〔千葉医学 77：207～212, 2001〕

〔Original Paper〕

Clinical relevance of dipyridamole stress Tc-99m-sestamibi myocardial SPECT for the early stage of acute myocardial infarction after reperfusion treatment

Takahiko Kinoshita, Yoichi Kuwabara, Takeshi Shikama
Koki Matsuno, Toru Kuroda, Akira Aouda
Kiyotaka Fujii, Nobuyuki Komiyama and Yoshiaki Masuda

(Received December 25, 2000, Accepted January 12, 2001)

SUMMARY

Objectives: This study aimed to evaluate coronary flow in acute myocardial infarction (MI) by stress myocardial perfusion imaging (MPI), and to compare that with metabolic status and perfusion at rest.

Methods: Twenty-three patients with acute MI who received successful angioplasty within 12 hours were studied. All patients underwent dipyridamole stress or rest technetium (Tc)-99m-sestamibi and ^{123}I-BMIPP SPECT imaging in the acute phase (mean 3.8 and 7.3 days respectively). For each images, segmental accumulations were semi-quantitatively graded by 4-point scoring system (0=normal, 1=mild reduction, 2=severe reduction, 3=defect) for 14 segments to yield the total defect score (TDS).

Results:

	Stress-MPI	BMIPP	Rest-MPI
TDS	13.1±9.5*	13.8±8.2#	9.1±8.9

*$P<0.001$ vs. Rest-MPI, #$P<0.001$ vs. Rest-MPI

TDS in stress MPI was significantly bigger than that in rest MPI, although it was not significantly different from that in BMIPP.

Conclusions: In the segments with infarction, dipyridamole stress MPI revealed to have greater defect than rest Tc in acute phase. This may indicate that the myocardium salvaged by reperfusion has disorder in coronary flow as well as metabolic disorder.

Key words: dipyridamole, ^{99m}Tc-sestamibi, SPECT, myocardial infarction, reperfusion

---

3rd Department of Internal Medicine, School of Medicine, Chiba University, Chiba 260-8670.
木ノ下敬彦, 桑原洋一, 鹿間 毅, 松野公紀, 黒田 徹, 粟生田輝, 藤井清孝, 小宮山伸之, 増田善昭：再灌流療法を施行した心筋梗塞早期における dipyridamole 負荷 Tc-^{99m}m 心筋 SPECT の臨床的意義の検討：その経過および I-^{123}BMIPP 心筋 SPECT との比較.
千葉大学医学部内科学第三講座 Tel. 043-222-7171.
2000年12月25日受付, 2001年1月12日受理.

I. Introduction

Dipyridamole stress nuclear myocardial perfusion imaging (MPI) is an established method to evaluate coronary heart disease[1]. Recent studies reported that dipyridamole stress MPI can be performed safely to determine risk stratification and treatment strategy in the acute phase of myocardial infarction (MI)[2-6]. And even in patients with reperfusion therapy, reversible perfusion defect is reportedly often observed[7]. However, clinical relevance of dipyridamole stress MPI is unknown in patients who underwent emergent percutaneous transluminal coronary angioplasty (PTCA), since their coronary anatomy are already revealed and revasculized. To evaluate clinical relevance, we performed dipyridamole stress MPI in the early phase of MI, and compared those with ^{123}I-BMIPP imaging and repeat dipyridamole stress MPI at the chronic phase.

II. Materials and Methods

Subjects

The study population is consisted of 23 patients (21 men and 2 women, mean 56 years old) who presented their first MI. All patients underwent emergency PTCA successfully within 12 hours from onset with remaining coronary stenosis <25% (LAD 15, LCX 1, RCA 7). Stent implantation was supplemented in 17 subjects. Blood samples were taken every 6 hours after the admission to determine peak creatine phosphokinase (CPK) level. All patients underwent dipyridamole stress MPI and ^{123}I-BMIPP imaging in acute phase, and dipyridamole stress MPI was repeated in 6 subjects without restenosis 6 months after onset. Patients with severe heart failure or serious arrhythmia were excluded from this study.

Dipyridamole stress ^{99m}Tc-sestamibi myocardial perfusion SPECT imaging

A same-day stress-rest protocol was used. Dipyridamole (0.14 mg/kg/min, 4min) was infused intravenously a mean of 3.7±0.86 days after onset of MI. 5 mCi of ^{99m}Tc-sestamibi was injected 2 minutes after the dipyridamole administration, and stress images were obtained 40 minutes after the injection. Four hours later, rest images were obtained 40 minutes after injection of 15 mCi ^{99m}Tc-sestamibi. Fifty mg of aminophylline was given to all patients intravenously 3 minutes after the sestamibi injection. Single photon emission computed tomography (SPECT) imaging was obtained using a triple-head gamma camera (PRISM 3000XP, PICKER inc.) equipped with medium energy general purpose collimators. Seventy-two projections (60 sec/stop, 24 stops, 64x64 format) were recorded over a 30 degree arc. Tomographic images were reconstructed into transverse, horizontal long axis, and short axis images after prefiltering by Butterworth method. A 12 lead electrocardiogram, heart rate, and blood pressure were recorded at baseline and every a minute for 12 minutes.

^{123}I-BMIPP SPECT imaging

BMIPP SPECT imaging was performed a mean of 7.2±1.0 days after onset of MI. BMIPP of 3 mCi was intravenously injected at rest after overnight fasting, and SPECT images were obtained 15 minutes later.

SPECT image analysis

The left ventricle was divided into 14 segments in each projection (Fig. 1). Segmental uptake was graded visually by use of a 4-point scoring system where 0 is normal, 1 is mild reduction of activity, 2 is severe reduction, 3 is absence of activity. The total defect score (TDS) was defined as the sum of

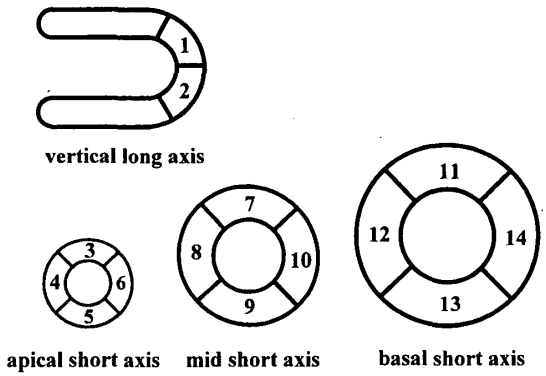

Fig. 1 Segmental analysis of SPECT image
Myocardium was divided into 14 segments and was graded visually by use of a 4-point scoring system. The total defect score (TDS) was defined as the sum of these scores.

these scores. Images were read and scored independently by two experienced nuclear medicine physicians, and were determined by consensus if there was initial disagreement.

Follow-up studies

Follow-up CAG was obtained in 16 among 23 patients at three to six months after the hospital discharge, and restenosis of the target vessel (>50% stenosis) was observed in 3 patients. Of the 13 patients without restenosis, 6 patients could be obtained follow up dipyridamole stress MPI in the same protocol as the acute phase.

Statistical analysis

Results are expressed as mean ± standard deviation (SD). Differences in continuous variables between two groups were tested by Student's *t* test or analysis of variance. Multiple comparison was performed with Sheffe's criterion. Agreements between categorical variables were determined by Kappa statistics. Associations between continuous variables were tested by linear regression analysis. Statistical significance was taken at $P<0.05$.

Ⅲ. Results

Clinical response to dipyridamole

Intravenous dipyridamole increased heart rate from 71 ± 10 to 82 ± 11 beats / min ($P<0.001$). Systolic blood pressure unchanged by dipyridamole infusion (120±17 to 112±13 mmHg, P=ns). One patients had asymptomatic ST depression of 0.1mm. Dipyridmole did not cause chest pain, severe arrythmia, or other symptoms in the studied patients.

Scintigraphic results

Results of TDS in stress MPI, rest MPI, and BMIPP image are shown in figure 2. Mean TDS in stress MPI was significantly bigger than that in rest MPI (13.1±9.5 vs. 9.1±8.9, $P<0.001$). Mean TDS in BMIPP images was not significantly deferent from that in stress MPI (13.8±8.2 vs. 13.1±9.5, P =NS), and it was significantly greater than that in rest MPI (13.8±8.2 vs. 9.1±8.9, P <0.001). Table 1 shows region to region agreement in defect scores among BMIPP images, stress MPI, and rest MPI. In regional analysis, defect score of BMIPP images also had better agreement with stress MPI than rest MPI (agreement=0.70 vs 0.63).

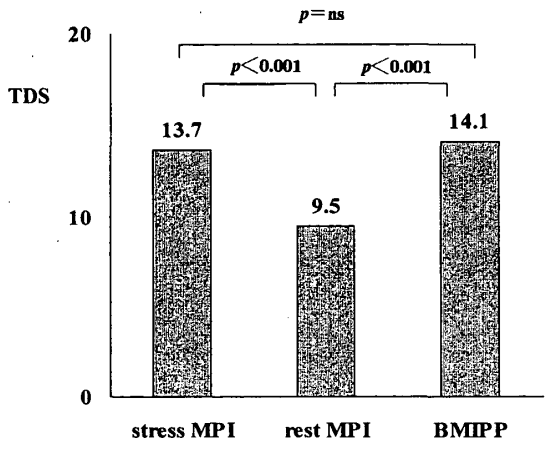

Fig. 2 Comparison between total defect scores (TDS) of stress MPI, rest MPI and BMIPP. TDS in stress MPI was significantly bigger than that in rest MPI.

Table 1 Agreement of regional defect scores of stress MPI, rest MPI and BMIPP.
Defect score of BMIPP images had a better agreement with stress MPI than rest MPI.

stress MPI defect score

BMIPP defect score	0	1	2	3
0	111	21	3	0
1	12	45	14	2
2	6	17	24	4
3	0	2	9	37

agreement 0.70
Kappa statistics 0.57
Spearman's correlation 0.78

rest MPI defect score

BMIPP defect score	0	1	2	3
0	125	9	2	0
1	37	31	4	0
2	12	27	10	3
3	1	4	14	29

agreement 0.63
Kappa statistics 0.43
Spearman's correlation 0.72

Correlation of TDS in MPI with peak CPK

Figure 3 shows linear correlation between TDS in stress MPI and peak CPK (left), and TDS in rest MPI and peak CPK (right). TDS in rest MPI had significant correlation with peak CPK (R=0.78 P=0.01), however TDS in stress MPI had only weak correlation with peak CPK (R=0.58 P=0.08).

Follow-up studies

Six patients without restenosis could obtain follow-up dipyridamole stress MPI studies. Among them, significant difference between TDS in stress MPI and rest MPI (11.5±2.9 vs. 6.8±1.5, $P<0.01$) was no more present at the re-study (8.2±4.9 vs. 6.8±6.2, P=0.22; Fig. 4).

IV. Discussion

It has been reported that dipyridamole stress myocardial perfusion imaging in the acute phase of MI can predict in-hospital and postdischarge cardiac events, and can define long-term risk in patients without emergent coronary angiography[2-6]. However, there are few reports regarding dipyridamole stress perfusion imaging studies in the patients who undergo emergency coronary angiography or PTCA. Patients who undergo revasculization in acute phase of MI should have no stenotic legion in the correspondent artery to infarct myocardium; therefore, stress test should theoretically show negative result.

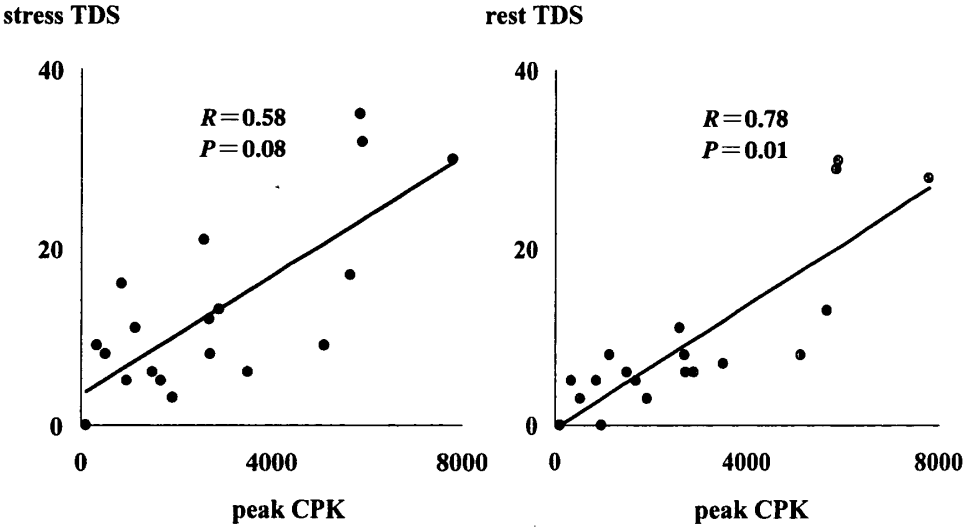

Fig. 3 Linear correlation between TDS in stress MPI and peak CPK (left), and TDS in rest MPI and peak CPK (right). TDS in rest MPI had significant correlation with peak CPK, however TDS in stress MPI had only weak correlation with peak CPK.

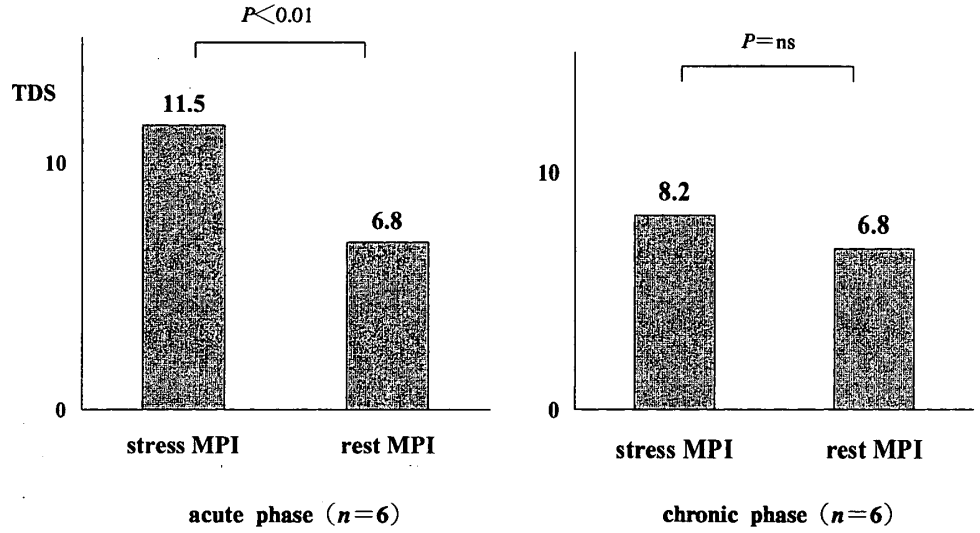

Fig. 4 Comparisons between TDS in stress MPI and TDS in rest MPI in chronic phase. Significant difference between TDS in stress MPI and rest MPI ($P<0.01$) was no more present at the re-study (P=ns).

In this study, dipyridamole stress myocardial perfusion imaging in early MI shows reversible perfusion defect at stress image even for the patient with emergent PTCA. Several reasons may be responsible for this phenomenon. Firstly, even after revascularization at major coronary artery, disorder in micro vessel might cause reduced coronary flow reserve[8,9]. Secondary, dysfunction of mitochondrial membrane would weaken intracellular sustain of Tc perfusion tracer in the damaged but salvaged myocardium after MI[10,11].

Extent and degree of perfusion defect in stress MPI well correlated with those of BMIPP. Reduction of accumulation in BMIPP image indicates reduced fatty acid use, and if perfusion is preserved in such area, this is considered to be area at risk. Consequently, reversible perfusion defect in dipyridamole stress MPI corresponds to the damaged but viable myocardium after acute MI.

The result of this study showed that the association between TDS in dipyridamole and peak CPK was short of significant, although there was good correlation between TDS in rest MPI and peak CPK. This result may also supports that reversible defect in dipyridamole stress MPI indicate the surrounding area of the infarct myocardium.

Repeat study of dipyridamole stress MPI showed that reversible perfusion defect observed in acute phase was no more present in chronic phase. This phenomenon indicates that the reversible defect in dipyridamole stress MPI is correspondent to viable myocardium and this abnormal finding will disappear hereafter.

Study Limitations

The study has several limitations. Firstly, only 23 subjects were enrolled in this study. Secondly, because of its adverse effect, there exist some patients (such as bronchial asthma) who cannot receive intravenous dipyridamole administration. Finally, there is time lag between dipyridamole Tc study and BMIPP study (3.7 vs. 7.2 days after MI onset respectively). That is to say, it is possible that the defect size of BMIPP image may be different if it was performed on the same day with dipyridamole stress MPI.

Conclusions

The present study demonstrates that dipyridamole stress MPI can be done safely in the acute phase of myocardial infarction after emergent PTCA, and detect the area of not only infarct myocardium but viable one which was damaged by the ischemic condition before coronary revasculization.

要　旨

【目的】
血行再建に成功した心筋梗塞早期に dipyridamole 負荷 Tc-99m 心筋 SPECT を施行し，可逆的集積低下出現の意義を心筋血流および脂肪酸代謝障害領域との関連および経過により検討する。
【方法】
完全血行再建を施行し得た初回心筋梗塞23例を対象とした。平均3.8病日に dipyridamole 負荷 Tc-99m 心筋 SPECT を施行し，負荷時および安静時SPECT像の欠損を14領域の total defect score (TDS) にて半定量的に評価した。平均7.2病日に施行した BMIPP シンチも同様に評価した。6カ月後に血管造影で再狭窄を認めない症例の一部に対して dipyridamole 負荷 Tc-99m 心筋 SPECT を再検した。
【結果】
負荷時の TDS (13.1±9.5) は安静時の TDS (9.1±8.9) より有意に大 ($P<0.001$) であり，BMIPP の TDS (13.8±8.2) と同程度であった。6カ月後の再検を行った6症例においては，負荷時TDSは急性期11.5±2.9から慢性期8.2±4.9へと有意に低下し，安静時の慢性期 TDS (6.8±6.2) と有意差は消失した。
【結語】
完全血行再建を施行した急性心筋梗塞において，早期 dipyridamole 負荷時 Tc-99m 心筋 SPECT の可逆的欠損領域は BMIPP の欠損領域と同等であり，急性冠血流低下による心筋障害の領域に重なることが示された。またこの領域は経過とともに著明に減少し，急性期冠血行再建療法により salvage された心筋領域を描出していると考えられた。

References

1) Albo PC, Gould KL, Westkott RJ, Hamilton GW, Ritchie JL, Williams DL. Noninvasive assessment of coronary stenosis by myocardial imaging during pharmacologic coronary vasodilatation. Ⅲ. Clinical trial. Am J Cardiol 1978; 42: 751-60.
2) Heller GV, Brown KA, Landin RJ, Haber SB. Safety of early intravenous dipyridamole technetium 99m sestamibi SPECT myocardial infarction. Early Post MI Ⅳ Dipyridamole Study (EPIDS). Am Heart J 1997; 134: 105-11.
3) Brown KA, Heller GV, Landin RS, Shaw LJ, Beller GA, Pasquale MJ, Haber SB. Early dipyridamole ^{99m}Tc-sestamibi single photon emission computed tomographic imaging 2 to 4 days after acute myocardial infarction predicts in-hospital and post-discharge cardiac events. Comparison with submaximal exercise imaging. Circulation 1999; 100: 2060-6.
4) Hung J, Moshiri M, Groom GN, Van der Schaaf AA, Parsons RW, Hands ME. Dipyridamole thallium-201 scintigraphy for early risk stratification of patients after uncomplicated myocardial infarction. Heart 1997; 78: 346-52.
5) Bosch X, Magrina J, March R, Sanz G, Garcia A, Betriu A, Navarro-Lopez F. Prediction of in-hospital cardiac events using dipyridamole-thallium scintigraphy performed very early after acute myocardial infarction. Clin Cardiol 1996; 19: 189-96.
6) Okada RD, Glover DK, Leppo JA. Dipyridamole 201Tl scintigraphy in the evaluation of prognosis after myocardial infarction. Circulation 1991; 84 (3 Suppl): I 132-9.
7) Kim S, Yamabe H, Yokoyama M. Impaired coronary circulation in acute myocardial infarction: a dipyridamole-thallium-201 study. Eur J Nucl Med 1997; 24: 210-4
8) Neumann FJ, Kosa I, Dickfeld T, BlasiniR, Gawaz M, Hausleiter J, Schwaiger M, Schomig A. Recovery of myocardial perfusion in acute myocardial infarction after successful balloon angioplasty and stent placement in the infarct-related coronary artery. J Am Coll Cardiol 1997; 30: 1270-6.
9) Ishihara M, Sato H, Tateishi H, Kawagoe T, Yoshimura M, Muraoka Y. Impaired coronary flow reserve immediately after coronary angioplasty in patients with acute myocardial infarction. Br Heart J 1993; 69: 288-92.
10) Flameng W, Andres J, Ferdinande P, Mattheussen M, Van Belle H. Mitochondrial function in myocardial stunning. J Mol Cell Cardiol 1991; 23: 1-11.
11) Ferrari R. Metabolic disturbances during myocardial ischemia and reperfusion. Am J Cardiol 1995; 76: 17B-24B.