Radionuclide Assessment of Stunned Myocardium by Alterations in Perfusion, Metabolism and Function

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A method for the diagnosis of stunned myocardium has not yet been established, although it has been retrospectively demonstrated in patients after intracoronary thrombolysis, unstable angina, and coronary revascularization. In this study, radionuclide cardiac imaging was carried out to evaluate the existence of stunned myocardium. 1) Gated blood pool scanning was performed in patients undergoing intracoronary thrombolysis both at the time of reperfusion (Rp) and 10 days later. In the $R_p < 4$ h group, about half of the initially abnormal segments showed complete improvement on quantitative wall motion analysis, which was more than in the $R_p > 4$ h and control groups. 2) In patients with acute myocardial ischemia, the correlation between thallium perfusion and regional wall motion was assessed semiquantitatively. In unstable angina, 5.8% of the ventricular wall segments showed dissociation between perfusion and wall motion (well-perfused asynergy). These segments had abnormal wall motion although perfusion was maintained, and were thought to be areas of stunned myocardium. 3) Fourteen dogs were studied using thallium and ^{123}I - β -methyl-iodophenyl pentadecanoic acid (BMIPP) fatty acid imaging to evaluate the relationship of perfusion to metabolism. In the reperfusion model, mismatching of the pattern of thallium and BMIPP uptake was observed. Reperfused myocardium probably has an increased triglyceride content, which is related to the degree of myocardial viability. In conclusion, stunned myocardium may be correctly diagnosed acutely on the basis of alterations in its perfusion, metabolism, and function by using radionuclide cardiac imaging.

REPERFUSION after brief episode of myocardial ischemia may result in prolonged myocardial dysfunction without necrosis, a phenomenon now known as "myocardial stunning"^{1,2}. A reliable method for the diagnosis of stunned myocardium has not yet been established clinically, although it is sometimes observed retrospectively in patients undergoing intracoronary thrombolysis, those with unstable angina, or patients receiving coronary revascularization.

Key words:

Stunned myocardium
Myocardial perfusion
Myocardial metabolism

It is important to assess stunned myocardium on the basis of alterations in its perfusion, metabolism, and function for the accurate diagnosis and treatment of ischemic heart disease^{3,4}. Radionuclide imaging appears to allow the determination of myocardial viability by using single-photon emission computed tomography. This study was undertaken to assess the functional recovery of the myocardium after stunning in patients undergoing intracoronary thrombolysis by using serial gated blood pool scans. In addition, the correlation between myocardial perfusion and regional wall motion was assessed

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Fig. 1. (a) Normal values of radial chord shortening (mean $\pm$ standard deviation) in each segment in the anterior and left anterior oblique (LAO) views.
(b) Determination of the changes of regional wall motion by the radial chord shortening method.

in patients with acute myocardial ischemia using thallium and gated blood pool scans, and the relationship of myocardial perfusion to metabolism was assessed by thallium and fatty acid myocardial imaging with occluded and reperfused infarcts.

MATERIALS AND METHODS

1. Serial assessment of left ventricular (LV) function by gated blood pool scanning

Twenty-three patients with acute myocardial infarction (MI) were investigated by gated blood pool scanning at the time of reperfusion and also 10 days later. Scanning was performed following in vivo red blood cell labeling with 20 mCi of ^{99m}Tc . Data were recorded in the anterior and 45° left anterior oblique (LAO) views by a mobile scintillation camera with a dedicated computer. Eighteen patients (78%) with successful reperfusion were divided into two groups: reperfusion after less than 4 h ($R_p < 4$ h, $n=9$, 4 anterior and 5 inferior MI) and after more than 4 h ($R_p > 4$ h, $n=9$, 4 anterior and 5 inferior MI). As a control group,

gated blood pool scans were also performed in the early hours following MI in an additional 42 patients who received conventional conservative treatment.

Regional wall motion of the left ventricle was analyzed quantitatively in the anterior and LAO views⁵ (Fig. 1). The wall motion was computed automatically in six zones as the average fractional changes in length of six radii per zone from end-diastole to end-diastole. A range of normal wall motion values was determined using 19 normal controls. Abnormal segments were defined as those showing under 30% radial shortening. Initially abnormal segments were defined as improving or worsening if their radial shortening increased or decreased by more than 10 points. Segments were defined as completely normalized if their radial shortening returned to normal (over 30%) by the tenth day. The changes in regional wall motion were expressed as the percentage of improvement of initially abnormal segments, and completely normalized segments were also expressed as the percentage of normalized to initially abnormal seg-

Thallium Myocardial perfusion		Regional Wall Motion	
ANT	LAO45°	ANT	LAO45°

● TI-Score 2 normal 1.5 mild hypoperfusion 1 moderate hypoperfusion 0.5 severe hypoperfusion 0 perfusion defect		● RWM-Score 3 normal 2 mild hypokinesis 1 severe hypokinesis 0 akinesis -1 dyskinesis	

Fig.2. Scoring of thallium perfusion and regional wall motion by semiquantitative methods in the anterior and left anterior oblique (LAO) views.

TABLE I IMPROVEMENT OF INITIALLY ABNORMAL SEGMENTS OF THE LEFT VENTRICLE IN QUANTITATIVE WALL MOTION ANALYSIS.

Group	n	Initially abnormal	Improved (normalized)	Unchanged	Deteriorated	P/I	N/I
● AMI							
Rp < 4h	4	25	17 (11)	7	1	68%	(44%)
Rp < 4h	4	25	11 (5)	11	3	44%	(20%)
Control	18	122	45 (14)	64	13	37%	(11%)
● IMI							
Rp < 4h	5	20	13 (11)	5	2	65%	(55%)
Rp < 4h	5	29	13 (10)	13	3	45%	(34%)
Control	24	136	51 (37)	70	15	38%	(27%)

AMI/IMI=anterior/inferior myocardial infarction

Rp=intracoronary thrombolysis

P/I=percentage of improved/initially abnormal segments

N/I=percentage of normalized/initially abnormal segments

ments.

2. Simultaneous assessment of thallium perfusion and regional wall motion

We investigated if there was a dissociation between regional wall motion and perfusion that could be used to identify stunned myocardium. The relationship of perfusion to regional wall motion was compared on the same day in 28 patients with acute myocardial ischemia. There were 12 with unstable angina, 8 with acute MI within 3 days of onset, 5 with recent MI (1-4 weeks from onset), and 3 with old MI. All patients had

thallium scans performed at rest and repeated 4 h later. Anterior and 45° LAO images were recorded for 10 min each with a gamma camera. After the delayed thallium scan was done, the patients underwent gated blood pool scanning with ^{99m}Tc-labeled red blood cells using the same views. Regional wall motion and myocardial perfusion were assessed independently and scored semiquantitatively for each segment of the left ventricular myocardium (Fig. 2).

3. Assessment of myocardial metabolism by fatty acid imaging

GBPS = gated blood pool scan RWM = regional wall motion
TL = thallium scan

Fig. 3. The correlation of thallium perfusion scores and regional wall motion scores in patients with acute myocardial ischemia

Fourteen dogs were studied using thallium and ^{123}I - β -methyl-iodophenyl pentadecanoic acid (BMIPP) to evaluate the relationship between myocardial perfusion and fatty acid metabolism. Eight dogs had left anterior descending arterial occlusion (6-h ligation) and 6 dogs had undergone reperfusion (3-hr ligation and 1-h reperfusion). Thallium and ^{123}I -BMIPP (both 3 mCi IV) imaging were simultaneously carried out and the relationship between thallium and BMIPP uptake in the infarcted area was evaluated in the excised hearts.

RESULTS

1. Serial assessment of LV function by gated blood pool scanning.

The functional recovery of regional wall motion is summarized in Table I. In the $\text{Rp} < 4$ h group, the improvement in initially abnormal segments was observed in 68% of the anterior MI segments and 65% of the inferior MI segments. A total of 44% of the anterior MI segments and 55% of the inferior MI segments improved completely after 10 days. In the $\text{Rp} > 4$ h group, improved

wall motion was observed in 44% of the anterior MI segments and 45% of the inferior MI segments, and did not differ compared to the control group (37% for anterior MI and 38% for inferior MI). In the $\text{Rp} < 4$ h group, LV function was still depressed immediately after intracoronary thrombolysis, but a significant improvement in regional wall motion was frequently observed 10 days later.

2. Simultaneous assessment of thallium perfusion and regional wall motion

In the patients with acute myocardial ischemia, the relationship of thallium perfusion to regional wall motion is shown in Fig. 3. The overall correlation between regional wall motion and the initial thallium perfusion images was $r=0.36$, which improved to $r=0.48$ for the delayed scans. These data showed that a dissociation of myocardial perfusion and regional wall motion existed at the time of the ischemic insult. There was a high incidence of myocardial segments which had normal perfusion and severe wall motion abnormalities. This dissociation between myocardial perfusion

TABLE II THE RELATIONSHIP OF THALLIUM PERFUSION TO FATTY ACID METABOLISM IN REPERFUSED AND OCCLUDED INFARCT MODELS. T1/2 SHOWS THE RATE OF BMIPP WASHOUT FROM THE MYOCARDIUM.

Group	BMIPP>TL	BMIPP=TL	BMIPP myocard. washout(T1/2)
Reperfusion n=6	5	1	274±157min
Occlusion n=8	2* (marginal)*	6	106± 15min

BMIPP= β -methyl iodophenyl pentadecanic acid
TL=thallium

and regional wall motion (well-perfused asynergy) was observed in 5.8% and 8.2% of segments in unstable angina and acute MI, respectively. On the other hand, such discordance was seldom observed in the patients with recent and old MI.

3. Assessment of myocardial metabolism by fatty acid imaging

Myocardial imaging with ^{123}I -BMIPP was excellent, owing to its higher uptake and longer retention in the myocardium. The mean half-time value generated from the BMIPP myocardial washout curve was significantly longer for reperfused myocardium than for normal or infarcted myocardium (274 ± 157 vs 96 ± 12 , and 106 ± 15 min, $p<0.05$). Myocardial imaging of the excised hearts showed the uncoupling of BMIPP and thallium (BMIPP uptake greater than thallium uptake) in 5 of the 6 reperfused hearts. On the other hand, all hearts with occlusion had persistent BMIPP and thallium defects in the infarcted areas, though 2 hearts also showed faint peri-infarct BMIPP uptake (Table II).

DISCUSSION

Myocardial stunning was first described as prolonged postischemic ventricular dysfunction by Brawnwald and Kioner¹. Though stunned myocardium is often observed in reperfusion models after a brief episode of myocardial ischemia, it is still unclear how to assess myocardial stunning in the clinical setting. In general, stunned myocardium has been diagnosed retrospectively after intracoronary thrombolysis when functional recovery occurs at a later stage. Myocardial viability should be assessed from the view-

points of myocardial perfusion, metabolism, and function.

Radionuclide cardiac imaging is able to assess perfusion by thallium scanning, metabolism by fatty acid imaging, and ventricular function by gated blood pool scanning^{3,4}.

1. Functional recovery after intracoronary thrombolysis

Studies performed in experimental reperfusion models have revealed that early reperfusion is critical to success. Reperfusion after less than 4 hr in man may lead to a significant reduction in the extent of an infarct⁶. The rapidity of myocardial necrosis can, however, vary widely among individuals due to the variable supply supply by collaterals and variations in residual blood flow. In the $\text{Rp}<4\text{h}$ group, the number of improved segments was significantly greater than in the $\text{Rp}>4\text{h}$ and control groups. In addition, half of the initially abnormal segments showed complete recovery after 10 days. These findings demonstrated that prolonged postischemic LV dysfunction existed in these patients following intracoronary thrombolysis. The late recovery of segmental function several weeks after coronary reperfusion has suggested that a substantial time period may be required to assess the ultimate effects of therapeutic intervention⁵.

2. Discordance between perfusion and wall motion

In general, myocardial perfusion matches regional wall motion at the site of old infarcts⁷. In unstable angina, we found a correlation between the thallium score and the regional wall motion score, but the relationship was far from the expected linear cor-

relation. We found that 5.8% of the segments showed well-perfused asynergy in unstable angina patients. These segments had wall-maintained perfusion but abnormal wall motion, and were thought to be areas of stunned myocardium. Thus, our study suggests that it is very important to evaluate perfusion and wall motion at the same time to diagnose myocardial viability.

3. Dissociation of perfusion and fatty acid metabolism

Attempts have been made to determine the metabolic integrity of the myocardium with radiolabeled free fatty acids, which are the preferred energy substrate for the heart.^{8,9} ¹²³I-BMIPP is one of the branched-chain fatty acids. It has suitable characteristics for single photon emission computed tomography (SPECT), since it demonstrates a high uptake and a long retention in the myocardium. A mismatched pattern of BMIPP and thallium uptake was observed in the reperfused dog model, while a matched pattern was observed in the occluded dog model. This may be explained as resulting from the release of BMIPP which had been stored as triglycerides and phospholipids. Reperfused myocardium probably has an increased triglyceride content, which may be related to the extent of the ischemia!¹⁰ Thus, BMIPP myocardial uptake reflects changes in the lipid pool size in association with changes in fatty acid metabolism.

Strauss et al. demonstrated the dissociation of BMIPP and thallium uptake after reperfusion in a clinical trial. Though the clinical application of BMIPP has not been well evaluated, the combination of BMIPP and thallium myocardial imaging supplies improved information on myocardial viability.

In conclusion, myocardial viability can be evaluated on the basis of alterations in perfusion, metabolism, and function by radionuclide cardiac imaging. Stunned myocardium may be correctly diagnosed at the time of acute stunning by these procedures.

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