda Denshi, Tokyo). Systemic arterial pressure was measured every minute with a sphygmomanometer. Peak O₂ uptake (peak VO₂) was measured with a Respiromonitor RM-300 (Minato Medical Science, Tokyo). The Respiromonitor RM-300 consists of a hot wire flowmeter and gas analyzer (MO-360, Minato Medical Science) that contains a sampling tube, filter, suction pump, and O₂ analyzer of zirconium element. Since peak VO₂ is influenced by age and gender, % peak VO₂, that is the percentage of predicted value for each age and gender reported by Itoh et al. [10], was also used. Percent peak VO₂ for males was calculated as peak VO₂ (ml/min/kg) / (−0.38 × age + 52.1) × 100 and that for females was calculated as peak VO₂ (ml/min/kg) / (−0.23 × age + 40.4) × 100. The exercise test was repeated after surgical closure of ASD.

1.3. Statistical analysis

All values are expressed as the mean ± S.D. Differences in mean values were compared among groups by analysis of variance (ANOVA). Linear regression analysis was performed to determine the relation between hemodynamic variables and % peak VO₂. Serial analysis was performed to determine the relation between hemodynamic variables and % peak VO₂. Serial changes within a group were compared by paired t test. A P value < 0.05 was considered statistically significant.

2. Results

2.1. Peak VO₂ before operation

Peak VO₂ and % peak VO₂ were significantly lower in group B (P < 0.01) and group C (P < 0.01) than in group A (19.3 ± 5.7, 17.6 ± 3.6, 27.6 ± 6.3 ml/min/kg, 61.7 ± 13.2, 56.7 ± 11.0, 83.5 ± 10.6%, respectively). However, there were no significant differences in peak VO₂ and % peak VO₂ between group B and group C. Although % peak VO₂ tended to be low when PAs exceeded 50 mm Hg, PAs and % peak VO₂ showed no significant correlation. There was no significant correlation between Qp/Qs and % peak VO₂. However, in patients except those in group C, there was a weak negative correlation between PAs and % peak VO₂ (r = 0.61, Fig. 1) and a significant negative correlation between Qp/Qs and % peak VO₂ (r = 0.86, Fig. 2). The regression line between Qp/Qs and % peak VO₂ was expressed as % peak VO₂ = −15.1 × Qp/Qs + 120.9.

2.2. Peak VO₂ after operation

In 22 of the 47 patients who underwent operation, postoperative exercise test underwent after surgical closure of ASD (mean 4.6 ± 2.0 months). There were no significant differences in the period of exercise test after surgery among the three groups (Table 1). Postoperative peak VO₂ increased significantly in group A (27.2 ± 5.1 to 31.1 ± 5.1 ml/min/kg, P < 0.05, Fig. 3A). Postoperative peak VO₂ also increased in group B (16.7 ± 3.3 to 21.5 ± 2.1 ml/min/kg, P < 0.01, Fig. 3A) even though some patients had high pulmonary arterial pressure. However, there was no significant difference between pre- and postoperative peak VO₂ in group C (16.8 ± 1.3–17.8 ± 2.8 ml/min/kg, NS, Fig. 3A). Changes between pre- and postoperative peak VO₂ in group A (P < 0.05) or group B (P < 0.01) were significantly greater than those in group C (4.0 ± 2.6, 4.8 ± 2.0, 1.0 ± 2.0 ml/min/kg, respectively, Fig. 3B). Therefore, postoperative peak VO₂ in group B was higher than that in group C (P < 0.01), however, remained lower than, that in group A (P < 0.01).

Fig. 1. The relation between PAs and % peak VO₂. Although PAs and % peak VO₂ showed no significant correlation, there was a weak negative correlation between PAs and % peak VO₂ (r = 0.61) in atrial septal defect (ASD) patients except those in group C. Percent peak VO₂ represents percentage of predicted peak VO₂ by age and gender. (PAs systolic pulmonary arterial pressure).

Fig. 2. The relation between Qp/Qs and % peak VO₂. Although Qp/Qs and % peak VO₂ showed no significant correlation, there was a significant negative correlation between Qp/Qs and % peak VO₂ (r = 0.86) in ASD patients except those in group C. The regression line was expressed as % peak VO₂ = −15.1 × Qp/Qs + 120.9. (Qp/Qs pulmonary-to-systemic flow ratio, See Fig. 1 for other abbreviations).
3. Discussion

This study showed that there was a significant negative correlation between Qp/Qs and % peak VO₂ in ASD patients except those with small or moderate left-to-right shunt and high pulmonary arterial pressure. The present study also showed reduced exercise capacity in adult patients with ASD who had large left-to-right shunt and/or high pulmonary arterial pressure. However, exercise capacity in patients with large left-to-right shunt increased after closure of ASD regardless of whether they had high pulmonary arterial pressure.

3.1. Exercise capacity in ASD

Several studies showed reduced exercise capacity in patients with ASD [4,6,10]. In children, exercise capacity in patients with Qp/Qs > 2.5 or PAs > 50 mm Hg was lower than that in the age-matched normal children [4]. In adults, Nakanishi et al. [15] showed a negative correlation between Qp/Qs and peak VO₂ corrected by age and gender in ASD patients without high pulmonary arterial pressure. Frick et al. [8] showed that, in patients with congenital heart defect, exercise capacity tended to be low when PAs exceeded 50 mm Hg. However, there was no relation between exercise capacity and pulmonary blood flow. The reason for this was that, in that study, patients with small or moderate left-to-right shunt and high pulmonary arterial pressure were not excluded. It might be another reason that the effect of age on exercise capacity [12] was not considered in that study.

The explanation of reduced exercise capacity can not be elucidated by the present study. Impaired left ventricular systolic and diastolic function secondary to chronic right ventricular volume and/or pressure overload [2,3,7,14,17] is a probable explanation. Abnormal distensibility of left ventricle in patients with ASD was shown [3]. Reduced left ventricular ejection fraction during exercise in patients with ASD was also shown [2,7,14,17]. This reduced ejection fraction was often seen in patients with higher Qp/Qs and weakly correlated with systolic pulmonary arterial pressure [2]. In patients with pulmonary hypertension, right-to-left shunt might occur during exercise inducing a decrease in the oxygen saturation of systemic arterial blood [13,19].

3.2. Postoperative exercise capacity in ASD

Several follow-up reports have indicated that surgical correction of ASD usually produced considerable symptomatic and hemodynamic improvement [1,5,6,9]. However, postoperative exercise capacity was lower than that in normal subjects [16,18] because of low cardiac output during exercise due to an inadequate augmentation in stroke volume [6,16], diminished compliance of the left ventricle [3], reduced heart rate response during exercise [16,18], or a low level of daily physical activity [18] after surgical closure of ASD.
These might exert more influence on postoperative exercise capacity in patients with large left-to-right shunt and/or high pulmonary arterial pressure than that in patients with small or moderate left-to-right shunt and without high pulmonary arterial pressure.

Several studies showed a significant reduction of pulmonary arterial pressure after surgical correction of ASD [1,5,9,11]. However, pulmonary arterial pressure in patients with elevated pulmonary vascular resistance decreased to a lesser extent or did not change significantly after surgery [1,5,9,11]. It might suggest that pulmonary arterioles in patients with elevated pulmonary vascular resistance sustained some extent of irreversible damage due to lifelong pulmonary artery volume and/or pressure overload. This irreversible damage to the pulmonary arterioles might prevent the improvement of postoperative exercise capacity in patients with small or moderate left-to-right shunt and high pulmonary arterial pressure. Therefore, early surgery to prevent this irreversible damage is important to improve exercise capacity in patients with ASD.

3.3. Study limitations

First, the present study was retrospective. The patients who did not undergo cardiac catheterization or could not exercise due to severe pulmonary hypertension were not included. Second, hemodynamic data during exercise could not be obtained. Further study that is supplemented by hemodynamic parameters during exercise is needed. Third, postoperative exercise test was performed in only 22 of the 47 patients who underwent operation. However, in any group, preoperative peak VO2 in these 22 patients compared with that in all patients in the present study was similar. Fourth, postoperative cardiac catheterization was not performed. However, we showed the pressure gradient across tricuspid valve estimated by Doppler echocardiography. The high pressure gradient that meant high pulmonary arterial pressure after operation was shown in group C.

4. Conclusions

The present study demonstrated that there was a significant negative correlation between Qp/Qs and peak VO2 corrected by age and gender in ASD patients except those with small or moderate left-to-right shunt and high pulmonary arterial pressure. The present study also demonstrated reduced exercise capacity in adult patients with ASD who had large left-to-right shunt and/or high pulmonary arterial pressure. However, exercise capacity in patients with large left-to-right shunt increased after closure of ASD regardless of whether they had high pulmonary arterial pressure.

References