Elevated standardised uptake value of the free wall of the right ventricular myocardium is correlated with enlarged left ventricular end-diastolic volume among patients with heart failure with reduced ejection fraction: A retrospective study

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Keywords: ^{18}F-FDG - Viability - End-diastolic volume - SUV - Right ventricle

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Received:
28 March 2022
Accepted revised:
29 June 2022

Abstract

This study aimed to investigate the relationship between the standardised uptake value of the free wall of the right ventricular myocardium (SUVrv) and left ventricular end-diastolic volume (LVEDV) among patients with heart failure with reduced ejection fraction (HFrEF) with coronary artery disease (CAD). This retrospective study included 50 patients with CAD and HFrEF scheduled for cardiac viability imaging with electrocardiography-gated fluorine-18-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography/computed tomography (PET/CT). The maximal SUVrv was measured. The LVEDV and left ventricular ejection fraction (LVEF) were automatically measured using quantitative gated single-photon emission computed tomography. Plasma brain natriuretic peptide (BNP) levels were obtained from medical records.The LVEF (0.24±0.06) was markedly reduced while the LVEDV (201.5±59.9mL) and BNP level (1348.1±1382.9pg/mL) were remarkably elevated. The SUVrv was 3.7±1.7 and was similar between patients with and without diabetes. The SUVrv was significantly positively correlated with the LVEDV and BNP level (r=0.35, 0.45; P=0.01, <0.01, respectively) but was unrelated to the LVEF (r=0.11, P=0.44). Herein, SUVrv was elevated and significantly positively correlated with LVEDV and BNP levels among patients with CAD and HFrEF but was unrelated to LVEF and diabetic status.

Hell J Nucl Med 2022; 25(2): 163-167 *Epub ahead of print: 3 August 2022* *Published online: 29 August 2022*

Introduction

Cardiac fluorine-18-fluorodeoxyglucose (^{18}F-FDG) viability imaging is a vital technique to assess heart failure with reduced ejection fraction (HFrEF) in patients with coronary artery disease (CAD) before the decision to revascularise [1]. If the myocardium in a fixed perfusion defect is viable, revascularisation will improve left ventricular (LV) function and patient quality of life [2]. Usually, ^{18}F-FDG uptake in the right ventricular (RV) free wall is investigated among these patients [3]. Investigations of this phenomenon in patients with pulmonary arterial hypertension [4]/pulmonary hypertension (PH) [5] additionally revealed that the standardised uptake value (SUV) of the RV free wall was reduced as pulmonary arterial pressure was relieved [6].

Electrocardiography (ECG)-gated cardiac ^{18}F-FDG viability imaging can provide several prognostic factors, including the LV ejection fraction (LVEF), LV end-diastolic volume (LVEDV), and LV end-systolic volume (LVESV). In patients with HFrEF, the LVEDV is strongly positively associated with the LV end-diastolic pressure (LVEDP) [7]. According to the Frank-Starling mechanism, myocardial contraction is stronger as LVEDP increases, leading to higher stroke volume and cardiac output. However, the LVEDP in patients with left heart failure may increase the RV afterload, which was the cause of PH in 65%-80% of patients [8]. Therefore, we postulated that the maximal SUV in the RV free wall (SUVrv) would be enlarged with an enlarged LVEDV. As the incremental LVEDV compensates for the loss of LV myocardium contractility, we posited that the maximal LV SUV (SUVlv) would not be associated with an enlarged LVEDV.

Subjects and Methods

Consecutive patients with CAD and HFrEF scheduled for cardiac ^{18}F-FDG viability positron emission tomography (PET)/computed tomography (CT) at our department between March 2018 and January 2022 were included in this retrospective study. Plasma brain natriuretic peptide (BNP) levels and LVEF measurements by echocardiography were obtained from patients' medical records. In our hospital, LVEF was measured using two-dimensional echocardiography with the modified Simpson's method [9] and recorded as LVEF[a]. Patients fasted for ≥6h before a finger-stick blood glucose assessment. Patients underwent cardiac ^{18}F-FDG viability imaging using an insulin-loading protocol. Intravenous regular insulin (dosage [IU]=0.02×[blood glucose (mmol/L)-2]×weight (kg) for patients without diabetes and 15% addition for patients with diabetes) was administered approximately 20min before ^{18}F-FDG injection [10].

ECG-gated cardiac ^{18}F-FDG data acquisition and analyses

The ECG-gated cardiac data were acquired with a three-dimensional list mode, 200×200 matrix, using PET/CT (Biograph mCT Flow64, Siemens, Malvern, PA, USA) with 10 min/bed position approximately 50min after ^{18}F-FDG (3.7MBq/kg) injection. The first 6min of attenuation-corrected ungated PET images were reconstructed with iterative TrueX (three iterations, 24 subsets) for SUV measurement. Attenuation-corrected eight-gated PET images were retrospectively reconstructed with iterative TrueX (three iterations, 24 subsets) for LVEDV, LVESV, and LVEF automatic assessment using quantitative gated single-photon emission computed tomography (QGS) 2012 version (Cedars-Sinai Medical Center, Los Angeles, CA, USA). The SUV measurements were performed using TrueD software (Siemens) [11]. The LVEF assessment using the QGS 2012 version was recorded as LVEF[b].

Statistical analyses

Results are expressed as the mean±standard deviation or percentage. Normal distribution was assessed using the Kolmogorov-Smirnov test. The t-test, chi-squared test, Fisher's exact test, and Pearson's correlation test were performed when necessary. Statistical significance was set at P≤0.05.

Results

The clinical and cardiac ^{18}F-FDG viability image characteristics of patients with HFrEF are listed in Table 1. These patients' LVEFs were markedly reduced with remarkably elevated LVEDV (201.5±59.9mL), LVESV (154.6±53.2mL), and BNP levels (1348.1±1382.9pg/mL). The SUVrv was significantly lower than the SUVlv (3.7±1.7 vs. 12.3±4.1; P<0.01). The LVEF[a] measurement with echocardiography was moderately correlated with the LVEF[b] measurement with ECG-gated ^{18}F-FDG PET (r=0.56, P<0.01). In a subgroup analysis, the SUVlv was significantly lower in patients with diabetes than in those without diabetes (9.8±3.1 vs. 13.2±4.1, P<0.01), while the SUVrv was similar between these two subgroups (3.4±1.7 vs. 3.8±1.7, P=0.44). The LVEDV and LVESV were also significantly lower in patients with diabetes than in those without diabetes (161.0±41.3mL, 121.9±36.8mL vs. 215.7±59.3mL, 166.4±53.6mL; P<0.01, <0.01, respectively).

The SUVrv was significantly positively correlated with the LVEDV, LVESV, and BNP level, but not with the LVEF[b] (Figure 1). The SUVlv was not correlated with the LVEDV, LVESV, LVEF[b], or BNP level (Figure 2).

Table 1. *Patients' clinical and cardiac ^{18}F-FDG viability image characteristics.*

	Whole group (n=50)	Non-diabetes (n=37)	Diabetes (n=13)	P-value
Age (years)	62.2±11.6	60.9±11.4	65.7±11.9	0.22
Sex (female/male)	10/40	9/28	1/12	0.12
Height (cm)	165.4±6.6	166.0±7.0	163.8±4.9	0.31
Weight (kg)	63.3±9.6	63.5±10.9	62.9±4.6	0.81
BNP (pg/mL)	1348.1±1382.9	981.5±1062.4	2363.2±1684.5	0.01
LVEF[a]	0.32±0.13	0.31±0.13	0.35±0.10	0.35
LVEF[b]	0.24±0.06	0.23±0.06	0.25±0.06	0.30
LVEDV (mL)	201.5±59.9	215.7±59.3	161.0±41.3	<0.01
LVESV (mL)	154.6±53.2	166.4±53.6	121.9±36.8	<0.03
SUVlv	12.3±4.1	13.2±4.1	9.8±3.1	<0.01
SUVrv	3.7±1.7	3.8±1.7	3.4±1.7	0.44

^{18}F-FDG, ^{18}F-fluorodeoxyglucose; BNP, brain natriuretic peptide; LVEF[a], left ventricular ejection fraction measured using echocardiography; LVEF[b], left ventricular ejection fraction measured using electrocardiography-gated ^{18}F-fluorodeoxyglucose positron emission tomography; LVEDV, left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume; SUVlv, maximal standardised uptake value of the myocardium of the left ventricle; SUVrv, maximal standardised uptake value of the free wall of the myocardium of the right ventricle

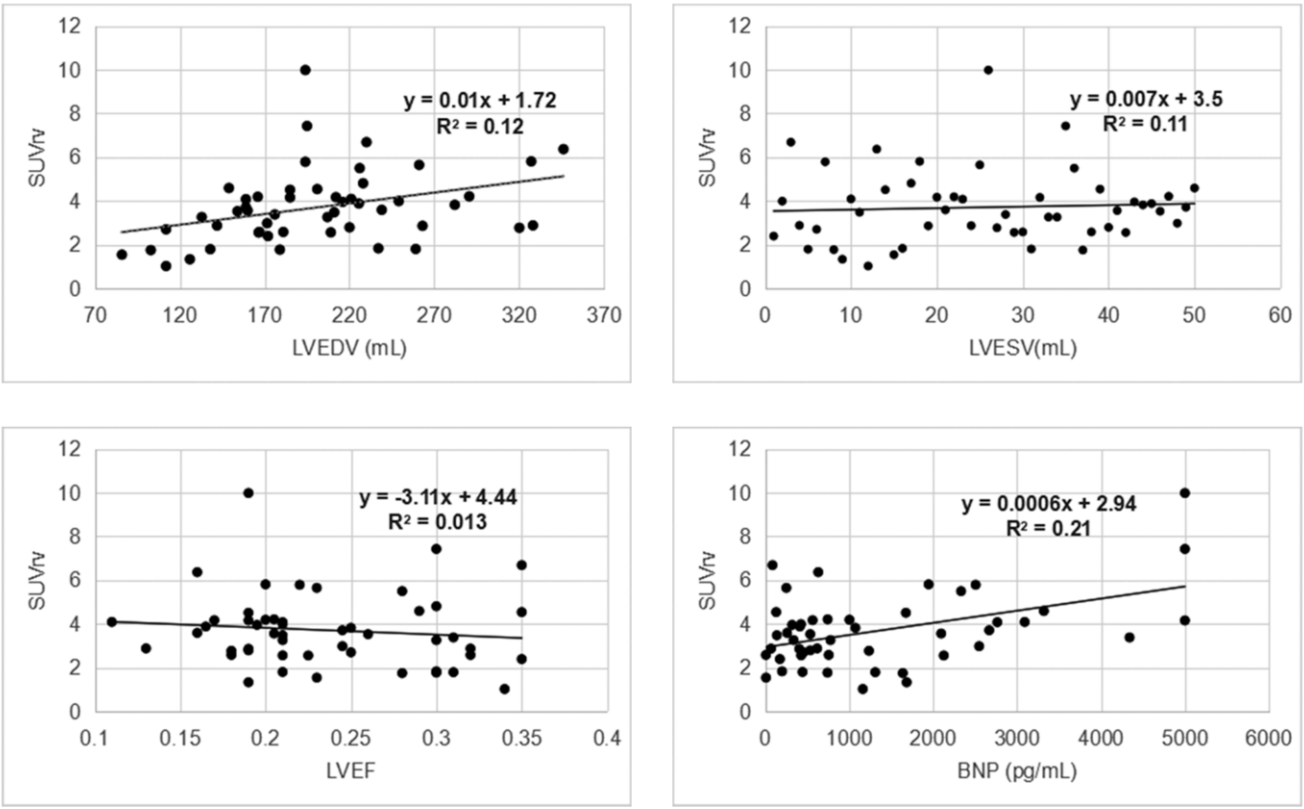

Figure 1. Correlation between the SUVrv and the left ventricular parameters and plasma BNP levels in patients with HFrEF.

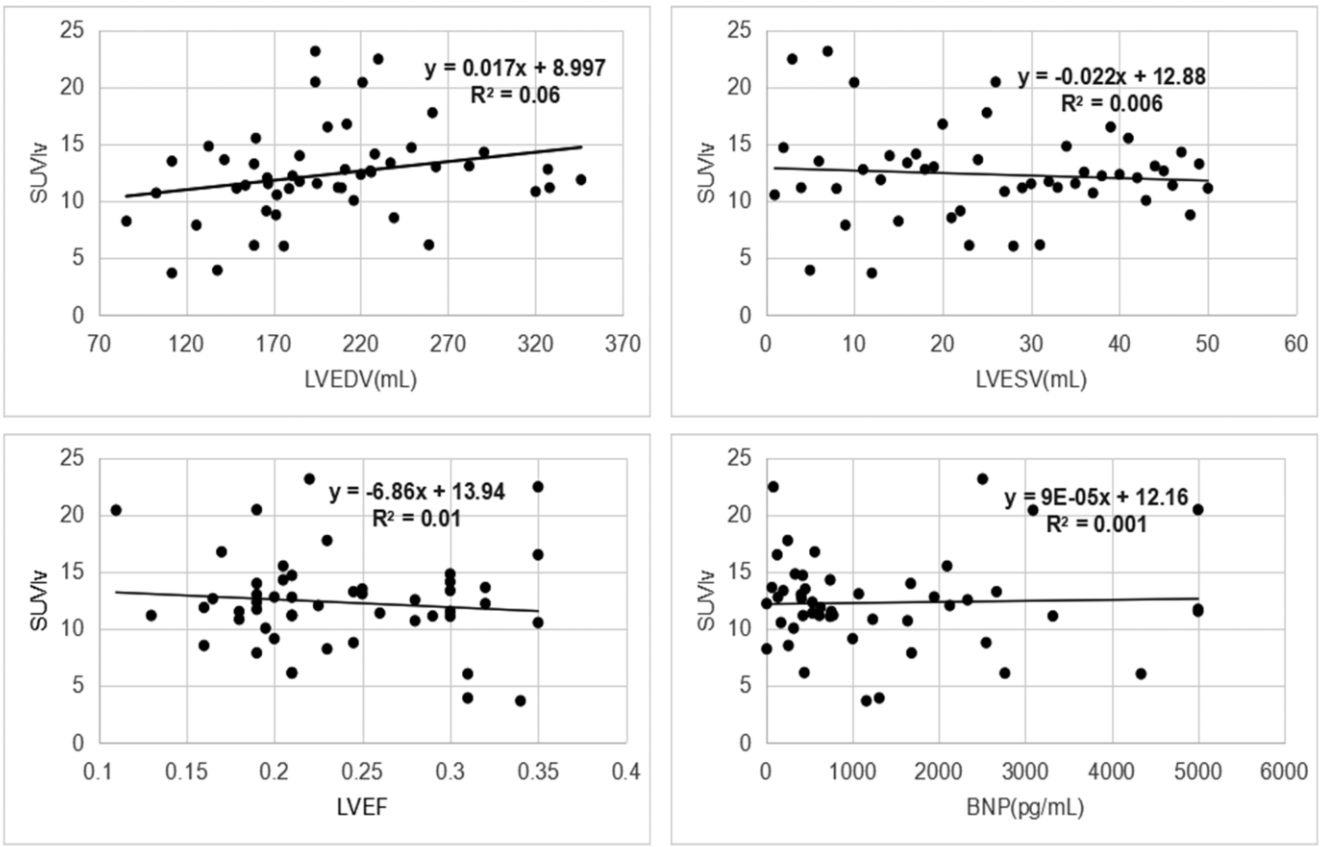

Figure 2. Correlation between the SUVlv and the left ventricular parameters and plasma BNP levels in patients with HFrEF.

Discussion

Clinical SUVrv

This study confirmed that the SUVrv was significantly positively correlated with the LVEDV in patients with CAD and HFrEF. Higher SUVrv [5] and RV myocardium glucose uptake rate values [3] in patients with HFrEF indicated higher mortality rates. For patients with HFrEF, PH with a reduced RV ejection fraction was an independent negative prognostic factor [12]. These reports imply that SUVrv is positively associated with PH. As the SUVlv is not associated with an enlarged LVEDV, which was confirmed in this study, the SUVlv cannot provide independent prediction information for patients with HFrEF.

SUVrv was dependent on pressure

The SUVrv was not associated with the LVEF[b] among patients with HFrEF in this study, similar to the findings published by Tsai et al. (2019) [3]. Compared with its weak correlation with the LVEDV (r=0.35, P=0.01), the SUVrv was moderately positively correlated with the BNP level (r=0.45, P< 0.01). As the BNP level is a significant independent predictor of the LVEDP [13], we infer that the SUVrv may depend on pressure load, instead of volume load, and the LVEF among patients with HFrEF.

SUVrv was unrelated to diabetes

In the present study, the SUVlv was impaired in patients with diabetes, as observed in our previous study [10, 14]. However, the SUVrv was not affected by diabetes in the current study. Several reports that focused on glucose uptake rate in the RV myocardium [4-6, 15, 16] did not describe this phenomenon. Tsai et al. (2019) [3] reported that the RV myocardium glucose uptake rate was not associated with overall survival in patients with HFrEF and diabetes. This implies that the SUVrv is more dependent on RV afterload than it is on diabetic status. In the subgroup analysis, patients with diabetes with similar LVEF had smaller LVEDV and LVESV than patients without diabetes. Enlarged LVEDV and LVESV are associated with worse prognoses [17], suggesting that diabetes is associated with increased morbidity and mortality [2].

Limitations

There were some limitations to this study, as follows. The study included a small sample size. As right heart catheterisation is an invasive procedure, it is not a routine examination for patients with HFrEF [8]. The LVEDP was not included in these patients' medical records. As a surrogate marker of LVEDP, LVEDV was included in our study. We hope to perform a prospective study to investigate the relationship between the SUVrv and the LVEDP in the future.

In conclusion, the SUVrv, but not the SUVlv, was elevated and significantly related to elevated LVEDV and BNP levels among patients with HFrEF. A higher SUVrv may indicate a poorer prognosis for these patients. The SUVrv depends on the RV afterload and is not associated with diabetic status among patients with HFrEF.

Ethics approval and consent to participate

This retrospective study involving human participants was in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The ethics committee of Quanzhou 1st hospital approved this retrospective study and waived the need for written informed consent from participants for the retrospective nature of the study.

Funding

This study was supported by the Natural Science Foundation of Fujian Province (2015J01516, 2018J01202, 2020J0-11280) and the Quanzhou Science and Technology Commission (2019C023R).

The authors declare that they have no conflicts of interest.

Bibliography

1. Dilsizian V, Bacharach SL, Beanlands RS et al. ASNC imaging guidelines/SNMMI procedure standard for positron emission tomography (PET) nuclear cardiology procedures. *J Nucl Cardiol* 2016; 23: 1187-226.
2. Ponikowski P, Voors AA, Anker SD et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur Heart J* 2016; 37: 2129-200.
3. Tsai SY, Wu YW, Wang SY et al. Clinical significance of quantitative assessment of right ventricular glucose metabolism in patients with heart failure with reduced ejection fraction. *Eur J Nucl Med Mol Imaging* 2019; 46: 2601-9.
4. Ohira H, deKemp R, Pena E et al. Shifts in myocardial fatty acid and glucose metabolism in pulmonary arterial hypertension: a potential mechanism for a maladaptive right ventricular response. *Eur Heart J Cardiovasc Imaging* 2016; 17: 1424-31.
5. Tatebe S, Fukumoto Y, Oikawa-Wakayama M et al. Enhanced ^{18}F-fluorodeoxyglucose accumulation in the right ventricular free wall predicts long-term prognosis of patients with pulmonary hypertension: a preliminary observational study. *Eur Heart J Cardiovasc Imaging* 2014; 15: 666-72.
6. Oikawa M, Kagaya Y, Otani H et al. Increased ^{18}F-fluorodeoxyglucose accumulation in right ventricular free wall in patients with pulmonary hypertension and the effect of epoprostenol. *J Am Coll Cardiol* 2005; 45: 1849-55.
7. LaCombe P, Jose A, Lappin SL. Physiology, Starling Relationships. 2021 May 9. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan.
8. Rosenkranz S, Gibbs JS, Wachter R et al. Left ventricular heart failure and pulmonary hypertension. *Eur Heart J* 2016; 37: 942-54.
9. Chen YC DR, Zhang KL, Dong YD et al. Accuracy of left ventricular function from electrocardiography gated myocardial perfusion SPECT by MyoMetrix in Chinese. *Nucl Sci Tech* 2017; 28: 37-42.
10. Chen YC, Pan MJ, Wang QQ et al. Intravenous insulin injection supplemented with subsequent milk consumption is a safer formulation for cardiac viability ^{18}F-FDG imaging. *J Nucl Cardiol* 2021. Online ahead of print.
11. Boellaard R, Delgado-Bolton R, Oyen WJ et al. ^{18}F-FDG PET/CT: EANM procedure guidelines for tumour imaging: version 2.0. *Eur J Nucl Med Mol Imaging* 2015; 42(2): 328-54.
12. Ghio S, Gavazzi A, Campana C et al. Independent and additive prognostic value of right ventricular systolic function and pulmonary artery pressure in patients with chronic heart failure. *J Am Coll Cardiol* 2001; 37: 183-8.

13. Maeda K, Tsutamoto T, Wada A et al. Plasma brain natriuretic peptide as a biochemical marker of high left ventricular end-diastolic pressure in patients with symptomatic left ventricular dysfunction. *Am Heart J* 1998; 135: 825-32.
14. Chen YC, Wang QQ, Wang YH et al. Intravenous regular insulin is an efficient and safe procedure for obtaining high-quality cardiac ^{18}F-FDG PET images: an open-label, single-center, randomized controlled prospective trial. *J Nucl Cardiol* 2022; 29: 239-47.
15. Saygin D, Highland KB, Farha S et al. Metabolic and Functional Evaluation of the Heart and Lungs in Pulmonary Hypertension by Gated 2-[^{18}F]-Fluoro-2-deoxy-D-glucose Positron Emission Tomography. *Pulm Circ* 2017; 7: 428-38.
16. Wang L, Zhang Y, Yan C et al. Evaluation of right ventricular volume and ejection fraction by gated ^{18}F-FDG PET in patients with pulmonary hypertension: comparison with cardiac MRI and CT. *J Nucl Cardiol* 2013; 20: 242-52.
17. Shah MA, Soofi MA, Jafary Z et al. Echocardiographic parameters associated with recovery in heart failure with reduced ejection fraction. *Echocardiography* 2020; 37: 1574-82.