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ST Segment Depression During Cardiopulmonary Exercise Testing in Patients with Pulmonary Arterial Hypertension

a. Study Purpose and Rationale

Pulmonary arterial hypertension (PAH) is a progressive disorder characterized by abnormally high blood pressure in the pulmonary artery. Clinically, PAH is defined as a mean pulmonary arterial pressure (mPAP) ≥25 mm Hg at rest, when measured with a pulmonary artery catheter. Patients with primary pulmonary hypertension have no identifiable underlying cause, while secondary pulmonary hypertension may be due to cardiac, pulmonary, or systemic diseases. Regardless of the etiology, over time, pulmonary blood vessels narrow in diameter, resulting in increased resistance to blood flow into the lungs, and eventual right heart dysfunction and failure. Historically, the prognosis for PAH has been quite poor. However, with the advent of various vasodilator therapies, outcomes have improved in recent decades. In 2012, data from the US REVEAL registry, a consortium of PAH patients, demonstrated 1-, 3-, and 5-year estimated survival rates of 96 ± 4%, 84 ± 5%, and 74 ± 6%, respectively. Despite this improvement, there is still much left to understand about the progressive nature of PAH and clinicians continue to have difficulty in determining who is at highest risk of poor outcomes.

Several prognostic tools have been studied and validated for use in patients with PAH to help guide their medical management. These include the six minute walk test, cardiopulmonary exercise test, and cardiac catheterization. Most patients with PAH complete these studies on at least an annual basis for monitoring; important measures include meters walked in 6 minutes, mean pulmonary artery pressure (mPAP), and oxygen consumption (VO2). While these measures are helpful to guide medication therapy, it is likely that there are other risk factors that contribute to the progression of the disease and result in poorer outcomes. Some variables that have previously been studied include elevated cardiac troponin, BNP, and NYHA classification, amongst others.

Within our institution, we have noted a subset of patients with PAH who develop asymptomatic ST segment changes on electrocardiograms collected during cardiopulmonary exercise testing (CPET). To date, no studies have shown if these ST changes during peak exercise in patients with PAH have prognostic significance.

b. Study Design and Statistical Analysis

This study is a retrospective analysis of data collected on patients with pulmonary arterial hypertension seen at Children's Hospital of New York Presbyterian (CHONY) between 2010-2015. All patients who completed cardiopulmonary exercise testing (CPET) in this timeframe were included in the study. Patients were excluded if CPET EKG data was not available. As CHONY exercise laboratory converted CPET results to electronic files in 2010, there is likelihood that some studies may not have been converted.

Primary outcome to be measured is mortality. Secondary outcomes to be measured include mean PA pressure, mean peak VO2, and 6 minute walk distance.

A chi-squared test will be used to compare mortality in patients with ST changes during CPET to those without ST changes. An unpaired T-Test will be used to compare mean PA pressure, mean peak VO2, and 6 minute walk distance in patients with ST changes during CPET to those without ST changes. A statistical significance is defined as <0.05. Given the study population is an incomplete cohort, with subjects of variable stage and severity of disease at onset of study, we will complete a Kaplan Meier analysis to assess survival curves.

A power analysis was conducted using a $p < 0.05$, a power of 80%, and predicted N of 300, with a ratio of 4 between the control group and study group. Based on this analysis we can detect an effect size of 7% for the primary outcome, mortality. For the secondary outcomes, we can show a difference of size of 47m for the 6min walk test, 5.7 mL/(kg·min) for pVO2, and 6.5mmHg for mPAP. These values indicate that the study is adequately powered.

c. Study Procedure
No procedures were performed for this study.

d. Study Drugs
No drugs were given for this study.

e. Medical Devices
No medical devices were used for this study.

f. Study Questionnaire
No questionnaires were used during this study.

g. Study Subjects
Subjects with pulmonary hypertension who completed cardiopulmonary exercise testing between 2010 and 2015. Patients were excluded from this study if EKG data collected during CPET were not available.

h. Recruitment of subjects
No recruitment was done for this study.

i. Confidentiality of Study Data
Investigators involved in the study have completed HIPAA training and communicate via secure hospital server. All data will be de-identified prior to external use. Therefore, No information will be published that could be directly linked to a study subject.

j. Potential Conflict of Interest
No investigator has proprietary interest in or might stand to benefit in any other way from the results of the investigation.

k. Location of Study
CPET data was collected in the exercise laboratory located on the seventh floor of Children's Hospital of New York Presbyterian (CHONY). Data analysis is done at CHONY. Data from medical notes, cardiopulmonary exercise testing, cardiac catheterization, echocardiography, and six minute walk tests were used.

l. Potential Risks
No potential risks are present for this study.

m. Potential Benefits
Development of a novel prognostic tool for patients with PAH.

n. Alternative Therapies
No alternative therapies exist.

o. Compensation to Subjects
No compensation to subjects made by this study.

p. Costs to Subjects
This study was of no cost to subjects.

q. Minors as Research Subjects
This a retrospective study involving data obtained from the medical records of minors. Approval from the Department of Pediatrics Committee on Human Investigation was obtained prior to the initiation of the study.

r. Radiation and Radioactive Substances
No radiation or radioactive substances used during this study.

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