COMPLEX THORACIC MALFORMATIONS:

IS THERE AN ASSOCIATION BETWEEN ADOLESCENT IDIOPATHIC SCOLIOSIS AND PECTUS EXCAVATUM?

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Introduction

Three-dimensional thoracic anatomy is one determinant of cardiopulmonary function.[1,2] The bony thorax is compromised of the sternum and vertebral column, connected by the ribs through the sternocostal and costochondral joints. The sternum, ribs and vertebral column develop from embryonic mesoderm during the first trimester with ossification continuing into early adulthood.[3,4] During adolescent growth both anterior (pectus deformity of the sternum) and posterior (kyphosis or scoliosis of the spine) thoracic deformities result in significant rib distortion and subsequent restriction of thoracic volume. Adolescent idiopathic scoliosis (AIS) is very common with mild deformity affecting 0.2 – 3% of the population (Table 1).[5,6] Severe scoliosis greater than 100° is much less common and may result in severe pulmonary compromise due to restrictive disease.[7,8] Pectus excavatum (PE) is also common affecting 0.7% of the population (Table 2).[9–13] The sternal depression of PE has been shown to effect thoracic volumes[14] and when severe, decreases pulmonary function and impinges on the function of the right ventricle.[1,15–17] Given the common prevalence of both thoracic malformations combination deformities should exist within patients (Figure 1). Despite common anatomic and developmental origins pectus excavatum (PE) is typically treated by pediatric surgeons with scoliosis addressed by spine surgeons and little dialogue between the two subspecialists.

Given the high prevalence of pectus and scoliosis as well as the common developmental pathways, we undertook this study to determine whether there was an association between the two thoracic deformities (Figure 1). The overlap of these thoracic malformations has yet to be thoroughly investigated.[18] Should AIS and PE coexist there is potential for collective cardiopulmonary deficit greater than either thoracic malformation alone. Combined thoracic deformities, or the "double crush to the thorax", may influence patients' immediate and long-term outcomes. Therefore, we undertook an investigation of the AIS population to assess the radiographic prevalence of PE with the hypothesis that both thoracic malformations occur more frequently than expected (Figure 1).

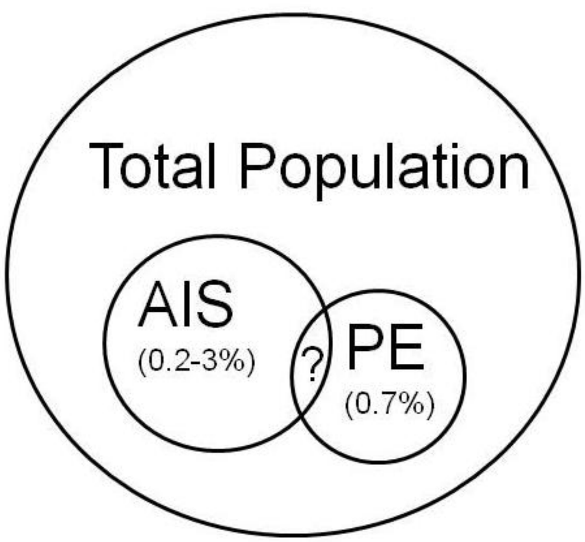
Table 1. Prevalence studies for Adolescent Idiopathic Scoliosis.

Citation	Prevalence	Subject Number	Method of AIS Diagnosis
Shands, Eisberg (1955)[19]	19:1000	194,060	Chest roentgenogram during a survey for pulmonary TB Cobb technique to define a curve of ≥ 10^o
Rogala, Drummond, Gurr (1978)[20]	45:1000	26,947	Clinical identification of structural abnormality on forward bending Subsequent roentgenographic Cobb technique to define a curve of ≥ 6^o

Table 2. Prevalence studies for Pectus Excavatum.

Citation	Prevalence	Subject Number	Method of PE Diagnosis
Clark, Grenville-Mathers (1962)[9]	12:1000	9,475	Sternal depression identified by clinical and radiographical evaluation
Chung, Myrianthopoulos (1975)[10]	2:1000	46,689	Method not defined. Assessment performed at birth.
Fonkalsrud, Dunn, Atkinson (2000)[11]	1.4:1000	unknown	Personal communication from March of Dimes Birth Defects Foundation, March 1995
Westphal, Lima, Neto, Chaves, Santos, Ferreira (2009)[12]	12.7:1000	1,332	Physical exam

Figure 1. Venn Diagram of the unknown relationship between AIS and PE.

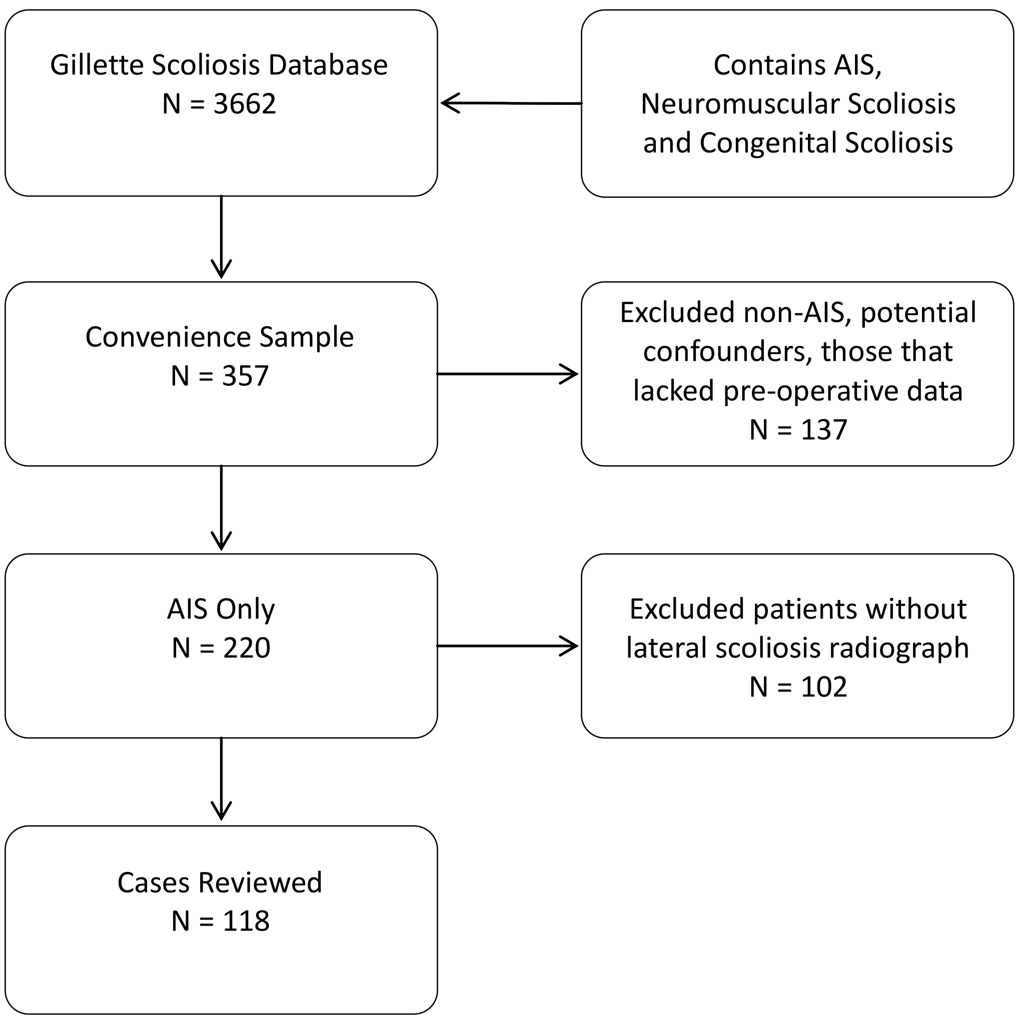


METHODS

A retrospective patient database was generated from a single institution, a large pediatric orthopedic referral center. Using the ICD-9 code for adolescent idiopathic scoliosis (ICD-9 737.3) a list of 3,662 patients were evaluated between 2002 and 2012 for scoliosis were identified (Figure 2). A convenience sample of 357 patients was reviewed until we obtained a sample size of 118. Of the 357 patients, 239 patients were excluded due to a diagnosis other than adolescent idiopathic scoliosis (134 patients) and incomplete radiographs/patient information (105 patients). Our study cohort includes 118 patients with preoperative lateral and posterior-anterior full-length scoliosis radiographs. Only patients with a Cobb angle of greater than 10° were included in the study.

Charts and radiographs were retrospectively reviewed. Age at radiograph and sex were recorded and the diagnosis of adolescent idiopathic scoliosis was confirmed. The preoperative standing scoliosis radiographs were used to collect the following radiographic parameters: coronal Cobb angle (Figure 3), thoracic kyphosis from T5-T12 (Figure 4) and Haller index (HI). A HI of 3.2 and greater were identified as having radiographic PE.[27] The HI measurement (Figure 5) was taken at the level of the greatest sternal depression parallel to the floor and is defined by: the transverse intra-thoracic length divided by the intra-mediastinal depth from the anterior boarder of the vertebral body to the posterior border of the sternum (Figure 5).[27] The HI measurements are taken parallel to the floor as performed in other studies.[28,29] Normal thoracic kyphosis in children is reported at 10-40°. Severe PE is defined as a HI greater than 3.2.[27] Multivariate logistic regression was applied to HI, Cobb angle, sex and age to determine if there was an association between severity of scoliosis, kyphosis and pectus deformity. HI values were dichotomized into positive (HI ≥ 3.2) and negative (HI < 3.2) cases for analysis. To define the interclass correlation for the measurement of the HI in patients with AIS a convenience sample of 10 sets of radiographs were selected and interpreted independently by a surgical resident (EAB), experienced pediatric radiologist (FGS) and experienced pediatric surgeon (DAS). Measurement errors for coronal Cobb angle have been well-reported in the literature. SPSS version 21 (SPSS; Chicago, IL) was used for statistical analysis.

Figure 2. Flow chart of study patients.



One hundred eighteen patients had standing lateral and posterior-anterior scoliosis radiographs. Using these radiographs scoliosis was re-measured (Figure 3), sagittal main thoracic angle (MTA) was determined from T5 – T12 (Figure 4) and the Haller index (HI) was determined (Figure 5). The HI indicates the severity of PE with the following measurements taken at the level of the greatest sternal depression: transverse intra-thoracic length divided by the intra-mediastinal length from the anterior boarder of the vertebral body to the posterior boarder of the sternum.[27] These measurements are taken parallel to the floor as performed in other studies.[28,30] Figure 5 illustrates a schematic of how the HI measurement is obtained. Figure 6 applies those HI measurements on a good quality representative radiograph. Figure 7 is a representative radiograph of a patient with considerable rotation of the rib cage illustrating the complexity in obtaining the HI in patients with scoliosis. Those with a coronal curvature (Cobb angle) of greater than 10 degrees were defined as having scoliosis. The MTA is defined as normal from 10 – 40 degrees. Severe PE is defined as a HI greater than 3.2.[27] Multivariate logistic regression was applied to HI, Cobb angle, sex and age. HI values were dichotomized into positive ($HI \geq 3.2$) and negative ($HI < 3.2$) cases for analysis. To define the interclass correlation for the measurement of the HI a convenience sample of 10 patients was selected and interpreted indpendently by a surgical trainee (EAB), experienced pediatric radiologist (FGS) and experienced pediatric surgeon (DAS). Interclass correlation statistics were performed. SPSS version 21 (SPSS; Chicago, IL) was used for the statistical analysis.

Figure 3. Schematic of Cobb angle measurement in Scoliosis.

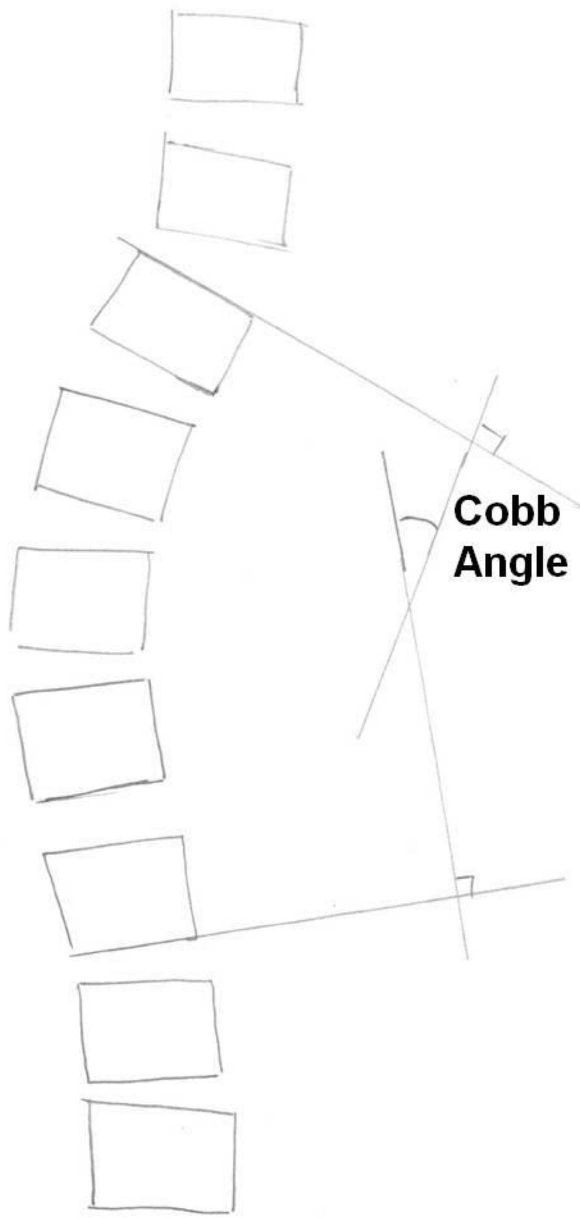


Figure 4- Schematic of sagittal main thoracic angle (MTA) measurement for angle of kyphosis.

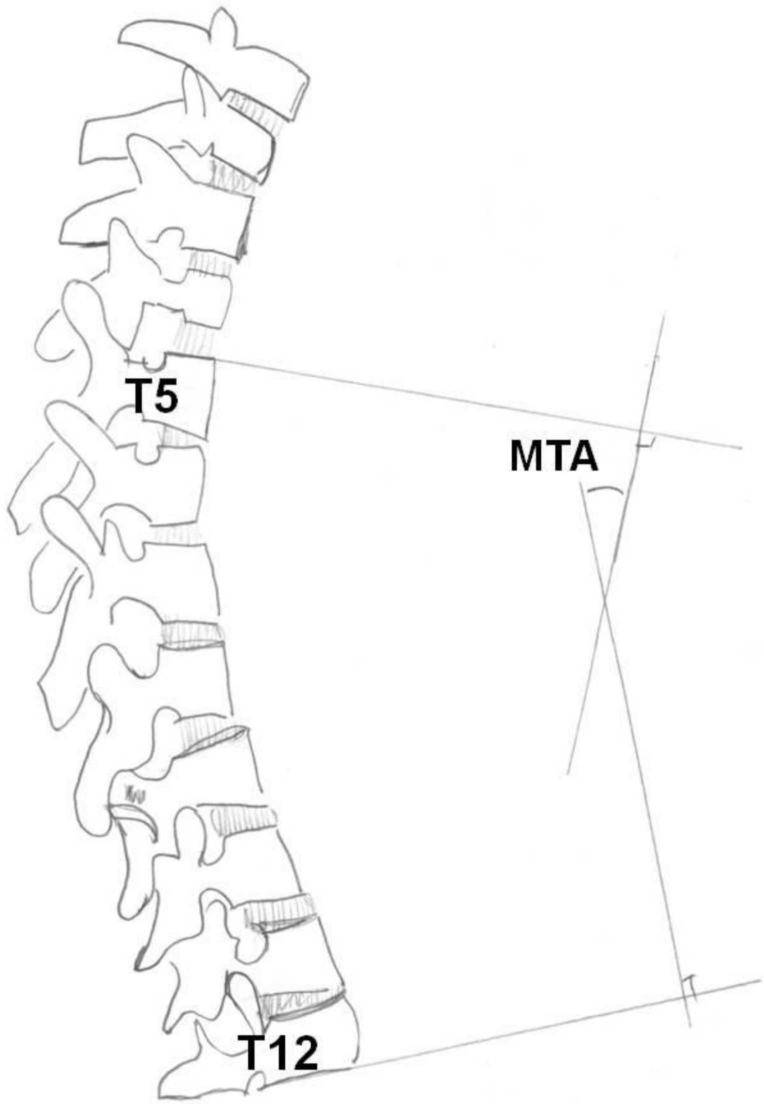


Figure 5- Schematic of the Haller index measurement for Pectus Excavatum.

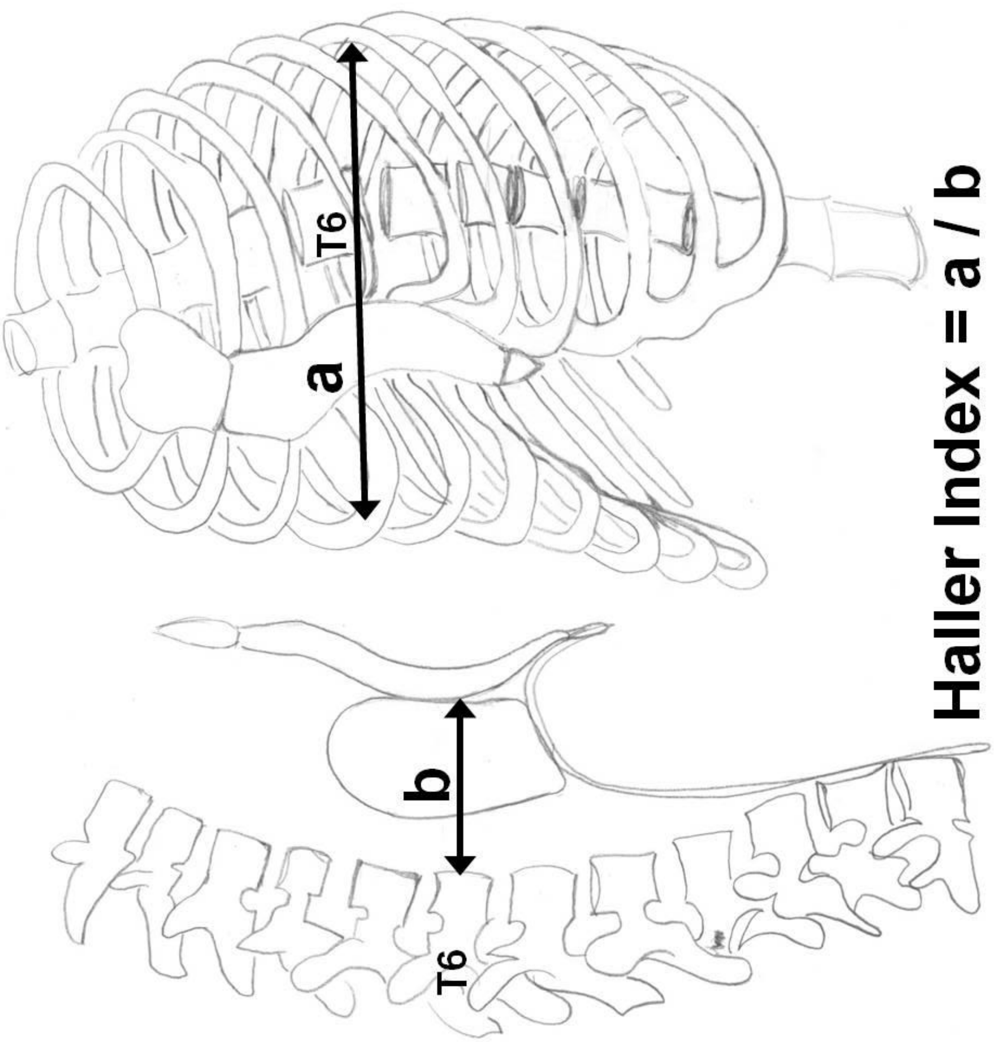


Figure 6. Representative standing scoliosis radiograph.

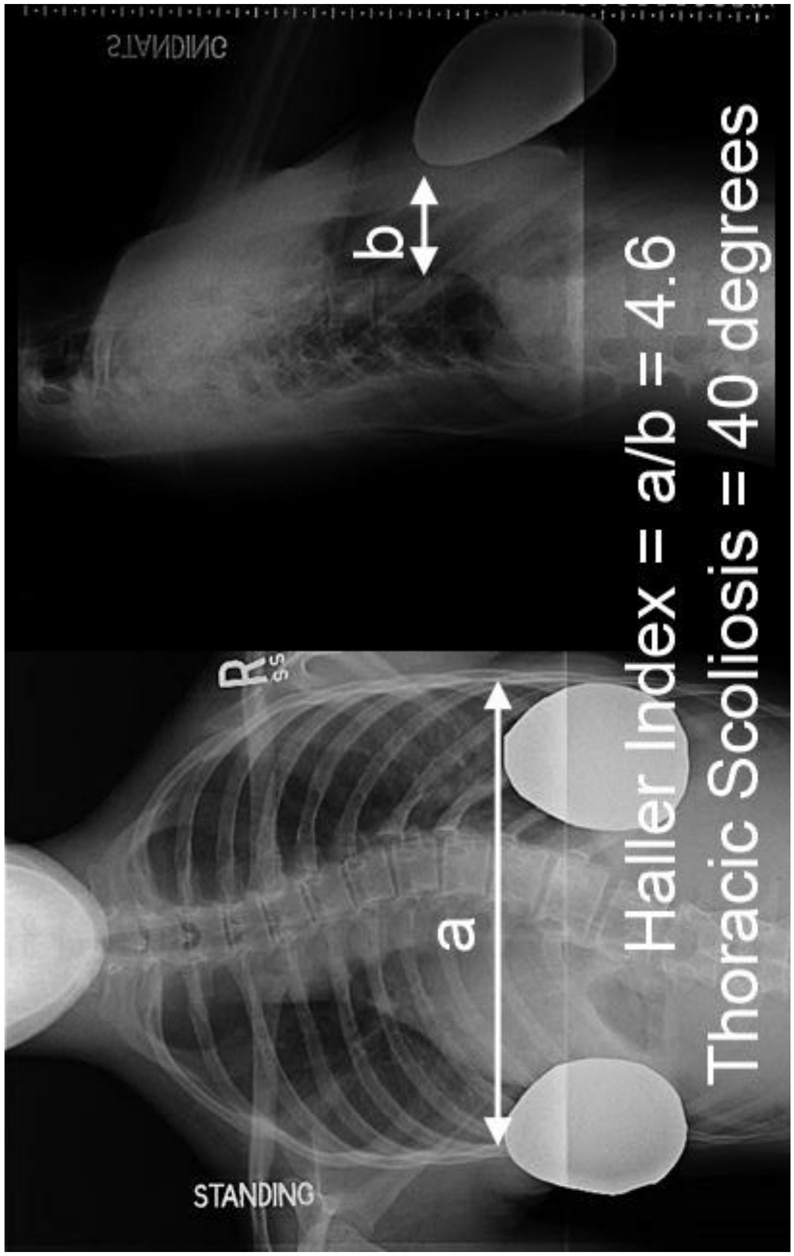
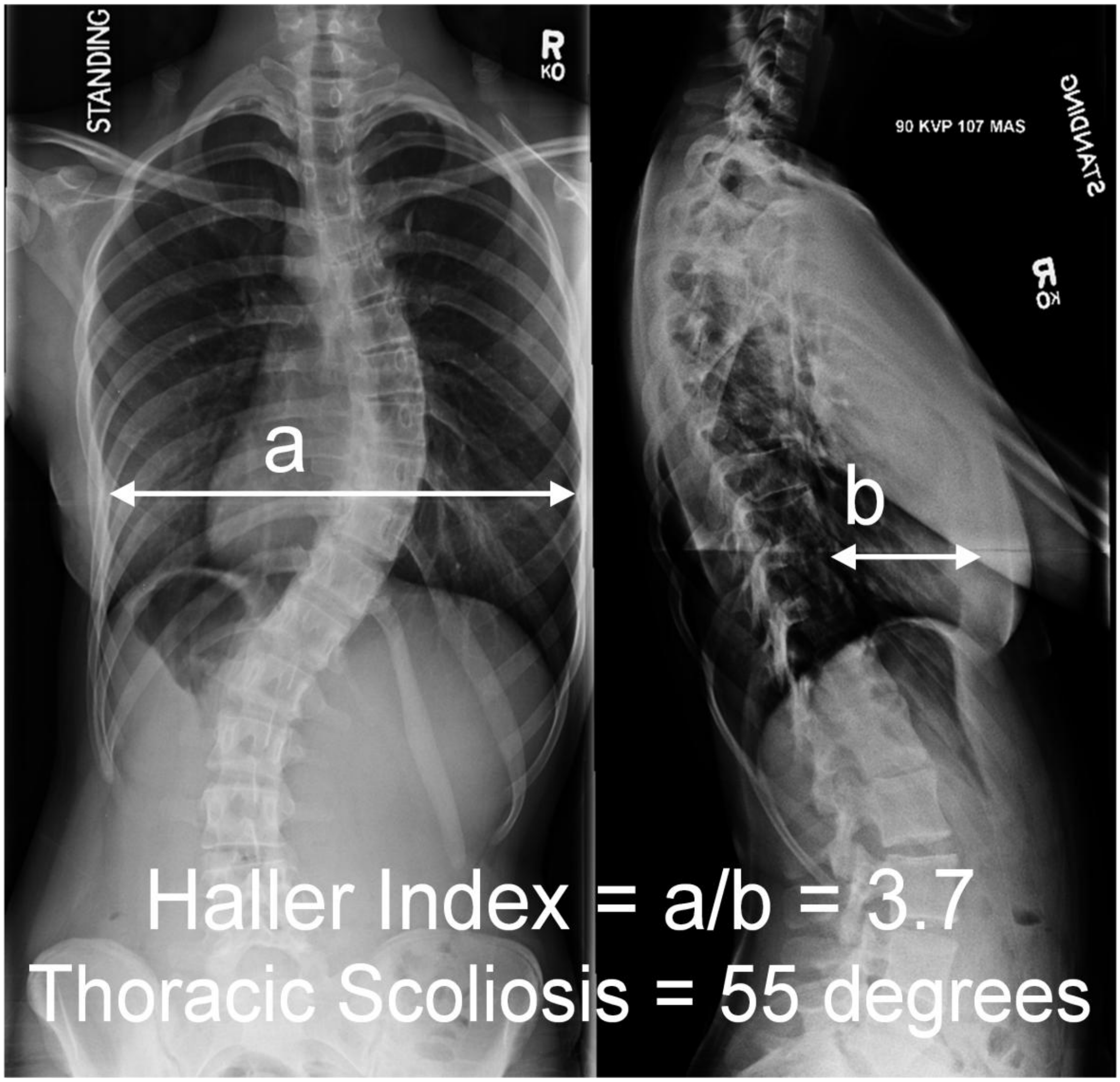


Figure 7. Challenging radiograph illustrating complex rib rotation.



RESULTS

Of the 118 patients, 103 were female (87%) with a mean age of 14 years (Table 3). Overall, 30% (35/118) of patients with AIS required surgery for scoliosis. A HI of greater than 3.2 was present in 25% (30/118) of the patients (Table 4). 27% (28/103) of the female patients with AIS had a HI ≥ 3.2 while only 13% (2/15) of the male patients with AIS had a HI ≥ 3.2. Of the AIS patients who required surgical correction for scoliosis (Table 4) 50% (15/30) had radiographic evidence of PE (HI ≥ 3.2); 93% (14/15) were female and 0.07% (1/15) were male.

Table 3. Demographic variables of 118 subjects.

	Number of Subjects
Gender	No. (%)
Male	15 (13%)
Female	103 (87%)
Age at radiograph (mean ± SD)	14±3 years
Cobb angle	10º to 91º
Corrective scoliosis surgery (No.)	30
Main thoracic angle T5-T12 (range)	1º - 45º
Haller index (range)	1.7 - 5.8

Table 4. Patients with Adolescent Idiopathic Scoliosis who have radiographic evidence of Pectus Excavatum.

	Haller Index ≥ 3.2
Haller Index > 3.2 (%)	30/118 (25%)
Female (103/118)	28/103 (27%)
Male (15/118)	2/15 (13%)
Cobb angle (range)	15° - 65°
Corrective scoliosis surgery (30/118)	15/30 (50%)
Main thoracic angle T5-T12 (range)	2° - 38°

An increased Cobb angle may appear to be associated with concomitant pectus excavatum as the association approaches significance (Table 5; OR 1.03, CI 1.00 – 1.06, p value 0.087). A decreased thoracic kyphosis was associated with an elevated HI (OR 0.95, CI 0.91 – 1.00, p value 0.048). The properties of the multivariate logistic regression model are as follows: c-static of 0.72 with a Hosmer-Lemeshow Chi-Square of 3.67, 8 degrees of freedom and a p-value of 0.89. The *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. As in our model, a *C* statistic of 0.72 suggests the model has acceptable discrimination and calibration. The interclass correlation coefficient between 3 raters (EAB, GFS, DAS) was 0.91, which suggests acceptable reliability between raters identifying the HI in patients with AIS. While this study is the first to define HI in AIS patients this high inter-rater reliability is consistent with other studies.

Table 5. Multivariate logistic regression model predicting the odds of HI ≥ 3.2.

	Odds Ratio	**Lower Confidence Limit**	**Upper Confidence Limit**	**p value**
Female	1.05	0.90	1.23	0.532
Age	1.80	0.34	9.57	0.488
Main thoracic angle	0.95	0.91	1.00	0.048
Cobb angle	1.03	1.00	1.06	0.087

An increased Cobb angle is associated with concomitant pectus excavatum but it is not statistically significant (Table 5; OR 1.03, CI 1.00 – 1.06, p value 0.087). A decreased main thoracic angle decreases the likelihood of also having pectus excavatum (OR 0.95, CI 9.1 – 1.00, p value 0.048). The properties of the multivariate logistic regression model are as follows: c-static of 0.72 with a Hosmer-Lemeshow Chi-Square of 3.67, 8 degrees of freedom and a p-value of 0.89. The *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. As in our model, a *C* statistic of 0.72 suggests the model has acceptable discrimination and calibration. The interclass correlation coefficient between 3 raters (EAB, GFS, DAS) was 0.91, which suggests acceptable reliability between raters identifying the HI. This high inter-rater reliability is consistent with other studies. [30]

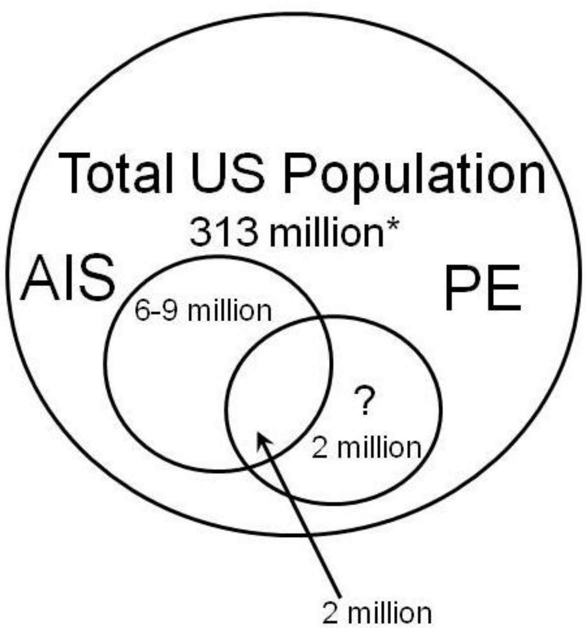
Discussion

Our results show the prevalence of PE in AIS is 25%, which is greater than expected in the general population. Furthermore, 50% of the AIS patients who required surgical correction for scoliosis had radiographic evidence of PE, which suggests a relationship between the Cobb angle and HI. This relationship between the anterior and posterior malformations of the thorax is complex as the multivariate logistic regression did not reveal a significant correlation between the severity of Cobb angle and HI. It is also plausible that the simplicity of the HI measurement does not characterize the full spectrum of the anterior chest wall deformity in PE, thus limiting the identification of characteristics of PE potentially associated with scoliosis. Our assessment of the MTA identified a potentially significant relationship with the HI. Our statistical modeling suggested a decreased MTA is associated with a lower likelihood of also having a concomitant PE whereas previous investigators hypothesized hypokyphosis was a compensatory deformity in response to the sternal depression of PE. A normal kyphotic curvature in the PE patient population has been reported by Waters, et. al.[22]

Looking from the perspective of the anterior chest wall deformity the prevalence of scoliosis in patients with PE is reported to be 6 – 27%; however, the studies generally lack information on how scoliosis was diagnosed and the magnitude of the Cobb angle.[11,21,23,24,31] The studies that include such information report modest Cobb angles that did not have surgical correction for scoliosis.[22,25] To our knowledge this is the first study that determined the prevalence of PE in patients with AIS. The identification of this population offers the opportunity to characterize an important patient population, one that may suffer from a double crush to the thorax from the combined deformities of AIS and PE. Given the estimated prevalence of AIS and PE in the general population (Table 1 and 2) and estimated population calculations performed elsewhere, it is possible that an estimated 2 million people have both AIS and PE undetected (Figure 8), assuming our results can be extrapolated to the general population. Certainly a major limitation to this generalization is the absence of reliable prevalence data for pectus excavatum (Table 1).

We have shown a greater than casual link between AIS and PE, which is important to understand when considering the three dimensional dynamic aspect of the thorax and its effects on physiology.[32,33] Respiration is a dynamic kinetic function of the thorax, which has been demonstrated to be impaired in each patient population, PE and AIS, separately.[32,34,35] Thoracic volumes are impaired in patients with thoracic malformations, whether the deformity is of the anterior, posterior or combination resulting in a double crush to the thorax.[31,36,37]

Figure 8. Population estimate of people with AIS, PE and the double crush to the thorax. *obtained from the US Census Bureau for 2012.



There are several studies that describe the decline of pulmonary function that begins in the third to fourth decade of life that report a decline of as much as 20% in FEV_1 and FVC.[38–40] PE and AIS have been shown to decrease PFT in otherwise healthy adolescents.[1,6,37] Taken together it is possible these processes limit the maximum achievable cardiopulmonary capacity of patients with combined thoracic malformations, thus portending a diminished quality and perhaps quantity of life. In understanding the population with a double crush to the thorax an attempt can be made to maximize the cardiopulmonary function for people with inevitable decline as they age. With our limited knowledge of complex chest wall malformations now coupled with our understanding that AIS is associated with an increased risk of a PE, every patient with AIS should be carefully evaluated for an anterior chest wall malformation.

AIS is well recognized to be genetic in origin.[41,42] PE is also likely genetic. It is unknown if there is linkage in the genetic components that influence phenotypic expression utilizing a final common pathway.[18] An alternative hypothesis is that both AIS and PE involve thoracic deformity with a buckling phenomenon. This buckling might be unifocal, either sternum or spine, or a combination of both. The end effect of decreased thoracic volume and impaired cardiopulmonary function results from either or both occurrences.

Limitations

There are a number of limitations of this study including those inherent in every retrospective review generated from an administrative database. The patients were from a tertiary referral hospital and likely not representative of the broader community. Approximately 33% of the initial database obtained administratively was incorrectly coded for AIS. Patient race was not collected. PE was diagnosed based on the radiographic HI. While the standing scoliosis radiographs were obtained using a routine protocol there are no data on whether breath holding or phase of respiration result in a marked difference in the identification of the HI.

Conclusions

We have studied this question of the association of complex thoracic malformations from the AIS aspect of the thorax and have discovered a 25% concurrence of PE, which is greater than expected in the general population. However, the magnitude of the Cobb angle did not correlate with the severity of the PE. Despite this, 50% of the AIS patients that required surgical correction of scoliosis had a HI ≥ 3.2 indicating a PE severe enough to be considered for surgical repair. Our findings suggest patients with AIS should have clinical and radiographic evaluations of their anterior chest wall to assess for pectus excavatum, and when discovered a multi-disciplinary approach applied to patients who are at risk for a double crush to the thorax. This is a starting point for continued research of the natural history of patients with complex malformations of the thorax based on scientific evidence.

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