ORIGINAL

The physiological uptake pattern of ^{18}F-FDG in the left ventricular myocardium of patients without heart disease

Hayato Nose[1], Hideki Otsuka[2], Yoichi Otomi[1], Kaori Terazawa[1], Shoichiro Takao[3], Seiji Iwamoto[1], Takashi Iwase[4], Hirotsugu Yamada[4], Masataka Sata[4], and Masafumi Harada[1]

[1]*Department of Radiology, Tokushima University Hospital, Tokushima, Japan,* [2]*Department of Medical Imaging, Tokushima University Hospital, Tokushima, Japan,* [3]*Department of Radiologic Science and Technology, Tokushima University Hospital, Tokushima, Japan,* [4]*Department of Cardiovascular Medicine, Tokushima University Hospital, Tokushima, Japan*

Abstract : Purpose : The purpose of this study was to evaluate the physiological uptake pattern of ^{18}F-FDG in the left ventricular myocardium of patients under preparation for tumor FDG-PET. Patients and Methods : We enrolled 188 patients without cardiac disease. The accumulation patterns were classified as either 'none', 'diffuse', 'focal' or 'focal on diffuse'. When a focal uptake was only observed on the basal wall, then the patterns were classified as having either a 'ring', 'over half' or 'spot' uptake. Results : The frequencies of the myocardial FDG uptake patterns were as follows : none, n=52 (27.7%) ; diffuse, n= 63 (33.5%) ; focal on diffuse, n=40 (21.3%) and focal, n=33 (17.6%). The age, blood glucose level, weight and dose of FDG did not differ significantly for each pattern. The focal and focal on diffuse patterns were seen in 73 patients, and 65 patients had a focal uptake only on the basal wall ; ring uptake in 29 patients, over half in 20 and spot uptake in 16 patients. Conclusions : The physiological myocardial uptake showed several patterns. Focal uptake was often seen in patients with cardiac disease, but it did not always indicate an abnormal finding when the accumulation was only on the basal wall. J. Med. Invest. 61 : 53-58, February, 2014

Keywords **:** *^{18}F-FDG PET, heart, physiological myocardial uptake, fasting state*

INTRODUCTION

^{18}F-fluorodeoxyglucose (FDG) positron emission tomography (PET)-based assessment of the myocardium is useful in the evaluation of primary cardiac tumors or cardiac metastasis, to examine the viability following myocardial ischemia and for the detection of inflammatory myocardial sarcoid lesions. However, because the cardiac FDG uptake shows several different patterns in the fasting state, it is often difficult to distinguish between normal or abnormal uptake. Therefore, it is recommended that glucose loading should be performed to increase this uptake prior to estimating the viability. In addition, heparin loading is carried out to suppress the physiological uptake of FDG in the myocardium before

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Address correspondence and reprint requests to Hayato Nose, MD, Department of Radiology, Tokushima University Hospital, 3-18-15 Kuramoto-cho, Tokushima 770-8503, Japan and Fax : +81-886-33-7174.

attempting the detection of inflammatory lesions, such as sarcoidosis.

In Japan, the use of ^{18}F-FDG PET was approved by the national health insurance program for evaluating cardiac sarcoidosis in 2012. It is therefore speculated that the number of ^{18}F-FDG PET examinations for cardiac sarcoidosis will increase. However, the normal heart frequently shows physiological uptake, and the physiological uptake is different for each patient, and may even differ within individual patients during different examinations. Therefore, it is often difficult to evaluate whether the uptake is abnormal or not.

In the present study, we evaluated the physiological cardiac accumulation of FDG under preparation for tumor FDG-PET.

METHODS AND MATERIALS

This retrospective study was approved by the institutional review board of Tokushima University Hospital.

A total of 207 consecutive outpatients who underwent FDG-PET/CT for tumor imaging between March 30, 2011 and May 13, 2011 at our hospital were enrolled in this study. The suspected diseases for which FDG PET/CT was used are shown in Table 1. Nineteen patients were excluded for the following reasons : 11 had cardiac disease (four cases of angina, four of arrhythmia, one old myocardial infarction, one congestive heart failure and one had undergone pericardiectomy), seven patients (four with esophageal cancer, three with lung cancer) had undergone radiation therapy during which the heart was included in the irradiated field ; and one patient had very poor imaging data due to obesity. Therefore, we investigated a total of 188 patients (84 males and 104 females ; mean age, 64.1 years ; and age range, 27-90 years).

FDG PET/CT

All patients prepared for the examination by fasting for at least six hours prior to tumor PET imaging. After verification of their blood glucose level, the patients were intravenously injected with 128-290 MBq/kg of FDG. Patients were then examined using a PET/CT scanner (Auiduo : Toshiba Medical Systems Corporation, Tochigi, Japan) one hour after FDG injection. Image acquisition was performed from the top of the head to the middle of the thigh. The attenuation-corrected PET images, non-attenuation-corrected PET images and CT images were reviewed, and the attenuation-corrected PET and CT images were co-registered using a commercial software program (Aquarius NET Viewer : TeraRecon Inc, San Mateo, CA, USA).

Table 1. Underlying diseases of the patients evaluated by FDG PET/CT

	n		n
Breast cancer	53	Parotid gland lesion	4
Lung lesion	28	cancer (3)	
cancer (21)		other (1)	
others (7)		Malignant melanoma	3
Esophageal cancer	21	Maxillary cancer	3
Uterine cancer	16	Renal cancer	2
Laryngeal cancer	13	Gallbladder cancer	2
Gastric cancer	11	Colon cancer	2
Pharyngeal cancer	10	Bone tumor	2
Malignant lymphoma	6	Unknown primary cancer	2
Pancreatic lesion	6	Tongue cancer	2
cancer (2)		Gingival cancer	1
others (4)		Oral cancer	1
Thymic lesion	5	Brain tumor	1
cancer (2)		Liver tumor	1
others (3)		Thyroid cancer	1
Rectal cancer	4	Prostate cancer	1
Ovarian lesion	4	Pleural tumor	1
cancer (3)		Cervical tumor	1
other (1)			

Analysis of the FDG PET images

The FDG uptake in the myocardium was classified into four patterns as described in two previous reports (1, 2) : 'none', 'diffuse', 'focal' and 'focal on diffuse' (Figure 1). The "none" pattern indicated no uptake of FDG in the myocardium or less uptake than was observed in the mediastinum. The "diffuse" pattern indicated a diffuse and homogeneous uptake of FDG in the left ventricle (LV) wall. The pattern was only classified as "focal" when a focal uptake was observed. The "focal on diffuse" pattern indicated a focal uptake overlying the diffuse pattern. However, if a focal nodular uptake was only seen in the lateral wall of the LV, we did not classify the pattern as a "focal" or "focal on diffuse" pattern, because normal papillary muscle often shows a focal uptake in the lateral wall. When the "focal" or "focal on diffuse" patterns were seen, we further classified these focal FDG uptake patterns into three additional patterns when it was only observed in the basal wall (Figure 2). These three patterns were the 'ring' pattern, 'over half' pattern and 'spot' pattern. The 'ring' pattern was characterized by a diffuse accumulation of FDG in the basal wall, the 'over half' pattern showed more than 50% accumulation, and the 'spot' pattern showed less than 50% accumulation. Two or three board-certified radiologists, who were blinded to all of the clinical information, performed the visual analysis and classified the uptake patterns.

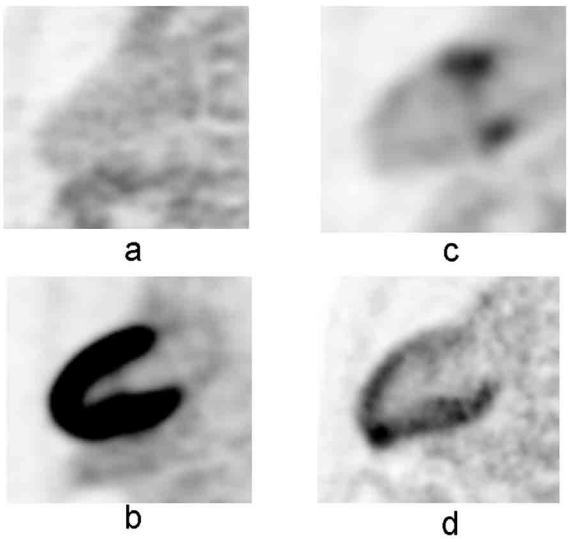

Figure 1. The left ventricular uptake pattern. a : none, b : diffuse, c : focal, d : focal on diffuse

Statistical analysis

The differences between the uptake patterns based on the age, blood glucose level and weight were evaluated using the Tukey test. A value of $p<0.05$ was considered to be statistically significant.

RESULTS

The frequencies of the myocardial FDG uptake patterns were as follows : "none", n=52 (27.7%) ; "diffuse", n=63 (33.5%) ; "focal on diffuse", n=40 (21.3%) and "focal", n=33 (17.6%) (Table 2). The age, blood glucose level, weight and dose of FDG did not differ significantly ($p>0.05$) for each pattern (Table 3). The "focal" and "focal on diffuse" patterns were seen in 73 patients, and 65 of these patients exhibited focal uptake of FDG in the basal

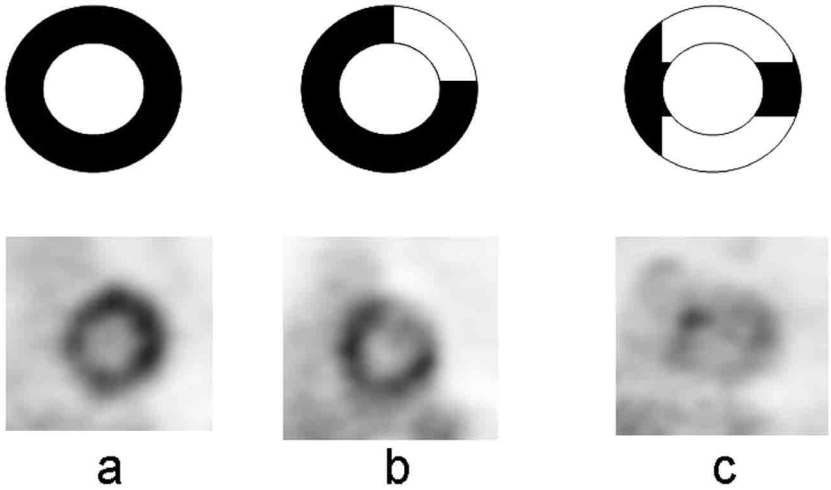

Figure 2. The uptake pattern in the basal wall. a : ring, b : over half, c : spot

wall only ('ring', n=29 ; 'over half', n=20 and 'spot', n=16) (Table 4). Patients with a "focal on diffuse" pattern did not have a 'spot' pattern, and only one patient had a "focal" pattern with a 'ring' pattern. Eight patients had focal uptake in other regions (apex, n=4 ; lateral, n=3 and anterior, n=1).

Table 2. Summary of the uptake patterns

Uptake pattern	n	%
None	52	27.7
Diffuse	63	33.5
Focal	33	17.6
Focal on diffuse	40	21.3
Total	188	100

Table 3. The relationship between the uptake patterns and parameters

Uptake pattern	None n=52	Diffuse n=63	Focal n=33	Focal on diffuse n=40
Age	65.0±12.0	61.8±12.8	68.0±9.7	63.2±12.1
Blood glucose level (mg/dl)	99.4±25.2	93.8±18.0	93.5±17.1	94.7±14.2
Weight (kg)	55.3±11.7	57.1±10.8	57.0±8.4	56.5±9.4
Dose (MBq)	201.8±41.3	210.4±33.7	208.0±29.1	209.9±35.6

None of the differences were statistically significant ($p > 0.05$)

Table 4. The area of focal uptake

		Focal	Focal on diffuse	Total
Basal segment only	Ring	2	27	29
	Over half	11	9	20
	Spot	16	0	16
Other segments		4	4	8
Total		33	40	73

DISCUSSION

The myocardium metabolizes fatty acids and glucose as energy sources. With sufficiently extended fasting, the myocardium shifts from a predominantly glycolytic metabolism to a fatty acid metabolism (3). In the clinical oncology setting, FDG PET is usually performed on patients who have been fasting for about six hours, so the fatty acid metabolism will be predominant over the glucose metabolism. However, cardiac FDG uptake often shows several patterns in the fasting state, and even in the same patient, the uptake can show different patterns at different times. There have been some previous reports on the physiological cardiac FDG uptake (4-8). In these reports, it was stated that the cardiac uptake showed various patterns, but that parameters such as the patient age, blood glucose level, weight and dose of FDG were not related to the uptake patterns in the myocardium. The myocardial metabolic rate is relative to the serum free fatty acid levels, but it does not depend only on the fasting period. In line with these findings, it was found in our study that the cardiac FDG uptake showed various patterns, but no parameters had a significant effect on these patterns.

Patients with cardiac disease, such as sarcoidosis (1, 2, 9-12), pulmonary hypertension (13), hypertrophic cardiomyopathy (14-16), a tumor or damage to the myocardium caused by radiotherapy (17-21) show abnormally high accumulation of FDG. In addition, cardiac sarcoidosis shows focal uptake (1, 2). We also investigated patients who showed focal FDG uptake. Thirty-three patients (17.6%) exhibited a "focal" pattern and 40 (21.3%) exhibited a "focal on diffuse" pattern. A total of 73 patients (38.8%) showed focal uptake. Thus, cardiac focal uptake was frequently seen in patients without cardiac disease. However, almost all of these patients (65/73, 89.0%) accumulated FDG only in the basal wall, which showed various patterns and degrees of focal uptake. Therefore, the uptake in the basal wall did not always indicate an abnormal finding when an examination was undertaken in the fasting state. However, patients without cardiac disease rarely show focal uptake of FDG in other regions. In our study, only eight of the 185 (4.3%) patients exhibited focal uptake in another region. If we decided that the focal uptake of FDG in the basal wall was normal, and focal uptake in another region was abnormal, the accuracy and specificity increased, but the sensitivity decreased, and we could not determine the true level of abnormal uptake in the basal wall.

Heparin increases the serum free fatty acid levels, reduces saccharometabolism and possibly minimizes the background myocardial uptake of FDG. Heparin also activates plasma lipoprotein lipase, which separates fatty acids. It is difficult to evaluate the cardiac uptake in the fasting state, so heparin loading should be carried out before injecting FDG.

When heparin loading is performed in patients without cardiac disease, the cardiac FDG uptake showed either the "none" pattern or the "diffuse" pattern, so we can easily evaluate the cardiac uptake. It is useful to use cardiac MRI or blood-flow scintigraphy in combination with this approach.

A major limitation of our study is that we labeled some patients as having no cardiac disease on the basis of only the clinical symptoms and anamnesis, so it could not be definitely confirmed that all of the enrolled patients were free from cardiac disease.

CONCLUSIONS

The physiological myocardial FDG uptake followed several patterns and frequently involved a focal uptake. Therefore, a focal uptake was often seen in patients with some cardiac diseases. However, this uptake did not necessarily indicate abnormal findings when the FDG accumulation only occurred in the basal wall. We should therefore be aware of the physiological uptake pattern when PET examinations are performed on patients in a fasting state.

REFERENCES

1. Ishimaru S, Tsujino I, Takei T, Tsukamoto E, Sakaue S, Kamigaki M, Ito N, Ohira H, Ikeda D, Tamaki N, Nishimura M : Focal uptake on ^{18}F-fluoro-2-deoxyglucose positron emission tomography images indicates cardiac involvement of sarcoidosis. Eur Heart 26 : 1538-1543, 2005
2. Ohira H, Tsujino I, Ishimaru S, Oyama N, Takei T, Tsukamoto E, Miura M, Sakaue S, Tamaki N, Nishimura M : Myocardial imaging with ^{18}F-fluoro-2- deoxyglucose positron emission tomography and magnetic resonance imaging in sarcoidosis. Eur J Nucl Med Mol Imaging 35 : 933-941, 2008
3. Neely JR, Morgan HE : Relationship between carbohydrate and lipid metabolism and the energy balance of heart muscle. Annu Rev Physiol 36 : 413-459, 1974
4. Shreve PD, Anzai Y, Wahl RL : Pitfalls in oncologic diagnosis with FDG PET imaging : physiologic and benign variants. Radiographics 19 : 61-77, 1999
5. Yamanouchi M, Yoshida K, Niwayama H, Nakagawa K, Aioi S, Shikama N : Effect of the duration of fasting on myocardial fluorine-18-fluorodexyglucose positron emission tomography images in normal males. Jpn Circ J 60 : 319-327, 1996
6. de Groot M, Meeuwis AP, Kok PJ, Corstens FH, Oyen WJ : Influence of blood glucose level, age and fasting period on non-pathological FDG uptake in heart and gut. Eur J Nucl Med Mol Imaging 32 : 98-101, 2005
7. Kaneta T, Hakamatsuka T, Takanami K, Yamada T, Takase K, Sato A, Higano S, Kinomura S, Fukuda H, Takahashi S, Yamada S : Evaluation of the relationship between physiological FDG uptake in the heart and age, blood glucose level, fasting period, and hospitalization. Ann Nucl Med 20 : 203-208, 2006
8. Gropler RJ, Siegel BA, Lee KJ, Moerlein SM, Perry DJ, Bergmann SR, Geltman EM : Non uniformity in myocardial accumulation of fluorine-18-fluorodeoxyglucose in normal fasted humans. J Nucl Med 31 : 1749-1756, 1990
9. Langah R, Spicer K, Gebregziabher M, Gordon L : Effectiveness of prolonged fasting ^{18}F-FDG PET-CT in the detection of cardiac sarcoidosis. J Nucl Cardiol 16 : 801-810, 2009
10. Okumura W, Iwasaki T, Toyama T, Iso T, Arai M, Oriuchi N, Endo K, Yokoyama T, Suzuki T, Kurabayashi M : Usefulness of fasting ^{18}F-FDG PET in identification of cardiac sarcoidosis. J Nucl Med 45 : 1989-1998, 2004
11. Mehta D, Lubitz SA, Frankel Z, Wisnivesky JP, EinStein AJ, Goldman M, Machac J, Teirstein A : Cardiac involvement in patients with sarcoidosis : Diagnostic and prognostic value of outpatient testing. Chest 133 : 1426-1435, 2008
12. Langah R, Spicer K, Gebregziabher M, Gordon L : Effectiveness of prolonged fasting ^{18}F-FDG PET-CT in the detection of cardiac sarcoidosis. J Nucl Cardiol 16 : 801-810, 2009
13. Kluge R, Barthel H, Pankau H, Seese A, Schauer J, Wirtz H, Seyfarth HJ, Steinbach J, Sabri O, Winkler J : Different mechanisms for changes in glucose uptake of the right and left ventricular myocardium in pulmonary hypertension. J Nucl Med 46 ; 25-31, 2005
14. Ishida Y, Nagata S, Uehara T, Yasumura Y, Fukuchi K, Miyatake K : Clinical analysis of myocardial perfusion and metabolism in patients with hypertrophic cardiomyopathy by single photon emission tomography and positron emission tomography. J Cardiol 37 Suppl 1 : 121-128, 2001

15. Ito Y, Hasegawa S, Yamaguchi H, Yoshioka J, Uehara T, Nishimura T : Relation between thallium-201/iodine 123-BMIPP subtraction and fluorine 18 deoxyglucose polar maps in patients with hypertrophic cardiomyopathy. J Nucl Cardiol 7 : 16-22, 2000
16. Park J-S, Cho I-H, Shin D-G, Kim Y-J, Hong G-R, Shim B-S : Hypertrophic cardiomyopathy complicated by left ventricular apical necrosis and aneurysm in a young man : FDG-PET findings. Korean J Intern Med 22 : 28-31, 2007
17. Jingu K, Kaneta T, Nemoto K, Ichinose A, Oikawa M, Takai Y, Ogawa Y, Nakata E, Sakayauchi T, Takai K, Sugawara T, Narazaki K, Fukuda H, Takahashi S, Yamada S : The utility of ^{18}F-fluorodeoxyglucose positron emission tomography for early diagnosis of radiation induced myocardial damage. Int J Radiat Oncol Biol Phys 66 : 845-851, 2006
18. Jingu K, Nemoto K, Kaneta T, Takai Y, Ichinose A, Ogawa Y, Yamada S : A case of high FDG-uptake into the myocardium after radiotherapy for esophageal cancer. Nippon Igaku Hoshasen Gakkai Zasshi 65 : 266-269, 2005
19. Ishikura S, Nihei K, Ohtsu A, Boku N, Hironaka S, Mera K, Muto M, Ogino T, Yoshida S : Long-term toxicity after definitive chemoradiotherapy for squamous cell carcinoma of the thoracic esophagus. J Clin Oncol 21 : 2697-2702, 2003
20. Small GR, Nicolson M, Buchan K, Broadhurst P : Pericardial malignant mesothelioma : a latent complication of radiotherapy? Eur J Cardiothorac Surg 33 : 745-747, 2008
21. Mukherjee S, Aston D, Minett M, Brewster AE, Crosby TD : The significance of cardiac doses received during chemoradiation of oesophageal and gastro-oesophageal junctional cancers. Clin Oncol 15 : 115-120, 2003