Assessment of Myocardial Viability by Using Newly Developed Myocardial SPECT Imaging

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Thallium myocardial imaging has been widely available for the detection of myocardial ischemia and assessment of myocardial viability in coronary artery diseases. However, myocardial imaging using SPECT and gamma-emitting radiopharmaceuticals has been developed for accurate evaluation of myocardial infarction and ischemia. The present study was undertaken to clinically evaluate myocardial necrosis, metabolism and sympathetic nerve activity. In this study, myocardial fatty acid metabolism was assessed using $^{123}$I-BMIPP, myocardial sympathetic neural activity was assessed using $^{123}$I-MIBG and myocardial necrosis was assessed using $^{111}$In-antimyosin Fab. Dual energy SPECT using these new agents and thallium gives precise characterization of myocardial viability in coronary artery disease. (*Jpn Circ J 1992; 56: 603–607)

THALLIUM myocardial SPECT (single photon emission computed tomography) has been widely used for the assessment of myocardial ischemia and myocardial viability in coronary artery disease. This technique is very useful in assessing the indications for percutaneous coronary angioplasty and follow-up procedures required. However, it has some limitations, since the amplitude of redistribution does not accurately reflect the degree of myocardial viability. Recently, re-injection or 24 h delayed thallium image has been used for the precise evaluation of myocardial viability. Myocardial viability should ultimately be evaluated with regard to myocardial necrosis, metabolism and sympathetic neural activity in addition to ventricular function and myocardial perfusion. The present study was undertaken to evaluate myocardial viability by using newly developed myocardial SPECT imaging. These procedures were carried out in coronary artery disease patients as follows: 1) myocardial metabolism was assessed by $^{123}$I-BMIPP ($\beta$-methyl iodophenyl pentadecanoic acid) 2) myocardial sympathetic neural activity was investigated using $^{123}$I-MIBG (metaiodobenzylguanidine) and 3) myocardial necrosis was studied using $^{111}$In-AM (antimyosin Fab).

MATERIALS AND METHODS

$^{123}$I-BMIPP myocardial imaging

Twenty-five patients with myocardial infarction were studied by simultaneous thallium and $^{123}$I-BMIPP myocardial SPECT to evaluate the relationship between myocardial perfusion and fatty acid metabolism. $^{123}$I-BMIPP and thallium of 111 MBq were injected simultaneously. There were 8 patients with intracoronary thrombolysis (ICT), 7 without ICT, and 10 with old

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Fig. 1. Simultaneous BMIPP and thallium myocardial SPECT in (a) patient with successful reperfusion and (b) without reperfusion. Note the dissociation between BMIPP and thallium detects in reperfusion case. L-A, T-A, and S-A = long, trans, short axial view.

Myocardial infarction. Their mean ages were 58 ± 11 years. Simultaneous $^{123}$I-BMIPP and thallium myocardial SPECT was carried out by using gamma camera (400 AC/T) equipped with an all-purpose parallell hole collimator interface to a STAR computer. Thirty-two planar acquisition were obtained at 40 second interval over a 180° arc extending from 45° RAO to 45° LPO projection. Tomographic slices, each 6 mm thickness, were reconstructed parallel to the vertical and horizontal long axes and the short axis of the left ventricle. The severity scores of BMIPP and thallium myocardial SPECT were calculated semi-quantitatively by segmental analysis using three representative slices (apex, middle, base) of short axial views (each showing 8 segments at 5 gradings each). The dissociation between perfusion and metabolism was evaluated by these scores in these patients.

$^{123}$I-MIBG myocardial imaging

Simultaneous $^{123}$I-MIBG and thallium myocardial SPECT was carried out in 14 patients with myocardial infarction to evaluate denervated but viable myocardium. The patients were given 111 MBq of $^{123}$I-MIBG, then, 74 MBq of thallium was injected intravenously 3–4 h after $^{123}$I-MIBG administration to allow sufficient clearance of the extraneural MIBG uptake. All patients were imaged serially at the acute phase (10 ± 2 days from the onset) and chronic phase (86 ± 10 days from the onset). These were 13 men and 1 woman. Their mean age was 58 ± 10 years. Eight patients had interventional treatment (percutaneous coronary angioplasty and/or intracoronary thrombolysis), however, no patients received elective percutaneous coronary angioplasty between the 1st and 2nd MIBG studies. Simultaneous $^{123}$I-MIBG and thallium myocardial SPECT was carried out by using a rotating gamma camera (400 AC/T GE) equipped with an all-purpose parallell hole collimator interface to the STAR computer. The extent of $^{123}$I-MIBG and thallium defects was evaluated visually on a bull's eye display generated from each short axial SPECT image.

$^{111}$In-AM myocardial imaging

Simultaneous $^{111}$In-AM and thallium myocardial SPECT was carried out in 33 patients with acute myocardial infarction to evaluate the usefulness of extent and uptake of $^{111}$In-Am in patients with reperfused and occluded infarcts. At about 48h after injection of 74 MBq of $^{111}$In-AM, 74 MBq of thallium was injected intravenously. All patients were studied between 5-10 days after injection. There were 30 men and 3 women. Their mean age was 63 ± 11 years. Simultaneous $^{111}$In-AM and thallium myocardial SPECT was carried out by using rotating gamma camera (400 AC/T) equipped with medium energy parallel hole collimator interfaced to the STAR computer. The extent and uptake of $^{111}$In-AM representative tomographic place was semiquantiatively assessed. Each representative tomographic plane was divided into 5 segments. AM uptake was graded semi-quantitatively as four scale (0–+3). AM uptake more than +1 was considered as positive. In addition, the relationship between AM uptake and thallium defect was evaluated at the representative same tomographic plane of dual SPECT.
RESULTS

**123I-BMIPP myocardial imaging**

Typical cases of acute myocardial infarction with and without intracoronary thrombolysis (ICT) are shown in Fig. 1. In successful ICT (Fig 1a), greater BMIPP defects were observed compared to thallium defects, while AMI without ICT showed similar BMIPP and thallium defects by simultaneous myocardial SPECT (Fig 1b). In 8 patients with successful ICT, significant dissociations of BMIPP and thallium were observed. The severity score was 5.1 ± 4.7 and 12.8 ± 8.8, respectively (P < 0.01). In 7 without ICT, severity scores of BMIPP and thallium were 14.5 ± 6.4 and 15.4 ± 6.2 ± 5.2, while in 10 with old myocardial infarction, those were 10.1 ± 11.2 and 14.2 ± 13.6, respectively (P = ns). Significant dissociations between BMIPP and thallium defects were not demonstrated in the latter two groups. In four cases of successful ICT, simultaneous SPECT was repeated in the chronic phase. BMIPP uptake and left ventricular function were gradually improved compared to thallium myocardial perfusion.

**123I-MIBG myocardial imaging**

Seven patients (group A) showed marked improvement; however, the remaining 7 (group B) did not show improvement of the 123I-MIBG defect from acute to chronic phase by bull’s eye display of simultaneous MIBG and thallium myocardial SPECT. The representative cases of group A and B are shown in Fig. 2. In a patients with anteroapical myocardial infarction (Fig. 2a), the 123I-MIBG defect was larger than thallium defect on day 8; however, neither defects are seen on day 69 conversely, in a patients with inferoposterior myocardial infarction (Fig. 2b), MIBG and thallium defect of similar size are observed on day 96. Of the 7 patients in group A, 4 still had a small defect during the chronic phase. Five of 7 had a high incidence of small infaracts, 5 of 7 underwent PTCA and 6 of 7 had reduced LVEF. Four of 7 had post-MI angina and all 7 had exercise-induced thallium redistribution at the infarcted area. On the other hand, 6 of 7 in group B had a high incidence of large defect and 4 had reduced LVEF. Two patients had post-MI angina and 1 had exercise-
induced thallium defect.

\textbf{\textit{111}}In-AM myocardial imaging

\textit{111}In-AM uptake was positive in 31/33 (94\%). The detection of infract location was 95\%, 89\% and 100\% of anterior, inferior and lateral infarction, respectively. Scan with thallium defect and corresponding AM uptake was classified as overlap positive (+). Typical cases with overlap (+) and overlap negative (−) were shown in Fig. 3. Overlap (+) at the infarcted area was observed frequently in 18 (55\%) of all patients. Among patients who were overlap (+), 10/18 (56\%) had emergent PTCA/PTCR, while those who were overlap (−) had 2/15 (13\%) with PTCA/PTCR. Overlap (+) at the infarcted area correlated with ischemic events such as reattack, PTCA, CABG and sudden death within 6 months of onset. Twenty-eight patients had coronary angiography. In overlap (+) patients with greater than 75\% residual stenosis, 5 (50\%) of 10 had ischemic events. However, among patients without residual stenosis, there was only 1 case of ischemic event. Patients who were overlap (−) also had only one ischemic event.

\textbf{DISCUSSION}

Myocardial metabolic and receptor imaging such as \textit{18}F-deoxyglucose and \textit{11}C-palmitate have been available using PET. However, PET studies can only be done in a research centers with an expensive imaging device and in-house cyclotron. Therefore, the newly developed myocardial imaging with gamma-emitters using SPECT is desirable.

\textit{123}I-BMIPP myocardial imaging\textsuperscript{3−2}

Attempts have been made to determine the metabolic integrity of the myocardium quantitatively with radiolabelled free fatty acids, which are the preferred energy substrate for the heart. \textit{123}I-free fatty acids were divided into 2 groups; straight and branched chain analogues. \textit{123}I-BMIPP is one of the branched-chain free fatty acids. It has suitable characteristics for SPECT, since it demonstrates higher uptake and longer retention in the myocardium. BMIPP myocardial uptake reflects the changes in lipid pool size in association with the changes in fatty acid metabolism. BMIPP cannot evaluate directly the β-oxidation of free fatty acid. In experimental studies, the dissociations of BMIPP and thallium uptake were observed in ischemic and cardiomyopathy models. In clinical trials, BMIPP defect was greater than thallium defect in myocardial infarction. Patients with ICT showed significant dissociation between thallium and BMIPP uptake. In 4 cases with successful ICT, BMIPP defects significantly decreased during the chronic phase. Myocardial fatty acid metabolism was more depressed compared to thallium perfusion at infarcted area. These areas demonstrated gradual recovery, which is associated with functional improvement. These data are valuable for patients management from the perspective of myocardial viability.

\textit{123}I-MIBG myocardial imaging\textsuperscript{3−5}

MIBG is an analogue of norepinephrine and it shares the same uptake mechanism at sympathetic nerve terminals. Thus, \textit{123}I-MIBG allows scintigraphic evaluation of myocardial sympathetic innervation. In animal experiments, sympathetic denervation and reinervation occur following acute myocardial infarction and the denervated but viable myocardium could be detected noninvasively by simultaneous MIBG and thallium myocardial SPECT. Similar results were obtained in the present
clinical study. In the acute phase, most patients had larger $^{123}\text{I}$-MIBG defects than thallium defect. Group A showed marked improvement at chronic phase. Thus, perinfarcted areas during the acute phase are more sensitive to afferent and efferent sympathetic denervation than to myocardial blood flow. These patients showed sympathetic reinnervation during the chronic phase, on the other hand, group B showed no improvements, since they had extensive necrosis.

$^{111}\text{In-AM myocardial imaging}^{6-8}$

$^{111}\text{In-AM}$, which can bind only to cardiac myosin which is exposed as a result of cell death and membrane disruption, was considered an accurate marker of myocardial necrosis. In our study, 31/33 (94%) patients had positive uptake. AM/TL overlap (+) at infarcted area was observed frequently in 18 (55%) of all patients. Of these 18, 10 (56%) had emergent PTCA/PTCR. Thus, the overlap (+) of $^{111}\text{In-AM}$ and thallium uptake demonstrated the mixture of necrotic and normal tissue in the reperfused myocardium, while the areas of $^{111}\text{In-AM}$ uptake and thallium defect were considered as complete necrosis. Therefore, the patients who had overlap (+) with residual stenosis were shown to be at further risk. In conclusion, newly developed myocardial imaging by using SPECT may give precise evaluation of myocardial viability in coronary artery disease.

REFERENCE


