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The association between skeletal muscle deficits and exercise performance in pediatric pulmonary hypertension patients

INTRODUCTION:

Exercise intolerance is common in patients with pulmonary hypertension (PH) and affects quality of life and prognosis. Exercise physiology in PH is complex, with many cardiopulmonary factors contributing to intolerance. Skeletal muscle atrophy and muscle dysfunction are associated with worse performance on 6-minute walk test (6MWT) in adults with PH. Muscle deficits have not been described in pediatric PH patients, yet pediatric patients have risk factors for low muscle mass and poor strength. The impact on exercise performance is unknown.

BACKGROUND:

Pediatric PH is associated with various vascular, cardiac, pulmonary, and systemic conditions. While therapies have improved in recent years, long-term outcomes remain poor. Exercise intolerance is common in PH patients, and improved performance on 6MWT is a common therapeutic target. Exercise physiology in PH is complex, with many cardiopulmonary factors contributing to intolerance. Association between peripheral skeletal muscle dysfunction and worse performance on 6MWT has recently been recognized in adult PH patients. Findings of skeletal muscle atrophy, impaired peripheral oxygen extraction, and reduced muscle contractility suggest that PH patients exhibit a generalized "myopathy" similar to patients with heart failure. Exercise training can improve exercise performance, quality of life, and functional class in adult PH patients and was beneficial in a pilot study of pediatric PH patients. But the mechanisms underlying this improvement continue to be investigated. Skeletal muscle deficits have not been described in pediatric PH patients, yet patients are potentially at risk due to inadequate physical activity, poor nutrition, vitamin D deficiency, chronic inflammation, low cardiac output, hypoxemia, and treatment with certain medications. The applicant previously described skeletal muscle deficits in association with worse exercise performance in children with complex, single ventricle congenital heart disease. Pediatric PH patients have similarities to this patient population. Characterization of skeletal muscle mass and strength in pediatric PH patients could improve understanding of modifiable determinants of exercise performance and open new therapeutic avenues in this high risk population.

HYPOTHESIS AND OBJECTIVES:

Pediatric PH patients have lower muscle mass and strength compared to healthy reference participants. If muscle deficits are identified, with or without association with exercise performance, the study will provide clinically significant targets for future interventions to improve functional capacity in this population.

SPECIFIC AIM 1:

To characterize skeletal muscle mass (as indicated by leg lean mass on densiometry) and muscle strength in pediatric PH patients (WHO Diagnostic Groups 1, 2, and 3) and to identify risk factors for decreased muscle mass and strength.

SPECIFIC AIM 2:

To explore the associations between muscle mass/strength and measures of exercise performance (on 6MWT, cardiopulmonary exercise test, and exercise cardiac MRI) in order to predict impediments to performance in pediatric PH patients.