Increasing Severity of Pectus Excavatum is Associated with Reduced Pulmonary Function

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Objective To determine whether pulmonary function decreases as a function of severity of pectus excavatum, and whether reduced function is restrictive or obstructive in nature in a large multicenter study.

Study design We evaluated preoperative spirometry data in 310 patients and lung volumes in 218 patients aged 6 to 21 years at 11 North American centers. We modeled the impact of the severity of deformity (based on the Haller index) on pulmonary function.

Results The percentages of patients with abnormal forced vital capacity (FVC), forced expiratory volume in 1 second (FEV₁), forced expiratory flow from 25% exhalation to 75% exhalation, and total lung capacity findings increased with increasing Haller index score. Less than 2% of patients demonstrated an obstructive pattern (FEV₁/FVC <67%), and 14.5% demonstrated a restrictive pattern (FVC and FEV₁ <80% predicted; FEV₁/FVC >80%). Patients with a Haller index of 7 are >4 times more likely to have an FVC of ≤80% than those with a Haller index of 4, and are also 4 times more likely to exhibit a restrictive pulmonary pattern.

Conclusions Among patients presenting for surgical repair of pectus excavatum, those with more severe deformities have a much higher likelihood of decreased pulmonary function with a restrictive pulmonary pattern. (J Pediatr 2011;159:256-61).

Previous investigations have demonstrated that the decreases in pulmonary function in pectus excavatum are modest, on the order of 80% to 85% of average values for the overall population. Most patients with pectus excavatum do not complain of symptoms in the resting state, but report symptoms with exercise. If the decrease in pulmonary function were caused by the pectus excavatum deformity, then the decrease in function might be expected to vary directly with the severity of the deformity. A relationship between pulmonary function and severity of chest wall depression has been determined in small studies; however, we are unaware of any study that actually used depth of chest wall depression to predict decreased pulmonary function. Consequently, we reexamined the lung function results in a large multicenter study, some results of which have been reported previously. We hypothesized that severity of chest wall depression could be used to predict decreased pulmonary function and would be associated with restricted, rather than obstructed, lung disease.

Methods

Out of 327 patients enrolled in a prospective multicenter study of pectus excavatum carried out at 11 North American pediatric medical centers, the design of which has been described in detail previously, we measured pulmonary function in 310, confining the study to those between 6 and 21 years of age who also had

CT Computed tomography
FEF₂₅-₇₅ Forced expiratory flow from 25% exhalation to 75% exhalation
FEV₁ Forced expiratory volume in 1 second
FRC Functional residual capacity
FVC Forced vital capacity
PFT Pulmonary function test
RV Residual volume
TLC Total lung capacity

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Supported by a grant from the Children’s Health Foundation of the Children’s Health System (Children’s Hospital of The King’s Daughters) of Norfolk, VA. A subset of patients underwent exercise cardiopulmonary function studies at several centers (not completed or reported here). That substudy was underwritten by a grant from Walter Lorenz Surgical, Inc, now Biomet Microfixation, Inc. The funding sources played no role in the collection, analysis, or reporting of data. D.N. served as a consultant to Biomet Microfixation, Inc. The authors declare no conflicts of interest.

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acceptable flow volume curves. In brief, patients and parents seeking surgical advice on correction of pectus excavatum presented to the center of their choice. Baseline spirometry data were obtained in the 310 patients. In 218 of these patients, lung volume data were available as well.

We included baseline pulmonary function tests (PFTs) and radiographs that were assessed using the multicenter study protocols on 9 patients who subsequently were excluded from the parent multicenter study because on careful radiologic studies, they turned out to have a Haller index score <3.2 on computed tomography (CT) scan. Although these cases were not eligible for the multicenter study, we included them in this analysis because they provided us with a wider spectrum of Haller index scores at the low end. Data collection for this study began in 2001 and ended in 2009.

Consent included both parental or guardian written informed consent and assent from the child, in accordance to the procedures of the local Institutional Review Board. Patients were excluded when any of the following applied: pectus carinatum, Poland’s syndrome or other complex chest wall anomaly, previous repair of pectus excavatum by any technique, previous thoracic surgery, congenital heart disease, bleeding dyscrasia, history of major anesthetic risk factors such as malignant hyperthermia, or pregnancy.

The primary study was funded by a grant from the Children’s Health Foundation of the Children's Health System (Children’s Hospital of The King’s Daughters) of Norfolk, Virginia. A subset of patients underwent exercise cardiopulmonary function studies at several centers (not completed or reported here). That substudy was underwritten by a grant from Walter Lorenz Surgical, Inc, now Biomet Microfixation, Inc (Jacksonville, Florida). The funding sources played no role in the collection, analysis or reporting of data.

Pulmonary Function

Spirometry with flow-volume curves was performed by multiple testing centers according to a uniform method. Total lung capacity (TLC) and functional residual capacity (FRC) were measured by plethysmography on a subset of 218 patients. All PFT results and flow-volume curves were examined by a single pulmonologist (R. Mellins), who was blinded to other patient data; curves were judged to be acceptable if there was a rapid takeoff at the beginning of expiration with no or little noise during the remainder of expiration and, in the few cases with premature termination, end expiration was within 15% of the extrapolated residual volume. A total of 310 patients had acceptable preoperative PFT results appropriate for inclusion in this analysis. Raw values for forced vital capacity (FVC), forced expiratory volume in 1 second (FEV1), and forced expiratory flow during the middle half of the FVC (FEF25-75) were normalized using Knudson’s equations, which should have a mean of 100% in a normal population. TLC was calculated using the predicted values of Zapletal et al. Each individual was further categorized as having reduced pulmonary function for each measure with percent predicted values of <80% for age, height, and sex.

Patients with an FEV1/FVC ratio of <67% were classified as having obstructed pulmonary function. We used FVC and FEV1 values of <80% predicted and an FEV1/FVC ratio of >80% as criteria for restrictive lung disease. For the subset of 218 patients with lung volume data, a TLC of <90% was added to the foregoing criteria to identify a restrictive pulmonary pattern. For this subset of patients, the relationships among TLC, residual volume (RV), FRC, and the Haller index were examined.

Haller index

CT scans were performed for each patient using a standardized protocol as previously described. Two independent radiologists evaluated each CT scan. Using the protocol, a research associate determined the Haller index score. The Haller index was calculated as the inner transverse thoracic diameter divided by the anteroposterior distance between the anterior thoracic wall and the spine at the narrowest point.

Statistical Analysis

All statistical analyses were performed using SAS for Windows release 9.2 (SAS Institute, Cary, North Carolina) or SPSS for Windows version 17.0 (SPSS Inc, Chicago, Illinois). All analyses were verified by a second analyst (J.P. or M.L.) using a different statistical program. All numeric variables were assessed for normality using normal probability plots and histograms. Because the majority of variables were non-normal, descriptive statistics are given as median and range. Asymptotic 95% CIs are presented for percentages. The statistical significance of differences between groups was assessed using Wald (logistic regression) or Cochran-Mantel-Haenszel (frequency tables) χ² or Wilcoxon-Mann-Whitney tests, as appropriate.

Plots of Haller index scores by PFT results were examined for linear or other relationships. It was immediately obvious that the relationships between Haller index and FVC, FEV1, and FEF25-75 were nonlinear for all 3 PFTs. This analysis further indicated a binary relationship, with a clear increase in the number of PFT values <80% predicted with more severe Haller index. This obvious visual relationship was confirmed by modeling the outcome and predictors several different ways, with <80% having the best fit to the data. The Haller index was used to predict having a PFT result of <80% in logistic regression models. The best model was selected based on –2log-likelihood and area under the receiver operating characteristic curve. Goodness of fit was assessed with the Wald χ² and Hosmer and Lemshow statistics.

Results

The study cohort was 87% male, 95% Caucasian, and 24% with a previous history of asthma. The mean Haller index score was 4.7, with a median of 4.3 and a range of 2.2 to 11.9. The results for the overall group, as well as for the patients with a Haller index score in the first quartile (<3.72) and those with a score in the fourth quartile (>5.1), are given
in Table I. There were no differences in median age, age range, or history of asthma between the first and fourth quartiles. Those with a more severe pectus deformity (fourth quartile) were more likely to have scoliosis (25.7% vs 14.5%) and to be female (23% vs 10%) than those in the first quartile. Those in the fourth quartile had significantly lower FVC, FEV1, FEF25-75 and TLC values. There were no significant differences in the FEV1/FVC ratio or RV between the two quartiles. Only 1.6% of patients had an FEV1/FVC ratio of <67%, so there was little evidence of airway obstruction at the time of testing. For the overall group, the RV value was 109% of predicted and the RV/TLC ratio was 26% (normal RV/TLC, 20% in this age group). Age, sex, history of asthma, and history of scoliosis had no impact on the association between Haller index and any PFT values (data not shown).

Figure 1 shows the relationship between FVC and Haller index score. A clustering in the lower right quadrant relative to the upper right quadrant indicates an increased probability of FVC values <100% of predicted for individuals with a Haller index score >75th percentile. There is a similar distribution of values for FEV1 and FEF25-75 (Figures 2 and 3; available at www.jpeds.com). There is a statistically significant relationship between Haller index and probability of having a TLC <80% of predicted (Table II and Figure 4; available at www.jpeds.com).

Figure 5 illustrates the percentage of patients with an FVC of <80% of predicted for all 4 quartiles by Haller index score. As shown, increasing Haller index score is associated with increasing percentage of patients with FVC <80% of predicted. This trend is statistically significant (P <0.0001), and there is no significant departure from linearity. The same significant linear relationship is seen for FEV1 and FEF25-75. Thus, although raw individual PFT results and Haller index do not have a linear relationship, when the PFT values are expressed as the probability of being ≤80%, they do have a linear relationship.

Table II shows the results of several logistic regression models that predict reduced or restricted pulmonary function. In general, for each unit increase in Haller index, the likelihood of having an abnormal PFT result increases by 1.3-1.5 times. To put this in context, the models suggest that patients with a Haller index of 7 are >4 times more likely than those with a Haller index of 4 to have an FVC of ≤80%. In the total study population of 310, for each unit increase in Haller index, patients were 1.4 times more likely to show a restrictive pattern; patients in the highest quartile (the fourth) had more than twice the frequency of a restrictive pattern compared with the lowest quartile. These relationships were unchanged when the analysis included only the subset of patients (n = 218) for whom a TLC <90% was included in the definition of restrictive pattern.

Table II also shows the relationships among the 3 main PFTs. In patients with a normal FVC, 61% had a normal FEF25-75 and 88% had a normal FEV1, and the relationship among the 3 PFTs is statistically significant. As shown in the regression models, FVC and FEF25-75 appear to be independently related to Haller index, and FEV1 appears to be related to Haller index through its relationship with FVC and FEF25-75.

**Discussion**

Our results suggest a meaningful effect of the depth of chest wall depression on pulmonary function in patients with clinically significant pectus excavatum, and that this is primarily lung restriction, not airway obstruction. It is important to bear in mind that "100%" in the Knudson predicted values represents the mean for the normal population, and if the population is normal, then the percent predicted values should be evenly distributed above and below 100%. As we have reported previously and shown here, this is clearly not the case in patients with pectus excavatum. These results further suggest that some of this shift in the distribution of

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Table I. Pulmonary function and demographic data by Haller index (median, 4.3)

<table>
<thead>
<tr>
<th></th>
<th>Overall</th>
<th>Haller index ≤median</th>
<th>Haller index &gt;median</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, median (range)</td>
<td>15 (6-21)</td>
<td>15 (6-21)</td>
<td>15 (6-21)</td>
</tr>
<tr>
<td>Some decreased PFT, % (95% CI)*†</td>
<td>53 (48-59)</td>
<td>44 (37-52)</td>
<td>62 (54-69)</td>
</tr>
<tr>
<td>History of asthma, % (95% CI)†</td>
<td>24 (17-30)</td>
<td>20 (11-29)</td>
<td>27 (18-36)</td>
</tr>
<tr>
<td>Males, % (95% CI)†</td>
<td>87 (83-91)</td>
<td>91 (86-95)</td>
<td>83 (77-89)</td>
</tr>
<tr>
<td>FVC, median % predicted (range)*</td>
<td>89 (60-126)</td>
<td>91 (64-126)</td>
<td>86 (59-125)</td>
</tr>
<tr>
<td>FEV1, median % predicted (range)*</td>
<td>88 (51-131)</td>
<td>90 (56-131)</td>
<td>85 (51-131)</td>
</tr>
<tr>
<td>FEF25-75, median % predicted (range)*</td>
<td>86 (23-161)</td>
<td>86 (23-160)</td>
<td>80 (34-138)</td>
</tr>
<tr>
<td>FVC/FEV1, median % (range)*</td>
<td>86 (57-100)</td>
<td>87 (57-100)</td>
<td>86 (68-99)</td>
</tr>
<tr>
<td>TLC, median % predicted (range)*</td>
<td>96 (62-137)</td>
<td>97 (71-137)</td>
<td>92 (62-136)</td>
</tr>
<tr>
<td>RV, median % predicted (range)</td>
<td>109 (6-312)</td>
<td>109 (38-312)</td>
<td>112 (6-203)</td>
</tr>
<tr>
<td>RV/TLC, median % predicted (range)</td>
<td>26 (2-53)</td>
<td>25 (9-53)</td>
<td>27 (2-45)</td>
</tr>
<tr>
<td>FRC, median % predicted (range)</td>
<td>101 (18-147)</td>
<td>102 (34-147)</td>
<td>100 (18-140)⁴</td>
</tr>
</tbody>
</table>

*P < .05 for difference between groups.
†At least one of FVC, FEV1, and FEF25-75 <80% predicted.
| n | 113.
| Available for 169 patients.
| Percent rather than % predicted.
Pulmonary function below 100% might be attributed to the depth of depression in patients with more severe disease. The effect on pulmonary function clearly is related to the severity of the chest wall deformity as evaluated on CT scan. Although the magnitude of the effect is modest, we do not know whether the work of breathing is increased as the result of the chest wall deformity, especially at the larger tidal volumes required during exercise. Until we understand this, we cannot assess the clinical relevance of the changes in lung function resulting from pectus excavatum.

The Haller index, although a useful measure of severity, does not take into consideration the different morphologic varieties of defects. Pectus excavatum is characterized by depression of the sternum and anterior chest either symmetrically or asymmetrically. There are a wide variety of morphologic variants, including focal, “cup-shaped” depressions, broad and shallow “saucer-shaped” depressions, trenches running from the area just below the clavicles to the costal margin, and mixed upper sternal protrusion and lower depression. Thus, individuals with the same Haller index could have defects that impair the bellows function of the chest wall in very different ways.

Previous studies on the association between pulmonary function and pectus excavatum have presented apparently conflicting results, with some studies showing an effect and others showing no effect. This report suggests a possible explanation for these discrepant results. Almost all previous studies on this topic treated pectus excavatum as a binary variable—the patient either had it or did not have it. Many of our patients with a Haller index of <5 have PFT results at rest in the normal range, and those with a higher Haller index are much less likely to have results in the normal range. This may help explain the apparent discrepancy in the literature. Groups of patients with Haller indices predominately in the range of 5 to 7 or higher would be more likely to show reduced pulmonary function than groups predominately in the range of 3.2 to 5, yet all of these patients would be considered severe by current clinical assessment.

For more than 60 years, reports have consistently alluded to symptomatic complaints of patients affected by this condition. Symptoms of limited ability to exercise, easy fatigability, and a subjective sense of inability to breathe easily are common. It can be speculated that the larger tidal volumes required by exercise, especially if somewhat constrained by the effect of the pectus excavatum deformity on rib motion and on the bellows function of the chest wall, could account for some of the symptoms under exercising conditions. Our results provide evidence that pulmonary function is related to the depth of the depression and probably in a causal way, and might explain why repairing the defect can result in improved pulmonary function and reports of improved exercise tolerance. This explanation does not exclude the additional possibility that impaired right ventricular function from external pressure of the deformed chest wall could interfere with cardiac output and cardiopulmonary function. Moreover, the present study provides no indications for surgical correction of pectus excavatum, which remains a clinical decision in which altered pulmonary function is one of several factors that need to be assessed.

Although increased RV and RV/TLC ratio are usually thought to represent evidence of airflow obstruction with

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**Table II. Logistic regression models of Haller index predicting the odds of reduced pulmonary function**

<table>
<thead>
<tr>
<th>Predictor</th>
<th>OR (95% CI)</th>
<th>P value</th>
<th>C statistic</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC &lt; 80%</td>
<td>1.392 (1.156-1.676)</td>
<td>.0005</td>
<td>0.63</td>
</tr>
<tr>
<td>FEV1 &lt; 80%</td>
<td>1.344 (1.124-1.607)</td>
<td>.0012</td>
<td>0.60</td>
</tr>
<tr>
<td>FEF25-75 &lt; 80%</td>
<td>1.415 (1.179-1.697)</td>
<td>.0002</td>
<td>0.63</td>
</tr>
<tr>
<td>Any of FVC, FEV1, and FEF25-75 &lt; 80%</td>
<td>1.528 (1.250-1.866)</td>
<td>&lt;.0001</td>
<td>0.63</td>
</tr>
<tr>
<td>TLC &lt; 80%</td>
<td>1.493 (1.151-1.937)</td>
<td>.0025</td>
<td>0.64</td>
</tr>
<tr>
<td>Restricted pulmonary function</td>
<td>6.529 (2.115-20.161)</td>
<td>.0011</td>
<td>0.61</td>
</tr>
</tbody>
</table>

* All models use the Haller index as a continuous predictor except, which is modeled as Haller <7 versus Haller >7.

C statistic indicates the area under the receiver operating characteristic curve. No relationship is a C statistic of 0.5; a perfectly deterministic relationship is a C statistic of 1.
air trapping on expiration, our finding that some patients with these findings had normal FEV₁/FVC ratios and normal FRC values argue against this interpretation. Another possible explanation for the increased RV and RV/TLC ratio is that in pectus excavatum the chest wall is not only stiffer than normal on inspiration from the resting (ie, FRC) level, but is also stiffer than normal on expiration below the resting level, so that lung emptying is incomplete.

Among the 83.9% of patients who neither had obstructive nor restrictive lung disease, 9.6% had an FVC value <80% and 37% had an FEF₂₅-₇₅ value <80%. In addition, examination revealed that many of these patients had decreased motion of the anterior sternum or paradoxical breathing, suggesting increased work of breathing. Although at present we cannot classify these patients, these data and other observations suggest that pulmonary function might not be completely normal in many of those who do not meet our criteria for obstructive or restrictive lung disease.

There are some limitations to this study that must be addressed. We cannot exclude the possibility that 12% of the 310 patients may have had mild airway obstruction, possibly in the small airways, manifested only by a decrease in the FEF₂₅-₇₅ value to <60%. These patients were equally likely to be in the lower and upper quartiles of Haller index, indicating no relationship between this level of mild obstruction and the severity of pectus excavatum. Although we did not study the response to bronchodilators systematically, post-bronchodilator study results were available in 7 patients, and in those 7, the FEF₂₅-₇₅ value improved by at least 29%; because these findings did not correlate with the Haller index, we believe it more likely that this was linked to reactive airways than to pectus excavatum.

We recognize that although clinically useful and practical to measure, the Haller index has limitations as a measure of severity. Very different effects on chest wall restriction with similar index values are possible, depending on the extent to which the costochondral junctions are distorted by the pectus excavatum.

Our analysis is limited to patients with more severe defects, even though a few had a rounded Haller index score <3.2. Our finding of a significant relationship within this limitation indicates that the relationship would possibly be stronger if our sample also had included patients with less severe deformities.

This limitation might have resulted in the low predictive value of our logistic regression models. Although all 3 models were significant (P < .001 for all) and showed no significant lack of fit, the area under the receiver operating characteristic curve was approximately 0.61 for each; in a strongly predictive model, this value would be closer to 1. This indicates that even though the models were able to predict decreased pulmonary function, the Haller index score explains only a portion of the probability of having a PFT of ≤80%, and inclusion of other measures in the future could increase the models’ predictive power. Such measures would include more details about the shape and position of the deformity and about the patient’s clinical history and comorbidities. In addition, tests of cardiopulmonary function under exercising conditions are more likely to reveal the impact of pectus excavatum on abnormal function. These measures will eventually be available at the completion of the parent multicenter study. Again, the fact that we were able to find a relationship within these limitations suggests that the actual relationship may indeed be stronger than we report here.

In conclusion, we have demonstrated in a large population of patients with pectus excavatum that increasing depth of chest depression is related to an increased likelihood of below-normal pulmonary function, primarily with a restrictive pattern. Future studies should examine other measures in combination with depth of depression to increase our understanding of the mechanisms and impact of this deformity on cardiopulmonary function in both the resting and exercising states.

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References

Appendix

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Figure 2. Percent Predicted FEV1 by Haller index among 310 North American pectus excavatum patients (vertical bar at upper quartile).

Figure 3. Percent predicted FEF25-75 by Haller index among 310 North American pectus excavatum patients (vertical bar at upper quartile).
Figure 4. Precent predicted TLC by Haller index among 218 North American pectus excavatum patients (vertical bar at upper quartile).