Area-at-Risk Determination by Technetium-99m-Hexakis-2-Methoxyisobutyl Isonitrile in Experimental Reperfused Myocardial Infarction

Patrick M. De Coster, MD, William Wijns, MD, Francisca Cauwe, BSc, Annie Robert, MS, Christian Beckers, MD, and Jacques A. Melin, MD

In a canine model of reperfused myocardial infarction, we tested the hypothesis that after reperfusion, technetium-99m-hexakis-2-methoxyisobutyl isonitrile (Tc-MIBI) tomographic imaging still reflects occlusion blood flow when the tracer is injected before reperfusion. Nine anesthetized dogs underwent 2 hours of coronary occlusion followed by 3 hours of reperfusion ending by being killed. Reference coronary blood flow was determined by radioactive microspheres injected during occlusion and after reperfusion. Biopsies in normal and ischemic myocardium and single photon emission computed tomography were obtained during occlusion and after reperfusion. Circumferential profiles were applied to axial slices divided into 5-degree sectors. The sectors were divided into 3 groups selected on the occlusion acquisition (normal, mildly reduced, and severely reduced) and compared with the postreperfusion acquisition. Tissular Tc-MIBI kinetics was assessed both by Tc-MIBI time-activity curves of normal and ischemic tissue obtained by biopsy and by the relative gradient between normal, ischemic, and necrotic postmortem tissue samples. In biopsy samples, Tc-MIBI content remained unchanged during occlusion and after reperfusion in normal as well as in ischemic tissue (4,662±2,237 counts/min/mg vs. 4,599±1,577 counts/min/mg in normal tissue, NS; 941±903 counts/min/mg vs. 1,087±721 counts/min/mg in ischemic tissue, NS). In postmortem tissue samples, there was a good correlation between occlusion microsphere blood flow and Tc-MIBI activity (r=0.91). In the necrotic samples, mean normalized Tc-MIBI activity (10±17%) was slightly higher than the normalized microsphere blood flow (3±3%, p<0.001) but markedly lower than the normalized microsphere reperfusion blood flow (63±31%, p<0.001). Comparing the single photon emission computed tomographic acquisitions before and after reperfusion, Tc-MIBI activity remained unchanged in normal as well as in mildly reduced or severely reduced segments. Thus, our data are consistent with the hypothesis that Tc-MIBI traces blood flow, does not redistribute significantly despite reperfusion, and can be used for imaging the area at risk. (Circulation 1990;82:2152–2162)

The extent of acute cellular injury and ultimate necrosis after coronary occlusion is influenced by the amount of myocardium that becomes ischemic (the size of the ischemic bed or area at risk) as well as by the severity and the duration of ischemia within the area at risk. In the clinical setting of acute myocardial infarction, a practical method able to delineate this area at risk is not presently available. Additionally, the area at risk would be an important baseline characteristic to compare between groups in clinical trials designed to evaluate the effect of interventions in the acute phase of myocardial infarction.

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Thallium-201 scintigraphy has been extensively used during the past decade for diagnosis1,2 and

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2Address for correspondence: Patrick De Coster, MD, University of Louvain, Medical School, Hospital of Mont-Godinne, B-5530 Yvoir, Belgium.

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FIGURE 1. Outline of the experimental protocol. LAD, left anterior descending coronary artery; SPECT, single photon emission computed tomography.

prognostic stratification\(^3,4\) of patients with acute infarction, and its use in the context of reperfused myocardial infarction has been recently reviewed by Beller.\(^5\) Sequential \(^{201}\)TI imaging has been shown to predict accurately the patency of reperfused arteries in acute myocardial infarction but suffers from major practical limitations.\(^6\) Uptake of \(^{201}\)TI reflects myocardial blood flow distribution for only a short period after intravenous injection because of the redistribution phenomenon.\(^7\) This requires an early scintigram during occlusion, which has become impossible to obtain because intravenous thrombolytic therapy is now routinely administered as early as possible after or even before hospital admission and should not be delayed. Recently, isonitrile complexes labeled with technetium-99m have been proposed as tracers of myocardial blood flow.\(^8-12\) These tracers have a small myocardial clearance that is not significantly different for the normal and ischemic myocardium.\(^{13}\) This small clearance would predict that the myocardial distribution of the tracer still reflects the blood flow at the time of injection even when measured a few hours later.

The aim of our study was to demonstrate the usefulness and the validity of a scintigram performed a few hours after reperfusion if the tracer was injected during the occlusion. The tracer used in the present study was an isonitrile complex (\(^{99m}\)Tc-hexakis-2-methoxyisobutyl isonitrile [Tc-MIBI]), which was injected during the occlusion period. Three independent data sets tested the hypothesis that delayed (after reperfusion) imaging still reflects the size of the ischemic bed or area at risk, including necrotic and ischemic tissue. Single photon emission computed tomography obtained after reperfusion was compared with a scintigram performed during the ischemic period; biopsies were performed during occlusion and after reperfusion; after killing, reference microsphere blood flows and Tc-MIBI activities have been determined in tissue samples characterized as viable or necrotic by histochemical and metabolic techniques.

Methods

Nine mongrel dogs weighing 19–27 kg were studied after a 12-hour overnight fast. The dogs were anesthetized with sodium pentobarbital (30 mg/kg), intubated, and ventilated with room air (Spiromat respirator, Dräger, Lubeck, Germany). Arterial blood gases were monitored, and oxygen was added to maintain values within the normal physiological range. Morphine sulfate (1 mg/kg i.m.) was given at induction and throughout the remainder of the experiment to maintain adequate anesthesia. The heart was exposed through a left thoracotomy and suspended in a pericardial cradle. Catheters were inserted into the left atrium and descending aorta (by femoral approach). One dog died 15 minutes after occlusion and was not included in the “Results” section.

Experimental Protocol

A summary of the experimental protocol is outlined in Figure 1. All dogs were pretreated with
lidocaine hydrochloride. The left anterior descending coronary artery was occluded with an atraumatic vascular clamp. Three dogs were defibrillated during occlusion before any tracer injection. Fifty microliters of 99mTc microspheres (15±1 μm, du Pont de Nemours, North Billerica, Mass.) was injected into the left atrium 30–45 minutes after coronary artery occlusion. Immediately after the withdrawal of the reference blood sample, 10–15 mCi Tc-MIBI was injected intravenously and the arterial input was obtained by rapid arterial sampling. A first single photon emission computed tomographic (SPECT) acquisition was performed 20 minutes after Tc-MIBI injection and followed by in vivo transmural biopsies. Biopsies were taken from both ischemic and normal myocardium with a Travenol Tru-Cut needle (Baxter Company, Deerfield, Ill.). The occlusive vascular clamp was suddenly released 90 minutes after occlusion in three dogs and 120 minutes after occlusion in five dogs. Fifty microliters of 111In-labeled microspheres was injected into the left atrium 100 minutes after reperfusion. A second SPECT acquisition was performed 120 minutes after reperfusion. Thereafter, 5–8 mCi 18F-2-deoxyglucose (FDG) was injected intravenously and the arterial input function was obtained by rapid arterial sampling. Twenty minutes before killing, blood samples were taken for the measurement of glucose, lactate, and fatty acid levels. A second set of biopsies was taken just before killing. Immediately thereafter, the left anterior descending artery was occluded with a snare, blue dye was injected into the left atrium for in vivo risk region determination, and the heart was arrested with concentrated KCl solution.

Postmortem Tissue Preparation

After killing, the hearts were excised and the ventricles were sectioned parallel to the atroventricular groove, forming five slices 1–1.5 cm thick. The basal surface of the heart slices and margins of the area at risk were traced onto acetate sheets. Biopsy sites were identified on the sheets. The slices were placed in a solution of triphenyl tetrazolium chloride (TTC) at 37° C for 30 minutes.

Endocardial and epicardial sampling for the measurements of 99mTc, 111In, 99mTc, and 18F activity was made in the center of the infarct (TTC–), in ischemic but noninfarcted myocardium (area unstained with blue but TTC+), in the zone immediately adjacent to the ischemic area, and in the nonschismic normal muscle. Ischemic samples were cut to avoid contamination by nonischemic and necrotic tissue. Necrotic samples were subdivided into homogenous confluent areas of necrosis and patchy necrosis. The size of myocardial infarcts and areas at risk was measured planimetrically. Samples were weighed and counted in a scintillation well counter. Myocardial blood flow was calculated with the following equation: Qm=(Cm×R)/Cr, where Qm equals myocardial blood flow (ml/min), Cm equals tissue counts (counts/min), R equals reference arterial blood flow, and Cr equals counts per minute in reference samples. Flow per 100 g was calculated by dividing blood flow by the sample weight. To take into account the different scatter fractions and half times, all samples were counted three times, that is, on the day of the experiment, and 24 hours and 2 weeks later. The following windows were used: 18F, 430–600 keV; 99mTc, 115–165 keV; 99mTc, 620–820 keV; and 111In, 300–430 keV. A computer program was used to correct for activity overlap between the energy windows. The rate of exogenous glucose use was calculated by applying the FDG model described by Sokoloff et al.14 Fixed values for the rate constants and a lumped constant of 0.67 were used to calculate the glucose metabolic rate in myocardial tissue (expressed in mg/min/100 g).15,16

Imaging Methodology

SPECT imaging was performed with a rotating gamma camera (400 AC/T, General Electric) equipped with a high-resolution low-energy collimator. This camera was interfaced to a dedicated computer (Micas V, Bartec, Farnborough, UK). The dogs were positioned on the imaging table right side down with the spine approximately parallel to the axis of rotation. Energy discrimination was provided by a 20% window centered on the 140 keV photopeaks. Planar system resolution of the imaging device was 8.4 mm without scatter. Acquisition was performed at 360 degrees around the dog’s chest by using a rotation radius of 28 cm. Sixty-four projection images were generated and stored without zoom in a 64×64 matrix. At each projection, data were acquired for a preset time of 15 seconds and contained approximately 200,000 counts in the entire field of view and 60,000 counts in the cardiac area. No corrections for center of rotation nor for uniformity were made. These parameters were verified before each study; center of rotation showed no variations and uniformity remained within acceptable limits in the center field of view (less than 3% variation). From the projection data, sinograms were generated covering the cardiac area from base to apex at one-pixel slice thickness (6.3 mm). Reconstruction was done with a Shepp-Logan filter. Ten axial views were obtained and a circumferential profile was applied to each slice. In this algorithm, an operator-selected circumferential region of interest is positioned around the left ventricle and divided into 72 equally spaced sectors (5 degrees each). Starting position for analysis is always 0 degrees in a standard x-y coordinate system. Curves are generated showing the mean value of summed sectorial activity plotted against anticlockwise angle. Those mean values were expressed as a percentage of maximal sector activity in each slice. Curves generated from both acquisitions were compared at each slice level.

Preparation of Tc-MIBI

We used vials containing 1 mg of [Cu(MIBI)4]BF4, 0.075 mg stannous chloride, 1 mg cysteine hydrochlo-
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ride, 26 mg sodium citrate, and 20 mg mannitol (duPont de Nemours). The contents of the vials were lyophilized and stored under nitrogen. For the preparation of the compound, 3 ml of a solution containing sodium pertechnetate $^{99m}$Tc (approximately 25 mCi) was added to the vial. The vial was then placed in a boiling water bath for 10 minutes. Twenty to 40 minutes later, 15 mCi of this solution was injected intravenously. The quality control of the injected dose was performed by using a radio-thin-layer chromatographic method. More than 90% of all injected doses were identified as Tc-MIBI. The precise structure of the cationic technetium complex is $^{99m}$Tc (MIBI)$_n$ where MIBI is 2-methoxy-2-methylpropyl isonitrile.

Data Analysis

Myocardial blood flows and tracer activities in ischemic and infarcted samples were normalized by dividing these values by the nonischemic zone activity in the corresponding left ventricular ring.

All results are expressed as the mean±1 SD. The mean values of flow and tracer activities for each dog within each region were used as individual data points in the analysis of variance. Statistical significance of changes in the variables under study (Tables 1 and 2) was computed by one-way analysis of variance for repeated measures with contrast (BMDP statistical software package). Paired Student's $t$ tests were used to compare microsphere blood flow with Tc-MIBI activity (Figure 2). A $p$ value greater than 0.05 was considered nonsignificant.

Results

Hemodynamic Data

At the time of Tc-MIBI injection (30–45 minutes after occlusion), mean heart rate (136±18 beats/min) and mean aortic pressure (96±20 mm Hg) were not significantly different from the preocclusion values (137±17 beats/min and 94±27 mm Hg) (Table 1). Three hours after reperfusion, heart rate (140±22 beats/min) and mean aortic pressure (96±28 mm Hg) remained similar to the control values.

Infarct Size and Myocardial Blood Flow

The range of infarct/risk region was expansive. Two dogs had no infarct at all, and the six remaining

<table>
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<td>Before &amp; After Tc-MIBI injection</td>
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<td>Heart rate (beats/min)</td>
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<td>Mean blood pressure (mm Hg)</td>
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Values are mean±SD.

| TABLE 2. Normalized Microsphere, Tc-MIBI, and Fluorodeoxyglucose Metabolic Rate |
|-------------------------------|-------------------|-------------------|-------------------|-------------------|
|                              | Adjacent to normal area | Ischemic area | Patchy necrosis | Necrosis |
| Microsphere blood flow (%)   |                   |                 |                  |        |
| During occlusion             |                   |                 |                  |        |
| Endocardium                  | 86±20             | 43±29*          | 11±6f            | 3±3    |
| Epicardium                   | 81±25             | 37±25*          | 14±13*           | 3±2    |
| All                          | 83±23             | 39±27*          | 13±12*           | 3±3    |
| After reperfusion            |                   |                 |                  |        |
| Endocardium                  | 94±21             | 82±10           | 77±34            | 64±33  |
| Epicardium                   | 92±25             | 65±28†          | 59±30            | 52±2   |
| All                          | 93±23             | 70±26†          | 63±31            | 63±31  |
| Tc-MIBI activity (%)         |                   |                 |                  |        |
| Endocardium                  | 92±14             | 49±23*          | 28±10‡           | 10±7   |
| Epicardium                   | 88±19             | 48±19*          | 26±12*           | 3±1    |
| All                          | 89±17             | 49±20*          | 26±11*           | 10±17* |
| FDG metabolic rate (%)       |                   |                 |                  |        |
| Endocardium                  | 95±22             | 55±18*          | 32±15            | 16±15  |
| Epicardium                   | 76±18             | 44±27*          | 19±9†            | 15±3   |
| All                          | 84±21             | 47±25*          | 22±12*           | 16±14  |

Values are mean±SD. Tc-MIBI, $^{99m}$Tc-hexakis-2-methoxyisobutyl isonitrile; FDG, fluorodeoxyglucose. $^*p<0.001$, $^a p<0.01$, $^b p<0.05$ vs. the previous column value.
dogs had 77%, 43%, 42%, 41%, 38%, and 13%, respectively, infarct/risk region ratio.

During occlusion, transmural blood flow in the normally perfused area was 141±89 ml/min/100 g, was reduced in the ischemic area (TTC+; risk region, 35±22 ml/min/100 g; p<0.001 vs. normal), and was markedly decreased in necrotic regions (TTC−; 2.9±3.3 ml/min/100 g; p<0.001 vs. ischemic region).

After reperfusion, blood flow increased in ischemic (78±32 ml/min/100 g) and in necrotic tissue (46±28 ml/min/100 g) but remained significantly (p<0.01) lower than in normal tissue (130±68 ml/min/100 g).

**Myocardial Tc-MIBI Activities and Glucose Metabolism**

Rapid arterial sampling showed that peak arterial activity was observed 15–33 seconds after Tc-MIBI injection. After 4 minutes, residual arterial activity represented 2.8±1.5% of peak activity.

Tissular Tc-MIBI kinetics were assessed both by the Tc-MIBI time/activity curves of normal and ischemic tissue obtained by biopsy and by the relative 99mTc gradient between the normal, ischemic, and necrotic regions in tissue samples after killing (at 4 hours after injection), compared with the microsphere-determined blood flow.

The myocardial 99mTc time-activity curves from the tissue obtained by biopsy in the ischemic and normal myocardial regions are shown in Figure 3 (individual values and mean±SD). The 99mTc count rates for the biopsy samples were between 185 and 7,695 counts/min/100 g. The weight of each sample was between 6 and 24 mg. The mean count rate in biopsies obtained during occlusion was 4,662±2,237 counts/min/mg in normal tissue (range, 2,013–7,695 counts/min/mg) and 941±303 counts/min/mg in ischemic tissue (range, 185–2,455 counts/min/mg). The mean ratio of ischemic to normal tissue expressed in a percentage was 26±22% (range, 3–61%). The Tc-MIBI activity in the samples obtained 3 hours after reperfusion was similar to the occlusion values. The mean count rate in normal tissue was 4,599±1,577 counts/min/mg (range, 2,384–6,478 counts/min/mg) and 1,087±721 counts/min/mg (range, 129–1,773 counts/min/mg) in ischemic tissue. The ratio of ischemic to normal tissue was 27±20% (range, 2.1–61%).

Table 2 and Figure 2 compare the mean normalized Tc-MIBI and microsphere activity in postmortem myocardial samples (3 hours after reperfusion). The comparison is made for endocardial and epicardial samples obtained from necrotic regions (TTC−, homogenous or patchy), ischemic but noninfarcted regions (TTC+, risk region) and areas immediately adjacent to the ischemic region. In ischemic samples, the mean normalized Tc-MIBI activity (49±20%) was lower than the microsphere activity after reperfusion (70±26%, p<0.001) and slightly higher than the microsphere activity during occlusion (39±27%, p<0.001). In the homogenous necrotic samples, the mean normalized Tc-MIBI activity (10±17%) was...
lower than the Tc-MIBI activity in ischemic samples ($p<0.001$) and than the microsphere activity after reperfusion ($63\pm31\%$, $p<0.001$). Similarly, in the ischemic samples, the Tc-MIBI activity in the necrotic samples was slightly higher than the microsphere activity during occlusion. The difference was small but reached statistical significance, that is, $10\pm17\%$ for Tc-MIBI versus $3\pm3\%$ for occlusion microspheres ($p<0.001$).

Comparison of the individual data (312 tissue samples) of tissue Tc-MIBI content and flow (microspheres) during the occlusion period showed a linear relation with a high correlation coefficient ($r=0.91$) (Figure 4). Although the agreement was good for normalized flow greater than $10\%$, a consistent excess of Tc-MIBI was observed for lower microsphere flow values. In contrast, no significant relation was found between Tc-MIBI content and reperfusion blood flow ($r=0.51$) (Figure 5). In both ischemic and necrotic tissue, Tc-MIBI content was consistently lower than the reperfusion blood flow.

The metabolic rate for glucose was $13.3\pm4.4$ mg/min/100 g in normal myocardium. Normalized values for glucose are shown in Table 2. The values in homogeneously necrotic samples ($16\pm14\%$) were slightly but not significantly lower than in patchy necrosis ($22\pm12\%$) and were smaller than in ischemic ($47\pm25\%$; $p<0.001$) or adjacent samples ($84\pm21\%$; $p<0.001$).

The arterial levels of glucose, fatty acids, and lactate were $371\pm24$, $22\pm8$, and $102\pm26$ $\mu$mol/100 ml, respectively.

**Myocardial Tc-MIBI Imaging**

SPECT images during occlusion were compared with the data acquired 2 hours after reperfusion. Figure 6 shows an example of a circumferential profile curve obtained from the acquisition performed during occlusion and 2 hours after reperfusion. Figure 7 shows an example of four tomographic slices before and after reperfusion in one representative dog. The 72 sectors (5 degrees each) of each slice were divided into three groups according to the percentage of maximal Tc-MIBI activity calculated during the first acquisition (occlusion period) (Figure 8). The first group of segments (normal uptake) included all the sectors in which the percentage of Tc-MIBI activity normalized at each slice level was higher than $70\%$. The segments in which Tc-MIBI uptake was mildly impaired constituted a second group ($30\text{–}70\%$ of maximal Tc-MIBI activity) and the severely abnormal segments were included in a third group (less than $30\%$ of maximal Tc-MIBI activity).

No visual changes were detectable in the defect size observed in the late acquisition (reperfusion) compared with the first acquisition (occlusion). This was confirmed by the circumferential profile analysis, as shown in Figure 8, comparing the mean values of Tc-MIBI activity in each group of segments during occlusion and in the same segments after reperfusion. In each of the three groups, the mean value of Tc-MIBI activity remained unchanged after reperfusion, compared with the occlusion data. In the nor-
mal segments, the mean value of Tc-MIBI activity was 84±2% during occlusion and 82±3% after reperfusion. In the segments with mildly impaired uptake, Tc-MIBI activity was 50±1% before and 52±2% (NS) after reperfusion. The mean value of difference was 2±1% (NS). Seventy-three percent of the mildly impaired segments showed less than 10% increase in Tc-MIBI activity after reperfusion, and 95% of these segments had less than 20% increase.

In the severely abnormal segments, the percentage of Tc-MIBI activity was 19±3% before and 20±4% after reperfusion, resulting in a mean value of difference of 1±1% (NS). No segment of this group became normal after reperfusion. The majority of the segments (88%) showed less than 10% variation in Tc-MIBI activity between serial SPECT images.

**Discussion**

The present study suggests that delayed scintigram with Tc-MIBI still reflects the occlusion blood flow, if Tc-MIBI is injected during occlusion, and can therefore be used for delayed imaging of the area at risk. Three independent data sets support this statement. First, the SPECT images obtained 2 hours after reperfusion showed a similar Tc-MIBI distribution compared with the scintigrams performed during occlusion. Second, by counting iterative biopsy samples, the ratio of Tc-MIBI activity in ischemic versus normal tissue was identical during occlusion and after 3 hours of reperfusion. Finally, in the postmortem tissue samples, the normalized Tc-MIBI activity was close to the reference microsphere occlusion blood flow and markedly lower than the reperfusion blood flow. The postmortem histochemical and metabolic characterization of tissue samples confirmed that Tc-MIBI reflects the entire area at risk, in both necrotic and viable tissue.

During the past decade, it has become evident that delineation of area at risk is crucial for the assessment of infarct-attenuating agents. Presently, all the available methods suffer from practical or theoretical limitations. Analysis of regional wall motion abnormalities tends to overestimate the size of the ischemic bed.17,18 Because they require an invasive procedure in the catheterization laboratory, practical restrictions are applicable to the intracoronary infusion of 99mTc macroaggregate19,20 or 201Tl.21 Intravenous 201Tl has been shown to accurately reflect regional blood flow when uptake is measured early after injection but is an unreliable indicator of myocardial injury in an experimental model of occlusion followed by reperfusion.22 Because of the redistribution phenomenon, delayed 201Tl uptake measured after reperfusion does not reflect occlusion blood flow but is considered a marker of viability.23 Nevertheless, 201Tl has been frequently used in clinical studies of patients within hours after acute myocardial infarction.1-6 With the advent of intravenous thrombolysis, the use of 201Tl in assessing the occlusion blood flow becomes unrealistic because the

**FIGURE 5. Scatterplot showing correlation between the individual 99mTc-hexakis-2-methoxyisobutyl isonitrile (Tc-MIBI) activities and the reperfusion microsphere blood flows (normalized values).**
FIGURE 6. Circumferential profiles on one axial slice; the left part of the figure represents the same axial slice reconstructed from the acquisition performed during occlusion (above) and 2 hours after reperfusion (below). The defect is indicated by the arrow. The corresponding circumferential profiles are shown on the right part of the figure. The curves are normalized to their own maximum.
reperfusion procedure should not be delayed. Therefore, there is an important need for a flow tracer still reflecting occlusion blood flow several hours after reperfusion.

The design of our protocol was chosen to reproduce a potentially frequent clinical situation in the setting of a thrombolytic therapy. For this reason, we preferred a rather long duration of occlusion (90 minutes) to a brief occlusion.24 Instead of other experimental studies performing scintigrams during persisting occlusion13,25 or after reperfusion, but also after a second injection of Tc-MIBI,24,25 we chose to compare occlusion and reperfusion scintigrams after a single injection during the occlusion period.

The SPECT acquisition performed 2 hours after reperfusion seems to be a reasonable delay for imaging the patient without interfering with the acute therapy. Our data are in agreement with previously reported animal studies, showing that Tc-MIBI accurately reflects blood flow distribution in normal and ischemic myocardium.13,24–28 Additionally, we also observed the already demonstrated close relation between Tc-MIBI distribution and occlusion blood flow despite the fact that the occluded vessel was reopened for 3 hours.

These experimental data could serve as validation of other clinical29–31 observations suggesting that Tc-MIBI distribution remained unchanged despite reperfusion and could be used as a marker of the area at risk. Importantly, this was shown in both viable and necrotic tissue.

The small difference between the microsphere occlusion blood flow and the Tc-MIBI activity in postmortem tissue samples can be explained either by a small redistribution not detectable by imaging technique or by some degree of overestimation of blood flow. From the postmortem tissue samples analyses, it is not possible to determine the relative contribution of these two hypotheses because the dogs were killed 3 hours after reperfusion. The remarkable stability of Tc-MIBI content in normal and ischemic biopsy during and after reperfusion argues against the redistribution hypothesis. Given the rapid blood clearance of Tc-MIBI, any redistribution would be limited by the very small quantity of residual circulating tracer. The study by Li and coworkers24 is in favor of the overestimation hypothesis. After a short occlusion (6 minutes), they showed Tc-MIBI content in the center if ischemic areas consistently exceeded microsphere blood flow. In another study, Sinusas and colleagues28 also showed a slight overestimation of blood flow with Tc-MIBI in the central ischemic zones.

In conclusion, the present data demonstrate that the uptake and clearance kinetics of Tc-MIBI make this tracer valid for the assessment of the ischemic area at risk during coronary occlusion. Compared with previously used tracers, Tc-MIBI offers practical advantages. In a clinical situation, Tc-MIBI can be...
administered at the early stage of infarction in the emergency room so that no undesirable delay in the administration of thrombolytic therapy will result. Delayed imaging can be performed at a convenient time, up to several hours later, when the thrombolytic therapy is completed and the clinical state of the patient is stable. Even after successful thrombolysis, the delayed images would still reflect the regional blood flow distribution during the occlusion period. The feasibility of tomographic Tc-MIBI imaging in acute myocardial infarction has been recently demonstrated. The present investigation provides the experimental validation of the delayed imaging after reperfusion, which is currently being evaluated in the clinical setting. A second study could be performed on a separate day after a second Tc-MIBI injection. As we have shown, the first set of Tc-MIBI images will delineate the extent of impaired myocardial perfusion (area at risk) at the time of occlusion, whereas the second set of images would presumably show the final extent of myocardial infarction. The comparison between both SPECT images could then provide an estimate of the amount of reperfused myocardium.

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**KEY WORDS** • area at risk • myocardial infarction imaging • technetium-99m-isonitrile
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