Article Title: Three-Dimensional Assessment of Pectus Excavatum

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Glossary of Abbreviations:

- 2D – Two-dimensional
- 3D – Three-dimensional
- CPET – cardiopulmonary exercise testing
- CI – Correction Index
- HI – Haller Index
- O2 Pulse – Oxygen Pulse
- PE – Pectus Excavatum
- $\dot{V}O_2/kg$ – peak Oxygen consumption indexed to weight in kilograms
Central Picture – Compression Angle – 3D angle from Superior Vena Cava to Pectus excavatum defect (fulcrum) to mid-atrium.

Central Message – The compression angle (Superior Vena Cava to Pectus excavatum defect to mid-atrium) may better predict physiological limitation in pectus excavatum than the Haller or Correction Indexes.
Introduction

Pectus Excavatum (PE) is a common chest wall deformity, affecting approximately 1 in 300-1000 individuals\(^1\) with negative physiological and psychological effects on patients\(^2\). The depressed sternum and ribs can compress the heart and/or lungs leading to impaired cardiac and/or pulmonary function. Common symptoms include early fatigue, decreased exercise tolerance, shortness of breath, rapid heartbeat, and chest pain. Surgical correction is currently the definitive treatment for PE. Preoperative evaluation consists of imaging and physiologic evaluation with cardiopulmonary exercise testing (CPET).

The Haller Index (HI), a two-dimensional (2D) measurement of intrathoracic width and length, is commonly used to assess the severity of PE\(^3\). However, the HI was developed retrospectively based on 33 patients who underwent surgical repair of PE compared to children without pectus. The HI reflects anatomic severity rather than physiological impact of PE. The most notable other 2D index is the Correction Index (CI).\(^4\) The CI was developed to avoid the overlap between PE patients and normal controls. Again, CI is a numerical representation of depth of the defect rather than cardiopulmonary limitation.

The aim of this study is to develop an anatomic measures of PE severity that correlates with physiological limitation. We use data from Cardiopulmonary exercise testing (CPET) with focus on peak oxygen consumption (\(\dot{V}O_2/kg\)) and Oxygen Pulse (O2 pulse) as these have been shown to be abnormal in PE patients and improve post repair\(^5\). Additionally, we leveraged three dimensional (3D) image acquisition to develop novel indices.

Patients and Methods
This retrospective study reviewed preoperative data from a consecutive 4-year period. The study was approved by the IRB (#15-071). Inclusion criteria included patients <18 year who underwent surgical evaluation at Phoenix Children’s, availability of 3D imaging with raw data, and a CPET with raw data. Patients with incomplete data were excluded. CPET was performed using an Ultima CPX metabolic cart (Medical Graphics). Exercise values were averaged and expressed as percent predicted using standard equations to facilitate comparison across different demographics. The O2 pulse served as a surrogate for stroke volume response. Volumetric, MR imaging datasets were used to generate 3D models using Mimics software (Materialise.com). A total of 30 Centroid points representing different thoracic, cardiac and pulmonary structures were created by the investigators using Geomagic Studio software (3Dsystems.com). Procrustes shape analysis was performed to co-register the varying patient sizes for relative distances between indices to be evaluated. The investigators generated 468 novel indices including angular indices (265), Triangular projection areas(106), vector differences (61) and relative length based relationships (36). Univariate, regression analysis was performed to evaluate the relationship between indices and CPET variables. An in-house, python script was created to perform an automated Procrustes and regression analyses, indices generation (lengths, angles, etc.), and identify indices with strongest correlations to CPET.

Results

The study included 26 patients (table 1) with a male predominance (84%). This research was approved by the IRB at Phoenix Children's Hospital. IRB 15-071, initial approval 10/9/2019. A waiver of consent was obtained for retrospective use of clinical data. \( \dot{V}O_2/kg \) was reduced in
88% of study patients with a reduced stroke volume response in 65%. Regression analysis showed poor correlation between \( \dot{V}O_2/kg \) and HI (\( R^2=0.00064, p=0.9 \)) as well as CI (\( R^2=0.0068, p=0.7 \)). There were 41 new indices that reached statistical significance in regression analysis with \( \dot{V}O_2/kg \) (\( R^2 0.15 – 0.43 \)). The correlation between O2 pulse and HI (\( R^2=0.059, p=0.2 \)) and CI (\( R^2=0.001, p=0.9 \)) did not reach significance. Of the new indices, 58 reached statistical significance in regression analysis with O2 pulse (\( R^2 0.15 – 0.39 \)). The index generating the highest \( R^2 \) with both \( \dot{V}O_2/kg \) (\( R^2 0.43, p<0.001 \)) and O2 pulse (\( R^2=0.39, p<0.001 \)) (figure 1) was the “Compression Angle”. The compression angle is the angle between the superior vena cava and the maximal point of depression of the PE defect (Fulcrum) to the mid-point of the right and left atrium (see central picture).

Comment

The Compression Angle had the highest correlation between the PE imaging and physiologic limitation. Despite the study’s limited size, over 50 3D indices were found to be significant in predicting physiologic impact of PE. We theorize that physiologic limitation in PE occurs due to compression of the heart, inhibiting the right heart in particular from augmenting its stroke volume during exercise. The Compression Angle describes the proximity of the PE to right heart structures in 3D and thus the degree of compression from the PE. This interaction between the chest wall and the heart is why we theorize that the compression angle and other indices correlate better than the HI and CI . Larger studies could help determine the clinical utility of novel indices such as the Compression Angle or other 3D measures in the pre-operative evaluation of PE and its anatomic variants.
References


## Tables

Table 1: Patient Demographics and Cardiopulmonary exercise testing

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total (26)</th>
<th>Male (22)</th>
<th>Female (4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Years)</td>
<td>14.2 (11.6 – 17.9)</td>
<td>14.1 (11.6 - 17)</td>
<td>14.8 (13.4 - 17.9)</td>
</tr>
<tr>
<td>Haller Index</td>
<td>4.3 (2.8 – 12.2)</td>
<td>4.3 (3.4 - 8.5)</td>
<td>5.4 (2.8 - 12.2)</td>
</tr>
<tr>
<td>Correction Index</td>
<td>29% (15% - 51%)</td>
<td>29% (15% - 51%)</td>
<td>22% (20% - 39%)</td>
</tr>
<tr>
<td>Exercise Capacity*</td>
<td>73% (43% - 98%)</td>
<td>73% (59% - 98%)</td>
<td>69% (43% - 83%)</td>
</tr>
<tr>
<td>Stroke Volume Response**</td>
<td>79% (46% - 114%)</td>
<td>77% (52% - 112%)</td>
<td>89% (46% - 114%)</td>
</tr>
</tbody>
</table>

*Exercise capacity is VO2/kg and is reported as percent of predicted

**The Oxygen Pulse serves as a surrogate for stroke volume response and is reported as a percent of predicted
Figure 1 – Scatter plot and trend lines for regression analysis of exercise capacity and stroke volume response with the Compression Angle, Haller Index and Correction Index.
Regression analysis between Index and CPET parameters

<table>
<thead>
<tr>
<th>Index</th>
<th>VO2/kg R², p-value</th>
<th>O2 Pulse R², p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compression Angle</td>
<td>R² 0.43, p&lt;0.001</td>
<td>R² 0.39, p&lt;0.001</td>
</tr>
<tr>
<td>Haller Index</td>
<td>R² 0.00064, p=0.9</td>
<td>R² 0.059, p=0.2</td>
</tr>
<tr>
<td>Correction Index</td>
<td>R² 0.0068, p=0.7</td>
<td>R² 0.001, p=0.9</td>
</tr>
</tbody>
</table>