Myocardial Technetium-99m-Teboroxime Activity in Acute Coronary Artery Occlusion and Reperfusion: Relation to Myocardial Blood Flow and Viability

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The purpose of this study was to test the hypothesis that ^{99m}Tc-teboroxime retention within the heart depends at least in part on the presence of viable myocytes. **Methods:** We used a porcine model of acute myocardial infarction with reperfusion and compared the myocardial uptake of labeled microspheres at 1 hr of reperfusion with that of ^{99m}Tc-teboroxime. Eleven domestic swine had measurements of hemodynamics and regional myocardial blood flow (microspheres) at baseline, at 10 and 50 min of left anterior descending (LAD) coronary artery occlusion and at 10 and 60 min of LAD reperfusion. Technetium-99m-teboroxime was injected intravenously at 60 min of reperfusion and the animal was killed 5–7 min later. The heart was then perfused with triphenyl tetrazolium chloride to identify infarcted and jeopardized myocardium in the occlusion zone and with Evans blue dye to mark normally perfused myocardium. After imaging, tissue sections were digested and colored microspheres were extracted and counted to determine myocardial blood flow. **Results:** After coronary occlusion, infarct zone (MIZ) to normal zone (NZ) blood flow ratios declined from 0.95 ± 0.27 (preocclusion) to 0.18 ± 0.15 at 10 min and 0.25 ± 0.35 at 50 min of occlusion (both $p < 0.05$). The MIZ:NZ count ratio at 60 min of reperfusion was less than the MIZ:NZ blood flow ratio in every animal and over the entire range of flow ratios (0.55–3.64). **Conclusion:** Technetium-99m-teboroxime requires viable myocytes for retention within the heart and is not exclusively a tracer of myocardial blood flow when imaged 5–7 min after injection. Additional in vivo imaging studies are required to determine the extent to which reduced retention of the tracer by reperfused but nonviable myocardium influences the appearance of clinical scans.

Key Words: technetium-99m-teboroxime; coronary reperfusion; myocardial infarction; myocardial viability, myocites

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Technetium-99m-teboroxime is a neutral lipophilic compound characterized by extremely high myocardial extraction (90%), even at high flow rates, during its first pass through the myocardium (*1–5*). These properties make it a very attractive tracer of myocardial perfusion. Since infarct-related artery patency is acutely critical and important over the longer term (*6*), myocardial imaging with a highly extracted "flow" tracer such as ^{99m}Tc-teboroxime may become frequently clinically employed more. It is unclear if the net retention of teboroxime in the heart is purely related to blood flow or if viable myocytes are also required. This is an important consideration because myocardial blood flow and myocardial viability may be uncoupled in the setting of acute myocardial infarction with reperfusion.

Data from in vitro experiments with perfused rabbit hearts indicate ^{99m}Tc-teboroxime binds to intact lipid membranes and thus has the potential to serve as a marker of viability (*1*). Another in vitro study, however, suggests teboroxime retention by fetal myocytes in culture may be relatively less sensitive to cell viability than either thallium or sestamibi (*7*). Further, since initial (1–2 min postinjection) accumulation (*2,3*) in the heart may be more flow dependent than late (5–7 min postinjection) tracer retention (*8*), the present study tests the hypothesis that ^{99m}Tc-teboroxime is not strictly a marker of myocardial blood flow when imaged late (5–7 min) but depends at least in part on viable myocardium for retention within the heart. We tested this hypothesis in a porcine model of acute myocardial infarction (coronary artery occlusion) with reperfusion by comparing the myocardial blood flow (microsphere technique) at 1 hr of reperfusion with that of myocardial ^{99m}Tc-teboroxime activity.

METHODS

Animal Preparation

Farm-bred domestic swine (n = 11; mean weight = 47 kg; range, 41–55 kg) were premedicated with ketamine (25 mg/kg i.m.)

and sodium thiamylol (total dose 0.5–1.0 g i.v.), intubated and anesthetized with halothane (0.5%–1.5%) and nitrous oxide (60:40 mixture with oxygen). Arterial blood gases were frequently monitored and maintained at appropriate levels throughout each study. After induction of anesthesia, each animal was anticoagulated with heparin (225 IU/kg i.v.). Full anticoagulation was maintained throughout the study.

Each animal was instrumented for the study as follows (*2,9,10*). A 7F pigtail catheter was advanced under fluoroscopic guidance into the left atrium. This catheter was used to administer colored microspheres for measurements of regional myocardial blood flow. Another 8F catheter was positioned in the aorta to monitor arterial blood gases and to reference withdrawal for microsphere determinations of regional myocardial blood flow. The femoral veins were cannulated bilaterally to administer fluids and medications during the study. A 3F angioplasty catheter was positioned in the middle third of the left anterior descending coronary artery. After placement of the angioplasty catheter, halothane and nitrous oxide were discontinued and the animal was permitted to awaken sufficiently to breath spontaneously and exhibit modest tremulousness. A constant intravenous infusion of sodium thiamylol was administered at 5–25 ml/hr (20 mg/ml) to maintain sedation and ensure that the animal was free of pain. The entire study protocol was reviewed and approved by the Animal Care and Use Committee of the Rhode Island Hospital and conformed to the "Position of the American Heart Association on Research Animal Use (adopted by AHA 11 November 1984)."

Hemodynamics, heart rate, arterial and left atrial pressures were monitored continuously throughout the study and recorded on chart paper with a Hewlett Packard eight-channel recorder (model 5588A, Palo Alto, CA). Intravascular and intracardiac pressures were recorded from fluid-filled catheters connected to Hewlett Packard force transducers (model 1280A).

Study Protocol

After instrumentation and a 30-min stabilization interval the experimental protocol was begun. Baseline measurements of hemodynamics and regional myocardial blood flow by colored microspheres were obtained (*11*). After completion of baseline measurements the left anterior descending coronary artery was occluded by inflating the balloon of the angioplasty catheter for 1 hr. Repeat measurements of hemodynamics and myocardial blood flow were obtained at 10 and 50 min of coronary artery occlusion. At the end of the hour, the balloon was deflated and the left anterior descending coronary artery reperfused for 1 hr. At 10 and 60 min of reperfusion, repeat measurements of hemodynamics and regional myocardial blood flow were again obtained. Technetium-99m-teboroxime (~15 mCi) was injected intravenously after completion of the 60-min data acquisition and the animal sacrificed 5–7 min later. The interval between tracer injection and sacrifice was chosen to approximate the time period over which clinical planar images might reasonably be obtained in a patient following ^{99m}Tc-teboroxime injection. The potential appearance of images limited to the initial 2–4 min after tracer injection are not directly addressed by the present protocol.

Postmortem Analysis of Myocardial ^{99m}Tc-Teboroxime Activity and Regional Myocardial Blood Flow

After the animals were killed, the area at risk in the distribution of the left anterior descending coronary artery was perfused with triphenyl tetrazolium chloride (TTC) to identify infarcted myocardium as described by others (*12*). Viable myocardium in the risk area stains brick red with TTC while necrotic muscle is unstained (pale white). The reference (i.e., normally perfused) region of the heart was identified by simultaneously perfusing the aortic root at the same pressure (100 mmHg) with Evan's blue dye. After completion of the staining procedure, the heart was sliced in bread-loaf style from apex to base into 1-cm thick sections. Each slice was traced on acetate and the location of blue, brick red and unstained segments carefully noted. Next, blue-stained, normal zones and TCC-negative infarct zones were removed from each section, weighed and imaged by placing them on the face of a Picker Dynamo gamma camera equipped with a general all-purpose collimator and interfaced with an MDS A^3 computer system (Ann Arbor, MI). Images were acquired in a 128 × 128 × 8 matrix for pre-set time (10 min) and counts recorded. Total counts in infarct and normal zone samples averaged 20 and 50 K, respectively (range, 7–87 K). Results were expressed as counts per gram in each zone. Count rates encountered were well within the linear range of the detector (~20 K/sec). Further, because the objective of the study was to test the hypothesis that infarcted myocardium would differ from normal tissue in terms of net tracer retention, noninfarcted tissue (TTC positive) in the risk area was not included in data analysis to be sure that only pure samples of normal and infarcted myocardium were studied.

To ensure precise 1:1 correspondence between ^{99m}Tc-teboroxime data and microsphere blood flow data, the same subsections which had been imaged to determine infarct zone and normal zone ^{99m}Tc-teboroxime activity were digested and counted for microsphere measurements of blood flow as described by others (*11*). It should be stressed that tissue used for the normal zone was obtained from myocardium on the side of the heart opposite the risk area. Finally, in these experiments which were performed to assess potential correlations between clinical images and myocardial blood flow, only transmural flow measurements were made (i.e., tissue samples were not divided into endocardial and epicardial subsections).

Statistical Analysis

All data are expressed as mean ± s.d. The significance of differences among group mean values of continuous variables (e.g., myocardial blood flow, ^{99m}Tc-teboroxime activity) were assessed by repeated measures ANOVA. If ANOVA demonstrated a statistically significant F statistic, then an appropriate contrast test was used to determine which means differed from one another (SuperAnova™, Abacus Concepts, Berkeley, CA). Values of $p < 0.05$ were considered statistically significant.

RESULTS

Hemodynamics

Mean arterial pressure did not change significantly versus baseline during the study. Left atrial mean pressure increased ($p < 0.05$) versus baseline at 10 min of coronary occlusion and at 10 and 60 min of reperfusion. Heart rate following coronary occlusion did not change significantly versus baseline. Following reperfusion, however, heart rate increased significantly ($p < 0.01$) versus baseline at both the 10- and 60-min measurement points (Table 1).

Regional Myocardial Blood Flow

Blood flow in the normal zone (NZ) did not change significantly from baseline at any time during the study protocol. Blood flow in the infarct zone (MIZ) as intended declined significantly ($p < 0.05$) versus baseline at both 10

TABLE 1
Hemodynamics*

	Baseline	Occlusion		Reperfusion	
		10′	50′	10′	60′
Mean arterial pressure (mmHg)	100 ± 22	98 ± 2	98 ± 15	92 ± 14	89 ± 19
Heart rate	79 ± 17	89 ± 14	91 ± 20	101 ± 23‡	110 ± 22‡
Left atrial pressure (mmHg)	7 ± 5	11 ± 6†	9 ± 8	13 ± 8‡	13 ± 6‡

*Mean ± s.d.; n = 11.
† = $p < 0.05$ vs. baseline.
‡ = $p < 0.01$ vs. baseline.

and 50 min of left anterior descending coronary artery occlusion. Following reperfusion, blood flow in the infarct zone increased significantly ($p < 0.05$) versus baseline at both 10- and 60-min. The baseline MIZ:NZ blood flow ratio declined ($p < 0.05$) versus baseline at both 10 and 50 min of coronary occlusion and increased ($p < 0.05$) above baseline levels at both 10 and 60 min of reperfusion (Table 2).

Myocardial Technetium-99m Teboroxime Activity

Figure 1 compares myocardial infarct zone ^{99m}Tc-teboroxime activity, expressed as infarct zone (MIZ) to a normal zone (NZ) counts/g ratio, with regional myocardial blood flow (MIZ:NZ ratio) after 60 min of reperfusion. The regression line of myocardial ^{99m}Tc-teboroxime activity versus flow is well below the line of identity. The MIZ:NZ ^{99m}Tc-teboroxime activity ratio (0.85 ± 0.32) also was reduced significantly ($p < 0.01$) versus the MIZ:NZ blood flow ratio 60 min after reperfusion (1.54 ± 0.94). Further, the MIZ:NZ ^{99m}Tc-teboroxime activity ratio was less than the MIZ:NZ blood flow ratio in every animal and over the entire range of flow ratios (0.55–3.64). There also was a positive correlation ($r = 0.65$, $p < 0.05$) between the absolute level of myocardial blood flow in the infarct zone at the time of ^{99m}Tc-teboroxime injection and the MIZ:NZ ^{99m}Tc-teboroxime activity ratio. The positive correlation indicates that higher absolute levels of flow in the infarct zone at reperfusion did not favor lower MIZ:NZ count ratios.

Figure 2 shows the exclusion of the three animals with reperfusion flow greater than 2.0 ml/min/g had little impact on the data. The absolute value of 60-min reperfusion flow in the infarct zone in this subset was 0.87 ± 0.56 (range 0.17–1.84). The slope of the line for the eight remaining animals was 0.48 with $r = 0.97$ ($p < 0.01$) and intercept = 0.18. The MIZ:NZ ^{99m}Tc-teboroxime activity ratio in this subset was 0.77 ± 0.33 with a 60-min reperfusion MIZ:NZ flow ratio = 1.21 ± 0.65 ($p < 0.01$).

DISCUSSION

The purpose of this study was to test the hypothesis that myocardial retention of ^{99m}Tc-teboroxime is not only a function of myocardial perfusion but also depends at least in part on the presence of viable myocytes. If myocardial ^{99m}Tc-teboroxime activity were dependent only upon myocardial perfusion then reperfusion flow and reperfusion ^{99m}Tc-teboroxime activity should have matched. The results of the present study, however, demonstrate that reperfusion ^{99m}Tc-teboroxime relative activity was less than relative myocardial blood flow at the time of tracer injection and thus supports the hypothesis that viable myocytes play a role in ^{99m}Tc-teboroxime retention by the myocardium. While more rapid tracer clearance in zones of higher flow in theory might explain differences in teboroxime activity at 5–7 min after injection, the absolute differ-

TABLE 2
Transmural Myocardial Blood Flow*

Zone	Baseline	Occlusion		Reperfusion	
		10′	50′	10′	60′
MIZ	0.87 ± 0.36	0.18 ± 0.19†	0.21 ± 0.22†	1.66 ± 1.06†	1.59 ± 1.35†
CX	0.95 ± 0.35	0.90 ± 0.37	0.98 ± 0.43	1.11 ± 0.68	1.00 ± 0.72
MIZ/CX	0.95 ± 0.27	0.18 ± 0.15‡	0.25 ± 0.35†	1.78 ± 1.08‡	1.54 ± 0.94†

*(ml/min/g; mean ± s.d.; n = 11).
† = $p < 0.05$ vs. baseline.
‡ = $p < 0.01$ vs. baseline.
MIZ = infarct zone; CX = circumflex zone; and MIZ/CX = flow ratio.

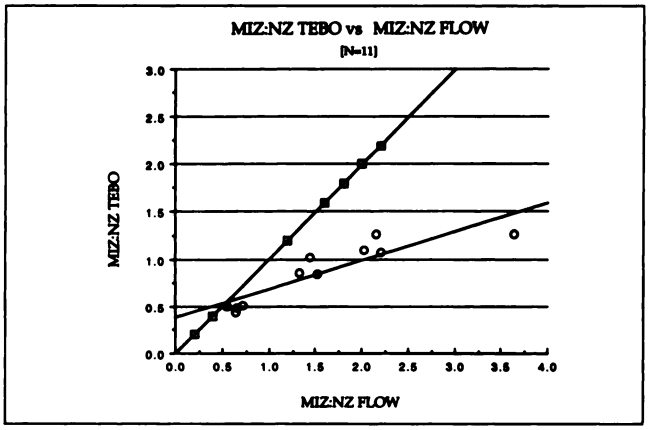

FIGURE 1. The infarct zone (MIZ):normal zone (NZ) ^{99m}Tc-teboroxime activity ratio is shown on the ordinate versus MIZ:NZ blood flow ratio on the abscissa. The line of identity is shown with squares (point spacing is arbitrary), the regression line and data with circles. The data demonstrate that ^{99m}Tc-teboroxime activity 5–7 min after tracer injection underestimates infarct zone reperfusion flow at all levels of flow.

ence between reperfusion blood flow in the MI versus normal zone was relatively small for the group as a whole (1.59 ± 1.35 versus 1.00 ± 0.72). Moreover, as previously noted, exclusion of the three animals with the highest reperfusion flows in order to create a subset having a nearly equal infarct and normal zone reperfusion flow (MIZ:NZ reperfusion flow ratio was 1.21:1 in this subset) did not change the results of the study (Fig. 2). Accordingly, it is unlikely that enhanced washout of teboroxime related to hyperemic flow can account for the relative excess of flow versus tracer activity in the infarct zone.

The conclusion that diminished teboroxime uptake relative to blood flow reflects nonviable myocardium in the infarct zone assumes that myocardial ^{99m}Tc-teboroxime activity actually could have been proportional to blood flow at the time of tracer administration. Since myocardial

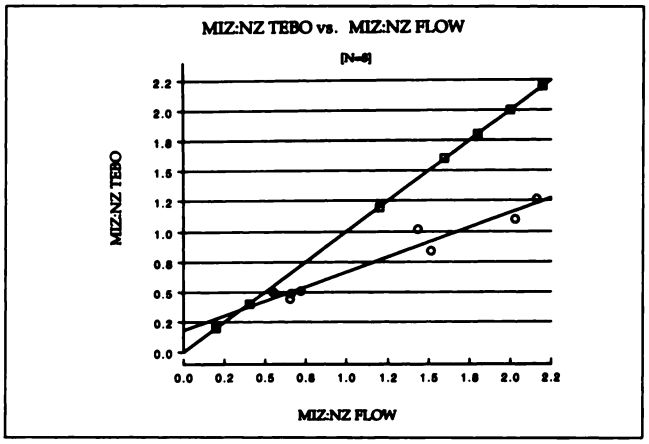

FIGURE 2. The same data shown in Figure 1 are plotted here minus three animals with infarct zone reperfusion flow > 2.0 ml/min/g. The relation between infarct zone ^{99m}Tc-teboroxime activity and flow does not change after exclusion of three animals with relatively high values of reperfusion flow.

uptake of all diffusable tracers, including ^{99m}Tc-teboroxime, may be flow limited, it is important to consider the possibility that under-representation of the tracer in proportion to blood flow at reperfusion might reflect physical limitations on tracer diffusion rather than biological factors (e.g., "viability"). There are several reasons to reject this hypothesis. First, absolute values of blood flow in the infarct zone at the 60-min reperfusion time averaged 1.59 ml/min/g and were greater than 2.0 ml/min/g in only three cases (2.47, 3.96 and 4.00). Prior studies from our laboratory (*2*) and others (*3–5,13*) have shown a close correlation between myocardial blood flow as measured by microspheres and myocardial ^{99m}Tc-teboroxime activity, particularly at levels of blood flow < 3.0 ml/min/g. Also, while others demonstrated a decrement in the linear relation between myocardial blood flow and ^{99m}Tc-teboroxime activity over time, the relation remained linear up to flow rates of 2.5 ml/min/g for at least 5 min after teboroxime injection (*8*). Second, as demonstrated in Figure 1, the ^{99m}Tc-teboroxime MIZ:NZ activity ratio was less than MIZ:NZ blood flow ratio at all levels from the lowest to the highest. Further, as shown in Figure 2, exclusion of the three animals with the highest reperfusion flows does not alter the conclusions of the study. Accordingly, it is unlikely that high levels of reperfusion flow in the infarct zone with corresponding decline in tracer extraction (and/or more rapid tracer washout) (*2*) can account for relative under representation of ^{99m}Tc-teboroxime activity in the region.

Comparison with Previous Studies

Experiments similar to the present one have been reported recently (*8,14*). One concluded that ^{99m}Tc-teboroxime was retained in acutely infarcted myocardium entirely in proportion to blood flow (*14*), while the other indicated that washout kinetics are altered in nonviable myocardium and that ^{99m}Tc-teboroxime underestimated reperfusion flow (*8*). The reason for differences between the results of our study and the previously published report (*14*) is unclear but may involve several factors. First, the earlier study employed rabbits and reperfused the infarct zone for 2 hr prior to injecting ^{99m}Tc-teboroxime and microspheres. The interval between tracer injection and sacrifice was not reported. Although a correlation between reperfusion flow in the infarct zone and ^{99m}Tc-teboroxime activity was observed (r = 0.81) the slope of the regression line and its relation to the line of identity was not stated.

In the current study, we also observed a correlation between ^{99m}Tc-teboroxime activity (expressed as MIZ:NZ ratio) and both the absolute value of reperfusion flow in the infarct zone at 60 min (r = 0.65) and the MIZ:NZ flow ratio (r = 0.90). Accordingly, differences in animal model, experimental design and data analysis likely account for differing conclusions between the two studies. Another study by the same group (*15*) is consistent with this interpretation since planar teboroxime images apparently were made very soon after tracer injection (i.e. <5 min) reportedly

failed to demonstrate uptake abnormalities in reperfused infarct zones. Comparison of serial scans made both early and late after tracer injection, however, was not reported (*15*).

The conclusions reached in the preliminary report of Chang et al. (*8*) are more similar than dissimilar to those of the present study. In particular, data reported concerning imaging between 8 and 12 min post-tracer injection indicated a good correlation between infarct zone flow and ^{99m}Tc-teboroxime activity (r = 0.86) but with slope of 0.47. The authors also noted that tracer clearance of ^{99m}Tc-teboroxime was enhanced versus normal (i.e., retention was reduced) in the infarct zone. Both observations are consistent with those reported in the present study in which the correlation between ^{99m}Tc-teboroxime activity (MIZ:NZ ratio) and flow (MIZ:NZ ratio) was 0.90 with slope of 0.31. It should be stressed that in ischemic but viable myocardium distal to a severe coronary stenosis, we previously reported the correlation between the IZ:NZ ^{99m}Tc-teboroxime activity ratio and flow (IZ:NZ ratio) was good (r = 0.74), but more importantly exhibited slope of 0.90 with intercept of zero (*2*). Accordingly, underestimation of flow by ^{99m}Tc-teboroxime at absolute levels of flow less than roughly 2–2.5 ml/min/g (average = ~1.5 ml/min/g) in the current study likely is indicative of sensitivity of ^{99m}Tc-teboroxime retention to the presence of nonviable myocardium rather than to the well known tendency of a diffusable tracer to underestimate flow at high levels and overestimate it a low levels.

The relation between myocardial blood flow at reperfusion and infarct zone tracer uptake also has been examined for ^{99m}Tc-sestamibi (*12*). In a canine experiment involving 3 hr of coronary artery occlusion followed by 3 hr of reperfusion, with ^{99m}Tc-sestamibi injected at 1.5 hr into reperfusion, the investigators reported that ^{99m}Tc-sestamibi defect size correlated closely (r = 0.98) with infarct size as measured by planimetery of TTC stained tissue sections. Infarct zone ^{99m}Tc-sestamibi activity also was reduced substantially versus reperfusion regional myocardial blood flow in severely and moderately ischemic tissue samples, but only modestly in mildly ischemic regions (regions classified based on flow during coronary occlusion). Thus, in severely and moderately ischemic tissue samples, blood flow was 75%–95% of normal zone flow during reperfusion, whereas ^{99m}Tc-sestamibi activity was only 25%–50% of that in the normal zone. In mildly ischemic samples, however, reperfusion blood flow was approximately 90% of normal with ^{99m}Tc-sestamibi activity very similar (80% of normal).

In the present study, reperfusion infarct zone flow actually exceeded that of the normal zone (~130%–160% of normal) while ^{99m}Tc-teboroxime activity was only 77%–85% of that in the reference zone. Accordingly, in acutely infarcted, reperfused myocardium, ^{99m}Tc-sestamibi activity in moderately and severely ischemic regions is reduced to roughly 33%–50% of reperfusion blood flow while ^{99m}Tc-teboroxime activity appears to be higher (approximately 40%–50% of prevailing levels of blood flow). It should be emphasized that the correspondence between blood flow measurements and ^{99m}Tc-teboroxime activity in the infarct zone was complete, since the same tissue samples used for determination of ^{99m}Tc-teboroxime activity also were used for determination of blood flow.

Comparison of the results of the present study to cell culture data concerning retention of teboroxime in viable and nonviable myocytes (*7*) is difficult because of marked differences in experimental models. Although the study of Maublant et al. (*7*) indicated that teboroxime was less sensitive than thallium and sestamibi to inhibition of cellular metabolism, their results must be considered carefully. In particular, the authors themselves noted (*7*) they had previously reported (*16*) no effect of ouabain on thallium accumulation and no effect of metabolic inhibition on sestamibi uptake in cell systems. When they changed experimental conditions, however, (more ouabian; longer period of metabolic inhibition) the results and conclusions changed as well (*7*). Further, the more recent cell system study of Maublant (*7*) indicated variously between 2% and 12% of baseline retention of sestamibi by nonviable cells, whereas data from an intact animal study demonstrated sestamibi accumulation equal to 30% of reperfusion flow in the most severely ischemic samples (*12*). It also should be noted that in the cell system teboroxime retention by nonviable cells varied markedly depending on how the cells were killed (*7*). Freezing reduced retention substantially to 30% of baseline whereas lysis apparently had little effect, reducing retention only to ~90%–95% of baseline (*7*). Accordingly, it is clear that conclusions regarding tracer accumulation in viable and nonviable cells in isolated systems are quite sensitive to experimental conditions imposed and results obtained from such systems do not always predict in vivo results.

Clinical Implications

Even the best of thrombolytic regimens for acute myocardial infarction are associated with failure to restore arterial patency in 20% of patients (*6*). Furthermore, to achieve the optimal survival benefit, TIMI grade III flow is required (*6*) but was present on the 90-min angiogram in only 53% of patients in the recent GUSTO trial (*17*). Since it is clearly not cost-effective to perform coronary angiography on every patient following thrombolytic therapy, a noninvasive method might have potential utility in evaluating reperfusion status following thrombolytic therapy. Although teboroxime retention in the infarct zone underestimated coronary blood flow to the region, inspection of Figure 1 demonstrates when the MIZ:NZ flow ratio was greater than 1, the MIZ:NZ TEBO ratio was in the range of 1. At lower flow rates, the underestimation of flow by teboroxime was more modest. Accordingly, the data indicate it may be possible to use teboroxime as a flow tracer to assess patency of an infarct-related artery despite the fact that myocardial blood flow will tend to be underestimated under these conditions. While early (2–4 min) im-

ages likely are best for this application, the data from the current study indicate that scans obtained at 5–7 min also may be useful. Whether or not combining early (2–4 min) and late (5–7 min) teboroxime images—analogous to the approach used for PET scans with ^{82}Rb (*18*)—will prove helpful in providing clinically useful information concerning both perfusion and viability status requires additional study and cannot be determined from the results of the present investigation.

Methodological Critique

The method used to count the tissue samples for ^{99m}Tc-teboroxime activity (i.e., in vitro imaging on the face of a gamma camera) has been utilized by others (*19*) and has the advantage of providing truly tomographic scans which are essentially free of scatter, background, attenuation and assumptions made in digital filtering and image reconstruction. Since the breadloaf slices were ~1 cm thick, tissue samples obtained from each section were also essentially the same thickness and thus counts/g in each zone could be fairly compared. Furthermore the half value thickness of ^{99m}Tc in water is 4.6 cm, and, thus, it can be shown even if slice thickness had varied by as much as 50% around the nominal value of 1 cm (i.e., 0.5–1.5 cm), that photon flux seen by the detector at most would have been altered by only 7%. Finally, in this experimental model, infarct zones were no more or less likely to be sectioned obliquely than normal zones, and thus any errors related to section thickness would cancel and could not account for systematic activity differences between regions.

Clinical images were not obtained because the objective of the study was to test the hypothesis that viable myocytes are required for retention of ^{99m}Tc-teboroxime by the heart. To test this hypothesis, it was essential to work with as pure a population of viable and nonviable cells as possible and to be able to very precisely compare tracer retention and transmural blood flow in one tissue type versus the other. In vitro imaging of very clearly defined, isolated samples of infarct and normal tissue therefore was employed. Since in vivo scans were not obtained in the present study, additional experiments will be required to assess whether differences in ^{99m}Tc-teboroxime activity detected by in vitro imaging are also apparent under clinical conditions.

CONCLUSION

Our data indicate that myocardial images obtained 5–7 min after ^{99m}Tc-teboroxime injection may underestimate blood flow to reperfused myocardium because nonviable (but perfused) muscle may not retain the tracer as well as residual, viable myocardium in the infarct zone. The magnitude of this effect on clinical images, however, is uncertain and may not preclude use of the tracer for applications such as determination of infarct-related artery patency. Nevertheless, based on data obtained in the present study in conjunction with a previous study (*2*) from this and other laboratories (*3,5,8,13,14*), we hypothesize that early (2–4 min) imaging with ^{99m}Tc-teboroxime may be more useful in assessing perfusion status because later images (5–7 min), although still perfusion-dependent, also may reflect a component of cell viability (*8*). The magnitude of the latter effect on clinical images of the myocardium remains to be determined.

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