EDITORIAL POINT OF VIEW

^{18}F-FDG PET Viability Assessment for the Improvements of Prognosis of the Patients with Left Ventricular Dysfunction —Is This Ready for Clinical Practice?—

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Abstract

Positron emission tomography (PET) has greater temporal and spatial resolution. ^{18}F-fluorodeoxyglucose (^{18}F-FDG) PET has also been used to assess pathophysiological condition and to identify the patients who have benefit from coronary revascularization therapy in ischemic left ventricular dysfunction. There have been numbers of studies looking at the diagnostic value of viable myocardium using ^{18}F-FDG PET. However, the prospective trials have been very limited and has been no previous study prospectively conducted by multi-center. Recently, the prospective multicenter clinical study in Japan showed the diagnostic usefulness of ^{18}F-FDG in predicting improvement in myocardial wall motion after coronary revascularization. This study has great contribution to strength the evidence of ^{18}F-FDG PET for detecting viable myocardium. Nuclear approach, including FDG-PET, can be a useful tool to identify viability in case of difficult to diagnose myocardial viability using myocardial perfusion SPECT. (Ann Nucl Cardiol 2016)

Keywords: FDG, Hibernation, Multicenter clinical study, Prognosis, Revascularization, Viability
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Chronic heart failure remains a substantial cause of death and disability in Japan and the rest of the world (1). Left ventricular dysfunction in ischemic heart failure is not always an irreversible process but can be improved significantly with recent optimal medical treatment, cardiac resynchronization therapy and invasive revascularization (2). The coronary artery revascularization plays still most important role for improving survival and functional capacity in patients with ischemic heart disease. Reversible causes of left ventricular dysfunction in chronic ischemic heart failure patients can be identified by means of nuclear cardiology technique. While single photon emission computed tomography (SPECT) approach using Thallium 201 (^{201}Tl) and ^{99m}Tc tracers has wildly contributed to provide information for identifying viable myocardium. ^{201}Tl retention in the myocardium reflects the cell membrane integrity of the Na/K pump. ^{99m}Tc-sestamibi binds to the mitochondria and could be a marker of myocardial viability and prognosis (3). Positron emission tomography (PET) uses high energy tracers, has greater temporal and spatial resolution. PET has also been used to assess pathophysiological condition and to identify the patients who can benefit from revascularization therapy (2,4), as shown in Fig. 1.

The myocardium has high energy demands and uses a variety of metabolic substrates, including fatty acid and glucose. Reversible left ventricular dysfunction occurs when the viability of myocardium is preserved and the contractility is reduced. Hibernating myocardium may represent a state of metabolic down regulation in response to reduced perfusion or oxygen supply. Under ischemic state, oxidation of fatty acid is decreased and glycolysis system becomes a dominant energy source. To obtain these metabolic pathological condition, the only approved PET tracer in Japan for viability assessment is ^{18}F- fluorodeoxyglucose (FDG) (5, 6). ^{18}F-FDG PET is a

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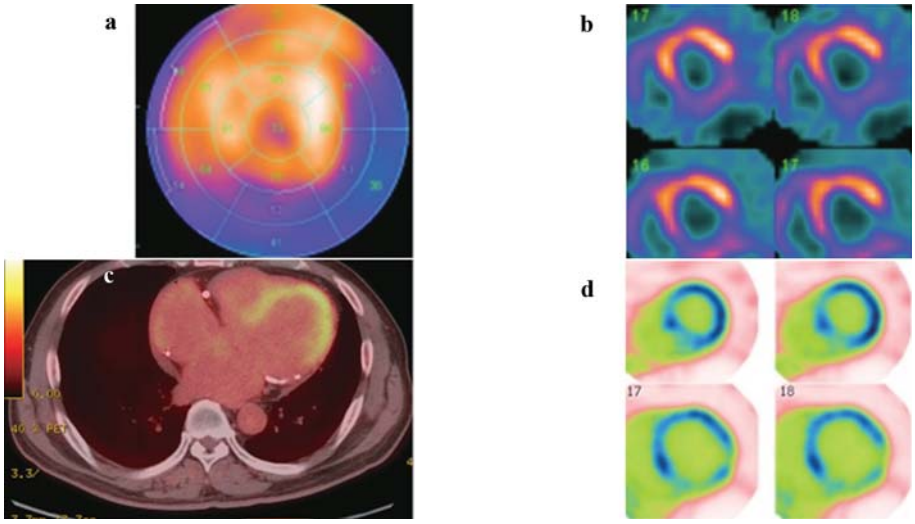

Fig. 1 Cardiac PET/CT for the assessment of viability
A 61 years-old male patient with prior myocardial infarction and history of revascularization for the 3-coronary vessels. ^{99m}Tc-sestamibi myocardial perfusion imaging showed defect in basal inferolateral area of the left ventricle shown in polar map (a) and short axis images (b). ^{18}F-FDG PET/CT axial images (c) reduced uptake in basal sub-endocardial lateral ^{18}F-FDG uptake. This corresponds with preserved uptake in apical to mid lateral area at short axis images on ^{18}F-FDG PET (d), which confirmed viable myocardium.

promising modality to prove and diagnose the viability in case of difficult to diagnose myocardial viability using myocardial perfusion SPECT (5), although there are the limitations. Firstly, ^{18}F-FDG PET imaging is less wildly available than SPECT. Secondly, insulin resistance in patients with type II diabetes may affect a reduced uptake of FDG into the myocardium.

Although FDG PET has been recognized important imaging approach for detecting viable myocardium, the prospective trials have been actually limited. Randomized controlled trial evaluating the utility of viability testing in patients with chronic ischemic cardiomyopathy had been conducted (2). The PET and recovery following revascularization (PARR)-2 study evaluated the utility of a management strategy using ^{18}F-FDG PET imaging to assist in decision making for revascularization versus medical therapy (2). The PARR-2 study reported that 30% patients in the PET subgroup had events vs. 36% in the standard care subgroup (2). Although there was no significant difference in the composite primary outcome of cardiac death, myocardial infarction or recurrent hospitalization between the two management strategies, there were some limitations that a number of patients (25%) were not managed according to the trial protocol and that the study subjects did not undergo the revascularization guided by the PET imaging results. Therefore an additional study was required only in the subjects adhering to PET-guided recommendation. In the sub-study of the PARR-2, it was demonstrated that there was a significant relationship between PET-defined hibernating myocardium and the improved outcome through revascularization (7). The result from this study added a quality of evidence, that ^{18}F-FDG PET is a useful imaging modality for detecting viable myocardium and gives us information for the decision-making on the invasive strategy (7).

In the article of this issue of *Annals of Nuclear Cardiology*, Matsunari et al reported the prospective multicenter clinical study that showed the diagnostic usefulness of ^{18}F-FDG PET in predicting improvement of myocardial wall motion after coronary revascularization (8). This was the first report in Japan that confirmed the ability of ^{18}F-FDG PET as a large-scale clinical trial for the detection of viability. It was concluded in accordance with previous studies (4,9), that ^{18}F-FDG PET is a valuable tool for risk stratification of the patients with left ventricular dysfunction and ischemic heart failure (8). The findings themselves are not exciting. However, the importance of the current study by Matsunari et al. is not only the first larger clinical trial using ^{18}F-FDG PET in Japan but also the first multi-center prospective trial looked at the clinical value of ^{18}F-FDG PET in clinical settings. In this regard, this study has great contribution to establish the evidence.

American College of Cardiology (ACC)/ American Heart Association (AHA) guidelines on revascularization, recommend CABG (class IIa, Level B) to improve survival for patients with ischemic heart disease and mild to moderate LV systolic dysfunction (EF 35-50%) (10). Clinical use of viability imaging in an appropriate use criteria in the ACC/AHA practice guideline has been previously given a class IIa recommendation (11). Recent European guideline recommends that PET or PET/CT can be used for assessment

of both ischemia and viability. ^{18}F-FDG PET can predict improvement in heart failure symptoms, functional status, quality of life, and global and regional systolic function post revascularization (12). ^{18}F-FDG PET is considered as an appropriate measure for viability assessment and, with some disagreement, for assessment of inducible ischemia as well. The disagreement should be explained by the limited availability of PET around European countries, rather than by the value of the PET (12).

The role of viability assessment in ischemic heart failure patients is also discussed in Japanese circulation society (JCS) guideline. Current JCS guidelines on nuclear cardiology tests gives the viability imaging of PET in patients with coronary artery disease a class I recommendation and level B of evidence (13). However, ^{18}F-FDG PET in Japan is mostly used for diagnosis of cancer and not widely used for cardiac disease. The selection of imaging modalities depends not only on accessibility but also local expertise and experience with the modalities and techniques. Since ^{18}F-FDG PET has been proved to be safe and beneficial in predicting left ventricular functional recovery by the current Japanese trial, nuclear approach, including ^{18}F-FDG PET, can be a useful tool to identify viability particularly for patients where conventional SPECT images fails to prove the viability. The current study by Matsunari et al. hopefully would pave the way to wide clinical use of ^{18}F-FDG viability imaging.

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Conflicts of interest

None

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