

CORRELATION BETWEEN RIGHT VENTRICULAR EJECTION FRACTION OBTAINED WITH GATED BLOOD POOL SPECT IMAGING AND RIGHT ATRIAL PRESSURE IN PATIENTS WITH PRIMARY PULMONARY HYPERTENSION

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A. Purpose and Rationale

Primary pulmonary hypertension (PPH) is a devastating disorder characterized by raised pulmonary artery pressure. The median survival prior to introduction of modern treatment modalities has been reported at 2.8 years. Since the introduction of IV prostacyclin, survival has greatly improved. After medical management options have been exhausted, a lung transplant is the only solution. The indications for transplantation originate from both clinical assessment and invasive evaluations of right heart failure. The measurements are derived from the right heart catheterization and are as follows: cardiac index less than 2 L/min², right atrial pressure greater than 15mmHg and mean PA pressure greater than 55mm Hg. In addition, some studies have shown that RAP<10 imparts better prognosis in PPH patients. More recently, we evaluated an alternative imaging modality -SPECT MUGA for risk stratification. The advantages of this approach include the non-invasive nature of the evaluation and its ability to provide three dimensional images of the full cardiac cycle with measurements of right ventricular diastolic and systolic volumes as well as ejection fractions. Preliminary results have shown that RV EF measured by SPECT MUGA of <25% is 78% sensitive and 95% specific as a marker of elevated RAP (greater than 10). The goal of this study is to validate these findings prospectively.

B. Study Design and Statistical Analysis

This is an observational study to be conducted at the CPMC Pulmonary Hypertension Center. All of the attending physicians in the center will be notified of the study existence by a letter. All the patients new to the clinic with existing diagnosis of primary pulmonary hypertension will be offered participation in the study and evaluated with right heart catheterization and SPECT MUGA as per currently accepted clinical practice. Both cardiologists interpreting MUGA and performing cardiac catheterization should be blinded to the results of each other's evaluations. The primary attending and the study investigator will be aware of both study results.

The primary outcome will be the negative predictive value of RV EF >25% as measured by MUGA with respect to finding normal RA pressure in subjects with PPH. Our hypothesis is that at least 90% of pts with RV EF >25% will have normal RAP. The analysis will be performed with chi-square test.

Taking into consideration preliminary data, MUGA has a high negative predictive value at the level of >25% for detecting clinically significant elevations of RA pressure. Based on these numbers, the power calculations yield the need to enroll 80 patients with RV EFs greater than 25%. The calculations were done with the goal to achieve a power of 80% at a significance level of 0.05

The rate of new patient admissions to the clinic is 20 patients per month. Calculating an average rate of PPH among these patients to be 10%, there will be 5 new patients per month. Based on preliminary data, 85% of all patients enrolled in the clinic have RV EF >25%, thus there will be 4.1 pts with high EFs enrolled per month. The study should take 1.6 years to recruit taking into consideration the need to analyze the data from 80 patients.

C. Medical Device

Both the right heart evaluation and SPECT MUGA are accepted modalities of evaluating patients with pulmonary hypertension. SPECT MUGA is a radionuclide angiography utilizing technetium 99m to label the patients' own red blood cells. A gamma camera is used to measure the radioactive tracers in the cavities of the heart over time. The camera computer generates a composite of the cardiac cycle with projected three dimensional images.

D. Study Subjects and Recruitment

Inclusion criteria: patients new to Pulmonary Hypertension Center at CPMC with diagnosis of primary pulmonary hypertension. The diagnosis is made according to the US National Institutes of Health registry as a mean pulmonary artery pressure of more than 25 nun Hg at rest, or 30 min Hg with exertion, in the absence of heart disease, chronic thromboembolic disease, underlying pulmonary disorder, or other secondary causes.

Exclusion criteria: allergy to contrast dye or current pregnancy.

Recruitment: described above.

E. Confidentiality of Study Data

Subjects' personal identifiers will be removed from all copies of medical records obtained by investigators and unique codes will be assigned at enrollment. Only the primary investigator and study coordinator will have access to all subject information.

F. Potential Conflict of Interest

None

G. Location of Study

CPMC-Pulmonary Hypertension Center

H. Potential Risks and Benefits

A potential risk of the study would include the risks of the right heart catheterization including bleeding, infection, arrhythmia, very small risk of perforation of the free wall of the heart which may be lethal. The risks of SPECT MUGA include exposure to small amounts of radiation. However, the risks and benefits are to be explained to the patients by their primary attending and obtained as part of the admission evaluation. The benefits of the study include better understanding of primary pulmonary hypertension and its treatments.

I. Compensation to Subjects

None is anticipated.

J. Radioactive Substances

A copy of this IRB proposal will be sent to Joint Radiation Safety Committee, however no additional exposure to radioactive substances above the usual evaluation is anticipated.