Improved cardiopulmonary exercise function after modified Nuss operation for pectus excavatum

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Abstract

OBJECTIVES: Patients with pectus excavatum have compromised cardiac function during exercise. We hypothesized that the Nuss technique would improve cardiopulmonary function during exercise.

METHODS: We investigated 75 teenagers (49 patients and 26 controls) at rest and during bicycle exercise prior to surgery and 1 year postoperative.

RESULTS: Prior to surgery, patients had a lower cardiac index 6.6 ± 1.1 l/min/m² when compared with controls 8.1 ± 1.0 l/min/m² during submaximal exercise, P = 0.0001. There was no difference in heart rate or increase in heart rate between the two groups. One year after surgery, cardiac index had significantly increased in the pectus group, P = 0.0054 although cardiac index was still significantly lower 7.2 ± 1.0 l/min/m² when compared with the control subjects (8.5 ± 1.6 l/min/m², P = 0.0008). Both the patients and the controls increased their VO₂ max during the one-year study period although the controls increased most. Right ventricular diastolic dimension increased in both groups over the one-year study period and left ventricular dimensions increased in the patients. Before operation, the patients had lower forced expiratory capacity FEV₁ 86 ± 13% when compared with controls 94 ± 10%, P = 0.009. Patients increased FEV₁/forced vital capacity over the one-year long study course although there were no differences between groups.

CONCLUSION: Patients with pectus excavatum have lower cardiac index at submaximal exercise when compared with healthy age-matched controls. Their cardiac index and FEV₁ are increased one year after the modified Nuss operation.

Keywords: Cardiopulmonary exercise • Pectus excavatum • Musculoskeletal disease • Lung function • Stroke index

INTRODUCTION

Pectus excavatum is known to cause symptoms such as fatigue, tachypnoea, discomfort and dyspnoea [1, 2]. Objective signs of compromised cardiopulmonary function are, however, not easily found and despite a vast amount of studies the conclusions are not consistent. Nevertheless, it is generally agreed that the influence of pectus excavatum on cardiorespiratory function is trivial at rest.

During exercise, the situation is different. We have, in a previous paper, found that cardiac index during bicycle exercise is decreased in children with pectus excavatum when compared with age-matched controls [3]. Our study confirmed the findings from the other two studies investigating teenagers with pectus excavatum and control subjects during exercise [4, 5]. The inability to increase stroke volume at higher cardiac output may be due to the shallow thoracic cavity.

The next question is whether surgical correction of pectus excavatum will relieve the symptoms, and whether the observed limitations in cardiopulmonary function during exercise can be reverted. With respect to the resting state, several studies have looked at changes in cardiac [2, 6–10] and pulmonary functions [2, 7–13] after operation for pectus excavatum. Results have shown no change in cardiac function [6, 7] and pulmonary function has varied from no change [11, 12] to slightly decreased [8] function.

Some of the studies also investigated the exercise capacity [2, 7, 8, 11] but they did not measure cardiac function during the exercise. The only study looking at cardiac function during exercise after pectus repair is the one by Peterson et al. [14], who investigated 13 patients with pectus excavatum before and 6 months after operation. Using radionuclide measurements of cardiac output and dimensions of the cardiac chambers, they found no change in cardiac output but increased chamber dimensions. The increased chamber dimension could however be explained by the growth of the teenagers between the baseline and the follow-up study.

The technique for surgical correction of pectus excavatum has changed to more minimally invasive techniques since Peterson did his study in the mid 1980’s and it is relevant to investigate children who have undergone a less invasive surgical procedure.
and include an age-matched control group in order to eliminate confounding from age-related changes.

This study questions whether minimally invasive operation for pectus excavatum in a teenager influences the cardiopulmonary function at rest and/or during exercise. At Aarhus University Hospital, Skejby, all patients undergoing surgical correction for pectus excavatum are operated with minimally invasive repair. The original technique was published by Nuss and colleagues in 1998 [15]. Since 2001, we have used a modified version of the procedure, where a shorter bar is implanted [16].

Our hypothesis was that the lower cardiac index and forced expiratory capacity within the 1 s (FEV1) found in patients with pectus excavatum would normalize after surgical correction, taking growth during the investigational period into consideration by comparing them with healthy age-matched controls.

**MATERIALS AND METHODS**

**Study population**

This study includes 49 patients with pectus excavatum operated at The Department of Cardiothoracic and Vascular Surgery at Aarhus University Hospital, Skejby, and 26 age-matched control subjects. Patients were 15.5 ± 1.7 years old and controls were 15.0 ± 1.9 years old at the time of the first examination before the patients underwent operation for pectus excavatum and 16.3 ± 1.7- and 16.0 ± 2.0 years old at the second investigation approximately one year later. There was no difference in body mass index between patients and control subjects, neither before nor one year after operation. Yet, the patients increased their body mass index when compared with before, whereas the controls display no change in body mass index. There was no difference in time interval between first and second investigations in the two groups.

All baseline measurements in this study comprised a subgroup of the study published by Lesbo et al. [3]. In this paper, all included teenagers have repeated analyses 12 months after surgery, still with the pectus bar in place. Control subjects were recruited by posters placed at Aarhus University Hospital, Skejby, and public schools nearby. Criteria for exclusion from both groups were severe lung disease, known heart disease and lack of Danish-skills. The study protocol was approved by the local ethics committee. Patients and controls gave written consent after oral and written information.

Statistical analyses were performed using StataIC 11.1 (Stata Corporation LP, Texas, USA). Data were normally distributed as estimated on normal distribution probability plots. Statistical analyses included Student's paired t-test for comparison within the same individuals over time and Student's unpaired t-test for comparisons between groups. Since a number of tests were performed, a difference was regarded as statistically significant if $P < 0.01$. We chose a lower significance level than normally used in order to reduce the risk of committing a statistical type 2 error.

**Magnetic resonance imaging**

The Haller index was measured with magnetic resonance imaging (MRI) to avoid unnecessary radiation [17].

**Echocardiography**

Fractional shortening, ejection fraction and structural abnormalities were described using transthoracic echocardiography. The scans were obtained with a 4 MS transducer coupled to a VIVID7® ultrasonic echo machine (GE Healthcare, UK). All examinations were done by the same echo technician.

**Spirometry**

Vital capacity (VC), forced vital capacity (FVC), FEV1 and peak expiratory flow (PEF) were measured. These measures were corrected for age, weight and height and compared with normal ranges. Data included in this study are percent values of the expected for the patients and control subjects.

**Cardiopulmonary exercise**

For cardiopulmonary exercise (CPX) evaluation, we combined a cycle ergometer test and a photoacoustic gas-rebreathing technique for non-invasive determination of the pulmonary blood-flow. This corresponds to the cardiac output, assuming no intracardiac shunts exist. The rebreathing system consisted of a three-way respiratory valve connected to a mouthpiece and a rubber bag, which in turn was connected to an infrared photo-acoustic gas analyzer (Innocor®, Innovision A/S, Odense, Denmark). To assure a closed system, the patient or control was equipped with a nose-clamp. The system used an oxygen-enriched mixture of an inert soluble gas (0.5% nitrous oxide) and an inert insoluble gas (0.1% sulphur hexafluoride) measured by photoacoustic analyzers over a 5-breath interval. The infrared photoacoustic technique has been described in detail by Clemensen et al. [18].

Minimum heart rate (at rest), maximal heart rate (during exercise), increase in heart rate, cardiac index and oxygen uptake/kg (VO2 ml/min/kg) were determined. Stroke index (SI) was calculated as maximum cardiac index divided by maximum heart rate. Exercise was performed in an air-conditioned laboratory (20–22 °C with moderate humidity). Participants cycled in the upright position to exhaustion, with a progressive protocol of 3 min work stages and 30 W increments. Prior to increasing work load a new breath test was made. Breath test could not be made at shorter intervals than 3 min due to the recommended time needed for clearance of gas particles. Pedalling cadence was 60 rpm. After instruction and 2–3 rebreathing procedures for practicing, the patient was placed on the bicycle and equipped with a pulse oxymeter.

The first rebreathing procedure was performed with the patient sitting relaxed on the bike (0 W). During incremental bicycle exercise, the rebreathing procedure was repeated every 3 min (at 30, 60, 90, 120 W and so forth). A sub-maximal exercise effort was considered with subjective evidence of fatigue (hyperpnoea, sweating), heart rate increase to 75-80% of the expected maximal heart rate, and the subject not wanting to continue cycling despite encouragement from the research team. All CPX tests were performed by the same research group.

The patients and controls were questioned about their habitual exercise and smoking habits. The exercise habits were scored from 1 to 4. One was exercise less than once a month, two was 1-3 times a month, three was 1–2 a week and four was more than 3 times per week.
RESULTS

The missing data on some of the examinations were randomly distributed and the actual number of patients participating in each test was given in the tables. Results were displayed as mean with SD.

Haller index

Haller index was 5.3 ± 2.3 in pectus patients while the Haller index in controls was 2.7 ± 0.3. The Haller index was not possible to measure by MRI after surgical correction due to the implantation of the metal bar.

Pulmonary function

Before surgical correction, FEV₁ was lower in pectus patients when compared with controls (Table 1). There was no statistically significant difference in FVC, FEV₁/FVC or peak flow between patients and controls. The pectus patients showed significantly increased FEV₁ and FEV₁/FVC 12 months after surgery whereas controls had an increased PEF.

Cardiopulmonary function

Echocardiographic measurements such as fractional shortening and ejection fraction showed no differences between the pectus patients and the controls neither before nor 12 months after the operation and there was no change in any group over time (Table 2).

Diastolic dimensions of left ventricle significantly increased among the patients over the 12 months follow-up. The controls showed an increase in right but not in left ventricular diastolic dimensions. No significant differences in the above values were detected between the pectus-operated patients and the controls (Table 2) neither before nor after 12 months follow-up.

Heart rate increased equally during exercise in pectus-operated patients as well as controls (Table 3). Maximum cardiac index and SI are the body surface area-corrected cardiac output and stroke volume, respectively. Maximum cardiac index during exercise was lower before the operation in the pectus group compared with the control group. At 12 months follow-up, the maximum cardiac index during exercise for the patients operated for pectus excavatum was 7.2 l/min/m². This was significantly improved compared with baseline, but still lower than the controls 8.5 l/min/m². The control group did not increase their maximum cardiac index during bicycling significantly after 12 months. SI was lower in patients than in controls before operation. This difference had disappeared at the 12 months follow-up visit.

Maximal oxygen uptake

The control group had increased their maximum oxygen uptake over the study period.

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Table 1: Spirometry in 40 pectus patients and 23 controls before and 12 months after surgical correction using the modified Nuss technique

<table>
<thead>
<tr>
<th></th>
<th>Baseline Patients</th>
<th>Baseline Controls</th>
<th>12 months follow-up Patients</th>
<th>12 months follow-up Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV₁, %</td>
<td>87* (13)</td>
<td>94 (10)</td>
<td>91** (13)</td>
<td>96 (14)</td>
</tr>
<tr>
<td>FVC, %</td>
<td>96 (14)</td>
<td>94 (12)</td>
<td>97 (13)</td>
<td>99 (14)</td>
</tr>
<tr>
<td>FEV₁/FVC, %</td>
<td>93 (7.5)</td>
<td>95 (7.3)</td>
<td>97** (8.5)</td>
<td>98 (11)</td>
</tr>
<tr>
<td>PEF, %</td>
<td>81 (14)</td>
<td>83 (14)</td>
<td>84** (17)</td>
<td>94** (15)</td>
</tr>
</tbody>
</table>

*Significant (P < 0.01) difference between patients and controls.
**Significant (P < 0.01) difference between baseline and 12 months follow-up.

Table 2: Echocardiography parameters in 37 pectus patients and 20 controls before and 12 months after surgical correction using the modified Nuss technique

<table>
<thead>
<tr>
<th></th>
<th>Baseline Patients</th>
<th>Baseline Controls</th>
<th>12 months follow-up Patients</th>
<th>12 months follow-up Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ejection fraction, %</td>
<td>65 (6.5)</td>
<td>66 (6.5)</td>
<td>64 (4.8)</td>
<td>64 (4.5)</td>
</tr>
<tr>
<td>Fractional shortening, %</td>
<td>34 (4.0)</td>
<td>35 (3.0)</td>
<td>35 (3.8)</td>
<td>34 (3.4)</td>
</tr>
<tr>
<td>Left ventricular diastolic diameter, cm</td>
<td>4.6 (0.4)</td>
<td>4.7 (0.5)</td>
<td>4.8** (0.4)</td>
<td>4.7 (0.5)</td>
</tr>
<tr>
<td>Left ventricular systolic diameter, cm</td>
<td>3.0 (0.3)</td>
<td>3.1 (0.4)</td>
<td>3.1 (0.3)</td>
<td>3.1 (0.3)</td>
</tr>
<tr>
<td>Right ventricular diastolic diameter, cm</td>
<td>2.1 (0.3)</td>
<td>2.1 (0.3)</td>
<td>2.2 (0.4)</td>
<td>2.2** (0.3)</td>
</tr>
</tbody>
</table>

*Significant (P < 0.01) difference between patients and controls.
**Significant (P < 0.01) difference between baseline and 12 months follow-up.

Table 3: Cardiac function tests during bicycle exercising in 38 pectus patients and 24 controls before and 12 months after surgical correction using the modified Nuss technique

<table>
<thead>
<tr>
<th></th>
<th>Baseline Patients</th>
<th>Baseline Controls</th>
<th>12 months follow-up Patients</th>
<th>12 months follow-up Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Min. heart rate, beat/min</td>
<td>87 (1.2)</td>
<td>86 (14)</td>
<td>82 (14)</td>
<td>80 (12)</td>
</tr>
<tr>
<td>Max. heart rate, beat/min</td>
<td>159 (17)</td>
<td>160 (34)</td>
<td>169 (20)</td>
<td>177 (16)</td>
</tr>
<tr>
<td>Maximum cardiac index, l/min/m²</td>
<td>6.6* (1.1)</td>
<td>8.1 (1.7)</td>
<td>7.2 ** (1.0)</td>
<td>8.5 (1.6)</td>
</tr>
<tr>
<td>Maximum VO₂/kg, ml/min/kg</td>
<td>26 (6.0)</td>
<td>31 (7.6)</td>
<td>28 (6.7)</td>
<td>35 ** (6.7)</td>
</tr>
<tr>
<td>Stroke index, ml/beat/m²</td>
<td>42* (8.3)</td>
<td>55 (25)</td>
<td>43 (7.7)</td>
<td>48 (10)</td>
</tr>
</tbody>
</table>

*Significant (P < 0.01) difference between patients and controls.
**Significant (P < 0.01) difference between baseline and 12 months follow-up.
Sports habits

Before operation, the patients exercised less than the controls, and there was no difference in training level one year after the operation, although this was mainly due to less activity in the control group.

DISCUSSION

We have previously found that maximum cardiac index at exercise in patients with pectus excavatum is only just above 80% of maximum cardiac index in healthy age-matched controls [3]. We set out to investigate whether the Nuss-operated teenagers would benefit from the operation by increasing their maximum cardiac index during exercise.

Maximum cardiac index during exercise increased 12 months after the operation. However, in spite of the significant increase, the maximum exercise cardiac index was not normalized completely. Two explanations for this increase after surgery are likely. First, the enlargement of the thoracic dimension in the anterior-posterior plane may facilitate filling of the heart especially during exercise. Secondly, the children may have appreciated their new bodily appearance and started to participate in sport activities and thus increased their exercise capacity.

Kowalewski also found that right ventricular diastolic diameter increased one year after operation for pectus excavatum, but he did not include a control group as we did [9]. Our control group increased the right ventricular systolic diameter over the one-year study time whereas no difference was detected in the patients. In contrast, the left ventricular diastolic diameter increased in the pectus patients but not in the controls. The different response is difficult to explain. Age-related growth would be expected to be comparable in the two groups. An increased thoracic cavity may facilitate left ventricular filling but the numerical changes are small and should be interpreted cautiously. Thus, we believe that the increase in cardiac dimensions can be attributed mainly to growth.

SI was lower in the pectus group compared with the controls and the difference disappeared after surgery. Thus, the improvement in cardiac output was caused by a greater combined increase in maximum heart rate and stroke volume among the pectus patients when compared with the controls.

The importance of age-matched controls is emphasized. In this study, the strength is the age-matched control group and the indexation of parameters such as cardiac output and stroke volume to body surface area in order to adjust for different physical development.

Controls but not pectus patients increase their maximum oxygen uptake from baseline investigation before surgery to 12 months after. This finding is difficult to explain since the controls decreased their activity level over the one-year study period. The pectus patients did not change their sports habits.

Whether one or the other explanation pertains to the finding, it is noteworthy that children with pectus deformities almost normalize their cardiac performance secondary to operation and still with the pectus bar in place. Further studies are needed, in order to see if removal of the bar will facilitate a complete normalization of the maximum cardiac index.

Respiratory function tests on pectus excavatum patients have been inconclusive. After open surgery no changes when compared with before have been noticed [5, 8, 11, 12]. A few of the studies have looked at respiratory changes after the newer less invasive Nuss procedure [2, 7, 8, 13]. Varying results have been reported from no change in respiratory function [2], to increased respiratory function after removal of the metal bars [13] or decreased function both before and after bar placement and bar removal [7, 8]. Sigalet et al. [7] is an extension of the study done by Bawazir et al. [8] and the combined data show that although the lung function continues to be lower than the population average, there is an increase in parameters over the treatment period. The weakness in all of these four studies was comparison to population average and lack of control subjects. In our study, we found an improvement in FEV1 in patients and not in controls from before operation to 12 months post-operatively.

LIMITATIONS

We have compared pectus patients before and after surgery and with age-matched controls using multiple comparisons with a substantial risk of committing a type 2 error. For these reasons, we have chosen a lower than normal significance level of 0.01.

CONCLUSION

Cardiac index during exercise was significantly lower in the pectus group compared with the control group prior to surgical correction by the modified Nuss procedure. Twelve months after the operation, pectus excavatum patients had significantly increased their cardiac index and FEV1 has normalized.

ACKNOWLEDGEMENTS

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Conflict of interest: Hans K. Pilegaard is consultant at Biomet.

References

Repair of pectus excavatum. Are we doing it better just to make it look better?

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In the beginning of the era of pectus excavatum surgery, only patients with the most severe forms of deformities were operated upon. The aim of the intervention was to release the compromised thoracic organs from the grip of the depressed sternum, and thus improve critically impaired cardiorespiratory function. The anatomical results were readily visible and the functional improvement was clinically evident.

As time passed, with the increasing experience and with the development of more effective and less traumatic procedures, the operative risk dropped dramatically and the operative indication for the repair of pectus excavatum was gradually extended to less severe deformities. Even so, it remains evident that most patients with advanced forms of the deformity indeed benefit physiologically from the repair and that the correction of mild deformities yielded but cosmetic improvement. The question as to whether moderate-to-severe sternal depressions may cause any functional restraint or even permanent physiological damage, which per se justifies surgical intervention, remained unanswered. This issue now bears special significance in providing informed consent, i.e. some parents may agree to surgery for the purpose to ‘cure’ the condition, i.e. improve cardiorespiratory function and/or eliminate foreseeable morbidity, but would not be in favour of an intervention for purely cosmetic reasons. The situation is further complicated by the stance of most insurance companies, which are reluctant to cover the expenses of reconstructive surgery done for purely cosmetic reasons.

There is a long line of studies that used primarily pulmonary, but also cardiac function tests, which attempted to prove the physiological value of pectus excavatum repair. Unfortunately, most, if not all, fell short of providing convincing proof that moderate-to-severe pectus excavatum may significantly impair cardiorespiratory function. The main difficulty which emerged in these studies was that such patients, the physiological parameters were not only after, but also before surgery were within the boundaries of accepted values. The methods for evaluation also had the potential to be influenced by the patient’s subjective input. Unfortunately, the article ‘Improved cardiopulmonary exercise function after modified Nuss operation for pectus excavatum’ [1] by Tang et al. does not overcome these difficulties, and thus fails to provide definite conclusions.