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Reverse redistribution of Tc-99m-tetrofosmin in patients with acute myocardial infarction

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We examined reverse redistribution (RR) of Tc-99m-tetrofosmin after a single injection in patients with acute myocardial infarction (AMI). Tc-99m-tetrofosmin myocardial SPECT was performed in 28 patients with AMI 10–14 days after the onset. Myocardial images were obtained 30 min and 180 min after the injection of 740 MBq of Tc-99m-tetrofosmin. The left ventricular wall was divided into 9 segments. Regional myocardial uptakes of Tc-99m-tetrofosmin were scored by 4-point scoring (0 = normal, 1 = mildly reduced, 2 = moderately reduced, and 3 = defect). RR was defined as an increase of more than 1 in the regional score in images at 180 min. RR of Tc-99m-tetrofosmin was observed in 17 of 20 patients with direct PTCA and 3 of 8 patients without reperfused therapy. RR was observed in 61 of all 252 segments. Coronary angiography performed 1 month later revealed that the infarct-related artery was patent in 19 of 20 patients (95%) with RR and in 3 of 8 patients (37.5%) with persistent defects (PD) ($p < 0.05$). In segment-by-segment analysis, the incidence of regional wall motion abnormality 1 month later was reduced in regions with RR compared to those with PD ($p < 0.0001$). In conclusion, RR of Tc-99m-tetrofosmin was frequently observed in patients with successful direct PTCA. As the segments with RR showed signs of preserved function 1 month later, this phenomenon may reflect a salvaged myocardium in AMI.

Key words: Tc-99m-tetrofosmin, reverse redistribution, acute myocardial infarction, PTCA

INTRODUCTION

Tc-99m-tetrofosmin is a myocardial perfusion agent with favorable imaging characteristics.[1–5] Once this tracer is taken up by the myocardium, its clearance is considered to be relatively slow and redistribution does not occur for several hours.[6] Nevertheless, we reported that myocardial images with Tc-99m-tetrofosmin often showed reverse redistribution in patients with hypertrophic cardiomyopathy[7] or complete left bundle branch block.[8] Reverse redistribution of Tl-201 was commonly observed in patients with acute myocardial infarction after reperfused therapy.[9,10] Weiss et al.[9] reported that reverse redistribution of Tl-201 was a sign of nontransmural myocardial infarction with patency of the infarct-related artery. Takeishi et al.[11] reported that reverse redistribution of another Tc-99m-labeled myocardial perfusion agent, Tc-99m-sestamibi was evident after direct PTCA in patients with acute myocardial infarction. They concluded that reverse redistribution of Tc-99m-sestamibi provides a clue for successful revascularization and predicts the preserved left ventricular function. Because time-related changes in myocardial Tc-99m-tetrofosmin distribution have not been previously examined in patients with acute myocardial infarction, this study was performed to investigate the prevalence of the Tc-99m-tetrofosmin reverse redistribution pattern in patients with acute myocardial infarction and to assess the clinical implication of this phenomenon.

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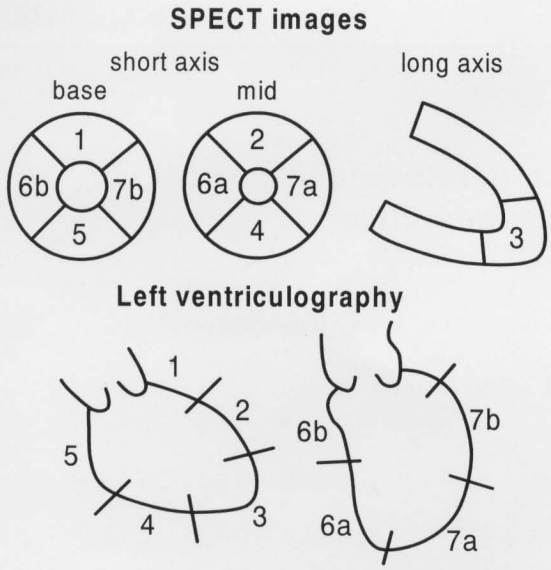

Fig. 1 Schematic representation of the left ventricular segmentation of SPECT and left ventriculography.

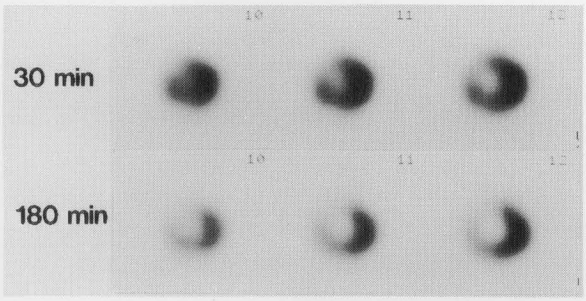

Fig. 2 Early and delayed Tc-99m-tetrofosmin myocardial SPECT images of a patient with anterior acute myocardial infarction with successful direct PTCA. Mildly decreased uptake of the tracer in the anterior and septal segments is observed on the early images (upper). Decreased uptake regions are expand, and more severely decreased uptake is observed on delayed images (reverse redistribution).

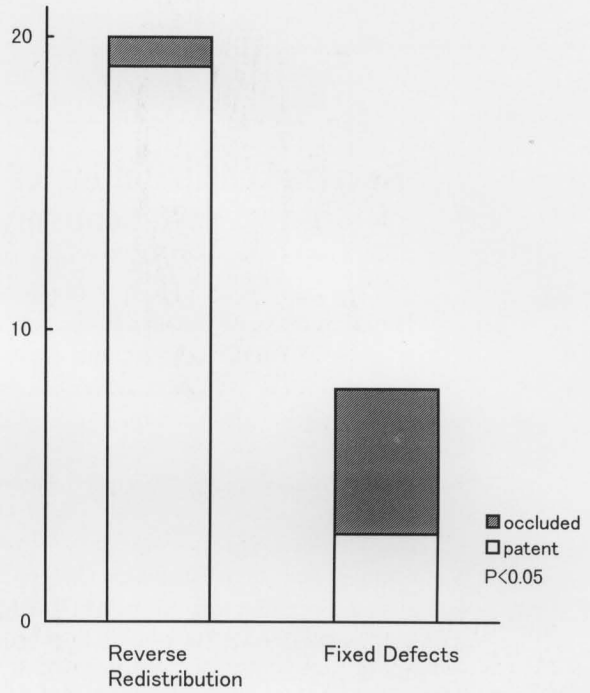

Fig. 3 Comparison of the patency of the infarct-related artery between patients with reverse redistribution and those with persistent defects.

METHODS

Subjects

The subjects were 28 consecutive patients with acute myocardial infarction, 22 men and 6 women, aged 39 to 79 years (mean 62 years). No patient had a history of previous myocardial infarction. The diagnosis of myocardial infarction was based on the presence of at least 2 of the 3 following criteria: a typical history of prolonged chest pain, transiently high serum enzyme levels including CK-MB fractions, and electrocardiographic signs of either a Q-wave or a non-Q-wave infarction. The infarct-related artery was the left anterior descending artery in 19 patients, the left circumflex artery in 2 patients, and the right coronary artery in 7 patients. Twenty patients admitted within 6 hours after the onset of symptoms received either standard angioplasty or coronary stent implantation. Successful revascularization was defined as less than 50% residual stenosis of the infarct-related artery. The remaining 8 patients did not receive PTCA because they were admitted to our hospital late after the onset of symptoms.

Tc-99m-tetrofosmin SPECT

Myocardial perfusion imaging with Tc-99m-tetrofosmin was performed 10–14 days after the onset. In each patient, 740 MBq of Tc-99m-tetrofosmin was intravenously injected at rest. Immediately after the injection, each patient drank a glass of milk to accelerate the tracer clearance from the hepatobiliary system. Data acquisition for SPECT imaging was performed twice; for early imaging at 30 min and for delayed imaging at 180 min after the Tc-99m-tetrofosmin injection, with a rotating digital gamma camera (Toshiba GCA 901A) equipped with a low-energy, high-resolution, parallel-hole collimator. Energy discrimination was provided by a 15% window centered at 140 keV. Thirty images were then obtained over a 180° arch from the 45° right anterior oblique to the 45° left posterior oblique position. Each image was accumulated for 30 seconds. The data were stored on a 64×64 matrix. After processing the projection images with a Butterworth filter, reconstructed processing was performed with a Shepp-Logan filter without correction for attenuation or scatter. Reconstructed transaxial images were reoriented in the vertical long-axis and short-axis of the left ventricle.

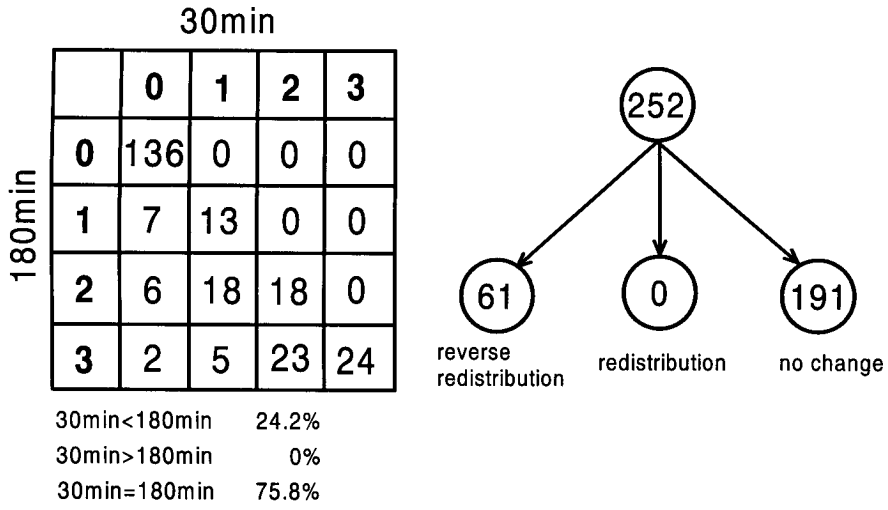

Fig. 4 Segment-by-segment comparison between early and delayed Tc-99m-tetrofosmin SPECT images.

The left ventricular wall on the vertical long axis and basal and mid short axis images were divided into 9 segments,[12] based on the angiographic ventricular segmentation recommendations of the American Heart Association (Fig. 1). The uptake of the tracer in each segment was scored by 2 experienced observers, who had no knowledge of the patient's clinical information, by 4-point scoring (0 = normal, 1 = mildly reduced, 2 = moderately reduced, and 3 = defect). Reverse redistribution was defined as an increase of more than 1 in the segmental score in 3-hr delayed images. The grading was decided on by consensus between the 2 observers. Myocardial distribution of Tc-99m-tetrofosmin in early and delayed images was compared.

Coronary angiography and left ventriculography

Coronary angiography was performed 1 month after the onset. Biplane left ventriculograms were obtained for assessment of left ventricular function. The left ventricular wall was divided into 9 segments (Fig. 1), and the regional wall motion of each segment was assessed as normal, mild hypokinesis, severe hypokinesis, akinesis or dyskinesis. The severity of asynergy in segments with persistent defects and those with reverse redistribution of Tc-99m-tetrofosmin was compared.

Statistical analysis

The differences in proportion (categorical variables) were examined by Fisher's exact test or the chi square test. A p value of < 0.05 was considered significant.

RESULTS

Case presentation

Tc-99m-tetrofosmin myocardial SPECT images of a patient with anterior acute myocardial infarction are shown in Fig. 1. In emergent coronary angiography, the left anterior descending artery was occluded and reperfused by direct PTCA. Tc-99m-tetrofosmin images were obtained 10 days after PTCA. Mildly decreased uptake of the tracer in the anterior and septal segments was observed on early images. Decreased uptake regions expanded, and more severely decreased uptake was observed on delayed images (reverse redistribution) (Fig. 2). Left ventriculograms 1 month after PTCA showed signs of mild hypokinesis in the anterior, apical and septal walls.

Reverse redistribution of Tc-99m-tetrofosmin

Successful coronary flow was achieved in all 20 patients with PTCA. Reverse redistribution of Tc-99m-tetrofosmin was observed in 17 of 20 patients (85%) with successful direct PTCA. The remaining 3 had persistent Tc-99m-tetrofosmin defects, but only 3 of 8 patients (37.5%) without direct PTCA had reverse redistribution and the remaining 5 had persistent defects ($p < 0.05$). Myocardial distribution of early and delayed Tc-99m-tetrofosmin images was compared on a segment-by-segment basis. Scores of initial images were equal to those of delayed images in 191 of 252 segments (75.8%). Reverse redistribution was observed in 61 of 252 segments (24.2%). No redistribution was observed in any segment (Fig. 3).

Coronary angiography and left ventriculography

Coronary angiography performed 1 month later revealed that the infarct-related artery was patent in 19 of 20 patients (95%) with reverse redistribution. The infarct-related artery was patent in only 3 of 8 patients with persistent defects (37.5%, $p < 0.01$) (Fig. 4). In 61 segments with reverse redistribution, normal, mild hypokinesis, severe hypokinesis, and akinesis or dyskinesis were observed in 13, 30, 12 and 6 segments, respectively. In 55 segments with persistent defects, normokinesis, mild hypokinesis, severe hypokinesis, and akinesis or dyskinesis

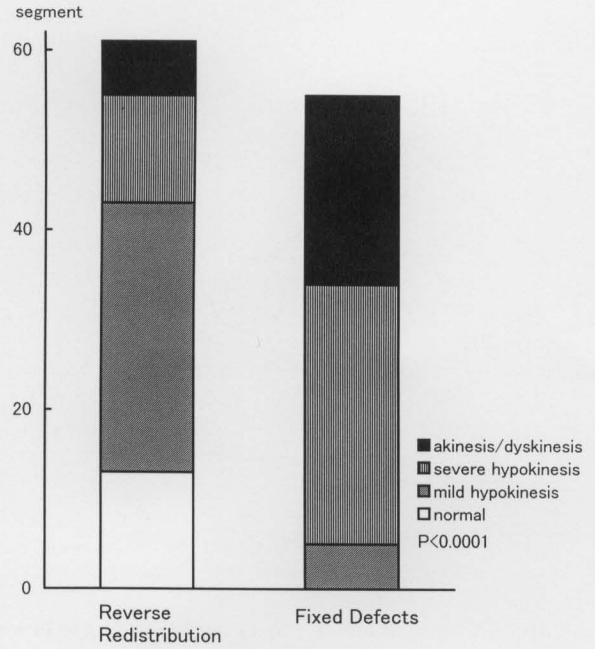

Fig. 5 Comparison of regional wall motion between segments with persistent defects and those with reverse redistribution.

were observed in 0, 5, 29 and 21 segments, respectively. The incidence of regional wall motion abnormality was reduced in patients with reverse redistribution compared to that in patients with persistent defects ($p < 0.0001$) (Fig. 5).

DISCUSSION

Our results indicated that reverse redistribution of Tc-99m-tetrofosmin was frequently observed in patients with acute myocardial infarction who received direct PTCA. This reverse redistribution of the tracer indicates salvaged myocardium.

Reverse redistribution of Tc-99m-tetrofosmin

After intravenous administration, Tc-99m-tetrofosmin is rapidly cleared from the blood and taken up by the heart, muscle, liver, spleen, kidneys and so on in proportion to the blood flow. The myocardial uptake is rapid but the retention is stable in contrast to the rapid blood and hepatic clearance. It has been considered that once this tracer is taken up by the myocardium, redistribution does not occur for several hours.[6,13] Although myocardial uptake of this tracer is mainly dependent on blood flow, the precise mechanism of Tc-99m-tetrofosmin uptake by myocytes has not been elucidated. Since the biokinetics of Tc-99m-tetrofosmin have not been clarified, in our facilities all Tc-99m-tetrofosmin images have been acquired twice: an early image at 30 min and a delayed image at 180 min after intravenous administration. We have noted that reverse redistribution of this tracer is often observed in patients with hypertrophic cardiomyopathy,[7] complete left bundle branch block[8] and acute myocardial infarction and so on. Acute myocardial infarction is one of the pathophysiologic states that shows this unusual finding. The mechanism of reverse redistribution of Tc-99m-tetrofosmin in patients with acute myocardial infarction remains unknown. Platts et al.[14] reported that Tc-99m-tetrofosmin uptake by myocytes is by a metabolism-dependent process that does not involve cation channel transport. They concluded that the most likely mechanism for this is by potential driven diffusion of the lipophilic cation across the sarcolemmal and mitochondrial membranes. Younes et al.[15] reported that the accumulation of Tc-99m-tetrofosmin by the mitochondria is related to their ability to transduce metabolic energy into electronegative membrane potential. Furthermore, Arbab et al.[16] reported that the uptake of Tc-99m-tetrofosmin through the cell membrane is partly related to the Na^+/H^+ antiporter system and only part of the accumulated Tc-99m-tetrofosmin inside the cells enters mitochondria. Since these experimental results could not discriminate between Tc-99m-tetrofosmin uptake and retention by myocytes, sarcolemmal or mitochondrial function may be related to Tc-99m-tetrofosmin uptake and/or retention by myocytes.

Reverse redistribution of Tc-99m-tetrofosmin in acute myocardial infarction

We proposed the following mechanism for reverse redistribution of Tc-99m-tetrofosmin in acute myocardial infarction. Tc-99m-tetrofosmin uptake may firstly occur in the infarct-myocardium after early revascularization. Tc-99m-tetrofosmin can enter injured but viable cells through the sarcolemmal membrane, because sarcolemmal function is maintained or incompletely impaired, but Tc-99m-tetrofosmin cannot be preserved in the infarct-myocardium. Accumulated tracer in the infarct-myocardium may be released due to mitochondrial dysfunction caused by ischemic injury. If the infarct-myocardium after early revascularization is injured but viable, release of accumulated tracer may occur for several hours due to their sarcolemmal and/or mitochondrial dysfunction caused by severe ischemia, which may result in reverse redistribution of Tc-99m-tetrofosmin. Therefore, patients with reverse redistribution would show improvement of regional wall motion abnormalities.

Study limitations

We determined reverse redistribution of Tc-99m-tetrofosmin by visual inspection. To verify our visual findings of reverse redistribution, the regional washout rate of the tracer in early and delayed images must be calculated. Since left ventriculography was not performed in the acute phase, we could not compare the regional wall motion for infarcted segments in the acute and chronic phases. We also judged regional wall motion abnormali-

ties by visual inspection. It is necessary to analyze regional wall motion abnormalities quantitatively with such techniques as the center line method.

Clinical implications

We demonstrated that reverse redistribution of Tc-99m-tetrofosmin in patients with acute myocardial infarction was frequently seen in the area related to the reperfused coronary artery. Most patients with reverse redistribution showed signs of a patent infarct-related coronary artery on coronary angiography 1 month after the onset. Regional wall motion abnormalities 1 month after were reduced in patients with reverse redistribution compared to patients without reverse redistribution. It has been reported that the presence of reverse redistribution in Tc-99m-sestamibi imaging indicates the patency of the infarcted artery and predicts the preserved left ventricular function.[11,17] Reverse redistribution of Tc-99m-tetrofosmin in acute myocardial infarction also discloses the patency of the infarct-related coronary artery, and predicts preserved ventricular contractility of the ischemic area in the late phase.

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