Newly Developed Myocardial Imaging by using Single Photon Emission Computed Tomography (SPECT)

Tsunehiko Nishimura, M.D., Toshihisa Uehara, M.D., Kohei Hayashida, M.D., Isao Mitani, M.D., Kazuo Haze, M.D., Hiroyuki Noda, M.D., and Hisateru Takano, M.D.

Thallium myocardial imaging is a useful technique to evaluate myocardial perfusion and myocardial viability in ischemic heart disease. However, myocardial imaging using single photon emission computed tomography (SPECT) and gamma-emitting radiopharmaceuticals has been recently developed for more precise evaluation of myocardial infarction and ischemia. The present study evaluates animal experiments and the clinical applications of these new myocardial imaging techniques. Areas considered in 1) myocardial necrosis assessed using 111In-antimonyosin, 2) myocardial fatty acid metabolism assessed using 123I-β-methyl-iodophenyl pentadecanoic acid (BMIPP) and 3) myocardial sympathetic neural activity assessed using 123I-metaiodobenzylguanidine (MIBG). Dual energy SPECT using these new agents and thallium gives precise characterization of the myocardial tissue in the infarcted and ischemic area.

Thallium myocardial imaging has been widely used for the assessment of myocardial perfusion and myocardial viability in ischemic heart disease. This technique is very useful in assessing the indications for and following-up procedures such as percutaneous coronary angioplasty. However, it has some limitations, since the amplitude of redistribution does not accurately reflect the degree of myocardial viability. Therefore, myocardial viability should be evaluated precisely with regard to myocardial necrosis, myocardial metabolism, and sympathetic neural activity.

In the present study, animal experience and the clinical application of myocardial imaging for the assessment of myocardial viability were evaluated. The following parameters were considered 1) myocardial necrosis using 111In-antimonyosin, 2) myocardial metabolism using 123I-BMIPP (β-methyl-iodophenylpentadecanoic acid), and 3) myocardial sympathetic neural activity using 123I-MIBG (metaiodobenzylguanidine).

MATERIALS AND METHODS
1. 111In-antimonyosin myocardial imaging
(1) In 12 dogs with more than 6h of ligation of left anterior descending coronary artery, 111In-antimonyosin and 99mTc-pyrophosphate were injected simultaneously. After the heart was excised, the extents of 111In-antimonyosin and 99mTc-pyrophosphate were compared with the results of TTC staining.
(2) Thirteen patients with acute myocardial infarction (7–14 days from the onset) were injected with 2 mCi of 111In-antimonyosin. There were 12 men and one woman with a mean age of 62 ± 8 years (51–79 years). Forty-eight hours

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Department of Radiology, Department of Cardiology and Department of Artificial Organs, National Cardiovascular Center, Osaka, Japan
Mailing address: Tsunehiko Nishimura, M.D., Department of Radiology, National of Radiology, National Cardiovascular Center 5-7-1, Fujihirohara Suita, Osaka 565, Japan

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after intravenous injection of $^{111}$In-antimyosin, the patients were injected with 2 mCi of thallium. Two sets of single photon emission computed tomography (SPECT) images were obtained simultaneously using dual energy window sets (173 and 247 keV for $^{111}$In, and 75 keV for $^{201}$Tl). The relationships between antimyosin uptake and thallium defect in the infarcted area were evaluated by transaxial SPECT images.

2. $^{123}$I-BMIPP myocardial imaging

Fourteen dogs were studied by using thallium and $^{123}$I-BMIPP to evaluate the relationship between myocardial perfusion and fatty acid metabolism. Eight dogs had left anterior descending coronary arterial occlusion (6h ligation) and 6 dogs had reperfusion (3h ligation and 1h reperfusion). Thallium and $^{123}$I-BMIPP myocardial imagings were carried out and the relationship between thallium and BMIPP uptake at infarcted area was evaluated in the excised heart.

3. $^{123}$I-MIBG myocardial imagina

1. In 8 dogs, acute myocardial infarction was produced by ligation of the left circumflex coronary artery. Images of MIBG and thallium SPECT were obtained 6h, 2 weeks, 4 weeks and 6 weeks later. The percent defect size was calculated from short axis views. The MIBG/TI ratio (the ratio of defect size) was determined. Two dogs were sacrificed at each point and tissue samples were obtained from infarcted, perinfarcted and normal myocardium. Changes in tissue norepinephrine content were measured.

2. Fourteen patients with acute myocardial infarction (7–14 days from the onset) were injected with 3 mCi of $^{123}$I-MIBG. There were 13 men and 1 woman with a mean age of 58 ± 7
years (48–68 years). Three hours after intravenous injection of $^{123}$I-MIBG, the patients were injected with 3 mCi of thallium. Two sets of SPECT images were obtained simultaneously using dual energy window sets (159 keV for $^{123}$I, and 75 keV for $^{201}$Tl). The relationships between MIBG and thallium defect at infarcted area were evaluated by transaxial SPECT images.

RESULTS

1. $^{111}$In-antimyosin myocardial imaging

   (1) In excised hearts, the extent of the infarcted area as assessed by $^{99m}$Tc-pyrophosphate and $^{111}$In-antimyosin correlated well ($r = 0.85$), however, the extent of $^{99m}$Tc-pyrophosphate was greater than that of $^{111}$In-antimyosin. Furthermore, the extent of $^{111}$In-antimyosin correlated well ($r = 0.92$) with that of TTC staining (Fig. 1).

   (2) By $^{111}$In-antimyosin imaging, positive uptake was demonstrated in 12 (92%) patients. The exception was 1 patient who had a small infarction. The area of thallium defect corresponded to that of antimyosin in 4 patients. The thallium defect was more extensive than antimyosin uptake in 2 patients. Antimyosin and thallium overlap was noted in 4 patients, 3 of whom had a history of successful PTCA and/or PTCR (Fig. 2).

2. $^{123}$I-BMIPP myocardial imaging

   Myocardial imaging with $^{123}$I-BMIPP was excellent, owing to its higher uptake and longer retention in the myocardium, and diminished liver and lung uptake. The mean half-time value generated from BMIPP myocardial washout curve was significantly longer in the reperfused myocardium than in normal and infarcted myocardium (274 ± 57 vs 96 ± 12, 106 ± 15 min, p < 0.05). Myocardial imaging of the excised heart showed the uncoupling of BMIPP and thallium (BMIPP uptake greater than thallium uptake) in 5 of 6 reperfused dogs. On the other hand, all occluded dogs had BMIPP and thallium persistent defect at infarcted area, though 2 had faint peri-infarcted BMIPP uptake (Fig. 3).

3. $^{123}$I-MIBG myocardial imaging

   (1) The typical discrepancy between MIBG and thallium defect was mostly observed 5 days after onset of infarction. The ratio of MIBG/Tl defect size was high (1.9 ± 0.2) 2 weeks after onset of myocardial infarction, but gradually decreased (Fig. 4). Tissue norepinephrine content gradually recovered (from 90 ± 12 to 540 ± 42 µg/g) in the peri-infarcted area, however, no recovery was noted in infarcted area (from 30 ± 10 to 38 ± 6 µg/g) at 6 weeks (Fig. 5).

   (2) Using $^{123}$I-MIBG and thallium myocardial imaging of acute myocardial infarction, 7 of 14 patients showed greater MIBG defect compared to thallium at the acute stage. However, 7 patients showed the same defect size at chronic

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Fig.5. Changes in tissue norepinephrine content (NE) in the non-infarcted (A), peri-infarcted (B) and infarcted myocardium.

stage (3 months after onset). Furthermore, in patients who had ventricular tachycardia, the MIBG defect size was greater than that determined by thallium.

DISCUSSION

Myocardial metabolic and receptor mapping has been available using positron emission computed tomography (PET) involving materials such as $^{18}$F-deoxyglucose, $^{11}$C-palmitate. However, PET studies can only be done in a research center with an expensive imaging device and cyclotron. Therefore, the newly developed myocardial imaging with gamma-emitters using SPECT is desirable. The present study was undertaken to evaluate myocardial tissue characterization with regard to necrosis, fatty acid metabolism and sympathetic neural activity using SPECT and newly developed radiopharmaceuticals.

1. $^{111}$In-antimyosin myocardial imaging

In animal experiments, the extent of $^{111}$In-antimyosin uptake showed excellent correlation with that of TTC staining. $^{111}$In-antimyosin, which can bind only to cardiac myosin, that is exposed as a result of cell death and membrane disruption, was considered an accurate marker of myocardial necrosis. In clinical trials, the infarcted area was visualized by positive uptake 7–14 days from the onset, though $^{99m}$Tc-tepyrophosphate uptake was observed 3–6 days from the onset. The relationship between thallium and antimyosin uptake reflected the myocardial area at risk. The overlap of $^{111}$In-antimyosin and thallium uptake demonstrated the mixture of necrotic and normal tissue in the repertused myocardium.

2. $^{123}$I-BMIPP myocardial imaging

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 under physiological conditions. $^{123}$I-free fatty acids were divided into 2 groups: straight and branched chain analogues. $^{123}$I-BMIPP is one of the branched-chain free fatty acids. It had suitable characteristics for SPECT, since it demonstrated higher uptake and longer retention in the myocardium. In animal experiments, the uncoupling of BMIPP and thallium uptake was observed in repertused myocardium. This may be explained as resulting from release of BMIPP which had been stored as triglyceride and phospholipid. Repertused myocardium probably has an increased triglyceride content, which indicates the extent of ischemia. Thus, BMIPP myocardial uptake reflects the changes in lipid pool size in association with the changes in fatty acid metabolism, although BMIPP can not evaluate directly β-oxidation of free fatty acid. Strauss et al demonstrated in a clinical study the presence of 3 patterns of BMIPP and thallium myocardial perfusion. They found that BMIPP uptake was greater than that of thallium in a zone supplied by vessels with severe stenosis, but with some flow on good collaterals. Though the clinical
application of BMIPP has not been evaluated, the combinations of BMIPP and thallium myocardial imaging supply different information about the zone of infarction and ischemia.

3. \( ^{123} \text{I-MIBG myocardial imaging} \)

MIBG is an analogue of norepinephrine and it shares the same uptake mechanism at sympathetic nerve terminals. Thus, \( ^{123} \text{I-MIBG} \) allows scintigraphic evaluation of myocardial sympathetic innervation. Therefore, we investigated the denervated but viable canine myocardium after acute myocardial infarction by serial MIBG and thallium SPECT. In animal experiments, sympathetic denervation and reinnervation occur following acute myocardial infarction and the denervated but viable myocardium could be detected noninvasively by combined MIBG and thallium SPECT.

In conclusion, newly developed myocardial imaging techniques using SPECT may give precise myocardial tissue characterization in infarcted areas. It may also be useful for the detection and follow-up of patients with ischemic heart disease.

REFERENCES


