Development of a Porcine Model of Posterior Thoracic Tether-Induced Thoracic Insufficiency Syndrome

Jerrianne Brandly[1], Klaus Hopster[1], Agathe Guillemet[1], Carly Ciociola[1], Brian Snyder[3], Patrick Cahill[2], Thomas P. Schaer[1]
[1]University of Pennsylvania School of Veterinary Medicine, Kennett Square PA, [2]Children's Hospital of Philadelphia, Philadelphia PA, [3]Boston Children's Hospital, Boston MA
jbrandly@upenn.edu

Disclosures: The authors declare no conflict of interest related to this research

INTRODUCTION: Thoracic Insufficiency Syndrome (TIS) in children with spinal deformities is associated with altered pulmonary development and impaired lung function. Severe cases require surgical correction, with multiple anesthetic events being particularly challenging for the anesthesiologist. The concave malformation of the chest wall severely limits diaphragmatic function and lung expansion and is associated with delayed and incomplete alveolar ventilation, compromising gas exchange and resulting in insufficient oxygenation [2]. Current clinical understanding of the pathophysiology and optimal treatment strategies remains limited due to the lack of suitable large-animal models that replicate the progressive deformity and pulmonary consequences of TIS [1]. Flow-controlled EXpiration (FLEX) ventilation is a newer procedure that modulates the otherwise passive expiration phase. Reducing the initial high-expiratory peak flow to a more linear flow allows the expiratory gas flow to persist throughout the entire expiratory phase. In a porcine model of acute respiratory distress syndrome, FLEX reduced ventilation-induced lung damage, decreased focal inflammation, increased dynamic compliance, and improved ventilation [3]. Furthermore, FLEX homogenized ventilation-perfusion matching by increasing ventilation in the dorsal/dependent lung regions in both lung-injured and lung-healthy patients [4].
The aim of this study was to compare changes in pulmonary function during spontaneous ventilation, conventional pressure ventilation (CPV), and FLEX ventilation in healthy, adult Yucatan mini pigs and age-matched animals with thoracolumbar spinal injury secondary to induced thoracolumbar spinal deformity. We hypothesize that the use of FLEX ventilation will improve lung compliance when compared to traditional ventilation methods, and that the TIS animals will continue to have decreased pulmonary capacity at 28 months.
METHODS: Under IACUC approval, three 6-week-old, 20 kg, female Yorkshire pigs were enrolled. In two animals, a lateral bending moment was induced by tethering the thoracic to lumbar spine using a subcutaneous posteriorly placed, laterally offset stainless-steel cable spanning two posterior pedicle screw clusters with a lateral offset at T9-10 and L4-5, respectively. The third animal served as an age-matched control. (. Radiographic, ultrasound, and computed tomography (CT) assessments were performed longitudinally to monitor spinal curvature and rib cage asymmetry. Pulmonary function testing was conducted at baseline and at serial timepoints post-tethering to assess pulmonary performance. The inspiratory tidal volume (TV) was measured while animals were breathing spontaneously. Dynamic lung compliance (Cdyn), the PaO_2/FiO_2 ratio, and the lung dead space ($P_{ET}CO_2/PaCO_2$ ratio) were analyzed during conventional pressure ventilation (CPV) and FLEX ventilation.
RESULTS: Posterior tethering resulted in progressive scoliotic and kyphotic deformities, leading to asymmetric reduction in thoracic volume on the tethered side. Cobb angles increase within the 15-week postoperative period to 29 and 31 degrees, respectively (**Figures 1a & b**). Pulmonary function testing revealed declining dynamic compliance and increased ventilation–perfusion mismatch, consistent with restrictive physiology, in the tethered animals (**Figure 2**). During CPV, Cdyn was reduced in the tethered pig (42 vs 49 mL/cmH_2O), which FLEX improved by 52% in the tethered group and by 22% in the control animals (**Figure 3**). Furthermore, FLEX reduced dead space from 23% to 11% in the tethered animals (Figure 4), resulting in more uniform ventilation and improved gas exchange.
DISCUSSION: This porcine model of spinal deformity recapitulates key anatomic and physiologic features of thoracic insufficiency, providing a translational platform for investigating disease progression, cardiopulmonary adaptation, and novel therapeutic interventions such as growth modulation and ventilatory strategies. The ability to combine advanced imaging with in vivo respiratory mechanics testing represents a major step toward bridging experimental and clinical understanding of TIS.
Conclusion: Posterior thoracolumbar tethering in juvenile pigs induces a progressive deformity and pulmonary impairment consistent with thoracic insufficiency, establishing a robust large-animal model for mechanistic and interventional studies of thoracic insufficiency.
SIGNIFICANCE/CLINICAL RELEVANCE:

REFERENCES: [1] Butler R, et. al, ORS, 2024 [2] Mayer O, et al, CPPAHC, 46(3), 2016. [3] Goebel U, et al. Br J Anaesth,113:474–483, 2014. [4] Wirth S, et al, Anesth Analg, 125: 1246-1252, 2017. [5] Wang Y, et al, JOSR 18(1), p.246, 2023. [6] Pehrsson K, et al, Spine, 17(9), pp.1091-1096, 1992.
ACKNOWLEDGEMENTS: This research was supported by The Wyss/Campbell Center for Thoracic Insufficiency (Children's Hospital of Philadelphia)

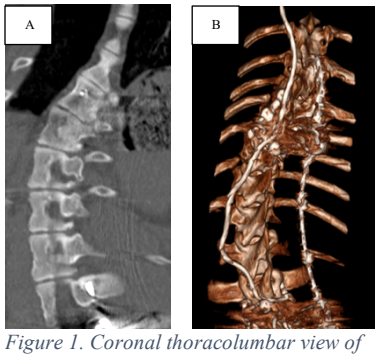

Figure 1. Coronal thoracolumbar view of spinal deformity in growing Yucatan minipigs (a). 3D rendering of the spinal deformity

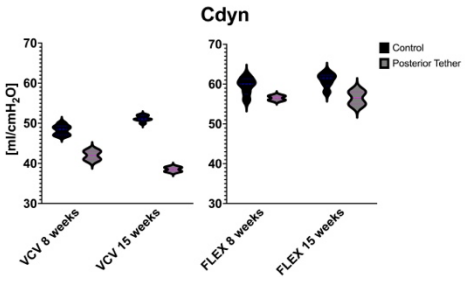

Figure 2. During CPV, Cdyn is reduced in the tethered pigs (42 vs 49 mL/cmH_2O). FLEX ventilation markedly improved Cdyn in TIS animals and by 22% in the control animals

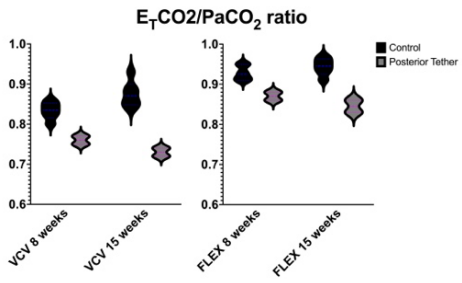

Figure 3. FLEX ventilation reduced dead space by 23% to 11% in the tethered animal, improving overall gas exchange.