ABSTRACT

Although acute respiratory distress syndrome is a life-threatening and frequent problem experienced by thousands of children each year, little evidence supports best ventilation practices during their critical illness. For over 25 years, pediatric critical care clinicians have debated the risk-benefit ratio of supine versus prone positioning and conventional mechanical ventilation (CMV) versus high-frequency oscillatory ventilation (HFOV) in the management of these young patients. Without pediatric-specific data, the debate of how best to care for children with *severe* Pediatric Acute Respiratory Distress Syndrome (PARDS) will continue and prevent progress in the field of pediatric critical care.

PROSpect (**PR**one and **OS**cillation **PE**diatric **C**linical **T**rial) is a two-by-two factorial, response-adaptive, randomized controlled clinical trial of supine/prone positioning and CMV/HFOV. Approximately 50 pediatric intensive care units (PICUs), about 2/3 U.S. and 1/3 international, with at least 5 years of experience with prone positioning and HFOV in the care of pediatric patients with severe PARDS, that can provide back-up extracorporeal membrane oxygenation (ECMO) support are participating. Eligible patients with severe PARDS are randomized within 48 hours of meeting eligibility criteria and within 4 days of endotracheal intubation to one of four groups: supine/CMV, prone/CMV, supine/HFOV or prone/HFOV. Subjects who fail their assigned positional and/or ventilation therapy for either persistent hypoxia or hypercapnia may receive the reciprocal therapy while being considered for ECMO cannulation. Our primary outcome is ventilator-free days (VFD) through day 28, where non-survivors receive zero VFD. We hypothesize that children with severe PARDS treated with either prone positioning or HFOV will demonstrate ≥2 more VFD. Our secondary outcome is nonpulmonary organ failure-free days. We will also explore the interaction effects of prone positioning with HFOV on VFD and investigate the impact of these interventions on 90-day in-hospital mortality and, among survivors, the duration of mechanical ventilation, PICU and hospital length of stay and trajectory of post-PICU functional status and health-related quality of life (HRQL). Up to 1,000 patients with severe PARDS will be randomized by age group and direct/indirect lung injury. Adaptive randomization will begin after 400 patients are randomized. After the 400th patient has been randomized and every 100 patients thereafter, new allocation probabilities will be computed based on ongoing intention-to-treat trial results, increasing allocation to well performing arms and decreasing allocation to poorly performing arms. Data will be analyzed per intention-to-treat for the primary analyses and per-protocol received.

This clinical trial will provide the definitive evidence necessary for the field to consider a major change in clinical practice in the care of critically ill children with severe PARDS.