REVIEW ARTICLE−EDUCATIONAL TRACK

^{18}F-FDG PET/CT for Detecting Cardiac Sarcoidosis: Preparation and Interpretation

Emi Tateishi, MD, PhD and Keisuke Kiso, MD, PhD

Received: July 17, 2018/Revised manuscript received: July 26, 2018/Accepted: July 27, 2018

Abstract

Since cardiac sarcoidosis (CS) portends adverse outcomes, early diagnosis of active inflammation in CS is essential for therapeutic and prognostic advantages. ^{18}F-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography (PET) has been used for the clinical evaluation of active inflammatory lesions in CS. While myocardium can utilize both free fatty acids and glucose as the substrates of energy metabolism, the physiological myocardial ^{18}F-FDG uptake often makes it difficult to detect the pathological ^{18}F-FDG accumulation. Prolonged fasting and low-carbohydrate diet are most commonly used for suppressing physiological myocardial ^{18}F-FDG uptake, and moreover unfractionated heparin administration is sometimes considered. Sufficient preparation allows for the establishment of increased ^{18}F-FDG uptake in myocardium as active inflammatory lesions. Typical patterns of pathological ^{18}F-FDG accumulation in myocardium are "focal" and "focal-on-diffuse" and these are often corresponded with myocardial perfusion abnormality. In case with inconclusive ^{18}F-FDG uptake, the simultaneous interpretation with myocardial perfusion imaging is useful and helpful to evaluate clinically significant ^{18}F-FDG uptake in CS.

Keywords: Cardiac sarcoidosis, Myocardial ^{18}F-FDG uptake, Perfusion-metabolic mismatch, Sufficient preparation

Ann Nucl Cardiol 2018; 4 (1): 151−154

Sarcoidosis is a systemic disorder with heterogeneous contribution of non-necrotizing granulomatous inflammation. Generally, it is associated with good prognosis; however, cardiac involvement in sarcoidosis, cardiac sarcoidosis (CS), portends adverse outcomes and causes sudden cardiac death especially in young patients. Early diagnosis of CS is essential for therapeutic and prognostic advantages. ^{18}F-fluorodeoxyglucose (^{18}F-FDG) is an analog of glucose and ^{18}F-FDG positron emission tomography (PET) has been proposed for non-invasively detecting active inflammatory lesions in CS because it can provide the image of enhanced glucose metabolism at sites of macrophage-mediated inflammation. The Japanese Ministry of Health and Welfare approved health insurance coverage of ^{18}F-FDG PET for evaluating inflammatory lesions of CS in 2012; thereafter, it becomes an indispensable imaging modality in clinical diagnosis, evaluation of disease activity, monitoring of therapeutic response, and assessment of prognosis for CS. In 2016, ^{18}F-FDG PET has been regarded as one of the major criteria in the Guidelines for Diagnosis and Treatment of CS published by the Japanese Circulation Society (JCS) and its collaborative organizations, including the Japanese Society of Nuclear Cardiology (JSNC) (1).

Effective preparation for cardiac ^{18}F-FDG PET

To diagnose CS accurately, it is necessary to produce the state with increased ^{18}F-FDG uptake in active inflammation and no uptake in the normal myocardium. Since myocardium can utilize free fatty acids (FFAs) and glucose as the substrates of energy metabolism, physiological myocardial glucose uptake has often impeded to find out active inflammation under normal resting conditions. Myocardial glucose utilization depends on several factors, such as availability of FFAs, medications, presence of diabetes, serum insulin levels, serum

doi: 10.17996/anc.18-00082

Emi Tateishi, Keisuke Kiso
Department of Radiology, National Cerebral and Cardiovascular Center, Suita, Osaka, Japan
E-mail: emitat@ncvc.go.jp

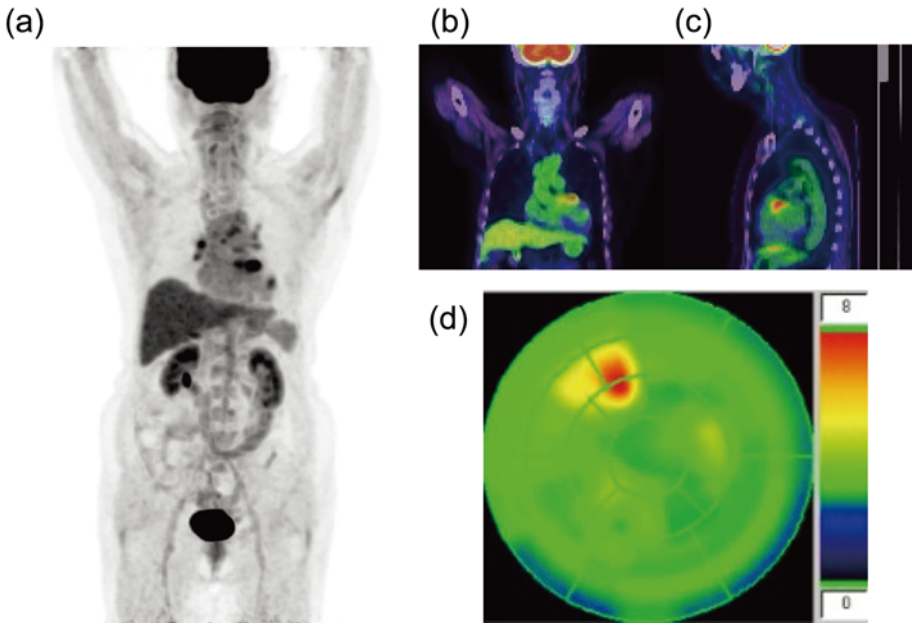

Fig. 1
Typical myocardial ^{18}F-FDG uptake pattern in cardiac sarcoidosis. Focal ^{18}F-FDG uptake was detected on the basal-anterior and mid-lateral wall of the left ventricle (LV). Increased ^{18}F-FDG uptake at mediastinal and bilateral hilar lymph nodes were also noted.
a : 3D maximum intensity projection (MIP).
b : Coronal PET/CT fusion image.
c : Sagittal PET/CT fusion image.
d : Bull's eye image.

glucose concentration and the duration of fasting. Though the optimal preparation has not been standardized and further investigations should be necessitated, prolonged fasting, dietary manipulation, and intravenous heparin, often in combination, have been commonly proposed for suppressing physiological myocardial ^{18}F-FDG uptake.

Prolonged fasting

Prolonged fasting effectively reduces serum insulin and glucose levels, and thereby suppresses physiologic myocardial glucose uptake. At least 12 h fasting is encouraged in JSNC recommendations for ^{18}F-FDG PET for CS published in 2014 (2). Recently, the Society of Nuclear Medicine and Molecular Imaging (SNMMI) and the American Society of Nuclear Cardiology (ASNC) provide the recommendation of fasting for 18 h or longer (3).

Low-carbohydrate diet

A low-carbohydrate diet could accomplish the switching of myocardial substrate metabolism from glucose to FFAs. In comparison with 12 h fasting alone, the combination of dietary manipulation with prolonged fasting resulted in significantly suppressed ^{18}F-FDG uptake in normal myocardium. Low-carbohydrate diet, less than 5 g of carbohydrate, is commonly required (4). In addition, high-fat diet may also decrease glycolysis in myocardium. Taking more than 35g of fat for the last meal has a possibility to suppress physiological myocardial ^{18}F-FDG uptake.

Adjunctive use of intravenous heparin

Since unfractionated heparin (UFH) induces lipolysis and increases plasma FFAs levels, intravenous UFH has been adjunctively used to suppress physiological ^{18}F-FDG uptake. The most published protocol is a single 50 IU/kg intravenous bolus of UFH approximately 15 min before ^{18}F-FDG administration (5).

Interpretation of ^{18}F-FDG uptake in myocardium

When ^{18}F-FDG PET is used to diagnose CS, it is important to consider the location and pattern of myocardial ^{18}F-FDG uptake. Postmortem studies have confirmed that sarcoidosis commonly involves on the basal ventricular septum, the left ventricular free wall, the papillary muscles and the right ventricle, in descending order of frequency (6). Focal ^{18}F-FDG uptake is a typical pattern for CS and focal-on-diffuse ^{18}F-FDG uptake may also represent active inflammation (Fig. 1). To further minimize false positive results, differentiating pathological ^{18}F-FDG uptake from physiological uptake should be carefully considered because fasting myocardial glucose metabolism varies among individuals. In some cases, ^{18}F-FDG uptake in myocardium can be observed even under fasting condition. Furthermore, the presence of myocardial ^{18}F-FDG uptake could be interpreted not only a sign of CS but also another etiology, such as hibernating myocardium by coronary artery disease and inflammatory

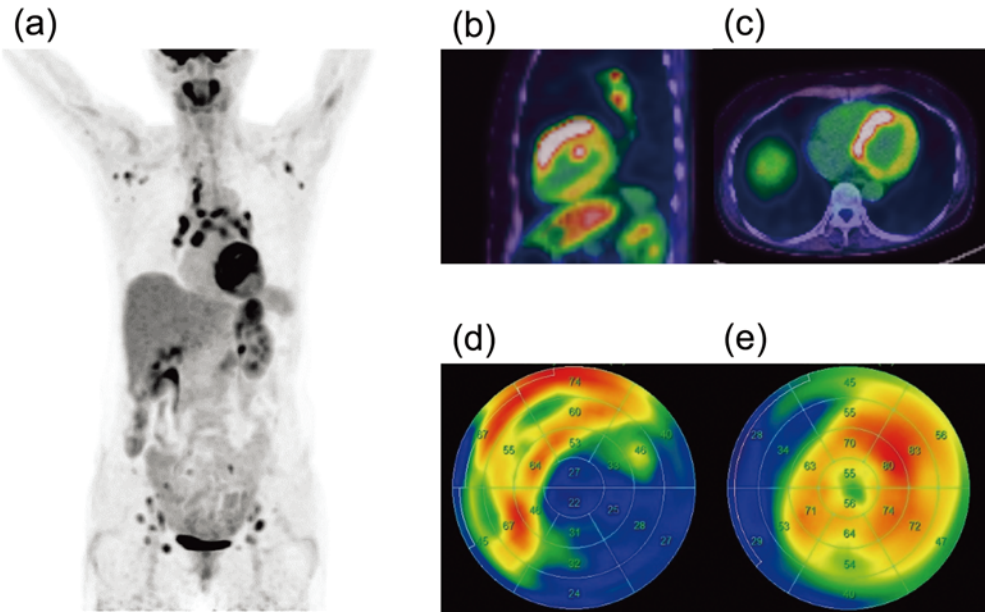

Fig. 2

A representative example of the perfusion-metabolic mismatch in a patient with histologically proven CS. Increased ^{18}F-FDG uptake at mediastinal, bilateral hilar and superficial lymph nodes were also observed in whole-body 3D maximum intensity projection (MIP) (a). Focal ^{18}F-FDG uptake can be observed in the anterior wall of left ventricle and the interventricular septum (b, c). In the presence of active inflammation, focal region of ^{18}F-FDG uptake was associated with myocardial perfusion defect, a perfusion-metabolic mismatch (d, e).

a : Frontal view of whole-body 3D MIP.
b : Sagittal PET/CT fusion image.
c : Transverse PET/CT fusion image.
d : Bull's eye image of myocardial 18F-FDG PET imaging.
e : Bull's eye image of myocardial perfusion SPECT imaging with ^{99m}Tc-MIBI.

myopathies.

According to the joint consensus of SNMMI and ASNC, the simultaneous interpretation of a resting myocardial perfusion and ^{18}F-FDG PET images is promulgated to diagnose CS. Pathological ^{18}F-FDG uptake is more likely to be associated with myocardial perfusion defects, which can be due to either compression of the microvasculature by inflammation or scarring (Fig. 2). ^{18}F-FDG uptake with normal myocardial perfusion is assumed about physiological ^{18}F-FDG uptake or early CS. The presence of ^{18}F-FDG uptake is valuable findings but not all of them correspond active inflammation of CS. On the other hands, the absence of ^{18}F-FDG uptake with a resting myocardial perfusion defect represents fibrosis or scarring, which may implicate the presence of previous CS. When a myocardial perfusion abnormality is present, the absence of ^{18}F-FDG uptake is not sufficient enough to rule out the cardiac involvement of sarcoidosis. It is important to deliberate about several factors affecting myocardial glucose uptake when diagnosing CS by ^{18}F-FDG PET.

See related self-assessment program: Go to ANC URL http://anc.jsncjournal.org/

Acknowledgment

The images in this article are from National Cerebral and Cardiovascular Center, Osaka, Japan.

Sources of funding

None.

Conflicts of Interest

None.

Reprint requests and correspondence:
Emi Tateishi, MD, PhD
Department of Radiology, National Cerebral and Cardiovascular Center, 5-7-1 Fujishirodai, Suita, Osaka, 565-8565, Japan
E−mail: emitat@ncvc.go.jp

References

1. The Japanese Circulation Society (JCS). Guidelines for the diagnosis and treatment of cardiac sarcoidosis (JCS2016) (Chair: Fumio Terasaki). Published on February 24, 2017 [in Japanese] (http: //www. j-circ. or. jp/guideline/pdf/JCS2016_

terasaki_h.pdf)
2. Ishida Y, Yoshinaga K, Miyagawa M, et al. Recommendations for ^{18}F-fluorodeoxyglucose positron emission tomography imaging for cardiac sarcoidosis: Japanese Society of Nuclear Cardiology recommendations. Ann Nucl Med 2014; 28: 393-403.
3. Chareonthaitawee P, Beanlands RS, Chen W, et al. Joint SNMMI-ASNC expert consensus document on the role of ^{18}F-FDG PET/CT in cardiac sarcoid detection and therapy monitoring. J Nucl Med 2017; 58: 1341-53.
4. Cheng VY, Slomka PJ, Ahlen M, et al. Impact of carbohydrate restriction with and without fatty acid loading on myocardial ^{18}F-FDG uptake during PET: A randomized controlled trial. J Nucl Cardiol 2010; 17: 286-91.
5. Manabe O, Yoshinaga K, Ohira H, et al. The effects of 18-h fasting with low-carbohydrate diet preparation on suppressed physiological myocardial ^{18}F-fluorodeoxyglucose (FDG) uptake and possible minimal effects of unfractionated heparin use in patients with suspected cardiac involvement sarcoidosis. J Nucl Cardiol 2016; 23: 244-52.
6. Tavora F, Cresswell N, Li L, et al. Comparison of necropsy findings in patients with sarcoidosis dying suddenly from cardiac sarcoidosis versus dying suddenly from other causes. Am J Cardiol 2009; 104: 571-7.