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ORIGINAL ARTICLE

Clinical significance of quantitative assessment of right ventricular glucose metabolism in patients with heart failure with reduced ejection fraction

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Abstract

Purpose Dynamic ^{18}F-fluorodeoxyglucose (FDG) PET can be used to quantitatively assess the rate of myocardial glucose uptake (MRGlu). The aim of this study was to evaluate the clinical significance and prognostic value of right ventricular (RV) MRGlu in patients with coronary artery disease and heart failure with reduced ejection fraction.

Methods Patients with left ventricular ejection fraction (LVEF) ≤ 40% were consecutively enrolled for FDG PET between November 2012 and May 2017. Global LV and RV MRGlu (μmol/min/100 g) were analyzed. Outcome events were independently assessed using electronic medical records to determine hospitalization for revascularization, new-onset ischemic events, heart failure, cardiovascular, and all-cause death. Differences between LV and RV MRGlu and associations with clinical characteristics and echocardiographic data were evaluated. Associations among FDG PET findings and outcomes were analyzed using Kaplan-Meier survival analysis.

Results Seventy-five patients (mean age 62.2 ± 12.7 years, male 85.3%, LVEF 19.3 ± 8.6%) were included for analysis. The mean glucose utilization ratio of RV-to-LV (RV/LV MRGlu) was 89.5 ± 264.9% ($r = 0.77$, $p < 0.001$). Positive correlations between RV MRGlu and maximal tricuspid regurgitation peak gradient ($r = 0.28$, $p = 0.033$) and peak tricuspid regurgitation jet velocity ($r = 0.29$, $p = 0.021$) were noted. LVEF was positively correlated with LV MRGlu ($r = 0.27$, $p = 0.018$), but negatively correlated with end-diastolic volume ($r = -0.37$, $p = 0.001$), end-systolic volume ($r = -0.54$, $p < 0.001$), and RV/LV MRGlu ($r = -0.40$, $p < 0.001$). However, RV MRGlu was not well correlated with LVEF. Forty-three patients received revascularization procedures after FDG PET, and 13 patients died in a mean follow-up period of 496 ± 453 days (1–1788 days), including nine cardiovascular deaths. Higher RV and LV MRGlu values, LVEF ≤ 16% and LV end-diastolic volume ≥ 209 ml of gated-PET were associated with poor overall survival and cardiac outcomes.

Conclusions In patients with coronary artery disease and ischemic cardiomyopathy, RV glucose utilization was positively correlated with RV pressure overload, but not LVEF. Global LV and RV MRGlu, LVEF, and LV end-diastolic volume showed significant prognostic value.

Keywords Heart failure · ^{18}F-fluorodeoxyglucose · Positron emission tomography · Rate of myocardial glucose uptake · Right ventricle

This article is part of the Topical Collection on Cardiology

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Introduction

Heart failure (HF) is associated with increased morbidity and mortality, decreased quality of life, and significant economic burden [1–5], and it can be categorized into subgroups according to left ventricular (LV) ejection fraction (EF). In patients with heart failure with reduced EF (HFrEF), the LVEF is ≤

40% with a larger end-diastolic volume relative to the stroke volume [6]. In Taiwan, the prevalence of heart failure is around 6%, and the annual cost of solely HF-related hospitalizations is as high as 2388 US dollars per patient [7]. Real-world data from the Taiwan HFrEF registry show low in-hospital mortality but high re-hospitalization rates compared to other countries; it also revealed suboptimal treatment adherence to guidelines during follow-up, suggesting that there is room to improve patient care [8, 9].

Dynamic positron emission tomography (PET) is a well-established method for quantification that has been successfully applied to neurologic, cardiac, and oncologic research, and it has also been used in drug development and precision medicine [10]. With regard to cardiology, the rate of myocardial glucose uptake (MRGlu) obtained by ^{18}F-fluorodeoxyglucose (FDG) cardiac PET can be used to quantify glucose metabolism and determine myocardial viability. Most dynamic FDG cardiac PET studies have focused on glucose utilization in the left ventricle rather than the right ventricle, and the latter were mainly for patients with pulmonary hypertension. In pulmonary hypertension, the right ventricular (RV)-to-LV MRGlu ratio increases as the disease progresses [11], either due to a significant reduction in LV glucose utilization or a net increase in RV metabolism [11, 12]. Elevated RV MRGlu implies RV impairment and RV pressure overload, and is a poor prognostic parameter in pulmonary hypertension [11, 12].

RV dysfunction has also been shown to be a potent indicator of poor outcomes for patients with left-sided heart failure, especially for those with an extremely low LVEF [13, 14]. Therefore, the aim of the study was to investigate RV metabolic alterations in patients with significant LV dysfunction. We hypothesized that RV glucose utilization as assessed using dynamic FDG PET would be linked to RV pressure overload and possibly correlated with LVEF. We also investigated the clinical significance and prognostic value of RV MRGlu in patients with coronary artery disease and HFrEF.

Material and methods

Patient population

This study was approved by the Institutional Review Board of Far Eastern Memorial Hospital (FEMH-IRB-101037-F), and all of the enrolled subjects provided written informed consent before inclusion. All procedures performed were in accordance with the updated guidelines and regulations. The study included patients with a clinical diagnosis of suspected coronary artery disease and heart failure who were referred by experienced cardiologists before coronary interventions or heart transplantations for dynamic FDG cardiac PET at Far Eastern Memorial Hospital between November 2012 and May 2017. All of the included patients had a LVEF ≤ 40% in either ultrasound or electrocardiogram-gated ^{201}thallium myocardial perfusion imaging with single-photon emission computed tomography (SPECT). All of the enrolled patients were New York Heart Association class II or III, and had been on stable pharmacotherapy for at least 4 weeks. Patients with significant valvular heart disease, idiopathic-dilated cardiomyopathy, hypertrophic cardiomyopathy, life expectancy less than 3 months, claustrophobia or a unstable condition preventing dynamic scanning, and those who were pregnant or breast-feeding were excluded (ClinicalTrials.gov: NCT02697669). Only the first dynamic FDG PET of each subject was included for analysis, and PET data with non-visualized RV uptake were also excluded.

Demographic, medication, laboratory test, electrocardiography, history of coronary angiography and/or bypass surgery, and prior echocardiography and myocardial perfusion imaging data were collected from the patients' statements and electronic medical records.

Doppler echocardiographic parameters

Doppler echocardiographic data including LVEF, left atrial dimension, LV end-diastolic and end-systolic dimensions, maximal tricuspid regurgitation peak gradient (TRmaxPG), and peak tricuspid regurgitation jet velocity (TRVmax) were collected. The status of right heart pressure could be inferred by TRmaxPG and TRVmax, and pulmonary hypertension was defined as resting mean pulmonary arterial pressure (mPAP) ≥ 25 mmHg [15].

According to recommendations from the 6th World Symposium on Pulmonary Hypertension, mPAP in normal subjects is around 14.0 ± 3.3 mmHg [15], and two standard deviations above the mean value, mPAP > 20 mmHg, is the threshold for abnormality [15]. MPAP can be estimated using Doppler echocardiography with the following formula: $mPAP = 0.61 \times SPAP + 2$ [16, 17], where SPAP is systolic pulmonary arterial pressure, and is calculated as TRmaxPG + right atrial pressure (RAP) or $4 \times TRVmax(m/s)^2 + RAP$ [16, 18]; RAP is traditionally assigned as 3, 8, or 15 according to the maximal inferior vena cava diameter and collapsibility index [19, 20].

Dynamic FDG cardiac PET protocol

The enrolled patients fasted for at least 6 h before undergoing dynamic FDG cardiac PET (GE Discovery VCT; GE Medical Systems, Milwaukee, WI, USA), and those with diabetes also abstained from anti-diabetic medications. The baseline blood sugar level (BS, mg/dl) was measured in all patients. Non-diabetic patients received 50 g of oral glucose, while diabetic patients received 20 g of oral glucose and 2 units of regular insulin intravenously if the baseline BS was < 150 mg/dl, or

4 units of regular insulin intravenously if the baseline BS was ≥ 150 mg/dl. The goal was to keep the BS < 140 mg/dl before dynamic FDG PET acquisition, and therefore we also used additional intravenous insulin injections when necessary.

Three hundred seventy megabecquerel (10 mCi) of FDG was intravenously administered over 2 min, and the dynamic scan was simultaneously initiated. The dynamic FDG PET data was collected for 50 min with list mode and 32 frames (12 × 10, 6 × 20, 6 × 60, and 8 × 300 s), and electrocardiogram-gating was performed for the last 20 min. All images were reconstructed using an ordered-subsets expectation maximization 20-subset three-iteration method, with an in-plane image resolution of 6 mm full width at half-maximum. The reconstruction matrix was 128 × 128 pixels [21].

Quantification of myocardial glucose utilization

The FDG cardiac PET scans were read by two experienced nuclear medicine physicians who were unaware of the clinical data, and also quantitatively analyzed using PMOD 3.7 software (PMOD Technologies, Zurich, Switzerland). To generate blood pool time-activity curves, we carefully determined the volumes of interest of LV and RV cavities. Using epicardium/endocardium outlines in three projections (short axis, vertical long axis, and horizontal long axis), volumes of interest were semi-automatically drawn with manual adjustments for the LV cavity, and then manually drawn for the right ventricle slice by slice in the standard short-axis position. Time-activity curves were fitted to a Patlak kinetic model, and then MRGlu (μmol/min/100 g) was measured using a lumped constant of 0.67 [12, 22]; where MRGlu = (Patlak slope × plasma glucose concentration)/lumped constant [21]. The LV and RV MRGlu values, LVEF, LV end-systolic, and end-diastolic volumes were attained for further analysis. Figure 1 is a representative example of a patient with HFrEF with RV FDG hypermetabolism.

Follow-up

We followed the clinical information via electronic medical records for at least 6 months after the index cardiac PET study. In addition to all-cause mortality and hospitalizations, major adverse cardiac events include cardiovascular death, acute myocardial infarction, coronary intervention, device implantation, cardiovascular surgery, heart transplantation, and hospitalization for acute heart failure. Survival was calculated from the date of FDG cardiac PET to the date of cardiac death (including heart transplantation) or all-cause death.

Statistical analysis

Numerical variables were expressed as mean ± standard deviation (SD), and categorical variables were expressed as frequency with percentage (%). Comparisons were analyzed using Fisher's exact test for categorical variables, *T* test for parametric numerical data, and Mann-Whitney *U* test for non-parametric numerical data. Correlations between two variables were determined using Pearson's correlation if the data were parametric, and Spearman's rank correlation if the data were nonparametric. Linear regression was used for regression analysis. To estimate optimal cutoff values of FDG PET parameters to predict the prognosis, we used receiver operating curves and Youden's index to achieve maximum sensitivity and specificity. We then used the Kaplan-Meier method and log-rank test to generate the survival curves of each endpoint. Data were analyzed using SPSS software version 24.0 (IBM Corp., Armonk, New York, USA). All p values were two-tailed, and a value of $p < 0.05$ was considered to be statistically significant.

Results

Patient characteristics

A total of 75 patients were included in this study, and their clinical characteristics are shown in Table 1. The mean age was 62.2 ± 12.7 years; 85.3% ($n = 64$) of the study cohort was male, and more than half ($n = 41$, 53.7%) of the patients had diabetes. The mean hemoglobin A1c level was 7.7 ± 2.0% in the diabetic patients and 6.0 ± 0.7% in the non-diabetic patients, indicating poor long-term glucose control in the study cohort, and especially in the diabetic group ($p = 0.001$). The mean TRmaxPG and TRVmax were 32.5 ± 16.1 mmHg and 277.4 ± 69.7 cm/s, respectively, resulting in calculated mPAP no less than 22.7 mmHg, and suggesting RV pressure overload, but not definitely pulmonary hypertension, in the included patients.

Dynamic FDG cardiac PET

The mean fasting BS was 119.8 ± 43.5 mg/dl and was higher in the diabetic group than the non-diabetic group (134.6 ± 48.7 mg/dl in 41 diabetic patients, versus 102.0 ± 27.8 mg/dl in 34 non-diabetic patients; $p = 0.018$). A mean of 30.3 ± 19.8 g of oral glucose was loaded, and 3.1 ± 2.1 IU of intravenous insulin was administered. The mean BS at FDG injection was 138.8 ± 31.3 mg/dl, and there was no significant difference between the diabetic and non-diabetic groups (133.3 ± 30.7 and 145.5 ± 31.2, respectively, $p = 0.92$). The dynamic FDG PET parameters including MRGlu values, their derivatives, LVEF, and LV volumetric data are listed in Table 2. There were no significant differences between the diabetic and non-diabetic groups.

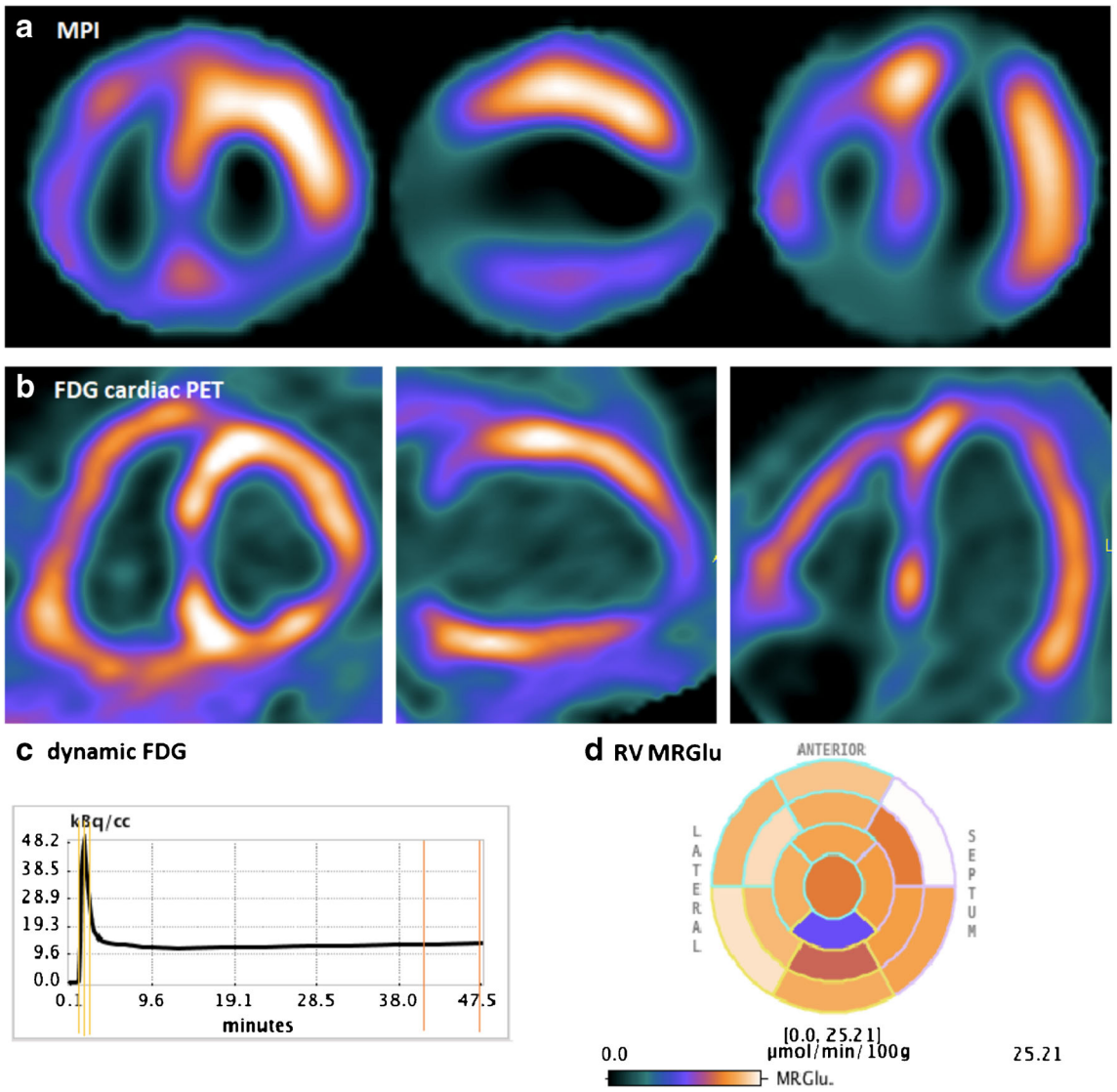

Fig. 1 1Representative images. ^{201}thallium MPI (**a**) and FDG PET (**b**) in 3-axis showed hibernating LV myocardium in the apex, inferior and inferoseptal walls, and obvious RV uptake. Dynamic FDG PET with Patlak kinetic analysis (**c**) of RV MRGlu (**d**) estimation were displayed

Correlations between MRGlu values and other parameters

RV MRGlu was positively correlated with LV MRGlu ($r = 0.77$, $p < 0.001$), and the mean RV-to-LV MRGlu ratio (RV/LV MRGlu) was 89.5 ± 264.9%. Other correlations between MRGlu values and LV volumetric data are listed in Table 3. LVEF was positively correlated with LV MRGlu ($r = 0.27$, $p = 0.018$) and negatively correlated with LV end-diastolic volume ($r = -0.37$, $p = 0.001$), end-systolic volume ($r = -0.54$, $p < 0.001$), and RV/LV MRGlu ($r = -0.40$, $p < 0.001$). Nonetheless, RV MRGlu was not significantly correlated with LVEF. Forty-one patients (54.7%) in the study cohort had diabetes mellitus. There were positive correlations between RV MRGlu and TRmaxPG ($r = 0.28$, $p = 0.033$) and TRVmax ($r = 0.29$, $p = 0.021$), implying that increased RV MRGlu was associated with RV pressure overload.

Survival analysis

We tracked the electronic medical records of each subject for at least 6 months until November 2017. The median follow-up period was 368 days (range, 1 to 1788 days). After FDG cardiac PET, 43 patients (43/75, 57.3%) received revascularization procedures. Thirteen patients (13/75, 17.3%) died during the follow-up period, of whom nine (9/75, 12.0%) died of cardiovascular causes.

Table 1 Characteristics of the enrolled patients ($n = 75$)

Clinical variables	
Age (years)	62.2 ± 12.7
Male gender	64 (85.3%)
Comorbidity	
Hypertension	55 (73.3%)
Diabetes	41 (54.7%)
Hyperlipidemia	40 (53.3%)
Smoking	45 (60.0%)
Current smoker	18
Ex-smoker	27
Prior cardiac events	
Previous myocardial infarction	29 (38.7%)
Previous intervention	53 (70.7%)
Medications	
Insulin	7 (9.3%)
Sulfonylurea	15 (20.0%)
Biguanide	12 (16.0%)
DPP4i	14 (18.7%)
Alpha-glucosidase inhibitor	4 (5.3%)
Statin	47 (62.7%)
Beta blocker	56 (74.7%)
Calcium channel blocker	13 (17.3%)
ACEi	21 (28.0%)
Angiotensin receptor blocker	30 (40.0%)
Hemoglobin A1c (%) ($n = 59$)	7.0 ± 1.8
MPI LVEF (%) ($n = 70$)	25.6 ± 10.0
Echocardiography ($n = 72$)	
Left atrium (mm)	44.0 ± 8.1
LV end-diastolic dimension (mm)	57.8 ± 10.2
LV end-systolic dimension (mm)	47.8 ± 12.0
LVEF (M-mode) (%)	35.9 ± 14.5
TRmaxPG (mmHg)	32.5 ± 16.1
TRVmax (cm/s)	277.4 ± 69.7

DPP4i, Dipeptidyl peptidase-4 inhibitor; *ACEi*, angiotensin-converting-enzyme inhibitor; *MPI*, myocardial perfusion imaging

The cutoff values of MRGlu (μmol/min/100 g) calculated using receiver operating curves were 25.18 for all-cause mortality and 35.06 for cardiovascular death in the right ventricle, and 39.06 for both endpoints in the left ventricle. Higher values of both RV and LV MRGlu were associated with worse survival, irrespective of overall survival or cardiovascular-specific outcomes (Fig. 2).

With regard to overall survival, the patients with RV MRGlu ≥ 25.18 μmol/min/100 g (log-rank = 7.68, $p = 0.006$), LV MRGlu ≥ 39.06 μmol/min/100 g (log-rank = 4.34, $p = 0.037$), LVEF ≤ 16% (log-rank = 10.32, $p = 0.001$), and LV end-diastolic volume ≥ 209 ml (log-rank = 3.98, $p = 0.046$) were more likely to have a poor outcome. However, LV end-systolic volume and RV/LV MRGlu did not provide incremental prognostic value. With regard to cardiovascular mortality, those with RV MRGlu ≥ 35.06 μmol/min/100 g (log-rank = 6.96, $p = 0.008$), LV MRGlu ≥ 39.06 μmol/min/100 g (log-rank = 4.94, $p = 0.026$), LVEF ≤ 16% (log-rank = 11.70, $p = 0.001$), LV end-diastolic volume ≥ 209 ml (log-rank = 4.00, $p = 0.045$), and LV end-systolic volume ≥ 182 ml (log-rank = 5.63, $p = 0.018$) had a significantly worse prognosis. Nonetheless, RV/LV MRGlu did not have any impact on cardiovascular survival.

Table 2 Data from dynamic FDG cardiac PET ($n = 75$)

Variables	
Fasting blood glucose (mg/dl)	119.8 ± 43.5
Blood glucose at FDG injection (mg/dl)	138.8 ± 31.3
Insulin injected (IU)	3.1 ± 2.1
LV MRGlu (μmol/min/100 g)	26.6 ± 21.1 [1.0–119.6]
RV MRGlu (μmol/min/100 g)	14.8 ± 14.4 [0.1–78.0]
RV/LV MRGlu (%)	89.5 ± 264.9
LVEF (%)	19.3 ± 8.6
End-diastolic volume (ml)	188.2 ± 69.3
End-systolic volume (ml)	154.4 ± 64.7
Follow-up days	496 ± 453 [1–1788]

Values are presented as mean ± SD [range]

Diabetic patients tended to have worse overall and cardiovascular survival, although not reaching statistical significance, which is not unexpected due to small sample size and limited follow-up period in the current study (Fig. 3). We performed subgroup analysis in patients with ($n = 41$) and without ($n = 34$) diabetes, which resulted in significantly worse cardiovascular survival when RV MRGlu ≥ 45.03 μmol/min/100 g (log-rank = 4.05, $p = 0.044$) and RV MRGlu ≥ 31.83 μmol/min/100 g (log-rank = 14.46, $p < 0.001$), respectively; while higher LV MRGlu values only resulted in non-significant trends of detriment for cardiovascular survival (LV MRGlu ≥ 38.77 μmol/min/100 g for diabetic patients, log-rank = 2.04, $p = 0.154$; LV MRGlu ≥ 22.03 μmol/min/100 g for non-diabetic patients, log-rank = 2.30, $p = 0.130$). Higher LV and RV MRGlu values were

Table 3 Correlations between MRGlu values and LV volumetric data

	RV MRGlu		LV MRGlu		LVEF	
	r	*p* value	*r*	*p* value	*r*	*p* value
LVEF	0.05	0.695	0.27	0.018		
RV/LV MRGlu	0.39	< 0.001	− 0.16	0.179	− 0.40	< 0.001
End-diastolic volume	0.36	0.002	0.25	0.034	− 0.37	0.001
End-systolic volume	0.32	0.005	0.18	0.120	− 0.54	< 0.001

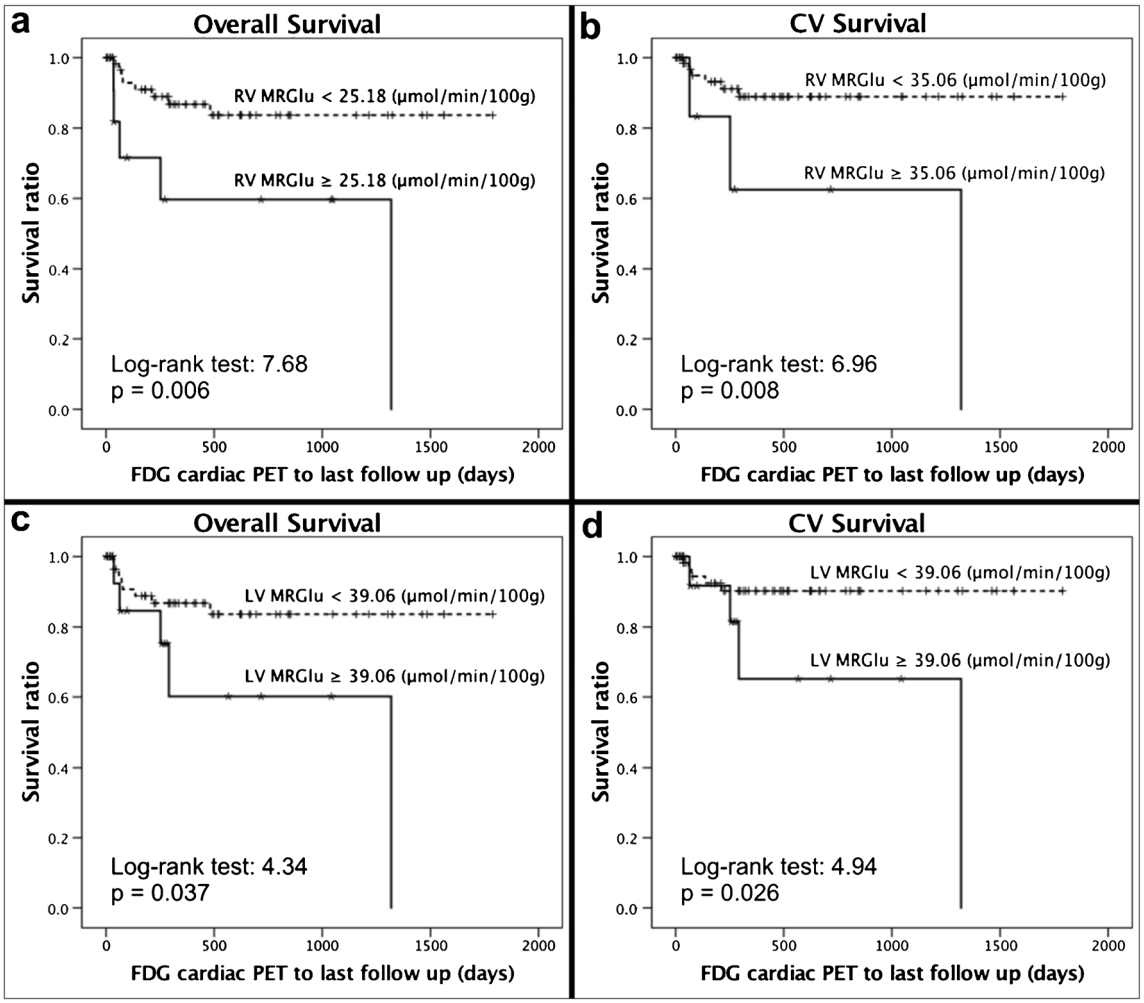

Fig. 2 Patients with (**a**) RV MRGlu ≥25.18 μmol/min/100 g had lower overall survival, and (**b**) RV MRGlu ≥35.06 μmol/min/100 g had lower cardiovascular survival. (**c**, **d**) LV MRGlu ≥39.06 μmol/min/100 g were associated with worse overall and cardiovascular survival

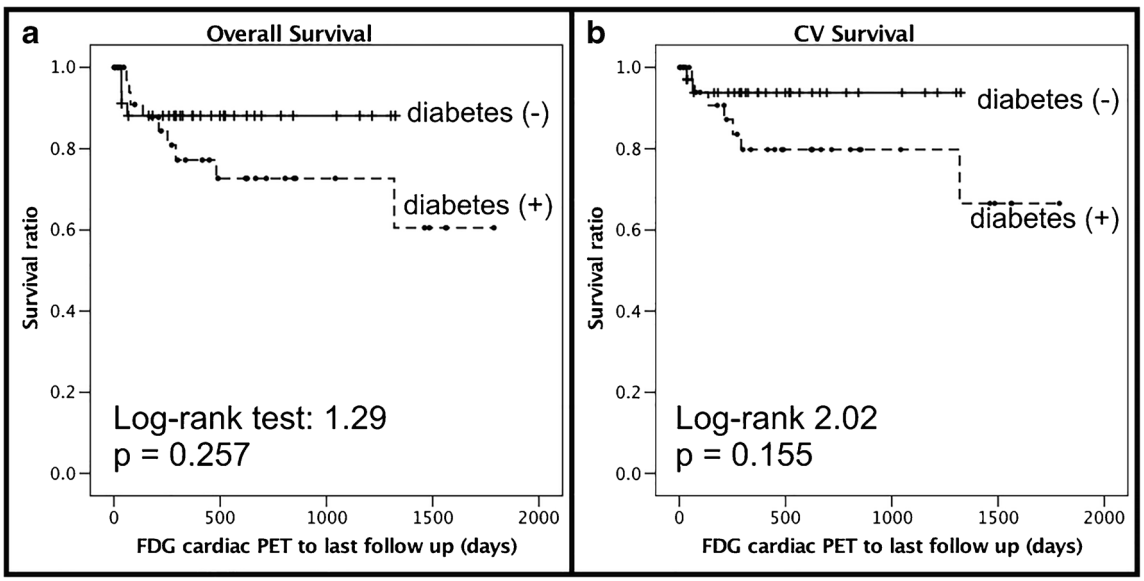

Fig. 3 Diabetic patients tended to have worse overall (**a**) and cardiovascular (**b**) survival, but not statistically significant in this study

associated with worse overall survival in non-diabetic patients, but not in diabetic patients.

Discussion

Studies focusing on RV dysfunction in ischemic cardiomyopathy are limited, especially those using FDG PET. It is not infrequent to observe increased RV activity on myocardial perfusion imaging for patients with left-sided heart failure; the increased RV uptake can not only be used to identify patients with balanced ischemia, RV hypertrophy, RV overload, or high pulmonary arterial pressure [23–25], but also indicate poor prognosis in these patients [26, 27]. In the present study, we used ^{201}thallium SPECT for perfusion assessments, whose tracer activity would not be affected by altered glucose metabolism. On the other hand, the subsequent PET has advantage for more precise and accurate quantification than SPECT due to better technical corrections for photon scatter, photon attenuation, and partial volume effect [28, 29].

The etiologies of pulmonary hypertension are classified into five groups [15, 30]. While left-sided heart failure (Nice group 2), similar to our study, is the most common cause of pulmonary hypertension [30], most published studies have focused on pulmonary arterial hypertension (PAH, Nice group 1) [12, 31, 32]. Patients with PAH usually have RV failure at the outset, resulting in adaptive RV hypertrophy, contractile dysfunction and chamber dilatation, followed by diastolic dysfunction of the left ventricle [30]. In contrast, patients with ischemic cardiomyopathy usually develop LV failure first, and the increased LV afterload subsequently leads to an increase in pulmonary pressure, then possibly RV failure or even death [30, 33].

We found positive correlations between RV MRGlu and pressure-overload indices, which is compatible with the findings of Bokhari et al. [34] in patients with idiopathic PAH. However, the findings are different to Ohira et al. [35] who reported that mPAP was positively correlated with semi-quantitative RV/LV FDG standard uptake value, whereas we found no significant relationship between quantitative RV/LV MRGlu and TRmaxPG/TRVmax.

Prior clinical and animal studies on pulmonary hypertension have reported increased RV FDG uptake [12, 31, 32] in diseased subjects compared to controls, and also a trend, but not significant, of lower LV glucose utilization [12] compared to controls. On the other hand, in chronic myocardial ischemia, viable tissues have been shown to have significantly higher MRGlu values than non-viable tissues [21], while non-viable myocardium has been associated with poor functional outcomes even after surgical revascularization [36]. Although data on the normal range of MRGlu in healthy subjects are lacking, we did observe more prominent RV activity and possibly less LV uptake in our ischemic cardiomyopathy cohort.

RV MRGlu was not well correlated with LVEF, implying that LV systolic dysfunction is not the only factor leading to RV dysfunction and RV pressure overload. The remodeling of myocardial glucose utilization in a failing heart is complicated and relies on several pathways to preserve adenosine triphosphate (ATP) supply, including increasing glucose transporter-1 (GLUT-1) dependence [37–39]. Heart failure is a complex syndrome associated with pulmonary vascular disease and right heart dysfunction [26]. It is widely accepted that the response of RV to pressure overload, rather than the severity per se, determines the prognosis [37, 40, 41]. Through ventricular interdependence, RV pressure overload can further influence LV geometry, and the resultant decreases in LV torsion and LV strain have also been associated with early mortality [42–44]. Our results suggest that MRGlu of LV and LV, even more significant in RV MRGlu, can provide incremental prognostic value in patients with ischemic cardiomyopathy; however, their ratio (RV/LV MRGlu) did not. This observation is similar to PAH in congenital heart disease (CHD-PAH), but different from idiopathic PAH [37]. This could be partly explained by the sequential order of LV and RV heart failure, in that for ischemic cardiomyopathy and CHD-PAH, RV adapts and remodels as a result of long-term LV failure. In addition, in the subgroup analyses, we noticed that higher MRGlu values in both LV and RV impaired the overall survival in non-diabetic group, but we did not observe similar phenomenon in those with diabetes. Possible explanations included that diabetic patients have higher mortality rate [45] but lower LV myocardial uptake [46] compared to those without diabetes, which added the complexity and led to non-significance, especially in the small subgroup sample size.

There are several limitations to this study. First, since the study primarily focused on patients with LV failure, we had limited data of RV function, including RVEF and other echocardiographic RV parameters. We did not routinely check serum free fatty acid and insulin levels at time of FDG PET. The lack of myocardial fatty acid PET imaging also hindered thorough observations of cardiac energetics [47] and myocardial metabolic remodeling in the patients with LV failure. Although Shan et al. [48] concluded that in patients hospitalized with heart failure, those with either reduced, borderline, or preserved EF had similar poor 5-year survival; further studies are needed to elucidate whether our conclusions can be extrapolated to patients with heart failure with borderline or preserved EF. Second, the follow-up period was relatively short (mean < 2 years). Third, the number of cases was not large, and the occurrence of the study endpoints (death/cardiovascular death) was infrequent. Fourth, the glucose loading protocol in our study, which was devised in 2012, is not completely consistent with the latest imaging guidelines [49]. However, the quality of our scans was clinically acceptable, and the simplified protocol was also clinically feasible. In addition, no significant differences in MRGlu values were noted between diabetic and non-

diabetic groups. Finally, the lack of normal controls made it difficult to interpret the MRGlu results, since no universally accepted normal range has been published.

Conclusion

In the patients with ischemic cardiomyopathy, RV myocardial glucose utilization was related to RV pressure overload. In addition, LVEF, LV end-diastolic volume, and global LV and RV MRGlu values also provided incremental prognostic value, indicating the importance of RV dysfunction in left-sided heart failure.

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Compliance with ethical standards

Research involving human participants and/or animals All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

Conflict of interest Except for financially supported by the Ministry of Science and Technology of Taiwan (MOST-101-2314-B-418-012-MY3, MOST-104-2314-B-418-008, MOST-105-2628-B-418-002-MY2, MOST-107-2314-B-418-006-MY3) and Far Eastern Memorial Hospital (FEMH-101-2314-B-418-012-MY3, FEMH-104-2314-B-418-008, FEMH-105-2628-B-418-002-MY2, FEMH-107-2314-B-418-006-MY3), no other relevant potential conflicts of interest exist. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. Corresponding author Yen-Wen Wu has received research grants from Ministry of Science and Technology of Taiwan and Far Eastern Memorial Hospital. The other authors declare that they have no conflict of interest.

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