Positron Emission Tomography Imaging May Provide a Novel Biomarker and Understanding of Right Ventricular Dysfunction in Patients with Idiopathic Pulmonary Arterial Hypertension

Bokhari et al: PET Imaging May Provide a Biomarker and Understanding of RV Dysfunction in PAH

Sabahat Bokhari, MD; Amresh Raina, MD;
Erika Berman Rosenweig, MD; Christian Schulze, MD; Justin Bokhari;
Andrew J. Einstein, MD; Robyn J. Barst, MD; Lynne L. Johnson, MD

Division of Cardiology, Department of Medicine, New York Presbyterian Hospital at Columbia University Medical Center, New York, NY

Correspondence to:
Sabahat Bokhari, M.D.
New York Presbyterian Hospital at Columbia University Medical Center
Division of Cardiology, PH 10-203
622 West 168th Street
New York, NY 10032
Phone: 212/305-8864
Fax: 212/305-4648
E-mail: sb605@columbia.edu

Journal Subject Codes: 11, 18, 26, 32, 60, 61.
Abstract

Background—The clinical course in PAH is variable and there is limited information on the determinants and progression of RV dysfunction. The objective is to develop PET metabolic imaging of the RV as a non-invasive tool in patients with pulmonary arterial hypertension (PAH).

Methods and Results—We performed PET scanning in 16 patients with idiopathic PAH (IPAH) (age 41±14yrs, 82% female) using $^{13}$N-NH3 for perfusion imaging and $^{18}$F-FDG for metabolic imaging. The myocardium was divided into 6 regions of interest (3 LV, 3 RV) and time activity curves were generated. A 2-compartment model was used to calculate myocardial blood flow (MBF) and Patlak analysis was used to calculate the rate of myocardial glucose uptake (MGU). All patients underwent cardiac catheterization, cardiac MRI and cardiopulmonary exercise testing with gas exchange (CPT). MBF, MGU and the ratio of RV/LV MGU were correlated to clinical parameters. PA pressure was 79±19/30±8 mm Hg, (mean 48 ± 10 mm Hg). MBF was 0.84±0.33 ml/g/m for the LV and 0.45±0.14 ml/g/m for the RV. Mean MGU was 136±72 nmol/g/m for the LV and 96±69 nmol/g/m for the RV. The ratio of RV/LV MGU correlated significantly with PA systolic and mean pressure (r=0.75 & 0.87, p=0.0085 & 0.001) and marginally with VO2 max (r=-0.59, p=0.05). RV free wall MGU also correlated well with mean PA pressure (r = 0.66, p = 0.03).

Conclusions—PET scanning with $^{13}$N-NH3 and $^{18}$F-FDG is a feasible modality for quantifying RV blood flow and metabolism in patients with IPAH.

Key Words: pulmonary artery hypertension, positron emission tomography, F18-FDG
### Abbreviations List

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAH</td>
<td>pulmonary arterial hypertension</td>
</tr>
<tr>
<td>IPAH</td>
<td>idiopathic pulmonary arterial hypertension</td>
</tr>
<tr>
<td>PET</td>
<td>positron emission tomography</td>
</tr>
<tr>
<td>MBF</td>
<td>myocardial blood flow</td>
</tr>
<tr>
<td>F18-FDG</td>
<td>fluorine 18-fluorodeoxyglucose</td>
</tr>
<tr>
<td>MGU</td>
<td>myocardial glucose utilization</td>
</tr>
<tr>
<td>LV</td>
<td>left ventricle</td>
</tr>
<tr>
<td>RV</td>
<td>right ventricle</td>
</tr>
<tr>
<td>PA</td>
<td>pulmonary artery</td>
</tr>
<tr>
<td>PVR</td>
<td>pulmonary vascular resistance</td>
</tr>
<tr>
<td>MRI</td>
<td>magnetic resonance imaging</td>
</tr>
</tbody>
</table>
Pulmonary arterial hypertension (PAH) is a progressive condition with a poor prognosis if not identified and treated early in the course of the disease. Before the advent of targeted PAH therapy, the National Institutes of Health Primary Pulmonary Hypertension Registry reported a mean survival of 2.8 years from diagnosis in patients with idiopathic PAH (IPAH).(1,2) More recently, intravenous epoprostenol has been shown to reduce mortality in IPAH patients (3-5) while endothelin receptor antagonists and phosphodiesterase inhibitors have improved hemodynamics and exercise capacity in PAH patients.(6-9)

Little attention has been devoted to how RV dysfunction may be best detected and measured, how RV dysfunction evolves structurally and functionally, or what interventions might best preserve RV function. Nevertheless, even the proportionately limited information related to RV dysfunction in PAH and its impact on the outcome of PAH suggests that RV dysfunction is an important contributor and that further understanding of these issues is of pivotal importance. Advancing knowledge through research about the molecular, cellular and functional characteristics of the RV and its vulnerability to disease will lead to progress in the treatment of PAH.

Morbidity and mortality in PAH has been correlated with mean pulmonary artery (PA) pressure, pulmonary vascular resistance (PVR), right atrial pressure, cardiac index, mixed venous oxygen saturation, exercise capacity, and New York Heart Association functional class.(10-14) Therefore, current clinical evaluation of patients with PAH includes invasive evaluation of hemodynamics via right heart catheterization, non-invasive imaging of right ventricular (RV) size and function, and measurement of
exercise capacity using the six minute walk test and/or cardiopulmonary exercise testing. However there is considerable variability in the clinical course of patients with PAH. Therefore, additional serum biomarkers(15,16) and noninvasive imaging modalities, which could identify patients at risk for RV dysfunction and adverse outcomes, might be useful in the clinical evaluation of patients with PAH.

One prior study has evaluated quantitative myocardial glucose utilization (MGU) in the RV, measured by dynamic $^{18}$Flourine-Fluorodeoxyglucose ($^{18}$F-FDG) positron emission tomography (PET) scanning, among a population of patients with varied etiology of PAH.(17) This study found no association between RV MGU and pulmonary artery (PA) pressure or PVR. However, it did find a correlation between the ratio of RV/LV MGU and PVR, albeit based on relatively reduced left ventricle (LV) MGU, rather than increased RV MGU. We hypothesized that MGU would be increased in the RV and in the LV among patients with IPAH and that RV MGU and that the ratio of RV/LV MGU would correlate with hemodynamic parameters and exercise capacity in these patients.

Methods

Patient Selection

Patients 18 to 65 years of age with IPAH, referred to New York Presbyterian Hospital/Columbia University Medical Center for treatment were recruited for this study. All patients underwent right heart cardiac catheterization, cardiopulmonary stress testing (CPT), two-dimensional echocardiography with Doppler and cardiac MRI within 30 days of PET imaging. All patients were stable and no active medical interventions were
performed between the tests and PET imaging. The severity of PAH was determined on the basis of right heart catheterization and assessment of clinical symptoms. Patients were excluded if they had diabetes, abnormal LV function, primary left sided valvular disease, or other forms of PAH. In addition, patients were excluded if they were pregnant, claustrophobic, unable to cooperate with the scanning protocol, or if they were unable to lie flat in the supine position for the duration of the PET scan. All patients gave written, informed consent and the protocol was approved by the Columbia University Institutional Review Board as well as by the Radioactive Drug Research Committee and the Joint Radiation Safety Committee of the University.

**PET Scanning**

In preparation for PET imaging, patients fasted overnight for at least 6 hours after a regular meal. The baseline fasting blood glucose was measured and patients were excluded from the study if their fasting blood glucose was greater than 125 mg/dl. The scanning protocol began with a 2 minute scan to ensure appropriate positioning within the scanner, followed by a 20 minute transmission scan using a Germanium-68 source. Although the intrinsic in-plane resolution was 6.5 mm (full width at half-maximum), images were reconstructed using an iterative algorithm and a Hann filter (cutoff frequency, 0.4), yielding an effective resolution of 10.5 mm. For resting myocardial perfusion imaging, the patients received an intravenous bolus of 0.28 mCi/Kg of $^{13}$N-NH3 with a simultaneous 2-D dynamic acquisition protocol (10 sec/frame x 12, 30 sec/frame x 2, 180 sec/frame x 1). The patients then received 50 grams of oral glucose load and one hour later were injected with 10 mCi of $^{18}$F-FDG intravenously. The PET
scanning began simultaneously, using a 2-D dynamic acquisition protocol over 60 minutes (10 sec/frame x 12, 30 sec/frame x 10, 120 sec/frame x 10, 300 sec/frame x 6). Plasma glucose was measured 0, 15, 30 and 60 minutes after \(^{18}\)F-FDG injection. PET images were acquired on a Siemens ECAT Accel high-resolution PET scanner. All images were corrected for scatter and measured photon attenuation. Image reconstruction was performed using iterative reconstruction and a Butterworth filter.

**Quantitative Analysis**

For quantitative analysis, the myocardium was divided into 6 regions of interest, 3 for the LV (anterior, lateral and inferior) and 3 for the RV (apex, free wall and septum). Time activity curves and input functions were generated for each region of interest and for the blood pool by placing a small region of interest within the basal LV blood pool on the mid-ventricular slice. A 2 compartment kinetic model was used to calculate myocardial blood flow in each region of interest using \(^{13}\)N-NH\(_3\). Patlak analysis was used to calculate the rate of MGU from \(^{18}\)F-FDG washout curves for each region of interest, and globally for the RV and LV. Values obtained from Patlak analysis were corrected for differences in uptake and phosphorylation of \(^{18}\)F-FDG and glucose using a lumped constant 0.67. The partial volume effect was corrected based on the RV free wall thickness measured by MRI and the recovery coefficient derived from the phantom study. The corrected MGU was calculated by the following equation: Corrected MGU = MGU/recovery coefficient. The recovery coefficient was 0.5 to 1.0. The partial volume recovery coefficient was calculated by convolution with Gaussian kernel representing the reconstructed PET image resolution. The transaxial MRI images corresponding to PET
images were selected and end-diastolic wall thickness of RV free wall, the interventricular septum and LV free wall were measured for partial volume effect correction of the PET emission data.

**Hemodynamic Evaluation, Exercise Testing and Additional Imaging**

Pulmonary and hemodynamic parameters were obtained by right heart catheterization. Cardiac output was measured by thermodilution (mean of 3 values). A symptom-limited CPT was performed on a cycle ergometer using a 10-watt ramp protocol. Heart rate was measured using a Marquette 12-lead ECG system and maximum oxygen consumption (VO2 max) on room air was measured using SensorMedics Vmax metabolic cart. All patients underwent two-dimensional echocardiography with Doppler color flow mapping and pulsed and continuous wave Doppler interrogation. In addition, patients underwent cardiac MRI scanning on a 1.5 Tesla GE Signa MRI scanner with EXCITE software, using a dedicated 8-channel cardiac coil with ASSET. MRI images were obtained using a gated steady-state free precession sequence (FIESTA) in sagittal, oblique, and short axis planes with 9 mm slice thickness, 1 mm inter-slice gap and 20 phases per cardiac cycle.

**Statistical Analysis**

Correlations between PET data and hemodynamic and cardiopulmonary exercise testing parameters were evaluated using the Spearman correlation coefficients. Statistical significance was defined as a p value less than 0.05. Data are presented as mean ± SD.
Results

Sixteen patients with IPAH were included in this study. Demographic, clinical and hemodynamic data are shown in Table 1. Patients were predominantly women (82%), with mean age 41 ± 12 years, (range 25-71 years). IPAH was diagnosed on an average of 20 ± 4 months before their enrollment in the study. PA pressure was 79 ± 19/30 ± 8 mm Hg, (mean 48 ± 10 mm Hg). Medical therapy for the study population is shown in Table 2. The majority of patients were treated with a standard targeted regimen for PAH including endothelin receptor antagonists, prostacyclin analogs, phosphodiesterase inhibitors, diuretics, digoxin and spironolactone. On cardiac MRI, the RV was enlarged (mean RV EDV 202 ± 31 ml), although RV function was largely preserved (mean RVEF 46 ± 6 %), see Table 3. End-diastolic wall thickness (EDWT) and end-systolic wall thickness (ESWT) were measured. Mean EDWT and ESWT values for RV and LV were not significantly different (9.2 ± 3.6 vs. 9.9 ± 4.1 and 11.6 ± 4.2 vs 12.4 ± 4.4; P = NS).

All patients underwent $^{13}$N-NH3 perfusion imaging. Resting myocardial perfusion was qualitatively and quantitatively normal for the LV (see Figure 1), (global LV blood flow 0.84 ± 0.33 ml/g/min, see Table 4). The RV was enlarged and hypertrophied on perfusion imaging (see Figure 1) and resting myocardial blood flow was 0.45 ± 0.14 ml/g/min.

RV Myocardial glucose uptake was clearly visible and therefore qualitatively increased in all patients (see Figure 2). Mean MGU was 136 ± 72 nmol/g/min in the LV and 96 ± 69 nmol/g/min in the RV. Although the RV/LV ratio of myocardial blood flow did not correlate with either systolic or mean PA pressure (r = 0.37 and 0.12, p = 0.33 and
0.78 respectively), see figure 3, the ratio of RV/LV MGU did correlate with PA systolic and mean PA pressure (r = 0.75 and 0.87, p = 0.0085 and 0.001 respectively), see Figure 3. There was no significant association between global LV MGU and mean PA pressure (r = 0.20, p = 0.6), although RV free wall MGU did correlate with mean PA pressure (r = 0.66, p = 0.03) with no significant association between global RV uptake and mean PA pressure (r = 0.41, p = 0.23). The RV free wall was compared separately, because there may be spillover of the activity from the left and right ventricle in the myocardium septum and apex.

Although most patients were NYHA class I or II, VO2 for these patients was reduced at 16 ml/kg/min (48% of age/gender predicted values). No adverse events occurred during or after the exercise stress test. The performance limiting symptom was shortness of breath in all patients. No patient reported retrosternal chest discomfort and no ischemic ECG changes were observed during exercise and recovery period. The mean exercise duration was 406 ± 22 seconds, heart rate at peak was 128 ± 8 bpm, systolic BP at peak was 139 ± 4 mm Hg and diastolic BP at peak was 80 ± 2 mm Hg (rest data is shown in Table 1). There was a trend towards a negative correlation between the ratio of RV/LV MGU and VO2 max (r = -0.59, p = 0.05). In addition, there was no significant negative correlation between the ratio of RV/LV MGU and exercise duration.

**Discussion**

While the LV is the initial target organ for atherosclerosis and systemic hypertension, the RV is the target organ for PAH. PET scanning using cyclotron-produced radio pharmaceuticals has been used to quantify LV blood flow and metabolism
in the myocardium in the normal state and in patients with left ventricular hypertrophy (LVH), atherosclerosis, and dilated cardiomyopathy. (18-24) The healthy heart relies primarily on fatty acid rather than glucose as a source of energy. In both LVH and dilated cardiomyopathy, there is a metabolic shift with an increase in myocardial glucose utilization (MGU) and a corresponding decrease in fatty acid metabolism, (18,19) and this shift appears to herald a decompensated state. There is experimental evidence to support the maladaptive aspects of this metabolic remodeling only in animal studies. A shift in substrate metabolism towards glucose utilization is associated with disturbed cardiomyocyte Ca++ homeostasis and an increase in cellular oxidative stress. (25) In addition a shift away from fatty acid utilization is associated with a less efficient alternative pathway for glucose oxidation which produces less NADH. MR spectroscopy studies have shown reduced PCr/ATP ratios in hypertrophied hearts with reduced FA oxidation. In the long term this metabolic remodeling probably contributes to the development of myocardial failure. (26) However this is not a proven hypothesis in humans. Furthermore, longer term follow up of RV function and studies of fatty acid metabolism would be required to confirm a maladaptive process.

Blood flow and substrate metabolism in the RV in the normal state have been poorly characterized. This is in large part because in the normal heart, the RV does little work compared to the LV and is thin walled. As a result, the normal RV takes up insufficient radiopharmaceuticals to be accurately measured, given the limited resolution of current PET scanners. However, in patients with IPAH, the hypertrophied and enlarged RV can easily be seen with PET imaging. While this compensatory hypertrophy has the beneficial effect to normalize wall stress, in experimental animals it has been
shown to shift nutrient substrate uptake from fatty acids to glucose. (27, 28) While fatty acid metabolism was not measured in the present study, the high MGU found and its relationship to afterload combined with the findings from experimental studies in chronic pressure overload support the premise that this increase in glucose utilization represents a metabolic shift away from fatty acid utilization.

The present study evaluated MBF and substrate metabolism for the RV and LV in IPAH to compare the two ventricles and to investigate whether RV and/or LV indices outlined by PET scanning correlate with its severity assessing by hemodynamic and or CPT. The results of this study provide insight into the effects of increases in the RV afterload on RV blood flow and RV substrate metabolism. This study demonstrated the feasibility of using dynamic PET scanning to quantify RV blood flow and metabolism in IPAH patients. We demonstrated a significant correlation between the ratio of RV/LV MGU and PA pressures. One prior study has evaluated quantitative MGU in the RV, measured by dynamic $^{18}$F-FDG PET scanning in varied etiologies of PAH patients by Kluge et al (17). These authors found no association between RV MGU and PA pressure or PVR but did find a correlation between the ratio of RV/LV MGU and PVR. However there are significant differences between their study and our study. Our study included only IPAH patients vs. their study included patients with varied etiologies of PAH. In our study the mean PAP was 48±10 vs. 60.8±19 in their primary PAH patients and the patients in current study were in NYHA Functional Class 1 and 2 vs. 2 and 3 in Kluge et al study. Their study used $^{99m}$Tc-tetrofosmine SPECT imaging for perfusion therefore, their data was analyzed semi-quantitatively. In contrast to our study where we used $^{13}$N-NH$_3$ PET for perfusion permitting absolute quantification analysis technique. In their
study, they did not find any correlation between RV glucose uptake and PA pressures, but they found a negative correlation between PA pressures and LV MGU, they attributed RV/LV MGU and PA pressure correlation to decreased LV MGU. In our study we did not find a negative correlation between LV MGU and PA pressure. In contrast to their study we performed CPT and found a trend towards a negative correlation between the ratio of RV/LV MGU and VO2 max. The differences in these studies may also be due to the differences in partial volume effect correction and the recovery coefficient. In their study MGU and perfusion were evaluated using different imaging modalities with different spatial resolution. Therefore there is a possibility that differences in recovery coefficients affected the right to left count ratios. The ventricular wall thickness in their study was not systematically evaluated. A more recent study by Oikawa et al looked at patients with PAH and found that increased RV FDG accumulation correlates with the severity of RV pressure overload. Additionally they found a reduction in RV uptake of 18F-fluorodeoxyglucose in patients with PAH who responded to treatment with epoprostenol, suggesting that some drugs that target the pulmonary vasculature may favorable change RV substrate metabolism. (29) In their study they did not quantify myocardial blood flow or MGU (Patlak quantification). In addition, they used EBCT or MRI for the measurement of RV structure. In contrast, all our patients underwent cardiac magnetic resonance imaging, which is considered the best technique to quantify RV volumes and size. They also had more patients with advanced PAH – Class II predominantly, rather than I/II which is the population one might target with such testing i.e. the early clinical disease without overt RV failure. Another recent study by Mielniczuk et al studied patients with heart failure, which included patients with diabetes,
ischemic heart disease and prior infarctions. (30) FDG uptake is variable in ischemic cardiomyopathy patients and this will have an effect on LV and RV SUV values. In their study RVEF was measured by ERVG and RV hypertrophy by echo. All our patients underwent cardiac magnetic resonance imaging, which is considered the best technique to quantify RV volumes and size. They did not quantify MGU (Patlak analysis) and right heart catheterization was not done for measuring RVSP. As compared to these studies our study is more comprehensive and in patients with IPAH (NYHA Class I/II). All our patients underwent MRI, right heart catheterization, quantification of myocardial blood flow, quantification of MGU and CPT. In contrast to the aforementioned studies we compared VO2 max with RV MGU. VO2 max is considered a strong predictor of survival in PAH patients.

The shift in MGU may be an early marker of RV dysfunction, possibly a preclinical marker before overt RV failure, given that RV function on MRI in our study was largely preserved and that most patients were NYHA Class I/II. The relations observed support the need for further investigation of MGU as a novel early biomarker that could be a therapeutic target in the treatment and/or monitoring of PAH. Monitoring MGU level may help to optimize treatment to improve function and outcome. A recent study by Oikawa et al showed reduction in RV SUV’s of FDG with treatment with IV epoprostenol. Whether the current treatments of PAH impact MGU would require further studies. In addition our study demonstrates a trend toward negative correlation with VO2 max, suggesting that this finding may have some prognostic impact.

The goal of our study was to develop PET parameters that could aid in the management of PAH patients and to use a metabolic parameter that can be measured with
a widely available radiopharmaceutical i.e. $^{18}$F-FDG. Although we used $^{13}$N-NH$_3$ (cyclotron produced) for measuring MBF, it is possible that generator produced rubidium 82 can also be used to quantify blood flow, which would allow these tests to be more widely performed. The results of this study provide insight into the effects of increases in the RV after load on RV blood flow and substrate metabolism. Whether RV myocardial metabolic changes contribute to the functional changes and whether myocardial metabolic modulation improves the mortality and morbidity of patients with IPAH will require further studies.

**Study Limitations**

We did not perform fatty acid imaging, therefore the metabolic shift with an increase in MGU and a corresponding decrease in fatty acid metabolism, was not evaluated. Although all patients in the present study had normal coronary angiography and normal MBF, we cannot exclude the possibility that myocardial ischemia due to severe RV hypertrophy might have increased the RV FDG metabolism. However, previous animal studies have shown that glucose utilization in rats is increased, whereas free fatty acid utilization is decreased in the hypertrophied myocardium with chronic LV or RV pressure overload. There is no control group in this study because in normal subjects RV wall is quite thin and MBF and MGU cannot be measured.

**Conclusions**

PET scanning with $^{13}$N-NH$_3$ and $^{18}$F-FDG appears to be a feasible modality for quantifying RV blood flow and RV metabolism in patients with IPAH. Further studies
are warranted to investigate using metabolic substrate imaging of MGU with PET as a tool to plan and follow therapy aimed at metabolic modulation in IPAH and hopefully PAH associated with other conditions.

Acknowledgements

The authors thank the nuclear technologists in the PET center for their help in studying these patients.

Disclosures

1) Sabahat Bokhari MD: None
2) Amresh Raina M.D: None
3) Erika Berman Rosenweig MD: None
4) Christian Schulze MD: None
5) Justin Bokhari: None
6) Andrew Einstein MD: None
7) Robyn J Barst MD: Speakers Bureau: Actelion, Amount: < $10,000, Gilead, Amount: < $10,000, Consultant/Advisory Board: Pfizer, Amount: >= $10,000, Actelion, Amount: >= $10,000, Novartis, Amount: >= $10,000, Ikaria, Amount: >= $10,000
8) Lynne L Johnson M.D: None
References


<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>41 ± 12</td>
</tr>
<tr>
<td><strong>Gender: male/female (%)</strong></td>
<td>3 (18%)/13 (82%)</td>
</tr>
<tr>
<td><strong>Fasting Blood Glucose (mg/dl)</strong></td>
<td>92 ± 8</td>
</tr>
<tr>
<td><strong>PA Pressures (Sys/Dia/Mean mm Hg)</strong></td>
<td>79 ± 19/30 ± 8/48 ± 10</td>
</tr>
<tr>
<td><strong>PCWP (Mean mm Hg)</strong></td>
<td>10 ± 6</td>
</tr>
<tr>
<td><strong>CI (L/min/m2)</strong></td>
<td>3.5 ± 0.4</td>
</tr>
<tr>
<td><strong>Blood Pressure (Sys/Dia Mean mm Hg)</strong></td>
<td>111 ± 11/68 ± 7</td>
</tr>
<tr>
<td><strong>Heart Rate (bpm)</strong></td>
<td>74 ± 7</td>
</tr>
<tr>
<td><strong>NYHA Functional Class</strong></td>
<td>1.5 ± 0.7</td>
</tr>
<tr>
<td><strong>BMI</strong></td>
<td>26 ± 6</td>
</tr>
<tr>
<td><strong>VO2 max (ml/kg/min)</strong></td>
<td>16 ± 2</td>
</tr>
</tbody>
</table>

PA = Pulmonary artery, PCWP = Pulmonary capillary wedge pressure, CI = Cardiac index, NYHA = New York heart association, BMI = Body mass index, VO2 max = Maximum oxygen consumption.
Table 2. Medical Therapy for IPAH Among the Study Patients (n=16)

<table>
<thead>
<tr>
<th>Medication</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warfarin</td>
<td>13 (82)</td>
</tr>
<tr>
<td>Digoxin</td>
<td>11 (73)</td>
</tr>
<tr>
<td>Endothelin Receptor Antagonist</td>
<td>10 (64)</td>
</tr>
<tr>
<td>Phosphodiesterase inhibitor</td>
<td>10 (64)</td>
</tr>
<tr>
<td>Prostacyclin Analog</td>
<td>9 (56)</td>
</tr>
<tr>
<td>Diuretic</td>
<td>7 (46)</td>
</tr>
<tr>
<td>Spironolactone</td>
<td>7 (46)</td>
</tr>
<tr>
<td>Calcium Channel Blocker</td>
<td>6 (38)</td>
</tr>
</tbody>
</table>
Table 3. Cardiac MRI Data for IPAH Patients (n=16)

<table>
<thead>
<tr>
<th>LV EDV (ml)</th>
<th>LV ESV (ml)</th>
<th>LV EDWT (mm)</th>
<th>LV LVEF (%)</th>
<th>RV EDV (ml)</th>
<th>RV ESV (ml)</th>
<th>RV LVEF (%)</th>
<th>RV EDWT (mm)</th>
<th>RV ESV (mm)</th>
<th>RV CO (L/min)</th>
<th>RV CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>137±15</td>
<td>51±6</td>
<td>9.9 ± 4</td>
<td>12.4 ± 4</td>
<td>202±31</td>
<td>109±26</td>
<td>46±6</td>
<td>9.2 ± 3</td>
<td>11.6 ± 4</td>
<td>6.8±2</td>
<td>4.1±1</td>
</tr>
</tbody>
</table>

LV = Left ventricle, RV = Right ventricle, EDV = End diastolic volume; ESV = End systolic volume; EF = Ejection fraction; EDWT = End diastolic wall thickness; ESWT = End systolic wall thickness; CO = Cardiac output; CI = Cardiac index
Table 4. Myocardial Blood Flow & Glucose Utilization in the Left and Right Ventricle

(n=16)

<table>
<thead>
<tr>
<th>MBF (ml/kg/min)</th>
<th>Lateral</th>
<th>Anterior</th>
<th>Inferior</th>
<th>Global</th>
<th>Septal</th>
<th>Free Wall</th>
<th>Apex</th>
<th>Global</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.89</td>
<td>0.87</td>
<td>0.76</td>
<td>0.84</td>
<td>0.59</td>
<td>0.33</td>
<td>0.41</td>
<td>0.45</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>MGU (nmol/g/min)</th>
<th>Lateral</th>
<th>Anterior</th>
<th>Inferior</th>
<th>Global</th>
<th>Septal</th>
<th>Free Wall</th>
<th>Apex</th>
<th>Global</th>
</tr>
</thead>
<tbody>
<tr>
<td>139</td>
<td>144</td>
<td>121</td>
<td>136</td>
<td>128</td>
<td>76</td>
<td>69</td>
<td>96</td>
<td></td>
</tr>
</tbody>
</table>

MBF = Myocardial blood flow. MGU = Myocardial glucose utilization
Figure Legends

**Figure 1.** $^{13}$N Ammonia Resting Myocardial Perfusion Images of the LV and RV with. Top panel illustrates short axis images of the LV and RV; bottom panel illustrates horizontal long axis images. Arrows illustrate enlarged RV.

**Figure 2.** $^{18}$F-FDG Resting Myocardial Metabolism Images of the LV and RV. Top panel illustrates short axis images of the LV and RV; bottom panel illustrates horizontal long axis images. Arrows illustrate enlarged RV.

**Figure 3.** Relationship of RV/LV MGU and MBF to Mean PA Pressure.

RV = Right ventricle, LV = Left ventricle, MBF = Myocardial blood flow, MGU = Myocardial glucose utilization, PA = Pulmonary artery
Positron Emission Tomography Imaging May Provide a Novel Biomarker and Understanding of Right Ventricular Dysfunction in Patients with Idiopathic Pulmonary Arterial Hypertension

Sabahat Bokhari, Amresh Raina, Erika Berman Rosenweig, Christian Schulze, Justin Bokhari, Andrew J. Einstein, Robyn J. Barst and Lynne L. Johnson

_Circ Cardiovasc Imaging._ published online September 16, 2011;
_Circulation: Cardiovascular Imaging_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2011 American Heart Association, Inc. All rights reserved.
Print ISSN: 1941-9651. Online ISSN: 1942-0080

The online version of this article, along with updated information and services, is located on the World Wide Web at:

http://circimaging.ahajournals.org/content/early/2011/09/16/CIRCIMAGING.110.963207

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation: Cardiovascular Imaging_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Circulation: Cardiovascular Imaging_ is online at:
http://circimaging.ahajournals.org//subscriptions/