Improved Rabbit model of Scoliosis and Thoracic Insufficiency Syndrome

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ABSTRACT/INTRODUCTION:
Thoracic Insufficiency Syndrome (TIS) is defined as the inability of the thorax to support normal respiration and/or lung growth. This description highlights the developmental dependence of the respiratory system on the thoracic skeleton and is often associated with severe early-onset scoliosis and fused ribs.

There is little clinical evidence to identify how TIS affects respiratory function and pulmonary development in the young child and likewise there is no accepted standard for the treatment of the disease. In the work presented in this abstract we seek to create a model for fused rib and scoliosis in rabbit that reproduces the severity of the most relevant features of clinically treatable TIS. Namely our model produces reduced respiratory capacity, respiratory asymmetry, increased chest wall compliance, and also an increase in red blood cells. The increase in red blood cells may be a compensatory response to respiratory distress [1].

METHODS:
Rib tethering surgery was performed in 4 ½ week old rabbits to create either a Unilateral chest wall constriction (right ribs 2-10, N=7) or a Bilateral constriction (right ribs 2-10 + left ribs 5-10, N=2). An age matched control group was also followed (N=4). At 6, 10, 14, & 28 weeks of age weight was recorded and breath hold CT scans and pulmonary compliance testing were performed. From 3D-CT reconstructions the Cobb angle, thoracic rotation angle, total lung volume, and left:right lung volume ratio was determined. Additionally, at 14 and 28 weeks of age the forced vital capacity was determined and blood samples were drawn for a complete blood count.

RESULTS:
P-values are given in parentheses when statistical significance was found.

Rate of growth in the rabbit, as measured by change in weight normalized by weight at 6 weeks, was less in both groups of disease rabbits at all time points. By 28 weeks of age the mean factors of growth were: 4.57 for Normal rabbits, 3.53 for Unilateral rabbits, and 2.74 for Bilateral rabbits (p<0.05).

Cobb angle and thoracic rotation angle were increased in both groups of disease rabbits at all time points. At 14 wks of age the mean Cobb angles were: 9° for Normal rabbits, 30° for Unilateral rabbits (p<0.01), and 47° for Bilateral rabbits (p<0.05) (Figure 1), the mean thoracic rotation angles were: 5° for Normal rabbits, 28° for Unilateral rabbits, and 30° for Bilateral rabbits.

Thoracic volumes, as determined from breath hold CT scans, were decreased in both disease rabbit groups. At 28 weeks old with the lungs held at deep-inspiration, mean thoracic volumes were: 157 ml for Normal rabbits, 140 ml for Unilateral rabbits, and 108 ml for Bilateral rabbits (p<0.05).

Left:right lung volumes, as determined from breath hold CT scans, were increased in both disease rabbit groups. At 28 weeks old, mean ratios were: 0.68 in Normal rabbits, 1.25 in Unilateral rabbits (p<0.01), and 0.96 in Bilateral rabbits.

Trans-respiratory compliance was decreased in both disease rabbit groups. At 28 weeks of age, the mean values for compliance averaged over a deep inspiration were: 5.63 ml/cmH2O for Normal rabbits, 4.46 ml/cmH2O for Unilateral rabbits, and 3.60 ml/cmH2O for Bilateral rabbits. Average compliance curves are shown in Figure 2.

DISCUSSION:
Both a Unilateral and Bilateral rib tether created rabbits with TIS exhibiting a decreased growth rate, increased Cobb angle, increased thoracic rotation angle, decreased thoracic volume, increased left:right lung volume ratio, decreased respiratory compliance, and decreased vital capacity. These values are comparable in severity to that observed clinically in patients that are candidates for surgical intervention by expansion thoracoplasty (Table 1). The increased red blood cell and hemoglobin concentrations in the disease models are likely a compensatory response to respiratory distress; a similar observation has also been seen clinically [1]. In continuing studies, this disease model will be a useful tool to understand the development of the lung microstructure in TIS and also to evaluate the effectiveness of expansion thoracoplasty surgery to improve pulmonary growth and respiratory function.

SIGNIFICANCE:
The unilateral tethered rib model simulates clinical spondylothoracic dysplasia, while the bilateral tethered rib model simulates Juene’s syndrome. These models appear to be sufficient to investigate the pathophysiology of TIS and to better understand the mechanism of action of expansion thoracoplasty.

REFERENCES: