Noninvasive Identification of Myocardium at Risk in Patients With Acute Myocardial Infarction and Nondiagnostic Electrocardiograms With Technetium-99m-Sestamibi

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Background. Patients who have chest pain without electrocardiographic ST elevation are not candidates for thrombolytic therapy in most clinical trials. This study examined the value of technetium-99m-Sestamibi tomographic imaging to assess myocardial perfusion in patients during chest pain without ST elevation.

Methods and Results. Tc-99m-Sestamibi was injected in 14 patients who had chest pain without ST elevation, who subsequently developed enzymatic evidence of myocardial infarction within 24 hours. Tomographic imaging was performed 1–6 hours after injection. Thirteen of 14 patients showed significant perfusion defects indicative of acute myocardial infarction consistent with absent perfusion (20±15% of the left ventricle; range, 2–53%); one patient had normal images. Because of the absence of definitive electrocardiographic changes, only five patients received reperfusion therapy within 6 hours of the onset of chest pain. Regional wall motion abnormalities were present in nine of nine patients undergoing contrast ventriculography and correlated with the location of the Tc-99m-Sestamibi perfusion defect. At the time of subsequent coronary angiography, total arterial occlusion was present in 11 of the 14 patients. The infarct-related artery could be identified in 13 of the 14 patients. In six of these 13 patients, the left circumflex was the infarct-related artery.

Conclusions. Patients who have chest pain without electrocardiographic ST elevation may have arterial occlusion and significant myocardium at risk. Tc-99m-Sestamibi imaging may be of benefit in identifying these patients early so that they can be considered for acute reperfusion therapy. (Circulation 1991;83:1615–1620)

Randomized trials of thrombolysis and preliminary studies of primary percutaneous transluminal coronary angioplasty for patients with acute myocardial infarction have shown clear benefit in reducing mortality and improving ventricular function.1–4 Heavy reliance has been placed on electrocardiographic ST elevation to identify patients who are candidates for acute reperfusion therapy.2–5 It has been well documented that a significant minority of patients, however, will have chest pain without electrocardiographic ST elevation and will subsequently show enzymatic evidence of myocardial infarction.6–10 Clearly, the ability to identify these patients early so that they may be considered for reperfusion therapy would be of benefit.

Technetium-99m-hexakis-2-methoxyisobutyl-isonitrile (99mTc-Sestamibi) is a radionuclide-labeled perfusion agent that is taken up by viable myocardium in proportion to blood flow, that demonstrates little or no redistribution, and that has favorable imaging characteristics.11,12 Its usefulness in assessing myocardium at risk, in assessing myocardial salvage after reperfusion therapy, and in estimating final infarct size was previously reported.13–15 The purpose of this study was to evaluate the results of 99mTc-Sestamibi imaging in patients who had acute chest pain without electrocardiographic ST elevation and who subsequently developed enzymatic evidence of myocardial infarction.
Methods

Study Group

The study group consisted of a consecutive series of patients with myocardial infarction who were enrolled in a prospective study of 99mTc-Sestamibi from February 1988 to June 1990 and who met the following criteria: 1) chest pain of at least 30 minutes in duration, 2) postmenopausal women or men older than 18 years, 3) injection with 99mTc-Sestamibi during acute myocardial infarction before any interventional therapy, 4) elevated creatine phosphokinase (CPK)–MB isoenzyme fraction making up more than 5% of the total CPK as determined within the first 24 hours from the onset of chest pain by an electrophoretic method.16 One hundred thirteen patients met these inclusion criteria. Patients were excluded from this study if the electrocardiogram recorded at the time of hospital admission showed significant ST elevation, which was defined as 0.1 mV or more in two limb leads or 0.1 mV or more in two contiguous precordial leads.5 Ninety-nine patients were excluded for this reason, leaving 14 patients in the final study group. One of these 14 patients was the subject of a previous case report.17

Electrocardiography

The 12-lead electrocardiograms were obtained in all patients at the time of hospital admission for acute myocardial infarction. The maximum ST depression in any lead was measured by calipers 80 msec from the J point and was graded as less than 0.1 mV or 0.1 mV or more. Q waves were considered pathological if they were 40 msec or more in width. Follow-up electrocardiograms (mean, 4.4 days) were obtained in all patients and were assessed for the development of pathological Q waves.

99mTc-Sestamibi Tomography

With previously described techniques, 99mTc-Sestamibi was prepared on a regular basis; 20–30 mCi was injected intravenously in all patients during acute chest pain before the initiation of any reperfusion therapy.13 Tomographic radionuclide images were obtained 1–6 hours later with a rotating gamma camera. Thirty images were acquired for 40 seconds each over a 180° arc, beginning at the 45° right anterior oblique angle and ending at the left posterior oblique angle. These images were processed as previously described.13,14 Quantification of the perfusion defect as a percentage of the left ventricle was performed with a five-slice modification of a previously described three-slice method.18 This method, which identifies the percentage of the left ventricle with absent perfusion, has been shown to agree closely with pathological infarct size in animal models of permanent occlusion.19,20 The five-slice method incorporates two additional slices to the previously described apical, midventricular, and basal slices (one slice midway between the apex and the midventricle and a second slice midway between the midventricle and the base) in an attempt to minimize undersampling of the left ventricle. The location of a perfusion defect was assigned by use of the 14-segment left ventricular short-axis model previously described by this institution.21

Coronary Angiography

All patients underwent coronary angiography during hospitalization (median, 3.8 hours; range, 1 hour to 5 days). The infarct-related artery was identified by analysis of the contrast ventriculogram and the coronary arteriogram and was determined to be occluded or patent according to established criteria.5 In one patient with multiple stenoses and prior infarction, the infarct-related artery could not be confidently identified. Collateral circulation to the infarct-related vessel was classified as present or absent.

Regional Wall Motion Analysis

Regional wall motion abnormalities were graded qualitatively by biplane contrast ventriculography...
TABLE. (CONTINUED)

<table>
<thead>
<tr>
<th>Patient</th>
<th>Infarct artery (%)</th>
<th>Time to angiography (hr)</th>
<th>Perfusion defect</th>
<th>Acute reperfusion*</th>
<th>RWM</th>
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<tr>
<td>1</td>
<td>90 LCx</td>
<td>120</td>
<td>6 Lateral</td>
<td>No</td>
<td>Apical</td>
</tr>
<tr>
<td>2</td>
<td>100 mid-LAD†</td>
<td>5</td>
<td>30 Anterior</td>
<td>No</td>
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<tr>
<td>3</td>
<td>95 mid-LAD</td>
<td>48</td>
<td>16 Anterior</td>
<td>No</td>
<td>---</td>
</tr>
<tr>
<td>4</td>
<td>100 Diagonal</td>
<td>2.5</td>
<td>19 Anterior/inferior</td>
<td>No</td>
<td>Anterior/lateral</td>
</tr>
<tr>
<td>5</td>
<td>100 proximal LCx†</td>
<td>2.5</td>
<td>21 Lateral</td>
<td>Failed PTCA</td>
<td>Inferior/lateral</td>
</tr>
<tr>
<td>6</td>
<td>100 proximal LCx†</td>
<td>18</td>
<td>4 Apical</td>
<td>No</td>
<td>Inferior</td>
</tr>
<tr>
<td>7</td>
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<td>19</td>
<td>22 Lateral</td>
<td>PTCA</td>
<td>Lateral</td>
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<tr>
<td>8</td>
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<td>1.4</td>
<td>30 Inferior</td>
<td>PTCA</td>
<td>---</td>
</tr>
<tr>
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<td>24</td>
<td>53 Lateral</td>
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<tr>
<td>10</td>
<td>100 distal LCx</td>
<td>3</td>
<td>0</td>
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<tr>
<td>11</td>
<td>100 SVG/LAD</td>
<td>2</td>
<td>22 Apical/septal</td>
<td>No</td>
<td>Anterior/lateral</td>
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<tr>
<td>12</td>
<td>100 RCA</td>
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<td>2 Inferior</td>
<td>No</td>
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<tr>
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<td>4.6</td>
<td>44 Anterior</td>
<td>Thrombolysis</td>
<td>Anterior</td>
</tr>
<tr>
<td>14</td>
<td>100 SVG/Ramus</td>
<td>1</td>
<td>14 Anterior</td>
<td>No</td>
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</tr>
</tbody>
</table>

*Acute reperfusion therapy within 6 hours of the onset of chest pain.
†Collateral circulation present.
‡Admitted with Q waves and developed large R waves in V1 and V2.
--- Contrast ventriculography not performed

MI, myocardial infarction; CPK, creatine phosphokinase; LV, left ventricle; %LV, defect size (absent perfusion) as a percentage of the left ventricle; RWM, regional wall motion abnormality; LVH, left ventricular hypertrophy; LBBB, left bundle branch block; RBBB, right bundle branch block; LCx, left circumflex coronary artery; LAD, left anterior descending coronary artery; RCA, right coronary artery; SVG, saphenous vein graft; PTCA, percutaneous transluminal coronary angioplasty.

(nine patients; six studied acutely). The site of wall motion abnormality was described as apical, inferior, lateral, or anterior.

Statistical Analysis

Data are presented as mean±SD or as median and range.

Results

The study population consisted of 10 male and four female patients (age range, 46–83 years), four of whom had a history of prior myocardial infarction (Table 1). Nine patients had chest pain of less than 6 hours in duration, six of whom had 99mTc-Sestamibi images obtained and interpreted within 6 hours from the onset of chest pain. The shortest time from hospital admission to completion of 99mTc-Sestamibi imaging was 45 minutes (two patients). All patients had elevated levels of CPK enzymes within 24 hours of admission (mean, 890±555 IU; range, 260–2166 IU; CPK-MB range, 7–34%) (Table 1). Only four of the 14 patients received successful acute reperfusion therapy (coronary angioplasty, three patients; thrombolysis, one patient) within 6 hours from the onset of chest pain. Tomograms and an electrocardiogram of an individual patient are shown in Figure 1.

Electrocardiography

No patient had 0.1 mV or more ST elevation on the electrocardiogram at hospital admission. Patient 5, with a prior history of inferior infarction, had inferior Q waves and subsequently developed increased R wave voltage in leads V1 and V2 suggestive of posterior infarction. None of the other patients had significant Q waves at hospital discharge.

Coronary Angiography

Nine patients had undergone angiography within 6 hours from the onset of chest pain; all of these patients had total coronary artery occlusions (Table 1). The remaining five patients had undergone angiography later in their hospital course; two of the patients had total coronary artery occlusions. Thus, a total of 11 patients had documented coronary artery occlusion. The infarct-related vessel was the left circumflex artery in six patients, the left anterior descending coronary artery in three patients, the right coronary artery in one patient, a saphenous vein graft in three patients, and was indeterminant due to multiple vessel total occlusions in one patient. Collateral circulation to the infarct-related artery was present in five patients (Table 1).

Myocardium at Risk

Perfusion defect size as a percentage of the left ventricle was widely variable (mean, 20±15%; range, 0–53%) (Table 1). Perfusion defect size was 17±16% of the left ventricle when the four patients with prior infarction were excluded. In patient 10, no perfusion defect was identified despite the subsequent elevation of CPK-MB enzyme levels. When present, the perfusion defect identified by 99mTc-
Figure 1. $^{99m}$Tc-Sestamibi tomographic image at the midventricular level along the horizontal long axis (top left panel), the vertical long axis (top right panel) and the short axis (bottom left panel) in patient 2 with a midleft anterior descending coronary artery total occlusion. Anterior defect indicating absent flow is present that makes up 30% of the left ventricle. Bottom right panel: Same patient’s electrocardiogram on initial hospital admission with chest pain. $^{99m}$Tc-Sestamibi, technetium-99m-hexakis-2-methoxyisobutylisonitrile.
Sestamibi imaging was consistent with the area supplied by the infarct-related artery in all cases.

Discussion

Recent randomized trials evaluating reperfusion therapy for acute myocardial infarction have specifically excluded patients without ST elevation on the electrocardiogram obtained at hospital admission.2-5 Previous reports demonstrated that 7-20% of patients with acute myocardial infarction will have normal or nonspecific electrocardiograms on hospital admission.6,9 Rouan et al9 found that 55% of 1,024 patients who had acute myocardial infarction did not have electrocardiographic ST elevation. Huey et al8 found that only 48% of patients with acute myocardial infarction due to left circumflex coronary artery occlusion will demonstrate electrocardiographic ST elevation. During coronary angioplasty, only 32% of patients with left circumflex balloon occlusion manifest electrocardiographic ST elevation compared with 84% and 92% for left anterior descending and right coronary artery occlusion, respectively.22 From these studies, it is reasonable to infer that a significant number of patients with myocardial infarction will not receive acute reperfusion therapy if ST elevation is a prerequisite for such therapy.

99mTc-Sestamibi imaging has been shown to correlate with myocardium at risk during coronary artery occlusion and subsequent infarct size in animal studies.19,20 The feasibility of this technique in assessing myocardium at risk in the clinical setting and in estimating myocardial salvage and infarct size using tomographic imaging13,14 and planar imaging15 has been previously reported.

The present study demonstrated that, in most patients (13 of 14 patients) without ST elevation who had acute myocardial infarction, 99mTc-Sestamibi imaging identified myocardium with absent perfusion at the time of hospital admission. Although this study was not designed to use 99mTc-Sestamibi tomographic imaging to triage patients with chest pain, two patients completed tomographic imaging with quantification of myocardium at risk in less than 1 hour from hospital admission. The myocardium at risk in this group (20±15%) was significant and was quite similar to that previously described for patients with inferior myocardial infarction and ST elevation (21±11%) using this technique.14 Only five of 14 patients with nondiagnostic electrocardiograms had undergone reperfusion therapy within 6 hours, reflecting the clinical practice to reserve acute reperfusion therapy for patients with ST elevation and acute myocardial infarction.

All of the patients who underwent coronary angiography within 6 hours had total coronary artery occlusion. This finding in a small study group contrasts with the belief that patients with non-Q wave myocardial infarctions generally do not demonstrate acute coronary artery occlusion.23 Larger studies are needed to clarify this issue. The prevalence of left circumflex artery occlusion in this group (46% of those in whom the infarct-related artery was identified) is clearly larger than reported in patients with ST elevation (8%).24 In those patients with abnormal images indicating acute myocardial infarction, the perfusion defect location correlated with the assumed territory of the infarct-related artery and regional wall motion, when available. We did not attempt to correlate myocardium at risk and CKP enzyme levels in this small group because of the use of acute reperfusion therapy in four patients and the presence of prior myocardial infarction in an additional two patients.

Limitations

This study considered a selected group of patients with nondiagnostic electrocardiograms and subsequent positive enzymes for acute myocardial infarction. All patients with chest pain and nondiagnostic electrocardiograms during this period were not injected with 99mTc-Sestamibi. Therefore, the clinical suspicion of significant coronary artery disease was increased in these patients. Our results may not apply to all patients without ST elevation who develop non-Q wave infarction. However, these results suggest that at least a subset of such patients have significant myocardium at risk that can be identified by this technique quickly enough to allow the initiation of reperfusion therapy.

The quantitative technique used here has a number of limitations that have been described previously.13 These include reduced accuracy and sensitivity for defects involving 5% or less of the left ventricle, which occurred in three patients in this group (two with measurable defects and one without). The study group included four patients with prior myocardial infarction, which will increase perfusion defect size. This may lead to overestimation of viable myocardium at risk because this technique cannot distinguish myocardial scar from myocardium at risk. The mean defect size was similar, however, when patients with prior myocardial infarction were excluded from analysis.

Radionuclide imaging with 99mTc-Sestamibi may be of benefit in evaluating patients with chest pain suggestive of myocardial infarction but without electrocardiographic ST elevation. The presence of significant myocardium at risk may identify patients who will benefit from acute reperfusion therapy. Further studies are needed to evaluate this possibility.

References


KEY WORDS • myocardial infarction • technetium-99m • reperfusion • radionuclide • tomography
Noninvasive identification of myocardium at risk in patients with acute myocardial infarction and nondiagnostic electrocardiograms with technetium-99m-Sestamibi.

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