Potential roles of ^{123}I -BMIPP SPECT to assess cardiac sarcoidosis

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Under normal fasting conditions, the healthy heart derives its energy from a variety of oxidizable substrates, including fatty acids, glucose, lactate, and amino acids. Among them, 60–70% of the energy production is obtained from fatty acid oxidation, and most of the remaining energy comes from glucose metabolism in the healthy myocardium. Under ischemic conditions, oxidative metabolism of free fatty acids is decreased due to the requirement of more oxygen compared to glucose for β -oxidation in mitochondria.

Such energy metabolism in the myocardium can be analyzed using suitable radiolabeled tracers. Iodine-123-labeled beta-methyl-p-iodophenylpentadecanoic acid (^{123}I -BMIPP) is a single-photon emission computed tomography (SPECT) tracer, which is an iodinated fatty acid analog used to assess myocardial fatty acid metabolism. ^{123}I -BMIPP was initially developed in the United States (US)¹; however, this tracer has not been approved for clinical use in the US and Europe despite its utility in clinical management. The Japanese community succeeded in the development of ^{123}I -BMIPP and it has now been approved for clinical use in Japan.^{2,3} ^{18}F -fluorodeoxyglucose (^{18}F -FDG), a glucose analog, is a positron emission tomography (PET) tracer used in myocardial viability assessment under controlled glycaemic conditions. ^{18}F -FDG is also used for the

evaluation of active inflammation such as cardiac sarcoidosis (CS) under long-fasting conditions.

Sarcoidosis is a multisystem inflammatory disorder, and its involvement in the myocardium is associated with a poor prognosis. For the diagnosis of CS, the combination of multi-modality imaging plays an important role because of the low yield endomyocardial biopsy. Cardiac magnetic resonance (CMR) with late gadolinium enhancement (LGE) and ^{18}F -FDG PET are the major criteria for the diagnosis of CS.⁴ Myocardial perfusion imaging and ^{123}I -BMIPP have also been used to diagnose CS.^{5,6}

The autopsy image obtained from a patient with CS showed the coexistence of different pathologies such as Langerhans-type cell granuloma formation, reactive fibrosis, hyalinizing scar tissues, and normal myocardium.⁷ Moreover, heterogeneous ^{18}F -FDG accumulation in the myocardium is observed in patients with CS.^{8,9} CS distribution can be determined using various modes of imaging and tracers as seen in Figure 1.

Several reports have indicated that a couple of imaging techniques have prognostic roles in patients with CS, including the size of positive ^{18}F -FDG uptake on PET, perfusion defect on SPECT, and abnormal contrast enhancement on magnetic resonance imaging (MRI).^{10–12} Furthermore, quantitative analyses and location of ^{18}F -FDG uptake (particularly in the right ventricle) are important prognostic markers in patients with CS.^{13,14}

Recently, Yamamoto et al. reported the usefulness of ^{123}I -BMIPP SPECT for predicting recurrence and major adverse cardiac events (MACEs) in patients with CS.¹⁵ In their study, 73 patients, including 28 patients who initially underwent ^{123}I -BMIPP SPECT and subsequently ^{18}F -FDG PET after the start of prednisolone therapy, were enrolled. In the follow-up period, 21 recurrences and 20 MACEs occurred. The results indicated that the total ^{123}I -BMIPP SPECT defect score and

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Figure 1. Schema of correlation between each test and pathological conditions of cardiac sarcoidosis. When myocardial physiological accumulation is suppressed, ^{18}F -FDG accumulates in highly active inflammatory lesions. Fatty acid metabolism delineated by ^{123}I -BMIPP is decreased in active inflammation and fibrosis. Myocardial perfusion decreased mainly in the fibrotic region and relatively decreased even in the granulomatous lesion site. LGE-MRI is observed mainly in fibrotic changes. ^{18}F -FDG, ^{18}F -fluorodeoxyglucose; ^{123}I -BMIPP, Iodine-123-labeled beta-methyl-p-iodophenylpentadecanoic acid; LGE, late gadolinium enhancement; MRI, magnetic resonance imaging.

SUVmax from ^{18}F -FDG PET were significantly associated with recurrence and MACEs. Among the several imaging tests used to assess CS, ^{18}F -FDG PET was the most sensitive to active inflammation. However, this study included patients who had already started prednisolone treatment, which might have affected the results of ^{18}F -FDG PET.

For ^{18}F -FDG PET to properly assess CS, dietary preparation to achieve the suppression of physiological myocardial uptake is necessary. Assessing recurrence and MACEs of CS using ^{123}I -BMIPP SPECT requires no special preparation such as long-fasting, high-fat diets, and low-carbohydrate diet prior to the scan.

There are several important issues that should be addressed in the near future. As shown in Figure 1, it is vital to understand the most important location or anatomical feature for assessing prognostic value. Several studies have performed quantitative analyses of active inflammation, myocardial fibrosis, or both as important prognostic markers in patients with CS.¹⁶ There may be specific locations in our imaging that can easily cause fatal arrhythmias, such as the septal wall. Clinicians usually select one or two imaging methods for the diagnosis and prognosis of these patients. Echocardiographies and/or resting myocardial perfusion imaging may also be helpful for prognosis. Additional studies are needed to compare the findings of different imaging techniques, particularly for risk analysis in patients with CS.

Disclosure

The authors declare no conflicts of interest.

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