

Original Article



Cardiac and Pericardial ¹⁸F-FDG Uptake on Oncologic PET/CT: Comparison with Echocardiographic Findings

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Conflict of Interest

The authors have no financial conflicts of interest.

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ABSTRACT

BACKGROUND: Interpretation of cardiac uptake on 18-fluorodeoxyglucose positron emission tomography/computed tomography (¹⁸F-FDG PET/CT) is often confounded by intense physiological FDG uptake and numerous benign conditions. The aim of the study was to describe the echocardiographic features in concordance with cardiac and pericardial ¹⁸F-FDG uptake on whole-body oncology PET/CT.

METHODS: We enrolled 43 consecutive patients (34 solid tumors, 8 lymphomas and 1 leukemia) who were newly diagnosed with non-cardiac malignancy showing incidental cardiac or pericardial ¹⁸F-FDG uptake on PET/CT and underwent transthoracic Doppler echocardiography (TTE) within 1 month of PET/CT. The maximum standardized uptake (SUV_{max}) of all lesions was measured.

RESULTS: Fifty-six ¹⁸F-FDG uptake lesions (32 pericardium, 7 myocardium, 9 cardiac chambers and 8 great vessels) were found, and pericardial effusion was the most common echocardiographic finding (22/43, 51.2%) among study population. Pericardial FDG uptake was shown as pericardial effusion (68.8%), intrapericardial echogenic materials (31.3%), pericardial thickening (28.1%), hyperechogenicity of myopericardium (18.8%), and restricted sliding movement or constrictive pericarditis (15.6%) on TTE. Lesions with regional wall motion abnormality ($p = 0.004$) or constrictive pericarditis ($p = 0.021$) had significantly higher mean SUV_{max} than those without. Myocardial FDG uptake demonstrated pericardial effusion (57.1%), regional wall motion abnormality (57.1%), and increased myocardial wall thickness (42.9%). All cardiac chamber FDG uptakes showed intracardiac mass on TTE.

CONCLUSIONS: Cardiac or pericardial ¹⁸F-FDG uptake on oncology PET/CT shows characteristic echocardiographic features according to which heart sites are involved.

Keywords: Cardiac metastases; ¹⁸F-FDG PET/CT; Echocardiography

INTRODUCTION

Cardiac metastases occur more frequently than primary cardiac tumors, with a highly variable incidence ranging from 2.3% to 18.3% in autopsy reports.¹⁾ Although in theory, any malignant tumor can metastasize to the heart, the most common tumors showing cardiac metastatic potential are lung cancer, breast cancer, hematologic malignancies and malignant melanoma.²⁻⁵⁾ Whole-body oncologic positron emission tomography/computed tomography (PET/CT) using 2-[¹⁸F]-fluoro-2-deoxy-D-glucose (FDG) is a useful imaging tool for cancer detection and staging that assesses tumor metabolic activity.⁶⁻⁸⁾ However, cardiac uptake of ¹⁸F-FDG on PET/CT has been overlooked due to intense physiological myocardial FDG uptake and numerous benign conditions.^{9,12)}

Transthoracic Doppler echocardiography (TTE) has been widely used as an initial imaging modality to provide information on hemodynamic consequences and the presence of cardiac metastases.^{13,16)} To the best of our knowledge, there have been no studies comparing cardiac or pericardial ¹⁸F-FDG uptake on PET/CT with findings on TTE in patients with non-cardiac malignancy. The aim of this study is to investigate echocardiographic features corresponding to cardiac or pericardial ¹⁸F-FDG uptake on whole-body oncologic PET/CT.

METHODS

Study population

Forty-three consecutive patients (32 men, 11 women; mean age, 62 ± 19 years) with newly diagnosed non-cardiac malignancy showing cardiac or pericardial ¹⁸F-FDG uptake on oncologic whole-body PET/CT who underwent TTE within 1 month of PET/CT were retrospectively reviewed. The present study was approved by the Institutional Review Board and conducted with ethical principles of the Declaration of Helsinki. Written informed consent was obtained from all patients before enrollment.

The primary tumors of all patients were histopathologically confirmed by analysis of surgically resected tumor or tumor biopsies. Patients with previous history of primary cardiac tumor or cardiac surgery, coronary artery disease, atrial fibrillation, significant valvular heart disease, chronic obstructive pulmonary disease, acute infection or sepsis and poor image quality were excluded.

¹⁸F-FDG PET/CT scanning

All scans were obtained using an integrated PET/CT inline system, either Biograph Duo or Biograph TruePoint (Siemens Medical Solutions, Knoxville, TN, USA). All patients fasted for at least 6h before the PET/CT study. Approximately 1h before PET/CT, each patient received an injection of 370-555 MBq of ¹⁸F-FDG. No patients had blood glucose levels > 130 mg/dL before the injection. There were 6-8 bed positions, and acquisition time was 2-3 min per bed position. Non contrast-enhanced CT was performed from the base of the skull to the upper thighs for attenuation correction and diagnosis (130kVp, 80mA, and 5-mm slice thickness; 120kVp, 50mA, and 5-mm slice thickness). PET immediately followed over the same body region, and images were reconstructed using a standard ordered-subset expectation maximization (OSEM) algorithm. The axial spatial resolution was 6.5 or 4.5mm at the center of the field of view.

Image analysis

All PET/CT images were reviewed at a workstation with fusion software (Syngo; Siemens Medical Solutions, Knoxville, TN, USA) that provided multi-planar reformatted images and displayed PET images after attenuation correction, CT images, and PET/CT fusion image. CT images were used to identify the location and morphological features of the lesion, in addition to its relation to surrounding tissues. ¹⁸F-FDG uptake in cardiac and pericardial lesions was quantified by calculating the maximum standardized uptake values (SUV_{max}), which were obtained by normalizing the tissue concentration of FDG activity and patient weight. All PET/CT scans were reviewed and interpreted by 2 board certified nuclear medicine physicians who were blinded to the clinical data and the applied imaging convention.

TTE

All ultrasound examinations were performed with a commercially available echocardiographic device (vivid 7 [GE Vingmed Ultrasound AS, Horten, Norway], with a 2.5-MHz phased array probe). Standard M-mode, two-dimensional (2D), and color Doppler measurements were obtained according to the American Society of Echocardiography (ASE) recommendations.¹⁷¹⁹ Briefly, echocardiographic data included morphology, size, location and echogenicity of metastatic lesions. Pericardial thickness greater than 4mm was defined as pericardial thickening. Left ventricular (LV) wall thickness and chamber dimension were measured from 2D-guided M-mode echocardiography. Regional LV myocardial wall motion was visually estimated by examining LV myocardial wall thickness and was classified as normal (normal wall thickening and motion), hypokinesia (reduced wall thickening and motion), and akinesia (absence of wall thickening and motion). Respiratory variation of $\geq 25\%$ in mitral inflow peak early (E) velocity with abnormal septal notching or abrupt diastolic flattening of the posterior wall was considered diagnostic of constrictive pericarditis. Pulmonary venous (PV) velocities were also recorded, and monophasic flow or flow velocities > 1.6 m/s were regarded as functionally significant obstructions. Right ventricular (RV) chamber dimension and wall thickness were measured from the apical four-chamber view and subcostal view, respectively. All echocardiographic examinations were performed by skilled sonographers and interpreted by experienced cardiologists who were blinded to clinical information of the study population.

Statistical analysis

Data were analyzed using SPSS 18 software (SPSS, Inc., Chicago, IL, USA). Continuous variables were presented as the mean \pm standard deviation (SD), and categorical data were presented as frequency percentages. Group comparison of mean SUV_{max} was performed by Mann-Whitney U test. A *p* value < 0.05 was considered statistically significant.

RESULTS

Among 43 patients with cardiac or pericardial ¹⁸F-FDG uptake on PET/CT, the most frequent site of primary tumor was lung (15/43, 34.9%), followed by lymph node (8/43, 18.6%), thyroid (4/43, 9.3%), breast (3/43, 7.0%), liver (3/43, 7.0%), stomach (2/43, 4.7%), pleura (2/43, 4.7%) and five other sites (chronic myeloid leukemia [CML], mediastinum, esophagus, ovary, and metastasis of unknown origin [MUO]). Of 15 patients with lung cancer, 10 patients (66.7%) had non-small cell lung carcinoma (five each cases of adenocarcinoma and squamous cell carcinoma) and five (33.3%) had small cell lung carcinoma. All patients with lymphoma had non-Hodgkin's lymphoma (diffuse large B-cell lymphoma in six patients and T cell lymphoblastic lymphoma in two patients). Thyroid cancer was follicular carcinoma in three

Table 1. Pathology of primary non-cardiac malignant tumors in 43 patients with cardiac or pericardial fluorodeoxyglucose uptake on whole-body ¹⁸F-fluorodeoxyglucose positron emission tomography-computed tomography

| Pathology | Cases, n (%) |
|---|--------------|
| Lung cancer | 15 (34.9) |
| Non-small cell lung carcinoma | 10 |
| Adenocarcinoma | 5 |
| Squamous cell carcinoma | 5 |
| Small cell lung carcinoma | 5 |
| Lymphoma (non-Hodgkin's lymphoma) | 8 (18.6) |
| Diffuse large B-cell lymphoma | 6 |
| T cell lymphoblastic lymphoma | 2 |
| Thyroid cancer | 4 (9.3) |
| Follicular carcinoma | 3 |
| Anaplastic carcinoma | 1 |
| Breast cancer (invasive ductal carcinoma) | 3 (7.0) |
| Hepatocellular carcinoma | 3 (7.0) |
| Stomach cancer (adenocarcinoma) | 2 (4.7) |
| Pleural mesothelioma | 2 (4.7) |
| Others* | 6 (13.9) |

*Chronic myeloid leukemia, mediastinum, esophagus, bladder, ovary, metastasis of unknown origin.

patients and anaplastic carcinoma in one patient. All three cases of breast cancer were invasive ductal carcinoma. The stomach cancer was adenocarcinoma and the pleural tumor was mesothelioma (Table 1).

FDG uptake in the heart

Although primary tumors tended to have a higher mean SUV_{max} than those of metastatic lesions in the heart, the difference was not statistically significant (Figure 1). Of 43 patients, 33 patients (75.0%) had only one metastatic FDG uptake, including the pericardium in 29 patients, myocardium in three patients, and cardiac chamber in one patient. Among the rest, there were seven cases (16.3%) with FDG uptake in two sites (cardiac chamber and great vessel in five patients, pericardium and myocardium in two patients) and three cases (6.9%) with FDG uptake in three sites (myocardium, cardiac chamber, and great vessels in two patients, and pericardium, cardiac chamber, and great vessel in one patient) (Table 2).

Echocardiographic features of metastatic FDG uptake lesions

Among study population, pericardial effusion was the most common echocardiographic finding (22/43, 51.2%) in concordance with ¹⁸F-FDG uptake on PET/CT. Table 3 shows

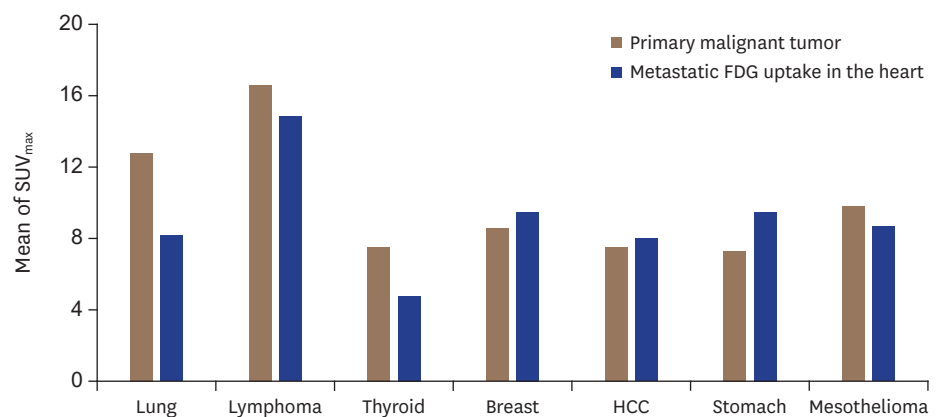


Figure 1. Comparison of mean SUV_{max} between primary tumor and metastatic cardiac FDG uptake. FDG: fluorodeoxyglucose, HCC: hepatocellular carcinoma, SUV_{max}: maximum standardized uptake value.

Table 2. Location of cardiac or pericardial fluorodeoxyglucose uptake on ¹⁸F-fluorodeoxyglucose positron emission tomography-computed tomography

| Location | Cases, n (%) |
|--|--------------|
| 1 lesion | 33 (75.0) |
| Pericardium | 29 |
| Myocardium | 3 |
| Cardiac chamber | 1 |
| 2 or more lesions | 10 (23.3) |
| Cardiac chamber + great vessel | 5 |
| Pericardium + myocardium | 2 |
| Myocardium + cardiac chamber + great vessel | 2 |
| Pericardium + cardiac chamber + great vessel | 1 |

Table 3. Echocardiographic features according to the location of FDG uptake on ¹⁸F-FDG positron emission tomography-computed tomography

| Location of FDG uptake | Cases, n (%) |
|---|--------------|
| Pericardial ¹⁸ F-FDG uptake | (n = 32) |
| Pericardial abnormalities | 25 (78.1) |
| Pericardial effusion | 22 |
| Intrapericardial mass or materials | 10 |
| Pericardial thickening | 9 |
| Hyperechogenicity of the myopericardium | 6 |
| Decreased sliding motion of the pericardium | 3 |
| Constrictive pericarditis | 2 |
| Myocardial abnormalities | 6 (18.8) |
| Regional wall motion abnormality | 4 |
| Increased myocardial wall thickness | 2 |
| Myocardial ¹⁸ F-FDG uptake | (n = 7) |
| Pericardial abnormalities | 6 (85.7) |
| Pericardial effusion | 4 |
| Hyperechogenicity of the myopericardium | 2 |
| Others* | 4 |
| Myocardial abnormalities | 5 (71.4) |
| Regional wall motion abnormality | 4 |
| Increased myocardial wall thickness | 3 |
| Cardiac chamber ¹⁸ F-FDG uptake | (n = 9) |
| Intracardiac abnormalities | 9 (100.0) |
| Mass in cardiac chamber | 4 |
| Pericardial abnormalities | 5 (55.6) |
| Pericardial effusion | 4 |
| Hyperechogenicity of the myopericardium | 1 |
| Myocardial abnormalities | 1 (11.1) |
| Regional wall motion abnormality | 1 |
| Other† | 7 |
| Great vessel ¹⁸ F-FDG uptake | (n = 8) |
| Disturbance of SVC, IVC or PV inflow | 5 (62.5) |
| Pericardial abnormalities | 4 (50.0) |
| Pericardial effusion | 3 |
| Hyperechogenicity of the myopericardium | 1 |
| Intracardiac abnormalities | 3 (37.5) |
| Mass in cardiac chamber | 3 |
| Myocardial abnormalities | 1 (12.5) |
| Regional wall motion abnormality | 1 |

¹⁸F-FDG: ¹⁸F-fluorodeoxyglucose, IVC: inferior vena cava, PV: pulmonary vein, SVC: superior vena cava.

*Intrapericardial mass or materials, pericardial thickening, decreased sliding motion of the pericardium, constrictive pericarditis. †Disturbance of SVC, IVC or PV inflow.

echocardiographic features according to the site of FDG uptake. Examples of each site are shown in **Figure 2**.

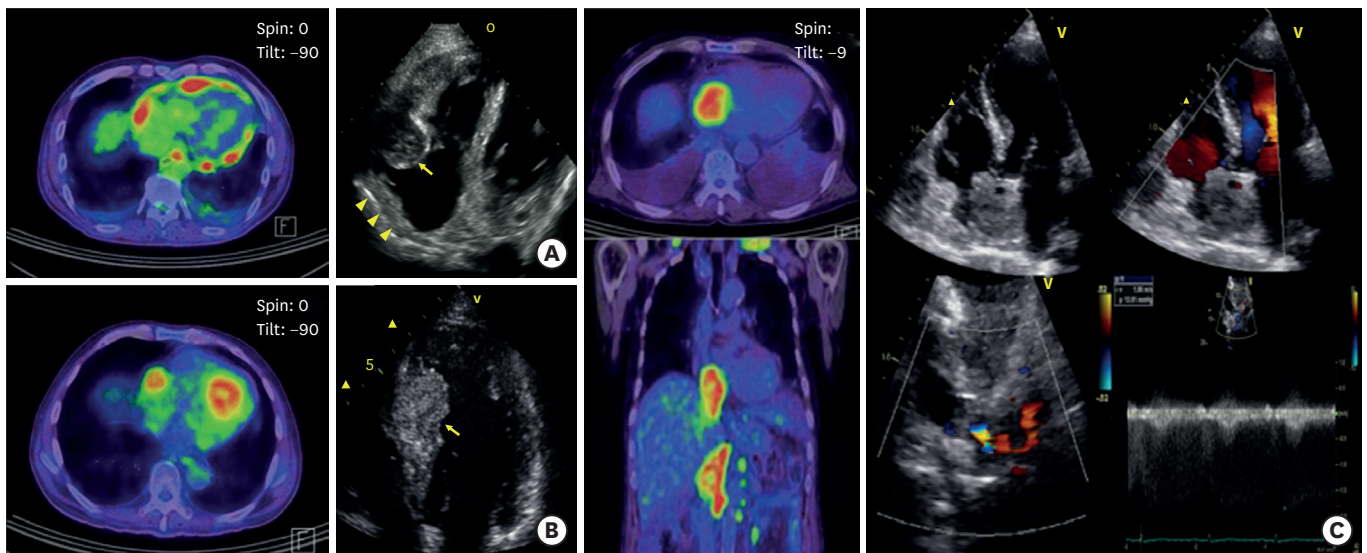


Figure 2. Cardiac and pericardial FDG uptake on whole body oncologic PET/CT and their echocardiographic features. (A) A 69-year-old man with multifocal pericardial FDG uptakes on PET/CT (left). TTE showed RV pericardial echogenic mass protruding into the RV and RA (right, arrow) with RV free wall hypokinesia and compressed RA by the pericardial mass (right, arrow head). (B) A 52-year-old man with focal FDG uptake and central photon defect in IVS on PET/CT (left). TTE revealed a round, homogeneous and hyperechogenic protruding mass on IVS with hypokinetic wall motion (right, arrow). (C) A 69-year-old man with intense FDG uptakes involving RA and IVC on PET/CT (left). TTE demonstrated a round, echogenic mass with irregular margin attached to the septum of the RA side (right upper) that is linked to an irregular heterogeneous echogenic mass from the IVC, showing flow acceleration at IVC entrance ($V_{\max} = 1.8$ m/s) (right lower). FDG: fluorodeoxyglucose, IVC: inferior vena cava, IVS: interventricular septum, PET/CT: positron emission tomography/computed tomography, RA: right atrial, RV: right ventricular, TTE: transthoracic Doppler echocardiography.

Of 32 patients with pericardial FDG uptake, 25 patients (78.1%) showed pericardial abnormalities including pericardial effusion (88.0%), intrapericardial mass or materials (40.0%), pericardial thickening (36.0%), hyperechogenicity of the myopericardium (24.0%), decreased sliding motion of the pericardium (12.0%), and constrictive pericarditis (8.0%). Despite only two cases showed pericardial and myocardial FDG uptakes simultaneously, 6 patients (18.8%) demonstrated myocardial abnormalities such as regional wall motion abnormality (RWMA) (66.7%) and increased myocardial wall thickness (33.3%). Of 29 cases with FDG uptake limited to the pericardium, 17 cases (58.6%) showed pericardial abnormalities on TTE and their mean SUV_{\max} was not significantly different from that of others with normal echocardiogram ($n=7$) (7.4 ± 4.7 vs. 6.4 ± 4.8 , $p = 0.684$) (data not shown). When comparing the mean SUV_{\max} of pericardial FDG uptake lesions according to the type of abnormal echocardiographic features, lesions with RWMA (14.3 ± 4.7 vs. 6.4 ± 4.0 , $p = 0.004$) or constrictive pericarditis (13.1 ± 3.4 vs. 6.6 ± 4.1 , $p = 0.021$) had significantly higher mean SUV_{\max} than those without. Furthermore, lesions showing pericardial thickening (8.4 ± 6.1 vs. 6.8 ± 4.1 , $p = 0.433$) or increased pericardial echogenicity (10.1 ± 5.9 vs. 6.7 ± 4.3 , $p = 0.138$) were more likely to have higher mean SUV_{\max} . However, the presence of pericardial effusion or intrapericardial materials was not associated with mean SUV_{\max} (Figure 3).

Of seven cases with myocardial ¹⁸F-FDG uptake, 6 patients (85.7%) revealed pericardial abnormalities such as pericardial effusion (66.7%), hyperechogenicity of the myopericardium (33.3%), and others (Intrapericardial mass or materials, pericardial thickening, decreased sliding motion of the pericardium, constrictive pericarditis in one patient each). Among 5 patients showing myocardial abnormalities on TTE (71.4%), RWMA in 4 cases (80.0%) and increased myocardial wall thickness in 3 cases (60.0%) were found.

All nine cases with cardiac chamber ¹⁸F-FDG uptake revealed a mass in the cardiac chambers including the RA (6/9, 66.7%), RV outflow tract (1/9, 11.1%), RV (1/9, 11.1%), and LA (2/9,

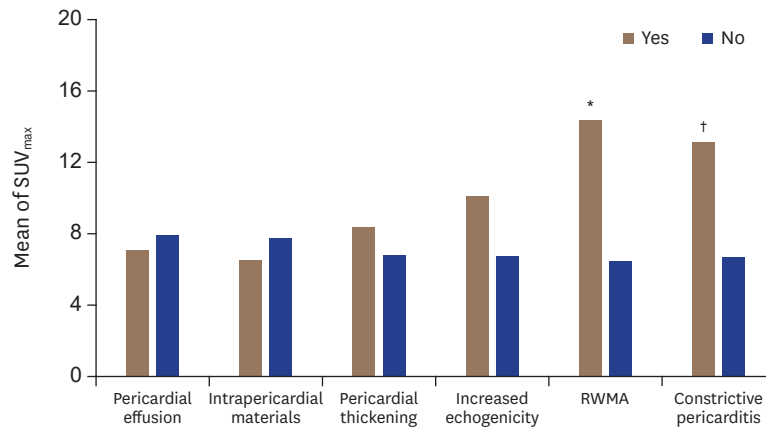


Figure 3. Comparison of mean SUV_{max} at isolated pericardial FDG uptake lesions with and without echocardiographic abnormal features (n = 29). **p* = 0.004, †*p* = 0.021. FDG: fluorodeoxyglucose, RWMA: regional wall motion abnormality, SUV_{max}: maximum standardized uptake value.

22.2%) on TTE. Eight cases with great vessel ¹⁸F-FDG uptake included disturbances of SVC, IVC, or PV inflow in 5 cases (62.5%), pericardial effusion in 3 cases (37.5%), and intracardiac mass in 3 cases (37.5%). FDG uptake confined to the great vessels was not found.

DISCUSSION

¹⁸F-FDG uptake reflects glucose metabolism, and its uptake on PET/CT has been widely used as an imaging biomarker for cancer detection in oncology.⁶⁻⁸⁾ Knowledge of pathological cardiac and pericardial FDG uptake on whole body PET/CT may provide important diagnostic clues to rule out metastatic involvement of the heart in patients with cancer or cancer screening.²⁰⁾ Here, we demonstrated for the first time echocardiographic features in concordance with cardiac and pericardial FDG uptakes that are incidentally encountered on oncology PET/CT among patients with non-cardiac malignancy.

Prior studies reported that the differentiation of focal pericardial FDG uptake from paracardiac lymph node uptake by ¹⁸F-FDG PET image is difficult.¹²⁾ In this study, all but two patients showed focal pericardial FDG uptake, and we could exclude paracardiac nodal disease through FDG PET/CT fusion image. Pericardium was the most common site of FDG uptake however, only 60% of them revealed abnormal echocardiographic features and their mean SUV_{max} was similar with that of normal echocardiogram. Although normal FDG uptake in the heart was adequately suppressed by prolonged fasting, the possibility of physiologic uptake or inflammation could not be completely excluded in our study. This result shows the limitation of oncology PET/CT for detecting cardiac metastasis, and also suggests that interpretation of cardiac FDG uptake, particularly in pericardium, should be cautious. Furthermore, we found that pericardial FDG uptake showing RWMA and constrictive pericarditis on TTE were more likely to have higher mean SUV_{max} compared to other echocardiographic features. These findings seem to be inconsistent with previous reports demonstrating reduced FDG uptake in lesions of RWMA on TTE. However, most studies have been conducted in patients with coronary artery disease for assessing myocardial viability using cardiac PET/CT protocol.²¹⁾²²⁾ Considering that FDG uptake is related to metabolism, increased FDG uptake showing RWMA on TTE may strongly suggest cardiac metastasis. Accordingly, it is thought that aforementioned abnormal echocardiographic features

reflecting hemodynamic impairment could provide important clinical clues for metastatic pericardial FDG uptake.

It is difficult to detect malignant myocardial FDG uptake on oncology PET/CT because physiologic variations in FDG uptake can obscure abnormal myocardial FDG uptake.^{9,11)} However, we used a strict preparation fasting regimen and excluded common patterns of normal physiologic FDG activity in the myocardium. In the present study, echocardiographic abnormalities were identified in all seven patients with myocardial FDG uptake. Interestingly, patients with myocardial FDG uptake alone showed not only myocardial structural or functional abnormalities but also pericardial abnormalities. These findings suggest that myocardial FDG uptake on oncology PET/CT could be a pathologic finding showing abnormal pericardial or myocardial abnormalities on TTE.

Most cases of FDG uptake in cardiac chambers on oncology PET/CT accompanied by involvement of the great vessels including the SVC, IVC, or PV, and some of them (7/9, 77.8%) also exhibited venous inflow disturbance on TTE. Considering that metastatic masses were usually located in RA or LA, our results suggest intracavitary cardiac metastases through a transvenous route. Echocardiography may be helpful to understand hemodynamic condition of these patients. Intracavitary space-occupying growth of a secondary heart tumor is rare, and it has been mainly reported in cancers of the kidney, liver, lung and thyroid.^{1,23)} Meanwhile, in our study, involvement of the cardiac chambers and/or great vessels was most frequently found in lymphoma. This seems to be related to the pathophysiology of lymphoma that can metastasize to the heart through hematogenous dissemination,²⁴⁾ along with relatively high proportion of lymphoma in our study population.

Our study has several limitations. First, this is a retrospective study with potential selection and information biases. Second, there was no comparison with other adjunctive imaging modalities such as CT or MRI. Finally, all cardiac and pericardial FDG uptake lesions were not confirmed by pathology. Risks related to myocardial biopsy limit their routine use in clinical practice, especially for cancer patients. Moreover, it is challenging to capture a small piece of affected cardiac tissue. Thus, clinical data was acquired and analyzed to rule out benign cardiac or pericardial lesions with increased FDG uptake on PET/CT.

In conclusion, echocardiographic abnormality for cardiac or pericardial ¹⁸F-FDG uptake on oncologic PET/CT is not uncommon, and its echocardiographic features differ according to which heart sites are involved. Echocardiography may provide incremental morphologic and hemodynamic information in combination with anatomic and metabolic data obtained by FDG PET/CT. Further longitudinal prospective studies with a larger sample size are needed to establish the optimal imaging approach for increased FDG uptake in the heart during cancer staging.

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