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Right heart catheterization measuring central hemodynamics in cystic fibrosis during exercise

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KEYWORDS
Cystic fibrosis;
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Summary
Background: Although pulmonary arterial hypertension (PAH) is a potential co-morbidity in cystic fibrosis (CF), right heart catheterization (RHC) is not commonly performed in this patient population until referral for lung transplantation.
Material and methods: An non-randomized observational pilot study was performed after an exercise protocol with an upright stationary bicycle was added to RHC performed in patients with CF undergoing evaluation for lung transplantation (LT).
Results: Twelve consecutive patients with advanced lung disease due to CF referred for LT completed RHC with exercise protocol. Transthoracic echocardiography (TTE) prior to the RHC did not identify evidence of PAH or significant structural abnormalities; right and left ventricular systolic function were normal. non-randomized RHC in this same cohort found 75% (9/12) had PAH with an elevation of the mean pulmonary artery pressure (PAP) at rest with a mean (±SD) of 27.8 ± 4.9 mmHg that significantly increased during exercise to 47.2 ± 5.4 mmHg, $p = 0.0025$. For the last 6 patients, pulmonary vascular resistance was calculated during exercise, with a significant increase from 3.15 ± 0.3 to 12.8 ± 0.6 Wood Units ($p = 0.0313$) comparing measurements at rest to exercise.
Conclusion: RHC at rest and during exercise was safely and effectively performed in patients with CF referred for LT. Furthermore, central hemodynamic measurements found significant worsening of PAH during exercise in a small cohort of CF patients with advanced lung disease.

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Introduction

The pathophysiology of pulmonary arterial hypertension (PAH) is complex and not completely understood due to multiple molecular mechanisms involved. Additionally, PAH occurs as a primary disorder or as a result of lung disease. The current diagnostic guidelines for PAH are based on hemodynamic measurements of right heart catheterization (RHC) performed at rest, (mean pulmonary arterial pressure (PAP) $>$ 25 mmHg), no pulmonary venous hypertension with a concomitant pulmonary capillary wedge pressure (PCWP) $\leq$ 15 mmHg, and a pulmonary vascular resistance (PVR) $>$ 3 Wood Units [1]. A mean PAP $>$ 30 mmHg during exercise was previously a component of the diagnosis of PAH, but this was abolished due to cutoff value of 30 mmHg being arbitrarily chosen and not supported by published data [2]. More recently, exercise-induced PAH was established as a potential spectrum of PAH, but this is currently undergoing debate whether it is clinically significant or a normal variant without clinical significance [3]. Patients with exercise-induced PAH can be asymptomatic [4,5], while others have exertional intolerance [6—10]. Some experts describe exercise-induced PAH as an early and even potentially treatable phase of PAH at rest, while others suggest that it is a stable variation of PAH [11—13]. With limited research in this area, the clinical significance of exercise-induced PAH remains unclear.

Due to progressive airway obstruction and chronic hypoxia, patients with cystic fibrosis (CF) are at risk for the development of PAH. A recent study demonstrated that mild PAH worsens survival for patients with CF [14]. However, a limiting factor in the clinical care of the population with CF is that transthoracic echocardiography (TTE) is used much more commonly in the evaluation for PAH than RHC due to the invasiveness of catheter placement. However, we hypothesized TTE is poor for the evaluation of PAH in patients with CF referred for lung transplantation and further hypothesized these patients with advanced lung disease can perform exercise during RHC.

Methods

Study design and setting

This non-randomized observational pilot study was approved by the Institutional Review Board at Nationwide Children's Hospital and The Ohio State University. An exercise protocol was added to the RHC for all patients with CF referred for lung transplantation where measurements were done at rest and during exercise. Initially, PVR calculations were obtained only at rest, but modifications to the RHC exercise protocol added PVR measurements during exercise for the latter half of the cohort. The electronic medical record was reviewed for pertinent data including demographics, body mass index, pulmonary function measurements, TTE reports, and RHC measurements. The primary outcome was RHC measurements compared to TTE.

Study population

All CF patients referred for lung transplantation between January 1, 2011 and June 30, 2012 were included in the study. The diagnosis of CF was based on an abnormal sweat chloride test or cystic fibrosis transmembrane regulator (CFTR) genotype [15].

Echocardiography and heart catheterization

The RHC was standardized for the entire cohort with access via the right internal jugular vein with advancement of the catheter to the pulmonary artery wedge position under fluoroscopic guidance. There was continuous monitoring of PAP at rest and during exercise on an recumbent stationary bicycle (Fig. 1). Prior to starting the exercise component, transducer position was recalibrated to the baseline level. For example, if the mean PAP was 22 mmHg at baseline at rest, the transducer was recalibrated to the appropriate position on the bicycle to a mean of 22 mmHg and then the procedure continued. The pulmonary capillary wedge pressure (PCWP) was recorded at the end of exhalation with deep breaths. For the last 6 patients evaluated, RHC measurements were obtained to calculate PVR at rest and during exercise using the calculation mean PAP $-$ mean PCWP/cardiac output. All RHC data were hand measured and calculated at the time of documentation.

Statistical analysis

Statistical analysis was performed using GraphPad Prism software (version 5.0). A paired *t* test was used where appropriate. Data is reported as mean $\pm$ standard deviation (SD). *P* values of $<$0.05 were considered statistically significant.

Results

Twelve consecutive patients with CF referred for lung transplantation completed the RHC with exercise protocol

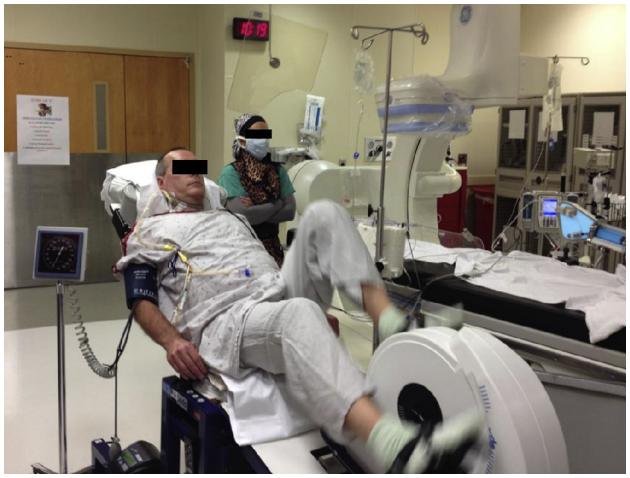

Figure 1 Adult patient with cystic fibrosis performing exercise on an recumbent stationary bicycle during right heart catheterization with catheter in the right internal jugular vein.