Regional Blood Flow, Oxidative Metabolism, and Glucose Utilization in Patients With Recent Myocardial Infarction

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Background. Metabolic imaging with positron emission tomography (PET) can detect tissue viability in clinical infarct regions. With appropriate tracer kinetic models and serial PET imaging, regional myocardial blood flow and rates of metabolism can now be quantified in patients with recent myocardial infarctions.

Methods and Results. Serial PET imaging with [15N]ammonia, [13C]acetate, and [18F]-deoxyglucose was performed in 22 patients with recent infarctions to measure regional blood flow (in milliliters per gram per minute), glucose metabolism (in micromoles per gram per minute), and oxidative metabolism (in clearance rate per minute). Hypoperfused clinical infarct regions were classified as "PET mismatch" if [18F] was increased relative to [15N] activity or "PET match" if [15N] and [18F] activities were reduced concordantly. Blood flows differed significantly between normal, mismatch, and match segments (0.63±0.20, 0.57±0.20, and 0.32±0.12 mL·g⁻¹·min⁻¹, respectively). The relation between oxidative metabolism and blood flow was piecewise linear and differed significantly between PET mismatch and PET match. Oxidative metabolism was less severely reduced than blood flow in mismatch regions but reduced in proportion to blood flow in match regions. There was considerable overlap of blood flows between both types of PET segments.

Conclusions. Quantification of regional blood flow and substrate metabolism in postinfarction patients revealed alterations in the relation between substrate delivery and consumption demonstrated previously only in invasive animal experiments. The preserved oxidative metabolism in myocardium with PET mismatches may be ascribed to a regional increase in oxygen extraction. Such increase together with preserved glucose utilization may be the prerequisite for survival of ischemically injured myocardium. (Circulation. 1993;88:884-895.)

Key Words • myocardial infarction • tomography • blood flow • metabolism

An acute coronary occlusion causes severe myocardial ischemia, which might progress to necrosis and scar tissue formation. Thrombolytic therapy, spontaneous reperfusion, or collateral blood flow can modify the evolution of an acute myocardial infarction and may salvage ischemically injured myocardium.1-3 Restoration of coronary blood flow may therefore lead to an improvement in segmental contractile function in some patients but prove ineffective in those with completed injury.4 Potentially salvageable myocardium can be identified with positron emission tomography (PET) and be distinguished from myocardium with a completed infarction.5-7 An earlier study performed with PET demonstrated qualitatively that glucose metabolic activity as evidence of persistent ischemia was preserved in nearly half of recent clinical infarct regions.8 More advanced PET instrumentation and biochemically validated tracer kinetic models now permit the noninvasive quantification of regional myocardial blood flow, oxidative metabolism, and glucose utilization. It was therefore the purpose of this study to characterize quantitatively the relations between regional myocardial blood flow and oxidative and glucose metabolism in patients with recent myocardial infarction and to examine whether such quantitative measurements would provide additional insights into the pathophysiology of recent myocardial injury in humans.

Methods

Patient Population

The study population consisted of 22 patients (age, 63±9 years) with a recent myocardial infarction documented by enzymatic and/or ECG criteria. A left bundle branch block precluded ECG infarct localization in 2 patients. Eight patients underwent coronary thrombolysis within 4 hours. Direct angioplasty was per-
formed in 2 patients within 8 hours of the onset of chest pain. There were 14 Q-wave and 6 non-Q-wave infarctions. Creatine phosphokinase (CPK) and CKMB serum levels averaged 1357±865 and 74±66 U/L, respectively (range, 190 to 3000 and 21 to 274 U/L). Additional demographic information is given in Table 1.

PET was performed at 86±38 hours (range, 21 to 170 hours) after the onset of chest pain, when patients were clinically stable. Sixteen patients were studied with [13N]ammonia, [11C]acetate, and 18F-deoxyglucose, and 6 patients were examined only with [13N]ammonia and 18F-deoxyglucose. Twenty of the 22 patients underwent coronary angiography (Table 1). PET was performed before angiography in 3 patients and after angiography in 17 patients. All patients were on oral or intravenous nitroglycerin, and 4 were heparinized at the time of the PET study. Each patient signed an informed consent form approved by the UCLA Human Subject Protection Committee.

Coronary Angiography

Coronary angiography was performed in 20 of the 22 patients within 2.8±1.8 days of the PET study. Contrast left ventriculograms were obtained in all but 1 patient with markedly elevated left ventricular end-diastolic pressure (Table 1). In this patient (10) and the 2 other patients without cardiac catheterization (Table 1, patients 7 and 18), the left ventricular ejection fraction was determined by two-dimensional echocardiography. The infarct vessel status was determined qualitatively according to the TIMI criteria (TIMI grade 0 or I, occlusion; TIMI grade II or III, patency).4

Two-dimensional Echocardiography

Regional wall motion was evaluated with two-dimensional echocardiography on the day of the PET study using four- and two-chamber and apical long-axis views. On each view, the myocardium was divided into six equal segments. Wall motion in each segment was graded by one observer (J.K.), who was unaware of the clinical and PET findings. Grading was on a four-point scale in which normal is 3, mild hypokinesis is 2, severe hypokinesis is 1, and akinesis/dyskinesis is 0. To facilitate the comparison between the PET and echocardiographic studies, a wall motion score was derived by dividing the sum of all echocardiographic scores for each of the seven anatomic segments (anteroseptal, anterior, lateral, posterolateral, inferior, apical, and posteroseptal) by the number of projections on which the segment was visualized. The 18 echocardiographic segments were assigned to the 7 tomographic segments as shown in Fig 1 and as reported previously from our laboratory.5-8

Positron Emission Tomography

Twenty-one patients were studied after oral glucose administration (100 g 1 hour before the 18F-deoxyglucose injection), and 1 patient with diabetes mellitus (Table 1, patient 5) was examined in the fasting state. After the patient was positioned in the whole-body tomograph (Model 931/8, CTI-Siemens, Knoxville, Tenn),9 a transmission scan was acquired for 20 minutes. After the intravenous bolus administration of [13N]ammonia (10 to 12 mCi), serial images of the myocardial tracer uptake were acquired for 21 minutes (12 frames of 10 seconds, 2 frames of 120 seconds, and 1 frame of 900 seconds each). Forty-five minutes later, after physical decay of [13N]activity, [11C]acetate (8 to 10 mCi) was injected as an intravenous bolus, and serial images were recorded for 26 minutes (6 frames of 60 seconds, followed by 10 frames of 120 seconds each). 18F-deoxyglucose was injected 1 hour later, and serial images were acquired for 69 minutes (8 frames of 15 seconds, 4 frames of 30 seconds, 1 frame of 300 seconds, and 6 frames of 600 seconds). Patient movement during image acquisition and between studies was minimized by a Velcro strap fastened across the patient’s chest. Venous glucose, free fatty acid, and insulin levels were determined at the beginning of the [13N]ammonia study and at the beginning and at the last 30, 20, and 10 minutes of the 18F-deoxyglucose study. Blood pressure and heart rate were measured repeatedly throughout the study. For comparison with blood flow, the rate-pressure product was averaged from two measurements during the first 2 minutes of the [13N]ammonia injection. For comparison with oxidative metabolism, the rate-pressure product was averaged from measurements at 10 and 15 minutes after injection, during the tissue clearance phase of [11C]acetate. The rate-pressure product remained constant throughout the entire study period in all patients.

Classification of Myocardial Segments on PET Images

Six to eight contiguous transaxial images were selected in each patient for analysis (Fig 1). Myocardial boundaries were determined with a previously described semiautomatic, operator-interactive edge detection method.10 Counts per pixel were averaged at 6° intervals for the entire circumference in each plane to obtain circumferential activity profiles. These profiles were then compared with a data base of normal activity profiles established in an identical fashion in 11 healthy volunteers.

Observed regional [13N] and 18F activity concentrations were normalized to the maximal [13N] activity concentrations in each plane and expressed as a percentage of maximal [13N] activity in each plane. If regional [13N] activity concentrations were within 2 SD of the normal mean in-plane activity, a segment was considered normal. If [13N] ammonium activity was reduced by more than 2 SD below the normal mean in at least 10 contiguous 6° sectors (within or between planes), myocardium was defined as hypoperfused. Depending on the 18F-deoxyglucose uptake, hypoperfused regions were categorized further into PET mismatch and PET match. Using previously established criteria,5-8 a hypoperfused segment with a concordant decrease in 18F activity in at least 10 contiguous 6° sectors was defined as blood flow–metabolism match, whereas a normalized 18F/13N count difference of >2 SD above the normal mean was defined as blood flow–metabolism mismatch. These rather large areas were chosen to ascertain that abnormalities on circumferential profiles reflected true abnormalities rather than statistical noise or misalignment between blood flow and glucose metabolic studies.

Quantification of Blood Flow and Glucose and Oxidative Metabolism

After segments had been classified as normal, mismatched, or matched (which required a minimal defect
TABLE 1. Characteristics of Patients With Recent Myocardial Infarction Undergoing PET

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PET, positron emission tomography; wall motion score: 0, akinetic; 1, severely hypokinetic; 2, mildly hypokinetic; Angio, coronary angiography; VD, number of stenosed coronary arteries; M, PET match; MM, PET mismatch; Q, Q-wave infarction; nQ, non-Q-wave infarction; LBBB, left bundle branch block; CABG, coronary artery bypass graft surgery; LCx, left circumflex coronary artery; LAD, left anterior descending coronary artery; RCA, right coronary artery; e, left ventricular ejection fraction determined by echocardiography.

*Thrombolytic therapy; †insulin-dependent diabetes mellitus; ‡direct percutaneous transluminal angioplasty.
extent of 60° within a plane or between adjacent planes on circumferential profile analysis), sectorial regions of interest (of at least 36° in width) were assigned to normal, mismatch, and match segments for quantification of regional functional processes. The reason for generating time/activity curves from regions of interest that were smaller than at least ten 6° regions of interest required for segment classification was to minimize lateral spillover of activity between adjacent and anatomic segments. Conversely, the regions for generating time/activity curves were at least 36° in size to reduce statistical noise, which would have been prominent if they were smaller. To ascertain identical placement of these regions to the 15N ammonia, 13C acetate, and 18F-deoxyglucose images, the same angle on the circumferential profile served as the starting point for the sectorial region of interest on each of the two or three image sets that were analyzed in each patient. The regions of interest were copied to the serial 15N ammonia, 13C acetate, and 18F-deoxyglucose images, and myocardial time/activity curves were obtained. Time/activity curves derived from adjacent image planes but located in the same anatomic segment (Fig 1) were averaged to form one time/activity curve for each anatomic segment. Last, a 25-mm² region of interest was placed in the center of the left ventricular blood pool and copied to the serial 15N ammonia and 18F-deoxyglucose studies to determine the arterial tracer input function.11

The time/activity curves were corrected for physical decay. The 15N and 18F tissue time/activity data were corrected for partial volume effects with a recovery coefficient that assumed a uniform thickness of 1 cm for the left ventricular myocardium.12,13 Although this assumption may not hold for all conditions, a recent study demonstrated similar diastolic wall thicknesses for ischemic and normal myocardium.14

Only the myocardial 15N activity curves were corrected for spillover of activity from the blood pool to the myocardium. Correction for spillover was performed by treating spillover as an additional parameter in the curve-fitting procedure in addition to the model parameters as previously described.15 Regions with excessively high spillover fractions (ie, the ratio of blood pool contamination to total tissue activity >80%) were excluded from analysis to avoid a marked underestimation of tissue tracer concentrations and hence, blood flows in these segments.16,17

The myocardial 13C acetate time/activity curves were not corrected for partial volume effects because clearance rates of 13C activity from the myocardium are relatively independent of the true activity concentrations.18 Moreover, the myocardial 13C acetate time/activity curves were not corrected for spillover of activity because (1) the clearance slope was derived from the time/activity curve at a time when [13C]acetate had largely cleared from blood and when residual activity
was relatively constant; (2) use of relatively small regions of interest (36°) minimized spillover from adjacent myocardial segments; and (3) rate constants obtained without spillover corrections are closely related to those obtained for spillover-corrected data. Therefore, spillover of activity at that time had probably relatively minor effects on the estimated clearance rates.

Because the effects of spillover are automatically removed in the Patlak graphical analysis, no spillover corrections for the \[^{18}\text{F}\]-deoxyglucose time/activity curves were required.\(^\text{20}\)

Regional myocardial blood flow was quantified from the arterial input function of \[^{[\text{13}}\text{N}\]ammonia and the myocardial tissue time/activity curves using a previously validated two-pool compartment model.\(^\text{16,17,21}\) Limiting the model fitting to only the first 2 minutes of data minimized the effects of contamination of the arterial input function by \[^{[\text{13}}\text{N}\]ammonia metabolites. Regional rates of myocardial glucose utilization were quantified with a three-compartment tracer kinetic model for \[^{18}\text{F}\]-deoxyglucose and a modified Patlak graphical analysis.\(^\text{12,20}\) Regional oxidative metabolism was estimated from the rate of clearance of \[^{[1\text{C}}\text{C}\]acetate from myocardium, which has been found to correlate closely with myocardial oxygen consumption.\(^\text{22-24}\) The tissue clearance rate, defined as \(k\), was determined by monoexponential least-squares fitting of the initial linear portion of the myocardial time/activity curve.

**Statistical Analysis**

Mean values are given with standard deviations. One-way ANOVA was used for comparison of intergroup differences, the nonparametric Mann-Whitney \(U\) test to compare the wall motion scores between segments with mismatches and matches, and the nonparametric Spearman’s rank correlation coefficient to relate wall motion scores to measurements of myocardial blood flow. Correlations between blood flow and metabolism were sought by least-squares linear regression analysis. For comparison of slopes of two regression lines, the \(F\) test was used.

To obtain the best fit for the relation between blood flow and oxidative metabolism, the optimum threshold between the low and the high flow range was determined by repeatedly fitting two regression lines simultaneously to the data by least-squares regression analysis.\(^\text{25}\) As a second step, the \(F\) test was used to test whether this relation was better described by a piecewise linear or a linear fit. In this case, the \(F\) test is a special likelihood ratio test for nested models.\(^\text{25}\)

Probability values of \(P<.05\) were considered to be statistically significant.

**Results**

**Coronary Anatomy**

Single-vessel disease was present in 10 patients, two-vessel disease in 7, and three-vessel disease in 3 (Table 1). The infarct-related artery was the left anterior descending in 8 patients, the left circumflex coronary artery in 4 patients, and the right coronary artery in 6 patients. In 2 patients with remote coronary artery bypass surgery, grafts to the first diagonal and left circumflex coronary artery were the infarct vessels. The

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**FIG 2. Diagrammatic classification of anatomic segments into normal, hypoperfused positron emission tomographic (PET) mismatch, and hypoperfused PET match as determined by circumferential profile analysis.**

left ventricular ejection fraction averaged 47±12% (range, 18% to 65%; Table 1).

**PET Findings in Clinical Infarct Regions**

Sixteen (73%) of the 22 patients were studied with \[^{[\text{13}}\text{N}\]ammonia, \[^{[1\text{C}}\text{C}\]acetate, and \[^{18}\text{F}\]-deoxyglucose, and 6 patients (27%) were studied only with \[^{[\text{13}}\text{N}\]ammonia and \[^{18}\text{F}\]-deoxyglucose. In 2 patients with plasma glucose levels of 350 and 400 mg%, the \[^{18}\text{F}\]-deoxyglucose images were of suboptimal quality, with only modest myocardial tracer uptake and relatively high blood pool activity. Although glucose metabolic rates could not be quantified, semiquantitative classification of myocardial segments according to \[^{[\text{13}}\text{N}\]ammonia and \[^{18}\text{F}\]-deoxyglucose uptake was possible. Also, blood flow and oxidative metabolism could be quantified in these 2 patients, who therefore were included in the analysis.

Circumferential profile analysis revealed flow defects in 20 patients, whereas blood flow was homogeneous in 2 patients (Table 1, patients 11 and 15). One (patient 11) of the 2 patients had a non-Q-wave infarction and a normal left ventricular ejection fraction. The other patient (patient 15) had a history of three-vessel bypass surgery, a left bundle branch block, and a left ventricular ejection fraction of 37%.

Seven segments per patient, or a total of 154 anatomic segments, were evaluated. Blood flow was found to be normal on circumferential profile analysis in 103 segments (67%) including 8 hypokinetic segments in the 2 patients with homogeneous blood flow (Table 1). Blood flow was reduced in 51 segments (33%). Of these, 29 segments (57%) in 13 patients were categorized to have a PET match and 22 (43%) in 10 patients (45%) to have a PET mismatch (Fig 2, Table 1). Both mismatch and match segments were noted in 3 patients.

Coronary arteriography was performed in 20 of the 22 patients. Of the 29 PET match segments, 20 were subtended by patent culprit vessels (TIMI grade II or III),\(^\text{4}\) whereas 9 were in the territory of an occluded vessel. In contrast, 16 of 18 mismatch segments were supplied by a patent but only two were subtended by an occluded infarct artery (TIMI grade 0 or I; \(P=\text{NS}\) by \(x^2\) analysis). Fig 3 depicts an example of transaxial \[^{[\text{13}}\text{N}\]ammonia, \[^{[1\text{C}}\text{C}\]acetate, and \[^{18}\text{F}\]-deoxyglucose images in a patient (patient 6 in Table 2). There is an
extensive blood flow–metabolism mismatch in the anterior septum, the anterior wall, the apex, and the inferior septum.

Regional Myocardial Wall Motion

The location of the hypoperfused segments corresponded to the ECG site of the infarct as well as to the site of regional wall motion abnormalities (Table 1). In the two patients with homogeneous blood flow, wall motion was diffusely impaired in one (patient 15) and was mildly hypokinetic in the territory of the infarct vessel in the other patient (patient 11). The severity of regional wall motion abnormalities in clinical infarct regions ranged from mild hypokinesis to akinesis (Table 1). The wall motion score averaged 1.0±0.6 in segments with PET mismatches and 0.9±0.3 in segments with PET matches (P=NS). There was no statistically significant correlation between the severity of segmental flow reductions and the segmental wall motion score.

Metabolic and Hemodynamic Findings

Average heart rates, blood pressure, and the rate-pressure product are given in Table 2. As further indicated in Table 2, glucose levels remained relatively constant throughout the 18F-deoxyglucose study.

Myocardial blood flow in 95 of 103 normal segments averaged 0.83±0.20 mL·g⁻¹·min⁻¹. The remaining 8 normal segments were excluded from the analysis because the spillover fractions exceeded 80%. In the hypoperfused segments, blood flows were significantly lower in the 29 PET match than in the 22 PET mismatch segments (0.32±0.12 vs 0.57±0.20 mL·g⁻¹·min⁻¹; P<.05; Table 3).

Oxidative metabolism was quantified in 76 normal, 17 PET mismatch, and 19 PET match segments in 16 patients. The clearance rates, k, averaged 0.063±0.012 min⁻¹ in normal myocardium but were significantly reduced in hypoperfused myocardium. They were significantly lower in PET match than in PET mismatch segments (0.037±0.010 min⁻¹ vs 0.055±0.010 min⁻¹; P<.001).

Rates of exogenous glucose utilization were quantified in 20 patients and averaged 0.57±0.28 μmol·g⁻¹·min⁻¹ in the 93 normal segments. As listed in Table 3, they were lower in the 22 PET mismatch and in 25 PET match segments. If glucose utilization rates in normal and in PET mismatch segments were compared in only those patients with PET mismatch segments (n=10), they were similar for both types of segments (0.42±0.2 vs 0.41±0.20 μmol·g⁻¹·min⁻¹). Conversely, in those patients with PET matched defects (n=13), rates of exogenous glucose utilization were significantly lower in PET match than in normal myocardial segments (0.20±0.1 vs 0.62±0.20 μmol·g⁻¹·min⁻¹; P<.001).

Blood Flow and Oxidative Metabolism vs Cardiac Work

To explore possible reasons for the interpatient variability of blood flow and oxidative metabolism in normal myocardium, both were compared with the rate-pressure product as an index of cardiac work. Mean values in each patient, obtained by averaging the values in all normal segments, were plotted against the rate-pressure product. Fig 4A demonstrates a linear relation of blood flow and oxidative metabolism to cardiac work. The same figure demonstrates further that these relations were independent of the left ventricular ejection fraction. Blood flow and oxidative metabolism in hypoperfused myocardium were unrelated to cardiac work. Also, no significant relations between the rate-pressure product and oxidative metabolism or blood flow in PET match and PET mismatch segments were observed.
TABLE 3. Quantitative Measurements of Blood Flow, Glucose Utilization, and Oxidative Metabolism

<table>
<thead>
<tr>
<th></th>
<th>Normal (mean±SD)</th>
<th>Range</th>
<th>Mismatch (mean±SD)</th>
<th>Range</th>
<th>Match (mean±SD)</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absolute values</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MBF (mL·g⁻¹·min⁻¹)</td>
<td>0.83±0.20</td>
<td>0.46-1.46</td>
<td>0.57±0.20*</td>
<td>0.27-0.89</td>
<td>0.32±0.12†</td>
<td>0.11-0.61</td>
</tr>
<tr>
<td>k mono (min⁻¹)</td>
<td>0.063±0.012</td>
<td>0.040-0.097</td>
<td>0.055±0.01*</td>
<td>0.037-0.073</td>
<td>0.037±0.01†</td>
<td>0.013-0.055</td>
</tr>
<tr>
<td>MRGlc (µmol·g⁻¹·min⁻¹)</td>
<td>0.57±0.28</td>
<td>0.14-1.30</td>
<td>0.41±0.20*</td>
<td>0.18-0.95</td>
<td>0.20±0.1†</td>
<td>0.08-0.54</td>
</tr>
<tr>
<td>Relative values</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% MBF</td>
<td>100±15</td>
<td></td>
<td>65±20*</td>
<td></td>
<td>42±18†</td>
<td></td>
</tr>
<tr>
<td>% k mono</td>
<td>100±10</td>
<td></td>
<td>84±15*</td>
<td></td>
<td>52±19†</td>
<td></td>
</tr>
<tr>
<td>% MRGlc</td>
<td>100±30</td>
<td></td>
<td>100±16</td>
<td></td>
<td>35±15†</td>
<td></td>
</tr>
</tbody>
</table>

MBF, myocardial blood flow; k mono, oxidative metabolism; MRGlc, metabolic rates of glucose consumption; % MBF, normalized blood flow; % k mono, normalized oxidative metabolism; % MRGlc, normalized metabolic rates of glucose consumption.

*P<.05 vs normal; †P<.05 vs ischemia and normal.

Relation Between Blood Flow and Metabolism

As demonstrated in Fig 5, no correlation existed between absolute rates of exogenous glucose utilization and absolute myocardial blood flow. This was because glucose metabolic rates in normal and hyperperfused myocardium varied considerably between patients and correlated with neither cardiac work nor plasma glucose, free fatty acid, or insulin levels. Glucose metabolic rates in PET mismatch and PET match segments were therefore normalized in each patient to those in normal myocardium (Fig 5). The normalized metabolic rates (in percentage of those in normal myocardium) were then compared with normalized blood flows (again in percentage of those in normal myocardium). As depicted in Fig 5B, normalized glucose metabolic rates declined in PET match segments in proportion to normalized blood flows. By definition and as expected, in PET mismatch segments they exceeded the relative blood flows and, on average, did not decline with blood flow. Interestingly, the normalized glucose metabolic rates for PET match segments occupied the lower and those for PET mismatch segments the upper end of the spectrum of flow reductions, although there was considerable overlap. For example, of the 20 segments with relative flow reductions of ≥50%, 15 (or 75%) had PET matches and only 25% PET mismatches. Conversely, there was considerable overlap between PET matches and mismatches for flow reductions from 30% to 50% (Fig 5B).

In contrast, segmental rates of oxidative metabolism correlated significantly with segmental blood flows. As illustrated in Fig 6, lower blood flows in normal myocardium and moderate reductions in hyperperfused myocardium were associated with disproportionately smaller decrements in oxidative metabolism. When blood flow fell below values of about 0.5 mL·g⁻¹·min⁻¹, oxidative metabolism declined more steeply. The data plots therefore demonstrated a piecewise relation between flow and oxygen consumption. To obtain the best fit for this data set, the optimum threshold between the low and the high flow range was determined by repeatedly fitting two regression lines simultaneously to the data by least-squares regression analysis. The best discriminator between the two pieces of the curve was found to be at a flow of 0.56 mL·g⁻¹·min⁻¹. As a second step, the F test was used to prove that the piecewise linear fit described the data better than a single linear fit (F=4.54>F=3.11; P<.05).

Because of the relatively wide range of blood flows in normal myocardium, largely as a function of interpatient differences in the rate-pressure products as shown in Fig 4, blood flows and rates of oxidative metabolism in PET mismatch and PET match segments were normalized to those in normal myocardium. The normalized blood flows are plotted against the normalized rates of oxidative metabolism in Fig 7. It is of interest that the slope between blood flow and oxidative metabolism was less steep for PET mismatch than that for PET match segments (P<.05). Of further note is that normalized oxidative metabolism was a relatively accurate discriminator between ischemic and infarcted tissue. Of 21 segments with >30% reductions of oxidative metabolism, 17 (or 80%) were classified as PET match and only 4 as PET mismatch. In contrast, 13 of 14 segments (93%) with reductions of <25% were classified as PET mismatch.

FIG 4. Scatterplot showing relation between the rate-pressure product and mean myocardial blood flow (A) and oxidative metabolism (k mono) (B) in normal myocardium. The data were fitted to a line by least-squares regression equations. □, Patients with an ejection fraction <45%; ○, those with ejection fractions >45%. This threshold was arbitrarily selected. In A, the regression line has a y intercept close to zero (y=0.00009x−0.07, r=0.74, P<.001; SEE, 0.15). In B, the regression line has a positive y intercept (y=0.000003x+0.03, r=.62, P<.01; SEE, 0.008).
Rates of glucose utilization relative to overall oxidative metabolism can be estimated from the ratio of k mono (expressed as percentage of that in normal myocardium) to normalized rates of glucose metabolism (as percentage of those in normal myocardium). This index was 1.0±0.13 in normal myocardium but increased to 1.30±0.46 in mismatch segments (P<.05). In contrast, it was reduced to 0.72±0.33 in segments with matched defects (P<.05 vs normal and mismatch).

**Discussion**

To the best of our knowledge, this is the first study that has quantified segmental blood flow together with rates of oxidative metabolism and glucose utilization rates in patients after a recent myocardial infarction. Blood flow and oxidative metabolism were more severely reduced in PET match than in PET mismatch segments. However, oxidative metabolism was less reduced than blood flow in PET mismatch segments. The considerable overlap of flows from mismatched to matched defects suggests that measurements of blood flow alone discriminate only poorly between these two types of injury. Rates of glucose utilization in normal and hypoperfused myocardium varied markedly between patients. Therefore, relative rather than absolute measurements of myocardial glucose utilization were found to discriminate better between potentially viable and nonviable myocardium. Last, and unexpectedly, oxidative metabolism declined with decreasing blood flow in a piecewise rather than a single linear fashion.

**Study Limitations**

There are several limitations to this study. One is the variation in time intervals from the onset of the acute event to the study.
cheast pain to the PET studies. This was dictated largely by the patient's clinical condition and thus the safety for transport to the imaging laboratory. Whereas some patients were studied as early as 21 hours after the onset of chest pain, others could not be examined until 1 week later. Therefore, disparities between blood flow and oxidative metabolism that possibly existed early after the acute event might have resolved by the time of the study. For example, both patients without flow defects were studied more than 72 hours after the acute event. Had they been examined earlier, blood flow or metabolic abnormalities might have been found. However, the variable timing of the PET studies after the acute event did not appear to affect the observed relations between blood flow, oxidative metabolism, and rates of glucose utilization. Separate analysis of these findings in patients studied within 3 days (n=9) and in those >3 days (n=13) after the acute event failed to uncover statistically significant differences. However, it is also possible that the relatively small sample size accounted for the absence of possible statistically significant differences.

As another potential shortcoming, the study included patients with and without early interventions such as thrombolytic therapy or direct angioplasty. The severity of the ischemic injury as well as the degree of reperfusion might therefore have varied between patients. Also, flow reductions with sustained glucose metabolic activity might have represented persistent ischemia in some patients but an adaptation to sustained flow reductions, defined as "hibernating myocardium," in others.27 Moreover, the absence of flow defects despite wall motion abnormalities in two patients with patent infarct arteries might have represented postischemic dysfunction or myocardial stunning.28 Last, myocardial stunning, hibernation, persistent ischemia, and necrosis might have coexisted in some patients. The present data therefore do not distinguish between different types of ischemic injury.

A third limitation is related to possible misalignments between segmental wall motion findings on echocardiography and estimates of functional processes derived from the PET images. Wall motion was examined in 18 segments on echocardiography and related to the 7 anatomic segments on the transaxial PET images as described previously in our laboratory.4-8 Despite the use of anatomic landmarks, for example, anterior and posterior papillary muscles or the insertion point of the right ventricular free wall into the septum, some degree of misalignment may have occurred. At the same time, it should be emphasized that the major thrust of this study was to characterize the relations between blood flow and glucose and oxidative metabolism rather than their relation to regional contractile function.

As another shortcoming, a uniform wall thickness of 1 cm was assumed for normal as well as PET mismatch and PET match segments in the present study. In patients with chronic coronary artery disease, diastolic wall thickness in myocardial regions with preserved 18F-deoxyglucose activity has been shown to be similar to that in normal myocardium.14 However, segments with more severe injury, for instance, those with matched perfusion–glucose metabolism defects, might have significantly reduced wall thicknesses.14 A reduction of about 15% in wall thickness as reported for the latter segments14 would have required correction by a recovery coefficient about 15% lower, which in turn would have resulted in about 15% higher estimates of blood flow in such segments. Such underestimation of blood flows might have contributed to the data scatter in the low flow range. However, such underestimation would not explain the observed piecewise linear relation between blood flow and oxidative metabolism.

**PET Mismatch and Match in Clinical Infarct Regions**

In this study, 45% of the patients and 43% of the clinical infarct regions exhibited blood flow–metabolism mismatches. This incidence is similar to that reported previously in early postinfarction patients.8 The findings suggest that contractile dysfunction was potentially reversible in such segments. Although long-term follow-up studies would be required to confirm this possibility, recently published observations in early postinfarction patients indicate that blood flow metabolism patterns do in fact predict with a relatively high degree of accuracy the long-term outcome in regional contractile function after successful revascularization.29

In four patients, blood flow–metabolism mismatches were detected within 3 days, whereas in six patients they were found 4 to 7 days after the acute event. Thus, the presence of mismatch was unrelated to the time between the infarction and the tomographic study and might be observed as long as 1 week after the acute event. The infarct vessel patency as defined by the TIMI criteria4 was unrelated to the presence of mismatch segments. However, the high number of matched segments subtended by a patent coronary artery (n=20) might indicate late reperfusion of the acutely injured segments. In contrast, all but two PET mismatch segments (n=16) were subtended by a patent infarct vessel, suggesting reperfusion during the early course of myocardial infarction.

**Relation Between Blood Flow and Cardiac Work**

The mean values for myocardial blood flow, oxidative metabolism, and exogenous glucose utilization in remote and presumably normal myocardium were similar to those reported previously in normal volunteers and normal myocardium of patients with coronary artery disease.30-32 However, individual values varied considerably between patients. As demonstrated in Fig 4, interpatient differences in rate-pressure product and thus in cardiac work were found to account for the relatively wide range of observed flows and oxidative metabolism. The relations of flow and of oxidative metabolism to the rate-pressure product in this study were similar to those observed previously with noninvasive techniques.16-18,33 These correlations held despite a wide range of left ventricular ejection fractions and thus variable amounts of dysfunctional myocardium. Similar relations between the rate-pressure product and oxidative metabolism in normal myocardium were reported recently.34 These variable fractions of dysfunctional myocardium may have been responsible in part for the scatter of the data about the regression line, although other determinants of oxygen demand may have contributed further. For example, end-systolic wall stresses, loading conditions, or different contractile states are significant contributors to oxygen demand but are not fully accommodated by the rate-pressure product as an index of cardiac work. The same reasons might also account for the lack
of a correlation between oxidative metabolism in match and in mismatch segments and the rate-pressure product. Although a recent study reported such a correlation for infarct segments, this correlation was only weak and did not discriminate between potentially viable and nonviable segments.24

Blood flows were reduced more severely than oxidative metabolism in PET ischemic segments (35% vs 16%, P<.001). In contrast, both blood flow and oxidative metabolism were proportionally and more severely reduced in segments with blood flow metabolism matches (58% and 48%, P=NS). Both types of ischemic tissue injury existed for intermediate reductions of blood flow. One factor accounting for this overlap is the variable degree of transmural injury between patients, which may relate to the heterogeneity of the patient population in terms of thrombolysis or angioplasty or in terms of different timings of the PET study after the acute event. Inadequate corrections for partial volume effects cannot explain the observed overlap. More adequate corrections (lower recovery coefficients) would increase blood flows in the most severely injured segments, thereby enhancing the observed overlap. Regardless of the underlying mechanism, the variability of blood flow in perfusion-metabolism matches and mismatches suggests that flow measurements alone do not fully discriminate between these two types of tissue injury.

In contrast, less overlap was observed for normalized rates of oxidative metabolism. This observation might be consistent with the recently reported notion that oxidative metabolism as assessed with [13C]acetate may be a useful discriminator between complete and incomplete infarction.29

Relation Between Blood Flow and Metabolism

A previous study in patients with subacute and chronic myocardial infarctions has reported a linear relation between blood flow and oxidative metabolism.30 Although this earlier study did not include segments with blood flows as low as in the present study, the observed piecewise relation was nevertheless unexpected. It raised the question whether it could be attributed to methodological or statistical problems.

Flow estimates by the PET approach are sensitive to partial volume effects, which were corrected for by a constant correction factor that assumed a uniform wall thickness. In contrast, estimates of the tissue clearance rates of [13C]acetate and thus of oxidative metabolism are largely independent of partial volume. Moreover, measurements of blood flow and metabolism in adjacent myocardial segments might represent dependent observations. For instance, spillover of tracer activity from areas of normal to those of reduced tracer activity might cause a statistical bias for the relation between blood flow and metabolism.

Several reasons argue against the possibility that methodological limitations accounted for the observed piecewise relation. First, in normal myocardium, where corrections for partial volume effects are less problematic, the slopes of the regression lines for blood flow and for oxidative metabolism vs the rate-pressure product clearly differ (Fig 4). The different steepnesses of these slopes indicate that decreases in blood flow are associated with smaller decrements in oxidative metabolism. Even if partial volume effects in normal regions with low flows were corrected inadequately, more accurate corrections and consequently higher estimates of flows would result in an even greater disparity of the slopes (as shown in Fig 4). This would further accentuate the observed piecewise relation. Although accurate corrections for partial volume in clinical infarct regions are admittedly problematic, which in part may account for the data scatter in the low flow range, they are unlikely to account for the steep decline in oxidative metabolism. More appropriate corrections might have modified the slope of the steeper portion of the piecewise relation, thereby further accentuating the piecewise character of this relation.

To obtain the best fit for the relation between blood flow and oxidative metabolism, the optimum threshold between the low and the high flow range was determined by repeatedly fitting two regression lines simultaneously to the data by least-squares regression analysis.25 As a second step, the F test was used to test whether this relation was better described by a piecewise linear or linear fit.

To minimize the contribution of lateral spillover to the measured tissue tracer concentrations, small regions of interest were used. However, to rule out the possibility that segmental measurements of blood flow and oxidative metabolism were influenced by adjacent myocardial segments and were in fact not independent, their relation was also analyzed by use of the mean values for normal, PET mismatch, and match segments within each patient. Such analysis confirmed the piecewise linear relation between blood flow and oxidative metabolism. The piecewise linear fit was significantly better than a single linear fit (F=6.7>F=5.6; P<.01; best threshold, 0.57 mL·g⁻¹·min⁻¹). Thus, neither statistical limitations nor partial volume or spillover problems were likely to have accounted for the piecewise linear relation.

In the present study, flows of about 0.55 mL·g⁻¹·min⁻¹ separated the flatter from the steeper portions of the piecewise relation. This value might represent a critical threshold. Together with the metabolic critical demand, and thus in demand, increases in the oxygen extraction fraction may in fact compensate for a decrease in blood flow and thus oxygen supply. Such compensatory mechanisms may no longer be adequate when blood flow decreases further. In support of such a possibility of a critical threshold of blood flow are recent animal studies with nuclear magnetic resonance spectroscopy that demonstrated a preservation of high-energy phosphate levels for flow reductions by as much as 50% of normal. If blood flow declined below this level, high-energy phosphate concentrations decreased.36

The observed piecewise relation is consistent with the data recently reported by Feigl et al.37 These investigators incorporated previously reported animal experimental observations into a theoretical model that describes the interdependence between perfusion pressure, blood flow, and oxygen consumption. The model predicts a piecewise relation between oxygen consumption and blood flow that is nearly identical to that found in the present study. Oxygen consumption, according to this model, falls only gradually for flows down to about 0.5 mL·g⁻¹·min⁻¹ but then declines more steeply with further decreases in flow. Increases in
the extraction of oxygen in this model accounted for the initially only gradual decline in oxygen consumption. Such increases in the oxygen extraction fractions might reflect a compensatory mechanism to maintain adequate oxygenation in hypoperfused myocardium.

Increases in oxygen extractions might also account for the different relation of normalized blood flow to oxidative metabolism in PET mismatch and match segments (Fig 7). The flatter slope of the regression line in PET mismatch than in PET match segments implies different oxygen extractions in these two tissue types. Values for oxygen extraction fractions in experimental animals range from 45% to 75% in normal myocardium, with increases to as much as 90% in hypoperfused myocardium.38,39 True values of oxygen extraction cannot be derived from the present data. However, the ratio between normalized oxidative metabolism and blood flow provides an index of oxygen extraction. Assuming an oxygen extraction fraction of 66% in normal myocardium as observed in patients with cardiac disease,40 a ratio of 1.25 in segments with mismatches, as calculated for flow reductions from 20% to 40%, would reflect a 25% increase of oxygen extraction to 82%. Such increases in oxygen extraction might maintain viability in hypoperfused myocardium and might offer an explanation for the recently reported high predictive accuracy of oxidative metabolism for the recovery of dysfunctional myocardium.29

Unlike oxidative metabolism, rates of glucose utilization did not correlate with blood flow or the rate-pressure product. This was because glucose utilization in normal myocardium varied considerably between patients. The observed variability of glucose metabolic rates between patients, despite standardization by oral glucose administration,41 may have been caused by (1) glucose intolerance in the majority of patients as evidenced by the high mean serum glucose levels in this population and (2) the effect of heparin on plasma free fatty acid levels and, consequently, on glucose utilization in four patients but also by other endocrine factors, for example, elevated plasma catecholamine levels.52,53 However, even demanding procedures such as the glucose–insulin clamp technique do not abolish the variability of glucose metabolic rates between patients.41

In agreement with previous animal experimental studies, glucose metabolic rates were lower in normal myocardium of patients with blood flow metabolism mismatches than in those with matched defects. An inhibition of glucose uptake in normal myocardium of patients with high rates of glucose metabolism in mismatch segments might account for this finding.44

Conversely, normalized glucose utilization in segments with matched defects correlated with normalized blood flow but, as expected, deviated from this relation in PET mismatch segments. This observation further suggests that normalized rather than absolute rates of glucose utilization are useful for identifying potentially reversible myocardial injury. The present data suggest that quantification of rates of glucose utilization is of limited use for assessing potentially reversible myocardial contractile dysfunction in patients with a recent myocardial infarction. The value of relative glucose metabolic studies for the prediction of reversible tissue dysfunction remains unclear. Serial assessment of regional wall motion will be required to determine the predictive value of preserved glucose utilization for functional recovery of recently injured myocardium.

Summary and Clinical Implications

This study identified two distinct patterns of blood flow and metabolism in clinical infarct regions. The relatively high incidence of blood flow metabolism mismatches suggests that ischemia can persist in a substantial fraction of clinically infarcted myocardium, even as long as 1 week after the acute event. Such regions cannot be identified solely by flow criteria, since modest to severe flow reductions are associated with both potentially salvageable and probably irreversibly injured myocardium. Mild to moderate flow reductions were associated with disproportionately smaller decreases in oxidative metabolism, probably because of an increase in the oxygen extraction. The latter may represent a compensatory mechanism for maintaining an adequate balance of high-energy phosphate. At the same time, it may also account for the usefulness of [11C]acetate as a marker of viability or reversible tissue dysfunction.20 The steep decline in oxidative metabolism with further flow decreases may in fact denote a critical threshold in myocardial ischemia that might separate reversible from irreversible tissue injury.

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References

6. Tillisch J, Brunken R, Marschall R, Schwaiger M, Mandelkern M, Phelps M, Schelbert H. Reversibility of cardiac wall motion abnor-
Regional blood flow, oxidative metabolism, and glucose utilization in patients with recent myocardial infarction.
J Czernin, G Porenta, R Brunken, J Krivokapich, K Chen, R Bennett, A Hage, C Fung, J Tillisch and M E Phelps

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