Cardiac function in adults following minimally invasive repair of pectus excavatum†

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Abstract

OBJECTIVES: To study if minimally invasive repair of pectus excavatum (PE) in adult patients would improve cardiopulmonary function at rest and during exercise as we have found previously in young and adolescent patients with PE.

METHODS: Nineteen adult patients (>21 year of age) were studied at rest and during bicycle exercise before surgery and 1 year postoperatively. Lung spirometry was performed at rest. Cardiac output, heart rate and aerobic exercise capacity were measured using a photo-acoustic gas-rebreathing technique during rest and exercise. Data are shown as mean ± standard deviation.

RESULTS: Fifteen patients completed the 1-year follow-up. No significant differences were found in neither cardiac output (14.0 ± 0.9 l min at baseline vs 14.8 ± 1.1 l min after surgery; \(P=0.2029\)), nor maximum oxygen uptake (30.4 ± 1.9 and 33.3 ± 1.6 ml/kg/min; \(P = 0.0940\) postoperatively). The lung spirometry was also unchanged, with no difference in forced expiratory capacity during the first second.

CONCLUSIONS: Correction of PE in adult patients does not improve the cardiopulmonary function 1 year after surgery as seen in children and adolescents.

Keywords: Pectus excavatum • Exercise • Nuss procedure • Cardiopulmonary function • Spirometry

INTRODUCTION

Pectus excavatum (PE) is the most common congenital deformity of the anterior wall of the chest, and occurs in 1 of 400 male live births with a male-predominance of four to six times [1, 2]. During the adolescent growth spurt, most of the chest depression increases in severity and many patients undergo surgery in their early teenage years [3].

For decades, no consensus on the effect of PE on cardiopulmonary function has existed and surgery was considered purely cosmetic. However, we have previously demonstrated that teenagers with PE exhibit decreased lung function, measured as forced expiratory capacity during the first second (FEV\(_1\)), in combination with an almost 25% lower cardiac function measured as maximal cardiac index (\(C_{\text{max}}\)) compared with a group of healthy age-matched controls during exercise [4]. All patients in the study underwent a modified, minimally invasive Nuss procedure [5]. The Nuss procedure is considered less invasive than the Ravitch procedure and is potentially less harmful to the chest flexibility and probably increases the volume of the chest more. One year following surgery, \(C_{\text{max}}\) was increased during exercise, but was still lower compared with age-matched controls [6]. Normalization of cardiopulmonary exercise function was achieved 3 years after surgical correction and bar removal [7].

Severe PE is also seen in adult patients, often causing psychological complaints and physiological weakening. There is no clear consensus on the effect of PE on cardiopulmonary function in this particular patient group. Neviere et al. [8] have demonstrated that adult PE patients on average have only 77% of the predicted peak oxygen uptake during exercise. One year after undergoing the modified Ravitch repair, oxygen uptake was improved to 87% of the predicted value [8]. The lung function declined maybe because of increased rigidity of the chest wall [8]. Although not documented, the combination with the improved oxygen uptake suggested that the beneficial effect of surgery was mainly on the cardiac function.

We hypothesized that both cardiac index and lung function would increase 1 year after the Nuss procedure compared with preoperative results as seen in young patients.

The aim of this study was to assess cardiac and pulmonary function at rest and during exercise and compare preoperative results with results 1 year after undergoing the Nuss procedure.

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MATERIALS AND METHODS

Participants

The study was a single-centre, prospective, controlled study. We included 19 patients (6 females), all scheduled to undergo the minimally invasive Nuss procedure for PE. All patients were older than 21 years of age at the inclusion time. Exclusion criteria were severe lung disease, pre-existing heart disease and lack of Danish language skills. Participants provided informed consent after oral and written information for a 1-year study period. The National Committee on Health Research Ethics approved the study protocol (1107217513). Assessments of cardiac/pulmonary function were conducted the day before patients underwent corrective surgery and 12 months postoperatively.

Statistical analysis

Before initiating the study, power calculations were made for volume of oxygen uptake/kg (VO2/kg) and cardiac output to ensure sufficient sample size. With an estimated standard deviation of 5%, a difference of 20% and a power of 80%, the number needed to investigate was 15. Statistical analyses were performed using StataIC 12.0 (StataCorp LP, TX, USA). Data were normally distributed as estimated on normal distribution probability plots. Initial and follow-up studies for the same individual were compared with the Student’s paired t-test. Due to multiple testing, a lower than normal level of significance was chosen: P < 0.01. All data are presented as mean ± standard deviation (minimum–maximum).

Questionnaire

Each patient completed a questionnaire examining his or her smoking habits and exercise habits. Exercise habits were scored from 1 to 4, where 1 was exercise less than once a month and 4 being more than three times per week. Participants were included in the smoking-group if they had been smoking more than 14 cigarettes per week for at least a year. The questionnaires were handed out at both examinations.

Cardiopulmonary exercise

In order to assess cardiopulmonary exercise capacity of the participants, we used a non-invasive, photo-acoustic gas-rebreathing technique, previously validated, combined with a bicycle ergometer fatigue-test [9]. A closed system was ensured with the participant being equipped with a nose-clamp and breathing through a mouthpiece connected to a three-way respiratory valve and a rubber bag, which again was connected to an infrared photo-acoustic gas analyzer-device (Innocor®, Innovision A/S, Odense, Denmark). The system used oxygen-enriched mixture of an inert soluble gas (0.5% nitrous oxide) and an inert insoluble gas (0.1% sulphur hexafluoride) measured by photo-acoustic analyzers over five breath intervals. Minimum–maximum heart rate, CImax and volume of oxygen uptake/kg (VO2/kg) were determined from this test. The maximum stroke index (SImax) was calculated as CImax divided by maximum heart rate. CImax and SImax are the body surface area-corrected cardiac output and stroke volume, respectively.

Participants were sitting upright on the bicycle, equipped with a pulse oximeter, in an air-conditioned laboratory. The rebreathing technique was used at rest and during exercise. Rebreathing tests were repeated every 3 min in order to secure washout of gas-particles from the system. Following each test, participants removed the mouthpiece and breathed in normal, atmospheric air. The participants pedalled at a steady pace of 60 rpm with incremental workload (steps of 30 W) until exhausted and no longer capable of continuing despite encouragement from the research team. A sub-maximal exercise effort was achieved with a heart rate of ~80% of expected maximum value as well as subjective evidence of fatigue (i.e. sweating and hyperpnoea). The tests were performed with the same equipment throughout the investigational period.

Spirometry

All participants underwent pulmonary function tests preoperatively and 1 year postoperatively. The same spirometer (Spirotac IV, Vitalograph®) was used throughout the study period. Forced vital capacity (FVC), FEV1, the ratio FEV1/FVC and the peak expiratory flow were recorded. All measured indices were related to size, age and gender-adjusted normal values and were expressed as a percentage of predicted standardized values derived from European Respiratory Society ’93 (age range 18–70), depending on the age of the participant [10].

RESULTS

Participant characteristics

Out of the 19 patients that were included, 15 patients completed the 1-year follow-up. The mean age at inclusion was 32 years. The missing data on some of the tests were randomly distributed. Number of patients participating in each test is presented in Tables 1–3.

Questionnaires

No difference was observed in the level of habitual activity (Table 1) before and after surgical correction of the PE. Smokers did not differ from non-smokers regarding lung function test scores or results from bicycle exercising tests, and the proportion of non-smokers did not change in the time period.

Cardiopulmonary exercise

Cardiopulmonary exercise capacity tests from baseline and 1 year postoperatively are outlined in Table 2 and Fig. 1. Heart rate

| Table 1: Smoking and exercise habits for patients and controls at baseline and 1-year follow-up |
|---------------------------------|---------------------------------|
| n = 15                          | Baseline                        |
|                                 | 1-year follow-up                |
| Exercise, category 1–4          | 2.4                             |
| (0.3)                           | (0.3)                           |
| Smokers                         | 5                               |
| non-smokers                     | 10                              |
|                                 | 10                              |

Results displayed as standard mean ± SD.

n: number of participants completing both tests; SD: standard deviation.
was (171 ± 16) after 1 year versus preoperatively (168 ± 9), P = 0.32. The 1-year follow-up CO max was 14.8 ± 3.8 l/min compared with 14.0 ± 3.2 l/min preoperatively (P = 0.20). Postoperative VO2 peak was 33.3 ± 5.4 ml/min/kg compared with the preoperative 30.4 ± 6.5 ml/min/kg (P = 0.09).

**Spirometry**

The pre- and postoperative lung function data are given in Table 3. At 1-year follow-up, patients did not improve FEV1 compared with baseline (90 ± 9 vs 89 ± 10%; P = 0.79). Forced expiratory volumes did not change during the year, and all patients scored within normal ranges of their predicted values. No significant improvement in the FEV1/FVC ratio was observed at follow-up (1-year 104 ± 10 vs preop 101 ± 10%; P = 0.01). Individual values are shown in Fig. 2.

**DISCUSSION**

In contrast to the findings in children and young adults, we did not find any significant change in the cardiopulmonary function in the adult patient corrected by the Nuss procedure after 1 year [4, 6, 7]. There was a tendency towards an increase in maximum oxygen uptake indicating that the adult patients might need a longer time to improve exercise capacity and lung function. This needs further investigation, and we have to await the retesting of the patients after 3 years when the bars have been removed.

Most patients report subjective improvement in exercise capacity following the Nuss procedure, which is not supported by our data [11, 12]. Our findings are in contrast to the study by Neviere et al. [8], who demonstrated improved maximal oxygen uptake (VO2 max) and O2 pulse (as a surrogate for stroke volume) 1 year after the open Ravitch. Neviere et al. [13] described in a later study that the inspiratory muscle strength is impaired before surgery.
and improved after surgery. The inspiratory muscles are important for generation of the negative pulmonary pressure that allows for increased venous filling and thus cardiac output and has been named the respiratory blood pump. This later study is highly comparable with ours in that 20 patients are included and the VO₂ max values are very similar to our values. In Neviere’s study, preoperative VO₂ is 30.8 ± 6.9 ml/min/kg whereas our VO₂ is 30.4 ± 6 ml/min/kg and postoperatively they find a VO₂ of 34.4 ± 8.6 ml/min/kg whereas we find 33.3 ± 5 ml/min/kg. This could indicate that the present study is underpowered with only 15 patients, and thereby not able to detect a small difference. However, our objective was to investigate any clinically significant differences after 1 year. Another hypothesis is that the modified Ravitch operation may allow for improvement in the ‘respiratory blood pump’ more efficiently in the adult population.

Interestingly, we have never demonstrated any decrease in lung function parameters after the Nuss procedure, neither in teenagers and adolescents nor in adults, whereas Neviere et al. demonstrated reduced lung function after the Ravitch procedure in their first paper but not in their later series of patients from 2010 to 2011 [4, 6–8, 13]. The changes found by Neviere et al. [8] were small and the measured values were within the normal limits except from expiratory minute ventilation, which was less than 60% both before and after surgery, indicating that PE is a disease with major impact on ventilation.

The Haller index (an index for the severity of the deformity calculated as the ratio of the transverse dimension of the chest to the anterior–posterior dimension) was not measured since no correlation between the adolescence patients’ Haller index and cardiopulmonary function was found either before or after corrective surgery [7].

Surgical correction of PE in adolescence patients has been shown to significantly improve patients’ self-esteem, social functioning and consequently leads to a better quality of life [14, 15]. The same is likely to hold true for adult patients, but this question needs further investigation.

Limitations

The inclusion of a control group consisting of PE patients who did not undergo surgery would have added an interesting level of information on the natural progression of cardiopulmonary function in this patient group. However, all patients were adults with no residual growth potential. Furthermore, the termination of each exercise test was based on subjective parameters, which adds a level of observer bias. Still, this bias was minimized by having the same observers use consistent termination criteria to perform the assessments throughout the study period.

CONCLUSION

For adult PE patients having minimally invasive repair, no significant improvement in cardiopulmonary function was found at rest or during exercise at 1-year follow-up. Nonetheless, a trend towards improved maximum oxygen uptake was seen and this finding adds to the growing body of evidence favouring surgical correction for PE in adults, not only because of the cosmetic nature, but also as a level of a potential physiological importance.

The cardiopulmonary function of this patient group will be addressed after 3 years and bar removal.

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Conflict of interest: Hans Pilegaard discloses a financial relationship with Biomet.

REFERENCES


APPENDIX. CONFERENCE DISCUSSION

Dr R. Schmid (Bern, Switzerland): Basically it is a negative study. I will ask one question after the other, not all at one time so it is easier to answer. What do
you think is the biggest difference between the groups? Why is there no difference in improvement?

Dr Udholm: Well, our study didn’t really come up with the answer to that question, but a theory could be that.

Dr Schmid: Interpretation.

Dr Udholm: Yes, yes. Well, one explanation could be that the older patient could be stiffer in the tissue and they simply need more time to adapt to the new chest wall.

Dr Schmid: You mentioned in the last sentence that the bar is still in place. Do you think this has an impact?

Dr Udholm: Well, the bar is still in place after 1 year with the adolescents, and we still saw an improvement there. Perhaps it could have some influence, but I don’t know.

Dr Schmid: The second question is, why do you measure forced expiratory volume in the first second? Why do you think there is a difference in forced expiratory volume in the first second when you measure lung volumes and not total lung capacity or residual volume?

Dr Udholm: Well, one of the reasons why it was important for us was because we found this difference in the adolescents in the forced expiratory volume in the first second. Regarding the smokers, the proportion of smokers preoperatively was the same postoperatively.

Dr Schmid: You also mentioned what we all experience in the clinic, that they showed a subjective improvement. Why do you think there is this discrepancy between subjective improvement and your measurements?

Dr Udholm: Well, that’s a good question, because almost all of our patients still have this subjective feeling that their cardiopulmonary function is better, that they can do much more exercise than they could before, but I don’t know why they feel like this when we don’t have the data to back it up.

Dr Schmid: Also in your paper you state that the rate of exercise they did was the same before and after, so it’s not their exercise performance.

Dr Udholm: They don’t exercise more, no.

Dr Schmid: But they feel better when they exercise.

Dr Udholm: They feel better, yes, exactly.

Dr Schmid: You measured VO2 max and you showed, and this was quite impressive, a decrease in VO2 max in some patients. How do you explain the decrease? Is this pain-related?

Dr Udholm: Well, after one year, most of the patients don’t feel any postoperative pain anymore, but some patients did feel like they had a lot of time to getting back to exercising, because they had one month on the couch, or even more. Perhaps that could explain why some even have a decrease.

Dr Schmid: Finally, the last question, in these adult patients, shouldn’t you correlate the exercise capacity with the Haller index you corrected; in other words, that you should normalise the amount of improvement you show clinically with the exercise capacity?

Dr Udholm: Well, of course, that would have been a very good idea to have a Haller index prior to surgery to see how deep the pectus was and see if that has any influence on the data, but we didn’t.

Dr Schmid: Thank you very much.

Dr H. Pilegaard (Aarhus, Denmark): I just have a comment on the Haller index. We tried to relate the Haller index in the young study we did, but there was no correlation between the capacity of the patient and the Haller index, so we couldn’t relate it to the deepness of the excavation.

Dr Schmid: The improvement of the Haller index, but maybe in the adults.

Dr Pilegaard: No, we had a normal Haller index when we saw the young patients, the adolescents. That study we did. I can’t remember the numbers in this study. But they were normalised in the first study we did and published. They had a normal Haller index after surgery.

Dr Schmid: After surgery, all of them?

Dr Pilegaard: All of them.

Dr Schmid: If you have a small pectus and you correct it, in the adult patients you wouldn’t think that you would improve the lung function, so these you should take out maybe.

Dr J. De Campos (Sao Paulo, Brazil): Congratulations on your paper and the presentation, and we are very anxious to know the final results when you remove the bar. I have two questions for you. First, these adult patients, maybe they have 1, 2, or more bars and it’s only 1 year after. Maybe this could be one explanation, because until now, you don’t have more capacity or something like that. You have at least 2 or 3 bars here in the chest wall.

Second, the way of life of these young adolescents, they change completely. Maybe this also can explain the difference. As Professor Schmid said, I don’t know if all these adult patients are doing more exercises or not or if you have some program that tries to push them to do more exercises. How do you explain this?

Dr Udholm: For the last question, we don’t have a program to push them to do more exercise. Regarding the way of life of the adolescents and the adults, that was why we compared them with the healthy age-matched controls, and we had these questionnaires about their exercise capacity to make sure that this wasn’t the explanation, that it was simply because they were doing more exercise at the 1-year and 3-year follow-up, because this was actually completely the same, and this patient group, actually a lot of them were really active postoperatively because many of them thought that this was the explanation why they couldn’t do what they thought that they needed to do, so they were really anxious to get out there afterwards.

Dr H. Elsayed (Cairo, Egypt): Can you just tell me how this would influence your practice in an adult patient who is not that concerned about the cosmetic effect and he has a mild to moderate pectus excavatum and you have not shown any physiological benefit? Is your study going to influence what you are going to tell him as to whether or not he should or should not have an operation?

Dr Udholm: Well, perhaps it would be best for Hans to answer that question.

Dr H. Pilegaard (Aarhus, Denmark): I think we have to wait for the results after 3 years because they might change. There was a trend that they were better, and we hear from the patients that they feel better, most of them. You said it’s not for the cosmetic reason. I think most of these patients with pectus excavatum are coming for the cosmetic reason in Denmark, even the old.

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In teenagers, the Nuss procedure for pectus excavatum (PEx) repair has the potential to improve lung function and normalize aerobic performance during incremental exercise testing. In a cohort of 70 adults, we have previously observed that aerobic capacity significantly improved one year after the Ravitch-type procedure [1]. In sharp contrast, Udholm et al. failed to demonstrate such improvements at the one-year follow-up in 15 adults undergoing the Nuss procedure [2]. Whether these contrasting results rely on different surgical approaches will be answered in the future by the 3-year follow-up proposed by Udholm et al. Meanwhile, interesting methodological issues mentioned by Udholm et al. deserve additional comments. First, Udholm et al. observed increases in postoperative peak VO2 that were consistent with our previous reports [1,3]. Study by Udholm et al. was underpowered, precluding any definite conclusion. Surprisingly, exercise testing was performed using a 30 Watt-increment to progressively increase workload. Of note, although VO2 max is linearly related to workload, high workload increments require sufficient time for VO2 to increase as well. This time delay can induce an oxygen debt limiting peak VO2 at the latest exercise steps. Absence of difference between pre- and postoperative peak VO2 in Udholm et al.’s study may be related, at least in part, to blunted VO2 kinetics. In order to limit confounding effects of reduced VO2 kinetics, determination of VO2 at ventilatory threshold and oxygen uptake efficiency slope may be useful to better characterize cardiopulmonary functional reserve in the context of symptom-limited submaximal exercise.

Secondly, authors claimed that exercise habit was similar before and after surgical correction. Exercise habits were evaluated with scoring system for categories, comparisons of which should be analysed using the Chi-2 trend rather than comparisons of means. Expression of postoperative VO2 changes according to individual fitness category could be informative as well. As suggested by Udholm et al., changes in exercise habit may be considered a confounding effect of PEx repair on postoperative peak VO2. Alternatively, it can be considered an expected result of PEx repair that has improved patients’ self-image and his motivation for social activities, including sports. Hence, beneficial impact of PEx repair on aerobic capacity may be related to direct improvement of cardiopulmonary response to exercise and through postoperative increases in exercise training, which will improve patient’s quality of life and reduce risk of premature mortality.

Overall, Udholm et al. have provided useful information on the 1-year follow-up after Nuss procedure in patients with PEx regarding changes in aerobic capacity. We feel that a standardized exercise testing protocol represents the most important issue that will allow study comparisons for evaluation of different procedures for PEx repair in adults.