Atrial septal defect in adults: echocardiography and cardiopulmonary exercise capacity associated with hemodynamics before and after surgical closure

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Abstract

The study aimed to evaluate pre and postoperative echocardiographic data and exercise capacity in relation to age and hemodynamics in adults with atrial septal defect (ASD). Fifty-two subjects with ASD (mean age: 38.6 ± 15 years) were enrolled. Echocardiography and cardiopulmonary exercise test were performed before and a year after surgery. Pre and postoperative data were analyzed for the entire group and then compared in terms of age: <40 and ≥40 years, right ventricular systolic pressure (RVSP): <30 and >30 mmHg and pulmonary to systemic flow ratio (Qp/Qs): <2.5 and ≥2.5. After surgery right ventricle dimension decreased in all patients, although it remained significantly larger in patients over 40 years. There was a negative correlation between peak oxygen uptake and preoperative RVSP (r = −0.69, P<0.001). Exercise capacity improved irrespective of the age at surgery, preoperative RVSP and Qp/Qs, although it failed to normalize in patients with RVSP >30 mmHg. Adults with ASD benefit from surgical closure irrespective of the actual age at surgery. Patient’s age at surgery and pulmonary hypertension crucially impact the results of surgical intervention. Early defect correction is therefore highly recommendable, specifically with a view to preventing the hemodynamic consequences of ASD.

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Keywords: Atrial septal defect; Cardiopulmonary capacity; Surgery; Adults

1. Introduction

Although it is generally held that surgery for ASD in adults usually results in considerable symptomatic improvement, little hard data are available on pre and postoperative exercise capacity, especially in terms of the actual factors that impact it. Cardiopulmonary exercise testing, a modern non-invasive method, is actually considered a reliable and objective technique for the evaluation and follow-up of cardiac function.

As ASD closure in adults is still deemed controversial [1], the present study aimed to evaluate pre and postoperative exercise capacity in relation to age and hemodynamic variables in terms of determining patients’ eligibility for surgical interventions.

2. Materials and methods

Fifty-two consecutive patients (women: 33; men: 19; mean age: 38.6 ± 15 years) with secundum (45 patients) or sinus venosus (7 patients) type ASD who had undergone a surgery for ASD at the Department of Cardiovascular Surgery and Transplantology in Krakow between 2000 and 2002, were enrolled into the study. In 6 cases with sinus venosus and one patient with secundum type ASD the defect was associated with partial anomalous pulmonary venous connection. Coronary artery disease was ruled out by coronary arteriography, as routinely performed in men over 40 and women over 45 years.

All patients underwent 2D color Doppler echocardiography a week before and a year after surgery. In 2D parasternal long axis view, the right ventricle diastolic dimension (RVd) was measured. The pulmonary to systemic flow ratio (Qp/Qs) was estimated in all patients and right ventricular systolic pressure (RVSP) was measured in patients with tricuspid valve incompetence using the simplified Bernoulli formula.

A symptom-limited, incremental cardiopulmonary exercise test (modified Bruce protocol) on a 2000 Treadmill was performed in every patient 7 days before and a year after surgery. The patients were encouraged to exercise to exhaustion. Maximal exercise capacity was assessed by exercise duration (T), peak oxygen consumption expressed both in milliter per kilogram per minute (VO2peak) and as percent of the predicted value (VO2%). Peak values of end-tidal carbon dioxide pressure (PETCO2) and VE/VO2, (a slope of the relation between ventilation and carbon dioxide production) were also determined.
Pre and postoperative CPX and echocardiographic data were analyzed for the entire group of patients and then compared in terms of age: <40 and ≥40 years, RVSP: ≤30 and >30 mmHg and Qp/Qs: <2.5 and ≥2.5.

Baseline clinical and hemodynamic data are summarized in Table 1.

All variables are expressed as mean ± standard deviation. A paired t-test was used to analyze pre and postoperative continuous data. The non-parametric Mann-Whitney U test was used to compare the differences between echocardiographic and CPX data between the respective subgroups (in terms of age, RVSP, Qp/Qs) both before and after surgery. Linear regression analysis was used to analyze the correlation between cardiopulmonary and echocardiographic data and possible influencing factors. A P-value <0.05 was considered significant.

3. Results

3.1. Clinical status

There were no major complications associated with surgery. The mean NYHA class decreased after surgery irrespectively of age: 2.0±0.35 vs. 1.1±0.33 in patients <40 and 2.4±0.49 vs. 1.4±0.5; P<0.001 in patients ≥40 years.

The rhythm disturbances increased after surgery (Table 2). Both before and after surgery atrial fibrillation/flutter were observed mainly in older patients (only 2 of 15 patients were <40) with pulmonary hypertension. Arrhythmia persisted in all patients who had been originally diagnosed with it prior to the surgery. No correlation between Qp/Qs and rhythm disturbances was encountered, though.

3.2. Echocardiography

No residual shunt was observed after a yearlong follow-up.

RVSP was calculated from the tricuspid regurgitation in 48 (92%) patients both before and after surgery. After ASD closure the mean value of RVSP decreased significantly from 36.7±10.5 (range 24–85 mmHg) to 26.7±17 mmHg (range 17–42 mmHg). Before the surgery the 1st tricuspid regurgitation was observed in 12 (25%), 2nd in 30 (62.5%), and 3rd in 6 (12.5%). After ASD closure, the number of patients with 1st tricuspid regurgitation increased to 29 (61%), whereas the number of patients with 2nd and 3rd tricuspid regurgitation decreased to 17 (35%) and 2 (4%), respectively. All patients with 3rd tricuspid regurgitation were over 40. There was no concomitant surgical procedure in terms of tricuspid annuloplasty.

There was a significant difference between preoperative RVₜ between the patients with Qp/Qs <2.5 and Qp/Qs ≥2.5 (36.8±8.4 vs. 43.5±1.1 mmHg; P<0.001) only, whereas no significant differences between RVₜ in terms of age and RVSP were found. Furthermore, RVₜ correlated significantly with Qp/Qs; r=-0.6; P<0.001. No significant correlations between preoperative RVₜ and patient’s age at surgery or RVSP were found. After the surgery RVₜ decreased significantly irrespectively of age, RVSP and Qp/Qs, although it remained significantly larger in patients >40 years, in comparison with the younger ones (31.1±5.3 vs. 24.6±2.3 mmHg; P<0.001) and in the patients with abnormal RVSP, when compared with patients with RVSP ≤30 mmHg (29.8±5.6 vs. 26.9±4.3 mmHg; P<0.05). The postoperative RVₜ correlated significantly with age at the time of surgery (r=0.61; P<0.001) and RVSP before ASD closure (r=0.3; P<0.05).

After ASD closure we noted a significant increase in exercise duration (723±308 vs. 896±241 s; P<0.001), peak oxygen uptake expressed both in milliliter per kilogram per minute – VO₂peak (23.4±8.9 vs. 29.3±10.2) and as percentage of the predicted value – VO₂% (63.6±18.4 vs. 82.6±20.2; P<0.001), whereas VE/VCO₂ decreased after ASD closure (28.5±5.5 vs. 27.1±4.2; P<0.001). No significant difference in PETCO₂ was encountered (5.0±0.7 vs. 5.0±0.8; ns).

CPX data measured at peak effort with respect to age and RVSP are summarized in Tables 3 and 4, respectively. Preoperative VO₂peak were significantly lower in patients with RVSP >30 mmHg as well as in those over 40, although when expressed as percentage of the predicted value (VO₂%) the difference remained significant only between patients with RVSP >30 and ≤30 mmHg. There was a significant negative correlation between preoperative RVSP and VO₂%; r=-0.69; P<0.001 (Fig. 1), whereas no significant correlations between VO₂% and age at surgery, or preoperative Qp/Qs were found.

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Table 1
Baseline clinical and hemodynamic data

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean range</th>
<th>No. of patients</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>38.6±15</td>
<td>&lt;40</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td>(17–68)</td>
<td>≥40</td>
<td>27</td>
</tr>
<tr>
<td>RVSP* (mmHg)</td>
<td>36.7±10.5</td>
<td>≤30</td>
<td>21</td>
</tr>
<tr>
<td></td>
<td>(24–85)</td>
<td>&gt;30</td>
<td>27</td>
</tr>
<tr>
<td>Qp/Qs</td>
<td>2.7±0.7</td>
<td>&lt;2.5</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td>(1.5–4.3)</td>
<td>≥2.5</td>
<td>27</td>
</tr>
</tbody>
</table>

*Data available on 48 (92%) patients; RVSP = right ventricular systolic pressure; Qp/Qs = pulmonary to systemic flow ratio.
Table 3
Pre and postoperative CPX data in terms of age <40 years and ≥40 years

<table>
<thead>
<tr>
<th></th>
<th>Before the surgery</th>
<th>After the surgery</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Age &lt;40</td>
<td>Age ≥40</td>
<td></td>
</tr>
<tr>
<td>T (s)</td>
<td>871 ± 272</td>
<td>585 ± 278</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>VO_{peak} (mL/kg/min)</td>
<td>28.0 ± 8.5</td>
<td>19.0 ± 6.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>VO_{%}</td>
<td>67.9 ± 18.1</td>
<td>59.7 ± 18.2</td>
<td>ns</td>
</tr>
<tr>
<td>VE/VCO₂</td>
<td>26.0 ± 4.1</td>
<td>30.9 ± 5.7</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>PETCO₂ (kPa)</td>
<td>5.2 ± 0.7</td>
<td>4.8 ± 0.7</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

*P<0.05, **P<0.01, ***P<0.001 in comparison with the preoperative value.
T = exercise duration; PETCO₂ = end-tidal carbon dioxide pressure; VE/VCO₂ = a slope of relation between ventilation and carbon dioxide production; VO_{%} = peak oxygen consumption expressed as % of the predicted value; VO_{peak} = peak oxygen consumption expressed in ml/kg/min; ns = not significant.

Table 4
Pre and postoperative CPX data in terms of RVSP ≤30 mmHg and >30 mmHg

<table>
<thead>
<tr>
<th></th>
<th>Before the surgery</th>
<th>After the surgery</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RVSP ≤30 mmHg</td>
<td>RVSP &gt;30 mmHg</td>
<td></td>
</tr>
<tr>
<td>T (s)</td>
<td>962 ± 171</td>
<td>542 ± 274</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>VO_{peak} (mL/kg/min)</td>
<td>31.2 ± 6.2</td>
<td>17.8 ± 6.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>VO_{%}</td>
<td>79.0 ± 11.4</td>
<td>54.2 ± 15.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>VE/VCO₂</td>
<td>26.0 ± 4.2</td>
<td>30.6 ± 5.9</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>PETCO₂ (kPa)</td>
<td>5.2 ± 0.8</td>
<td>4.8 ± 0.6</td>
<td>ns</td>
</tr>
</tbody>
</table>

*P<0.05, **P<0.01, ***P<0.001 in comparison with the preoperative value.
Abbreviations as in Table 3.

Preoperative value of PETCO₂ was significantly lower in patients ≥40 years in comparison to younger patients (4.8 ± 0.7 vs. 5.2 ± 0.7; P<0.05), whereas no significant difference between patients <40 and ≥40 years after defect closure was determined.

4. Discussion
4.1. Echocardiography

In the present study, Qp/Qs proved the only variable that significantly influenced the right ventricle dimension prior to surgery. A significant correlation was established between Qp/Qs and the right ventricle dimension, which is also in keeping with the findings of Wanderman et al. [2]. No significant differences were encountered in the right ventricle dimension prior to surgery in terms of age and RVSP. Other investigators reported similar observations [3].

Within a year of the surgery we found a very significant reduction in RV dimension, irrespective of a patient’s age at surgery, preoperative RVSP and Qp/Qs. This implies reversibility of an increased RV after ASD correction and may partially account for a better prognosis in patients after defect closure. However, the postoperative RV remains significantly larger in patients operated on when over 40, in comparison to those who underwent surgery at a younger age. The present study demonstrated that individual age at surgery was inversely related to postoperative RV. It appears that long-standing right ventricle overload leads to right ventricle remodeling and effectively impacts the surgical outcomes. Other investigators reported similar findings. Paerlman et al. [3] described a decrease in RV dimension after surgery in 28 out of 31 patients, although...
RV dilation persisted in 77% of them, despite successful ASD closure.

Many authors emphasize that there is no interdependence between shunt volume and postoperative RV dimensions, which is also fully consistent with our own findings [2–4].

4.2. Cardiopulmonary exercise capacity

Despite high pulmonary blood flow and right heart volume overload, patients with uncomplicated ASD often report only minor subjective complaints. Nevertheless, the present study demonstrated an evidently reduced cardiopulmonary exercise capacity. Peak oxygen uptake was reduced preoperatively to 63% of the predicted value. The diminished exercise performance corroborates the findings reported by other investigators. In the study of Fritsh et al. [5] peak oxygen consumption was as low as 62%, whereas Helber et al. [6] demonstrated a decreased exercise capacity down to 50–60%. The reduced peak oxygen uptake was observed even in a group of selected asymptomatic adults with ASD [7].

With respect to our own subgroup analysis in terms of age, RVSP and Qp/Qs, abnormal RVSP was established as the exclusive parameter affecting cardiopulmonary exercise capacity in adults with uncorrected ASD. In patients with RVSP > 30 mmHg peak oxygen consumption was as low as 54% of the predicted value, whereas in patients with normal RVSP it came up to 79%, a substantial difference definitely warranting a closer look. Patients with higher RVSP also reached significantly earlier the anaerobic threshold, as well as at a lower level of oxygen uptake.

Our findings happen to be very much in line with those of Oelberg et al. [8], who attributed the impaired cardiopulmonary exercise capacity to an abnormal pulmonary artery pressure and its subsequent rise during physical exercise. Reduced pulmonary venous return due to poorly recruit-able pulmonary circulation incapable of handling a large increase in blood flow, as required by physical exercise, could limit the cardiac output through underfilling of the left ventricle. The above hypothesis is corroborated by the results of their study in which they performed CPX and Doppler echocardiography during exercise to compare oxygen uptake and RVSP at rest and at peak effort in ASD patients, and had it subsequently matched against the healthy controls. There was a sudden increase in right ventricle systolic pressure in patients with uncorrected ASD during exercise, whereas no significant change in RVSP in controls was encountered. They also found a significant negative correlation between oxygen uptake and RVSP both at rest and at peak effort. A negative correlation between these variables was also evidenced in our own study.

Subgroup analysis in terms of age revealed significantly shorter exercise duration and lower peak oxygen uptake both at anaerobic threshold and at peak exercise in patients over 40. In these patients exercise performance was manifestly diminished in comparison to the younger ones. It should be noted at this junction however, that the above referenced parameters are impacted by age. In order to have the above variables compared effectively all values should be converted into the respective percentages of the predicted value, adjusted for specific age, as only then could the comparison yield accurate data.

Our study revealed an apparent tendency towards a decrease in the peak oxygen uptake expressed as the percentage of the predicted value in patients over 40, although this difference failed to reach significance. In the study of Brochu et al. [7], no significant differences in VO₂ % between patients under and over 40 years of age were encountered.

We did establish, however, that VE/VCO₂ slope before surgery was significantly steeper in older patients. VE/ VCO₂ characterizes the ventilatory response to physical exercise. Linear increase of both carbon dioxide and ventilation is evident during incremental exercise in a healthy subject. It still remains unclear why in the patients with chronic heart diseases there is an increase in ventilatory response during exercise. In patients with congestive heart failure this might well be attributable to an increased dead space ventilation, pulmonary circulation disorders, ventilation/perfusion mismatch, disturbances in respiratory reflex control originating in hypersensitivity of peripheral chemoreceptors and muscle ergoreceptors [9].

No study to date seems to have focused on the equivalent for carbon dioxide in ASD patients, although an increased value of VE/VCO₂ might reasonably be believed to be indicative of a more severe impairment of cardiopulmonary exercise capacity in these patients.

Similar working assumption was followed by ourselves with respect to PETCO₂. In patients over 40 years, PETCO₂ was significantly lower in comparison to the younger ones. It is widely acknowledged that establishing PETCO₂ value is of paramount importance in an assessment of severity of heart failure. As reported by many investigators, the decrease in PETCO₂ in patients with congestive heart failure is caused by increased pulmonary dead space ventilation, excessive ventilation of poorly perfused alveoli and impairment in pulmonary gas exchange [10].

The above course of reasoning might then give some grounds to believe that a lower value of PETCO₂ in older patients with ASD may be indicative of greater impairment of lung function in these patients.

Subgroup analysis in terms of Qp/Qs did not reveal any significant differences in cardiopulmonary exercise capacity before the surgery. The same observation was reported by other authors [7,8]. Interestingly, Giardini et al. [11] reported the correlation between the extent of peak VO₂ improvement after transcatheter closure and Qp/Qs magnitude.

Helber et al. [6] documented complete normalization of cardiopulmonary exercise capacity 10 years after surgery for ASD. In the present study, we managed to demonstrate a significant improvement of cardiopulmonary exercise capacity within a year of ASD closure. Irrespective of age, RVSP and Qp/Qs a significant increase in exercise duration, oxygen uptake – both at anaerobic threshold and peak effort was noted, whereas VE/VCO₂ decreased after ASD closure. This improvement was most manifest in the subgroup of patients with preoperative pulmonary hypertension. Nevertheless, cardiopulmonary exercise capacity in these patients remained significantly lower in comparison to the ones with normal RVSP before surgery.
It should be emphasized at this point that after ASD correction we found no significant differences in CPX data (expressed as a percentage of the predicted value) between patients subjected to surgical intervention under and over 40 years of age. The same results were reported by Brochu et al. [7] who encountered similar improvement in cardiopulmonary exercise capacity after transcatheter closure of ASD, irrespective of whether the defect was closed before or after the respective patients reached 40.

Despite having observed considerable improvement in exercise performance, the decreased anaerobic threshold and VO₂% less than 80% of the predicted value were encountered in 17 and 46% of patients, respectively. These results are consistent with the findings of Reybrouck et al. [12], who concluded that exercise performance was normal when surgical closure of ASD was performed before the age of 5 years rather than later in life.

The short follow-up is the main weakness of the study. Our data show ASD closure to be beneficial irrespective of age at surgery, although many abnormalities persist at one-year follow-up study. A longer follow-up period would be required to assess the actual benefits of surgery.

5. Conclusions

Adult patients with ASD benefit from surgical closure of ASD irrespective of the actual age at surgery, as assessed by echocardiography and CPX data. Patient’s age at surgery and pulmonary hypertension crucially impact the outcome of surgical intervention. Early defect correction should therefore definitely be aimed for, specifically with a view to preventing the hemodynamic consequences of ASD.

References