The Relationship Between Right Ventricular Function and Increased Right Ventricular [18F] Fluorodeoxyglucose Accumulation in Patients with Heart Failure

Running Title: Mielniczuk et al: RV Metabolism in Heart Failure

Lisa M Mielniczuk MD FRCPC1, David Birnie MB ChB MD1, Maria C Ziadi MD1, Robert A deKemp PhD1, Jean N DaSilva PhD1, Ian Burwash MD FRCPC1, Anthony T Tang MD FRCPC2, Ross A Davies MD FRCPC1, Haissam Haddad MD FRCPC1, Ann Guo MEng1, May Aung CNMT1, Kathryn Williams BSc MS1, Heikki Ukkonen MD3, Rob SB Beanlands MD FRCPC1

1. Division of Cardiology, University of Ottawa Heart Institute, Ottawa ON, Canada
2. Division of Cardiology, University of Victoria, Victoria, BC, Canada
3. Division of Cardiology, Turku University Hospital, Turku, Finland

Correspondence to:
Dr. Lisa Mielniczuk
University of Ottawa Heart Institute,
40 Ruskin Street, Ottawa, Ontario, K1Y 4W7 (Canada).
Tel: 613-761-4059
Fax: 613-761-4877
E-mail
lmielniczuk@ottawaheart.ca

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Abstract

**Background**—Left heart failure is characterized by alterations in metabolic substrate utilization, and metabolic modulation may be a future strategy in the management of heart failure (HF). There is little known about cardiac metabolism in the right ventricle and how it relates to other measures of right ventricular function. This study was designed to measure glucose metabolism in the right ventricle (RV) estimated using \[^{18}\text{F}\] fluorodeoxyglucose (FDG) PET imaging and to determine the relationship between right ventricular function and FDG uptake in patients with heart failure.

**Methods and Results**—A total of 68 patients had cardiac \[^{18}\text{F}\] FDG PET scans with measurement of right ventricular FDG uptake as a standardized uptake value (SUV). Perfusion imaging was acquired at rest with rubidium-82 or \[^{13}\text{N}\]-ammonia. Right ventricular function was determined using ERVG. Relative RV FDG uptake was determined as the ratio of RV:LV SUV. Fifty-five % of these patients had ischemic cardiomyopathy (CM). The mean LVEF and RVEF were 21±7% and 35±10% respectively. There was a correlation between RVEF and the ratio of RV/LV FDG uptake whether the entire LV myocardium (-0.40, p<0.001) or LV free wall (-0.43, p<0.001) was used. This relationship persisted in the subgroup with nonischemic CM (-0.37, p=0.04). RV FDG uptake was weakly related to increased right ventricular systolic pressure but not related to LV size, function nor LV FDG uptake. The correlation between RVEF and RV/LV FDG was maintained after partial volume correction (r=-0.68, p<0.001).

**Conclusions**—Right ventricular dysfunction is associated with an increase in the RV FDG uptake, the magnitude of which may correlate with severity.

**Key Words:** heart failure, right ventricle, FDG PET
Abbreviations and Acronyms

EF = ejection fraction
ERVG = equilibrium radionuclide ventriculography
FDG = 18Fluorodeoxyglucose
HF = heart failure
LV = left ventricle/ventricular
MI = myocardial infarction
13NH3 = N-13-ammonia
NYHA = New York Heart Association
PET = positron emission tomography
ROI = region of interest
82Rb = Rubidium-82
RV = right ventricle/ventricular
SPECT = single photon emission tomography
SUV = standardized uptake value
Right ventricular (RV) dysfunction is associated with a poor prognosis in patients with preexisting coronary artery disease, significant heart failure, and in patients with pulmonary arterial hypertension. Alterations in myocardial substrate utilization have been implicated in the pathogenesis of contractile dysfunction and heart failure (HF). Studies of substrate utilization in left HF have demonstrated that fatty acid utilization may be unchanged or slightly increased in early HF but substantially decreased in advanced HF, with a concomitant increase of glucose utilization in early HF and subsequent decline in advanced HF as insulin resistance develops in the myocardium. Whether the shift towards glucose utilization represents an adaptive response or a maladaptive response predisposing the heart to further myocardial dysfunction also remains uncertain. Few have studied RV metabolism in detail. Despite this, several lines of evidence suggest RV metabolism may be different.

It has been demonstrated that there are substantial differences among patients in their tendency to develop right heart failure. Recent literature suggests that the heterogeneity in clinical course may be caused by polymorphic variation in gene expression and that the link between cardiac contractile function and gene expression may be altered energy substrate metabolism. An understanding of the metabolic changes associated with right ventricular failure and dysfunction may lead to a potential target for the use of metabolic modulation in the treatment and prevention of right HF.

This study was designed to measure glucose metabolism in the right ventricle (RV) estimated using [18F] fluorodeoxyglucose PET scans and to determine the relationship between right ventricular function and FDG uptake in patients with heart failure.
Methods

Patient Population. Sixty-eight patients were enrolled from two sources. Firstly, 60 consecutive adult patients (over 18 years of age) with history of congestive HF who had a left ventricular (LV) ejection fraction (EF) \( \leq 35\% \) documented by radionuclide ventriculography (ERVG), symptoms consistent with New York Heart Association (NYHA) functional class II-III despite optimal medical therapy; and a QRS duration \( \geq 130 \text{ ms} \) based on baseline electrocardiogram) who were recruited for the PREDICT study\(^{17}\), were prospectively enrolled at the University of Ottawa Heart Institute. This study evaluated the effect of lateral wall scar on reverse remodeling and clinical response to cardiac resynchronization therapy (CRT). For the most part, these patients did not have severe pulmonary hypertension. In order to include a patient population with a wider range of pulmonary hypertension, we also included a cohort of 8 consecutive patients with ischemic cardiomyopathy and significant pulmonary hypertension who were enrolled in the CADRE database, a regional registry study evaluating cardiac PET use in Ontario.\(^{18}\) Ischemic etiology was defined as having both a documented history of myocardial infarction (MI) and evidence of significant coronary artery disease on coronary angiography (at least one stenosis \( \geq 70\% \) in \( \geq 2 \) major arteries). Significant pulmonary hypertension was defined as a mean pulmonary artery pressure \( \geq 40 \text{ mmHg} \) or an RVSP\(>50 \text{ mmHg} \) on a right heart catheterization or echocardiogram done within 60 days of the PET study. All patients enrolled provided informed consent for inclusion. The study was approved by the Human Research Ethics Board of the University of Ottawa Heart Institute.
Study Procedures

Echocardiographic Assessment of wall thickness

Transthoracic echocardiographic analysis was performed using a Phillips Sonos 5500 Ultrasound System. The pressure difference between the right chambers was calculated using the modified Bernoulli equation [Gradient (ΔP), mmHg ΔP = 4 v²; whereby v² = accelerated velocity across a stenosis] and the measured Doppler velocity of the regurgitant tricuspid flow jet. The right ventricular systolic pressure (RVSP, in mmHg) and right atrial pressure were assessed through standard recommended techniques.

Wall thickness was measured from two dimensional echocardiographic images. Each measurement was taken three times and then averaged. The diastolic right ventricular free wall was measured in the subcostal view and parasternal views were obtained to measure posterolateral left ventricular wall thickness.19

ERVG Imaging and Analysis

Patients underwent ERVG planar imaging at baseline. The ERVGs were acquired with a standard electrocardiogram gated equilibrium technetium-99m red blood cell blood pool imaging protocol.20,21 For quantitative analysis of global RVEF and LVEF data obtained from the LAO view was used.

PET Rest Perfusion and Metabolism Imaging Protocol

Patients underwent a rest perfusion and a metabolism positron emission tomography (PET) scan. All patients were required to fast prior to the PET study and underwent monitoring of the blood glucose levels. Patients were positioned in the Siemens/CTI (Knoxville, TN) ECAT ART camera (n=52) or in the GE Discovery Rx/VCT camera (n=16). A 4 minute cesium-137 single transmission scan22,23 was performed for
attenuation correction in the Siemens/CTI scanner. For the GE PET system, a scout scan and a low-dose CT (15 cm FOV) were performed.

The PET perfusion imaging was acquired at rest using a standard protocol with rubidium-82 ($^{82}$Rb) or $[^{13}$N]-ammonia as described previously. Immediately following the transmission scan, 8-10 MBq/kg of $^{82}$Rb or 5-10 MBq/kg of $[^{13}$N]-ammonia was administered intravenously. Static perfusion images were acquired.$^{24,25}$

For FDG imaging, nondiabetic patients were studied after an oral glucose load; whereas an insulin-euglycemic clamp was used for those with diabetes.$^{25-27}$ A standard dose of 5 MBq/kg (< 550 MBq) of FDG was injected intravenously as a bolus 30 minutes after the glucose load. For diabetic patients with insulin-euglycemic clamp, plasma glucose levels were checked every 5 min. FDG injection was performed after having 3 stable plasma glucose levels and stable glycemia (optimal glycemia = 5 mmol/L). FDG PET image acquisition was started 45 minutes after FDG injection to ensure accurate myocardial tracer uptake.$^{28}$

**Image Processing.** Transverse PET images were reconstructed using Fourier rebinning (FORE)-filtered back-projection (FBP) with a 12 mm 3D Hann window of the ramp filter. Photon attenuation and scatter corrections were applied using the ECAT v7.2 software. Automatic reorientation of the images into short-axis sections was achieved using our FlowQuant© software.$^{29}$

**Determination of RV and LV uptake and data analyses.** Areas of maximal LV and RV uptake were identified visually on the static transaxial images. Once identified, 4 small regions of interest (ROI size > 2 x 2 pixels) were drawn on the whole right ventricular (RV) free wall, interventricular septum, whole LV and LV lateral wall of the
end-diastolic transaxial image. The standardized uptake value (SUV), a well-established index of tissue FDG uptake per unit volume, was calculated as follows:\textsuperscript{30}

\[
\text{SUV} = \frac{\text{mean ROI count (cps/pixel) \times body weight (kg)}}{\text{injected dose (mCi) \times calibration factor (cps/mCi)}}
\]

where cps is counts per second. All measures were performed twice for both right and left ventricles.

In the subset of patients with RV and LV wall thickness measurements available, partial volume recovery coefficients (RC) were calculated by convolution with a gaussian kernel representing the reconstructed PET image resolution. Partial volume recovery-corrected FDG activity values were then calculated as SUV/RC.

\section*{Analyses}

The primary objective of this study was to determine the relationship between RVEF and RV glucose uptake, estimated using RV FDG SUV as well as the ratio of mean RV SUV/mean LV SUV. The mean RV SUV/peak LV SUV (in regions confirmed to have normal perfusion) was also determined in order to correct for any variability in FDG uptake in the LV due to previous scar. Secondary objectives included: the determination of the relationship between RV FDG uptake with RV size, LVEF and LV size; as well as evaluating the relationship between RV FDG uptake and estimates of pulmonary pressures.

\section*{Statistical Analysis}

All values are expressed as mean ± SD for normally distributed data and medians with first and third quartiles for non-normally distributed data. Pearson correlation and simple linear regression analyses were used to relate LVEF and markers of metabolism.
Correlation coefficients were compared using a Z-test after Fisher Z-transforms. Comparisons between the tertiles of RV FDG groups were made with t-tests for unequal variances and Chi-squared tests where appropriate. All p-values were two-sided and a p value of less than 0.05 was considered statistically significant. All statistical analyses were performed using STATA software, version 9.2 (Stata corp., College Station, Texas).

Results

Baseline Characteristics

Table 1 demonstrates the characteristics of the study population. All patients had advanced HF with a mean LVEF of 21% and a mean RVEF of 35%. Seventy-five % of patients were NYHA class III. A total of 45% of the subjects had non-ischemic cardiomyopathy. Moderate pulmonary hypertension was common, with a median RVSP of 52 mmHg (minimum 25 mmHg, maximum 81 mmHg). The average right ventricular wall thickness was 0.45± 0.074 cm (median 0.45 cm, Q1,Q3: 0.42, 0.5 cm).

RV function and FDG Uptake

There was a statistically significant relationship between increased FDG uptake in the RV and decreases in RVEF (r=-0.32, p=0.008) (Figures 1 and 2).

FDG uptake in the RV relative to the LV was represented as i) the ratio of RV SUV:LV SUV, for the entire LV myocardium and ii) RV SUV: LV SUV limited to uptake in the LV free wall, given the high proportion of subjects with a baseline left bundle branch block. The normal RV: whole LV standardized uptake value (SUV) in healthy volunteers without cardiomyopathy ranges from 0.26-0.31 according to data obtained in our laboratory. The relationship between RVEF and relative RV:LV FDG uptake was
also significant regardless of whether the whole LV was used \((r=-0.40, p<0.01)\) or isolated to LV lateral wall FDG uptake alone \((r=-0.43, p<0.001)\) (Figure 3). The significance of the RV/LV ratio was due to increased RV FDG uptake as there was no correlation between LV glucose uptake and RV function or size.

Since FDG uptake may be variable particularly in ischemic cardiomyopathy, we evaluated the RV uptake/LV peak uptake (in segments confirmed to have normal perfusion). Similar significant relationships were observed as with the ratio of the mean SUVs. To further evaluate the effect of potential variability in FDG uptake in the LV of patients with ischemic cardiomyopathy, the data were stratified by a history of ischemic vs. nonischemic cardiomyopathy. Both groups continued to display a relationship between increased RV/LV FDG uptake and decreases in RVEF: \((r=-0.37, p=0.04)\) for nonischemic cardiomyopathy, and \(r=-0.47, p=0.004\) for those with ischemic cardiomyopathy. There was also no change between absolute RV FDG uptake and RVEF in this stratified analysis \((r=-0.33, p=0.05)\) for nonischemic cardiomyopathy and \(r=-0.33, p=0.04\) for ischemic cardiomyopathy). In contrast, LVEF was not related to RV FDG uptake \((r=0.06, p=0.65)\) nor the RV:LV FDG uptake ratio \((r=-0.09, p=0.49)\).

When compared to subjects in the first and second tertile of RV SUV values, subjects in the third tertile had significantly lower RVEF \((25\pm11\%\text{ vs. } 36\pm25\%, p=<0.001)\) than the other two tertiles (Table 1).

**Partial Volume Effect on the RV FDG uptake vs RV function relationships**

In order to consider the effect of partial volume on FDG measurements due to differences in RV wall thickness, we evaluated the relationships or RV SUV parameters to RVEF in 26 patients who had echocardiography within 60 days of FDG PET. Table 2 shows the relationships for the entire data set and the subset who underwent
echocardiography without and with partial volume correction of FDG data. After correction for partial volume, the correlation coefficients for the relationship between RV FDG SUV parameters and RV function remained significant (p ≤0.03 for all 3 relationships) (Figure 4); and were numerically greater than values from the original dataset (Table 2). Statistical comparisons between correlation coefficients were not significantly different, although there was a trend for significant improvement in the relationship between RVEF vs RV/wholeLV FDG SUV data when partial volume correction was applied (p=0.095).

**Pulmonary Hypertension and RV Uptake**

The majority of patients in this study had some degree of pulmonary venous hypertension, with a median RVSP or (systolic pulmonary artery pressure if available) at baseline of 52 mmHg. Worsening pulmonary hypertension was weakly related to increased RV FDG uptake (r=0.36, p=0.04) but not LV FDG uptake (r=0.02, p=0.91) nor was it related to the ratio of whole RV:LV uptake(r=0.05, p=0.85) (Figure 5). When partial volume correction was considered in a smaller cohort (n=16 where both RVSP and RV wall thickness could be determined), the correlation coefficient was not significantly different because the relationship was no longer statistically significant. (r=0.19, p=0.43 for subset without partial volume correction and r=0.05, p=0.85 for subset with partial volume correction) (Table 2).

**Reproducibility of RV FDG Image Analysis**

To evaluate for intra-observer test reproducibility, a subset of scans from 30% of the total population were re-read by the same image analyst (MA) approximately six
months later. The intra-class correlation for the whole LV uptake was 0.94 (0.84, 0.98, p<0.0001) and 0.99 (0.97, 0.99, p<0.001) for the whole RV.

To evaluate for inter-observer test reproducibility, the same subset of scans was read by two independent image analysts (MA and MZ). The inter-class correlation was 0.99 (0.97, 0.99, p<0.0001) for the whole LV uptake and 0.95 (0.87, 0.98, p<0.001) for the whole RV.

**Discussion**

This study demonstrates that RV glucose uptake increases with decreasing RVEF. The ratio of uptake in the RV versus the LV increased with progressive RV dysfunction, independent of a history of ischemia and baseline LV glucose metabolism. Finally, in a cohort of patients with known LV failure, the severity of pulmonary hypertension was weakly correlated to RV glucose metabolism. Importantly, RV FDG SUV parameters and RVEF relationships were not adversely affected by partial volume recovery correction.

Alterations in myocardial substrate metabolism have been implicated in the pathogenesis of HF and contractile dysfunction. Animal models of left HF have demonstrated that the progression from cardiac hypertrophy to ventricular dysfunction is associated with a decrease in the expression of genes encoding for fatty acid oxidation and a shift in metabolism with glucose becoming the primary energy substrate. A similar shift in metabolism has been demonstrated in patients with idiopathic dilated cardiomyopathy using PET imaging. However it has also been proposed that the reliance of the myocardium on glucose may produce a relatively energy-deficient state that over a long time could result in decreased contractile performance. It is possible that although glucose metabolism may be beneficial in early HF, over the long term this
may lead to maladaptive myocardial responses contributing to the development of worsening HF. An understanding of the alterations and clinical significance of myocardial metabolism in heart failure is an important initial step in developing strategies to target metabolic modulation as a potential therapy for patients with HF.

The evaluation of RV failure is an important goal in the management of pulmonary arterial hypertension (PAH); although few studies have examined RV metabolism in detail. Increased RV free wall myocardial glucose utilization has been demonstrated in rat models of PAH. Oikawa and colleagues demonstrated that RV FDG accumulation increased in accordance with the severity of pulmonary vascular resistance in patients with PAH. In contrast to these results, a similar study reported by Kluge et al. suggested that in patients with PAH, the increased ratio of right-left FDG accumulation with increased pulmonary vascular resistance, was not related to increased RV FDG, but a corresponding decreased LV FDG accumulation. Importantly, these authors did identify a significant linear relationship between RV FDG uptake and increasing Tei index, an echocardiographic marker of progressive RV dysfunction.

Consistent with the work of Kluge and colleagues, the current study also demonstrated a linear relationship between RV function and RV FDG uptake, and a weak but statistically significant relationship between worsening pulmonary pressures and increased RV FDG. However, in contrast to Kluge et al., we did not identify any relationship between RV systolic pressures and changes in LV FDG uptake. This difference may be explained by the fact that in the study by Kluge et al., all subjects had normal LV systolic function, while in the current study all subjects had significant LV dysfunction. It is possible that differences in: i) methodology including glucose loading protocols (with or without acipamox) and ii) patient populations may explain the heterogeneity of the results regarding RV FDG and pulmonary vascular resistance. For
example, the presence of RV infarction could potentially contribute to decreased RV FDG uptake. However, the relationship between RVEF and RV FDG metabolism was similar when the data were stratified by ischemic and nonischemic cardiomyopathy. In addition, the findings were not altered when corrected for the peak LV SUV in normally perfused segments.

Finally, some heterogeneity may be due to the potential time delay between PET scan and echocardiographic assessment of pulmonary pressures, due to underlying lability in this measurement. Further studies are needed to determine whether the increased RV FDG accumulation promotes or results from progressive RV failure.

Some methodological limitations require discussion. It is known that FDG uptake is only a surrogate for true glucose metabolism; thus it is possible that the true difference in glucose metabolism between the two ventricles or as it relates to right ventricular function or afterload might be missed or underestimated. Nevertheless, FDG uptake does provide an in vivo means to probe alterations in glucose metabolism in the human RV. While our inter- and intra-observer variability were excellent, data on the reproducibility of RV FDG measurements are limited. Future studies should consider defining its reliability to further characterize potential utility in measuring RV metabolism. RV EF and volumes were measured with planar ERVG imaging. Although planar radionuclide ventriculography is accurate and reproducible for the LV, the technique is less robust for the RV. This methodology may also contribute to some underestimation of the correlation between RVEF and RV metabolism. Cardiac MRI is often considered the best technique to quantify RV volumes and size. However, in this population, 25% of the patients had either a pacemaker or implantable cardioverter defibrillator—thus making a significant proportion of the study population ineligible for
an MRI. Measurements of RV hypertrophy were estimated by echocardiographic analysis, which also has limitations due to poorer resolution compared to MRI.

Nevertheless, given the potential impact of the partial volume effect due to differences in RV wall thickness, we evaluated the relationships of RV SUV parameters to RVEF in a subset of patients. After correction for partial volume, correlation coefficients were either similar or numerically increased when compared to the data without partial volume correction. This has two important implications: i) the relationships of RV FDG SUV parameters and RVEF are likely valid observations and ii) the partial volume correction is important when measuring and interpreting glucose utilization in the RV.

The correlation coefficients for the relationship of RV SUV parameters to RVSP numerically decreased in the echo subset and after partial volume correction. These relationships were no longer significant (with or without partial volume correction). This is likely due to loss of statistical confidence from a much smaller sample size. As such, conclusions regarding RVSP and RV FDG relationships must be made with caution. Whether the relationship is partly driven by partial volume effect (in contrast the RVEF vs. RV FDG parameters which was not adversely affected by partial volume correction) will require evaluation in larger studies.

Many of the patients in the current study were evaluated on the Siemens/CTI ECAT ART PET system which has inferior resolution to most current PET/CT systems. This may have contributed to some of the variability observed and further emphasizes the importance of partial volume correction.

Data on invasive pulmonary pressures were not available in all subjects, thus limiting the robustness of conclusions regarding FDG and PA pressure relationships. Although there is good correlation between invasively measured RV systolic pressure and echocardiographic estimates;\(^42\) the relationship between hemodynamics and RV
metabolism in patients with left heart failure needs to be confirmed in future studies involving an invasive assessment of pulmonary pressures.

The LV SUV values were somewhat lower than previously reported by Morita et al.\textsuperscript{43} This likely reflects the nature of our population, which includes patients with ischemic heart disease and prior infarction as well as patients with diabetes. In addition, 75% of the patient cohort in the current study had a baseline left bundle branch block, which can also decrease FDG uptake. Importantly the RV/LV ratios are comparable to the literature and are the primary focus of our findings.

Finally experiment-wide Type I error was not controlled by any formal procedure, and may therefore be inflated due to multiple testing.

Right heart failure worsens prognosis in patients with cardiopulmonary disease. There is a need for novel management strategies and patient specific markers to identify and treat patients at risk. Accordingly, there are two clinically important findings from this study. Firstly, RV dysfunction appears to be associated with metabolic changes in substrate utilization. Whether this is an adaptive or maladaptive response in the pathophysiology of right heart failure requires further study. Either way, the relationships observed support the need for investigation of FDG PET as a novel biomarker that could be a therapeutic target in the treatment of right heart failure, whereby determining RV FDG uptake and/or monitoring its response may help optimize treatment to improve RV function and outcomes. Secondly, partial volume correction for PET is important when measuring and interpreting glucose utilization as a potential biomarker of RV metabolism and needs to be consider in future studies.

**Conclusions.** RV FDG accumulation increases with progressive RV dysfunction in a cohort of patients with left heart failure. The findings support the need for further
research to confirm the utility and prognostic significance of RV FDG PET imaging. While partial volume effects may be problematic in the RV, when a correction was applied the correlations observed with RV function did not appear to be adversely affected and at least one parameter trended for improvement. This supports the validity of the RVEF versus RV FDG parameter observations and the importance of partial volume correction in analysis of RV metabolism using PET.

Whether a shift towards glucose metabolism in the failing RV has potential long-term significance as a marker that could influence therapy for RV dysfunction and failure requires further evaluation in prospective studies. Such studies are now ongoing.
Sources of Funding

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Disclosures

Dr. Beanlands is a consultant for Lantheus Medical Imaging and DraxImage and has received research funding from MDS Nordion and GE for unrelated projects. Dr. deKemp is a consultant for DraxImage for unrelated projects.
References


Table 1. Baseline Characteristics of Study Cohort

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>(total n=68)</th>
<th>T1 or T2 (n=46)</th>
<th>T3 (n=22)</th>
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<tbody>
<tr>
<td>median age (Q1, 3)</td>
<td>69 years (60, 76)</td>
<td>65± 12</td>
<td>67 ±11</td>
</tr>
<tr>
<td>Female sex</td>
<td>9 (13%)</td>
<td>16%</td>
<td>5%</td>
</tr>
<tr>
<td>Ischemic CM</td>
<td>37 (55%)</td>
<td>50%</td>
<td>67%</td>
</tr>
<tr>
<td>NYHA class III</td>
<td>51 (75%)</td>
<td>72%</td>
<td>80%</td>
</tr>
<tr>
<td>Left bundle branch block</td>
<td>48 (71%)</td>
<td>75%</td>
<td>62%</td>
</tr>
<tr>
<td>History of hypertension</td>
<td>31 (46%)</td>
<td>50%</td>
<td>38%</td>
</tr>
<tr>
<td>Current smoker</td>
<td>13 (19%)</td>
<td>23%</td>
<td>10%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>30 (45%)</td>
<td>40%</td>
<td>62%</td>
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<tr>
<td>History of revascularization</td>
<td>37 (55%)</td>
<td>50%</td>
<td>48%</td>
</tr>
<tr>
<td>Therapies</td>
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</tr>
<tr>
<td>Beta blockers</td>
<td>64 (94%)</td>
<td>97%</td>
<td>86%</td>
</tr>
<tr>
<td>ACE I or ARB</td>
<td>65 (95%)</td>
<td>95%</td>
<td>99%</td>
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<td>Diuretics</td>
<td>62 (92%)</td>
<td>89%</td>
<td>95%</td>
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<tr>
<td>Digoxin</td>
<td>29 (42%)</td>
<td>38%</td>
<td>50%</td>
</tr>
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<td>Ventricular Size/function</td>
<td>Median</td>
<td></td>
<td></td>
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<tr>
<td>(Q1, Q3)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>RVEF</td>
<td>35 % (23, 43)</td>
<td>36± 11 %</td>
<td>25 ±11 % *</td>
</tr>
<tr>
<td>LVEF</td>
<td>21 % (16, 23 ±9)</td>
<td>19 ± 6%</td>
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</tr>
<tr>
<td>Parameter</td>
<td>Value 1</td>
<td>Value 2</td>
<td>Value 3</td>
</tr>
<tr>
<td>--------------------</td>
<td>---------</td>
<td>---------</td>
<td>---------</td>
</tr>
<tr>
<td>LVESV</td>
<td>226 ml</td>
<td>237 ±109</td>
<td>247 ±73</td>
</tr>
<tr>
<td>LVEDV</td>
<td>285 ml</td>
<td>307 ±116</td>
<td>310 ±82</td>
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<tr>
<td>RVSP</td>
<td>50 mmHg</td>
<td>49 ±11</td>
<td>52±16</td>
</tr>
<tr>
<td>Metabolic parameters</td>
<td>Median (Q1, Q3)</td>
<td>Median (Q1, Q3)</td>
<td>Median (Q1, Q3)</td>
</tr>
<tr>
<td>RV SUV</td>
<td>1.7 (1.2, 2.4)</td>
<td>1.7± 0.9</td>
<td>2.2± 1.9*</td>
</tr>
<tr>
<td>LV SUV</td>
<td>2.9 (2.1, 3.6)</td>
<td>2.7 ±1.0</td>
<td>2.5 ±1.0</td>
</tr>
<tr>
<td>RV SUV/LV SUV ratio</td>
<td>0.60 (0.51, 0.75)</td>
<td>0.52 ±0.1</td>
<td>0.87 ±0.23*</td>
</tr>
</tbody>
</table>

* denotes a significant difference between tertile 1 / 2 and tertile 3 (p<0.05)
Table 2. Correlations for RVEF and RV SUV parameters

<table>
<thead>
<tr>
<th>Correlation</th>
<th>Column 1 (Entire Data Set – Original Data (n=68))</th>
<th>Column 2 (Echo Subset – Original Data (n=26)*</th>
<th>Column 3 (Echo Subset – partial volume corrected values (n=26)*)</th>
<th>P value for comparison (columns 1 and 3)</th>
<th>P value for comparison (columns 2 and 3)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>RVEF with</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RV SUV uptake</td>
<td>$r = -0.32$, $p=0.008$</td>
<td>$r = -0.22$, $p=0.3$</td>
<td>$r= -0.44$, $p=0.03$</td>
<td>0.57</td>
<td>0.41</td>
</tr>
<tr>
<td>RV/whole LV SUV</td>
<td>$r= -0.40$, $p&lt;0.01$</td>
<td>$r= -0.62$, $p=0.001$</td>
<td>$r= -0.68$, $p=0.002$</td>
<td>0.095</td>
<td>0.68</td>
</tr>
<tr>
<td>RV/LV lateral wall SUV</td>
<td>$r = -0.43$, $p&lt;0.001$</td>
<td>$r = -0.44$, $p=0.03$</td>
<td>$r = -0.59$, $p=0.003$</td>
<td>0.40</td>
<td>0.55</td>
</tr>
<tr>
<td><strong>RVSP with</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RV SUV uptake</td>
<td>$r = 0.37$, $p=0.04$</td>
<td>$r = 0.19$, $p=0.43$</td>
<td></td>
<td>0.27</td>
<td>0.63</td>
</tr>
</tbody>
</table>
Figure Legends

Figure 1. Examples of increased RV/LV FDG uptake in right ventricle in two patients with ischemic cardiomyopathy. Short axis images of myocardium demonstrate increased FDG uptake in the RV free wall. Patient #1 is a 68 year old male with a previous anteroseptal myocardial infarction. His LVEF is 20% with an RVEF of 30%. The RV SUV is 1.9, with a whole LV SUV of 2.55 and an RV/LV ratio of 0.75. Patient #2 is a 59 year old male with previous CABG, LVEF of 18%, and RVEF of 37%. The RV SUV is 1.7 with a whole LV SUV of 2.58 and an RV/LV ratio of 0.66.

Figure 2. Pearson correlation between RVEF and: a) RV FDG SUV (r=-0.32, p=0.008); b) RV FDG SUV in those in the third tertile only. (r=-0.2, p=0.37)

Figure 3. Pearson correlation between RVEF and the ratio of RV FDG SUV/whole LV SUV (r=-0.40, p=<0.001) and RVEF and the ratio of RV FDG SUV/LV lateral wall SUV (r =-0.43, p=<0.001)

Figure 4. a) Pearson correlation between RVEF and a) RV FDG SUV/RC (r=-0.44, p=0.03); b) the ratio of RV FDG SUV/RC : whole LV SUV/RC (r=-0.68, p=0.0002) and c) the ratio of RV FDG SUV/RC : LV lateral wall SUV/RC (r =-0.59, p=0.003)

Figure 5. Pearson correlation between RV systolic pressure (or peak systolic pulmonary pressure) and RV FDG SUV. (r=0.36, p=0.04)
The Relationship Between Right Ventricular Function and Increased Right Ventricular $^{18}\text{F}$ Fluorodeoxyglucose Accumulation in Patients with Heart Failure
Lisa M. Mielniczuk, David Birnie, Maria C. Ziadi, Robert A. deKemp, Jean N. DaSilva, Ian Burwash, Anthony T. Tang, Ross A. Davies, Haissam Haddad, Ann Guo, May Aung, Kathryn Williams, Heikki Ukkonen and Rob S.B. Beanlands

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