The future of cardiac disease assessment using ^{18}F -FDG PET/CT

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Fluorine-18 labeled fluorodeoxyglucose (^{18}F -FDG) is the most commonly used positron emission tomography (PET) tracer in the world, mainly in the oncology field. ^{18}F -FDG uptake is related to metabolic activity; therefore, it can be used to characterize and localize many types of tumors. In nuclear cardiology, ^{18}F -FDG PET was first used to assess the metabolic viability of coronary artery disease in the 1980s [1, 2]. Glucose is one of the main substrates for the myocardium. Myocardial cells take up ^{18}F -FDG similar to glucose. In addition, ^{18}F -FDG is accumulated in inflammatory foci because of the activation of inflammatory cells, such as lymphocytes and macrophages. Therefore, ^{18}F -FDG PET is being used for the evaluation of cardiac sarcoidosis (CS) since the 2000s [3]. Intravenously administered ^{18}F -FDG is distributed throughout the body by the bloodstream and is found to accumulate more in sites of high glucose consumption. Interestingly, ^{18}F -FDG accumulates in cells differently depending on the disease and pathological conditions (Fig. 1). A review by Minamimoto presented an intriguing issue of myocardial and pericardial abnormalities using ^{18}F -FDG PET/computed tomography (CT) [4].

The main energy sources of the myocardium are glucose and free fatty acids (FFAs). In normal cardiomyocytes, glucose utilization is dominantly observed after meals, whereas FFA utilization is observed during long fasting periods. Hence, variation in myocardial ^{18}F -FDG uptake is observed in standard ^{18}F -FDG PET/CT performed after 4–6 h of fasting, and consequently, abnormal myocardial and pericardial signs are overlooked. Myocardial ^{18}F -FDG uptake is

completely different in fasting conditions and cardiac disorders. Myocardial viability is evaluated by assessing ^{18}F -FDG accumulation. In the infarcted scar tissue, the accumulation of ^{18}F -FDG is absent because of the non-availability of glucose metabolism. On the contrary, ^{18}F -FDG accumulation is observed in the viable myocardium is maintained because of the dominance of anaerobic glucose metabolism. To assess myocardial viability, oral glucose loading or an insulin-glucose clamp is applied to enhance physiological ^{18}F -FDG uptake in the myocardium.

^{18}F -FDG uptake reflects glycolysis in tumors. In cardiac tumors, ^{18}F -FDG uptake by the tumor tissue and the presence of malignancy are correlated [5]. In addition, glucose is consumed in the inflammatory process; therefore, significant ^{18}F -FDG uptake by active inflammatory lesions, such as CS, is observed. To accurately evaluate active myocardial lesions, suppression of physiological myocardial ^{18}F -FDG uptake through diverse methods, such as long fasting and low-carbohydrate diet and/or high-fat diet, is necessary.

The guidelines for the diagnosis of CS include abnormal findings on ^{18}F -FDG PET as one of the main signs of clinical diagnosis [6, 7]. The pattern of ^{18}F -FDG accumulation in the left ventricular myocardium is often divided into four categories: none, diffuse, focal, and focal on diffuse [8]. None and diffuse accumulation of ^{18}F -FDG are regarded as physiological patterns. However, the patterns of physiological ^{18}F -FDG accumulation are variable, and the normal variants include crista terminalis and lipomatous hypertrophy of the interatrial septum. In addition, Minamimoto reported the physiological uptake in detail, facilitating our understanding [4]. Sometimes ^{18}F -FDG uptake is observed in the atrial wall and in the right ventricle, which might be associated with atrial fibrillation and ventricular pressure overload in patients with pulmonary hypertension, respectively.

^{18}F -FDG PET/CT has diagnostic potential for various myocardial conditions (Table 1). Given the potential

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Table 1 FDG uptake pattern in the heart

	Uptake pattern
Physiological uptake	
LV wall	Diffuse, none, predominantly in the basal level, predominantly in the lateral and posterior walls
Normal variant	
Crista terminalis	Focal uptake in the right atrium
LHIS	Focal uptake in the interatrial septum
Uptake in the atrial wall	
AF	Along the atrial wall
Increased atrial pressure	Along the enlarged atrial wall
Uptake in the right ventricle	
Physiological	Lesser frequent uptake compared with that in the LV sometimes observed in healthy young adults with diffuse uptake in the LV
Increased ventricular pressure and overload (i.e., PH and valvular heart disease)	Diffuse uptake in the LV and RV
Pathological uptake in the left ventricle	
Coronary artery disease	Focal uptake or defect along the coronary territory
Myocardial hypertrophy	Uptake along the hypertrophic wall decrease in the region with tissue characterizations such as fibrosis
Left bundle branch block	Reduced septal FDG uptake
Takotsubo cardiomyopathy in the acute and subacute phases	Decreased uptake in the hypocontractile segment in the case of stimulated physiological uptake relatively increased uptake in the hypocontractile segment in the case of suppression of physiological uptake
Chemotherapy; possible early sign of cardiotoxicity	Increased uptake in the myocardium during chemotherapy with anthracyclines that remains elevated for at least 1 year
Radiation therapy	Increased uptake in the radiation therapy field
Cardiac sarcoidosis	Focal or focal on diffuse uptake in the active lesion
Cardiac tumor	Intense uptake in most malignant tumors compared with benign tumors
Cardiac amyloidosis	Diffuse uptake

AF atrial fibrillation, LHIS Lipomatous hypertrophy of the interatrial septum, LV left ventricle, PH pulmonary hypertension, RV right ventricle

diagnostic challenges imposed on radiologists and nuclear medicine physicians, this article provides information regarding the physiological and abnormal uptake in the myocardium [4]. ^{18}F -FDG accumulation is observed not only in CS but also in other heart diseases, such as coronary artery disease, hypertrophic cardiomyopathy, takotsubo cardiomyopathy, and cardiac tumors, even under conditions that

suppress physiological ^{18}F -FDG uptake. ^{18}F -FDG uptake in these diseases is sometimes difficult to distinguish from that in CS or from physiological uptake [4, 9, 10]. In order to point out the abnormal ^{18}F -FDG uptake in the cardiac lesion, it is essential to increase our knowledge and experience even during daily oncologic interpretation of PET/CT.

Fig. 1 Typical ^{18}F -FDG PET findings and patient preparation for cardiac diseases. Accumulation of ^{18}F -FDG in the left anterior descending artery territory is not observed in the infarcted scar tissue (a) under glucose loading conditions because of the non-availability of glucose metabolism. An increase in ^{18}F -FDG accumulation is observed in cardiac lymphoma (b) and cardiac sarcoidosis (c) on suppression of myocardial physiological uptake. ^{18}F -FDG, fluorine-18 fluorodeoxyglucose

Declarations

Conflicts of interest The authors declare no conflicts of interest.

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