Simultaneous Assessment of Myocardial Perfusion and Left Ventricular Function During Transient Coronary Occlusion

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Objectives. We used technetium-99m sestamibi imaging to evaluate the magnitude of changes in left ventricular function and perfusion and to investigate their interdependence during transient coronary occlusion.

Background. Transient coronary occlusion during coronary angioplasty provides a unique opportunity for examining the effects of acute myocardial ischemia on left ventricular function and perfusion.

Methods. Thirty-five patients with normal left ventricular function underwent first-pass radionuclide angiography with technetium-99m sestamibi using a multicrystal gamma camera during balloon occlusion of a coronary artery. Single-photon tomography was performed 2.1 ± 1.7 h later. Subsequently, all scans were repeated at rest.

Results. The mean size ± SD of the perfusion defect during coronary occlusion was 23 ± 18%, with significantly larger defects observed for occlusions of the left anterior descending coronary artery (39 ± 20%) than for occlusions of the left circumflex (15 ± 11%) or right (15 ± 9%) coronary artery (p < 0.05). The mean change in ejection fraction from recovery to occlusion was -17 ± 17% and was significantly larger for left anterior descending (-26 ± 21%) and left circumflex (-15 ± 11%) than for right (-8 ± 10%) coronary artery occlusions (p < 0.05). For the entire group, ejection fraction during occlusion correlated significantly with perfusion defect size (r = 0.63, p = 0.0004), whereas the extent of ischemic myocardium correlated with the decrease in ejection fraction (r = 0.69, p = 0.0001). The defects present during occlusion reversed within a few hours.

Conclusions. Changes in left ventricular function and perfusion develop pari passu during coronary occlusion and are more severe when the left anterior descending artery is occluded. Although a significant correlation exists between the extent of the perfusion defect and the severity of the decrease in ejection fraction, there is a substantial individual variation with respect to changes in both myocardial perfusion and ventricular function during acute coronary occlusion.

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Coronary occlusion during percutaneous transluminal coronary angioplasty provides an intriguing in vivo model for examining the effects of acute myocardial ischemia on ventricular function and perfusion and may have potential implications for assessing patients with acute myocardial infarction or unstable angina. Jones et al. (1) documented a fair overall correlation between perfusion defect size and left ventricular dysfunction during exercise. More recently, these investigators have shown changes in perfusion and function to be significantly greater during coronary occlusion than with exercise (2). Previous studies using echoangiography (3–6), hemodynamic measurements (1,7,8) or perfusion imaging (9–11), have attempted to assess the extent of jeopardized myocardium during coronary angioplasty. However, no studies have addressed the simultaneous effect of coronary occlusion on left ventricular function and myocardial perfusion. The recent introduction of the tracer technetium-99m sestamibi allows such a simultaneous evaluation to be performed. The purposes of this investigation, therefore, were to 1) concurrently evaluate left ventricular function by first-pass radionuclide angiography and myocardial perfusion by single-photon emission computed tomography during transient coronary occlusion at various anatomic sites; 2) examine the interdependence between changes in myocardial perfusion and function during coronary occlusion; and 3) assess the completeness of scintigraphic reperfusion in a model of transient occlusion followed by reperfusion.

Methods

Patient characteristics. The study group consisted of 35 nonconsecutive patients (26 men, 9 women, mean age 62 ± 12 years [range 37 to 79]) with normal baseline left ventricular function (mean left ventricular ejection fraction 62 ± 9% by contrast ventriculography) who underwent elective percutaneous transluminal coronary angioplasty. All patients had normal
wall motion, with the exception of one patient with a prior non-Q wave myocardial infarction who had mild focal hypokinesia. The indications for coronary angioplasty were either unstable angina (n = 16), exertional angina (n = 12) or an exercise test positive for ischemia (n = 7). The average New York Heart Association angina class was 2.8 ± 1.2. Seventeen patients had a normal baseline electrocardiogram (EKG), but the remaining 18 had various baseline ECG abnormalities (9 with nonspecific T wave abnormalities, 3 with a paced rhythm, 3 with left bundle branch block and 2 with left ventricular hypertrophy). Patients with a previous Q wave myocardial infarction or significant left ventricular systolic dysfunction (i.e., left ventricular ejection fraction <45%), were excluded. Patients were also excluded if coronary angioplasty could not be performed because of inability to cross the stenosis (n = 2) or if coronary dissection occurred and resulted in clinical or hemodynamic instability (n = 4). In one patient the study was rejected because ventricular tachycardia occurred during coronary inflation. Five patients had a previous non-Q wave myocardial infarction. All patients received cardiac medications within 12 h of angioplasty; these comprised calcium channel blockers in 26 patients, nitrates in 21, beta-adrenergic blocking agents in 6 and digoxin in 1 patient. In six patients, first-pass radionuclide angiography was attempted, but studies could not be obtained because of technical difficulties with the multicrystal camera in the catheterization laboratory. For these patients, only the perfusion data are reported. The protocol was approved by the Institutional Review Boards of The Methodist Hospital and Baylor College of Medicine and all patients signed informed consent.

Coronary angioplasty. An arterial sheath was introduced percutaneously into the femoral artery and used for the angioplasty procedure. A venous sheath was inserted into the femoral vein and was subsequently used for injection of technetium-99m sestamibi. The coronary artery undergoing angioplasty was opacified in multiple views before dilation. Coronary angioplasty was performed with the use of standard techniques. On average, 3 ± 1 (range 2 to 6) inflations were performed, each lasting from 40 to 300 s (mean ± SD 84 ± 11 s) with first-pass radionuclide angiographic images obtained during the second inflation, ~3 to 5 min after completion of the first inflation. Arterial blood pressure was monitored at the tip of the guiding catheter during balloon inflation. Patients were continually monitored with a three-lead ECG (leads II, V2 and V4) and recordings were obtained immediately before, during and after balloon inflations.

An invasive cardiologist who did not know the scintigraphic results measured the severity of coronary stenosis on the coronary cine angiograms using an electronic caliper.

First-pass radionuclide angiography. Imaging protocol. A Scinticor SIM-400 gamma camera, consisting of a mobile detector interfaced by way of a fiber optic link to a Macintosh computer was used. The first-pass radionuclide angiographic studies were acquired in digital format using a 20 × 20 pixel by 16-bit matrix with a time resolution of 25 ms/frame; all data were stored on an optical disc for processing and analysis.

After completion of the first balloon inflation, 11.8 ± 0.75 (range 9.8 to 13.6) mCi of technetium-99m sestamibi was loaded into the femoral tubing with use of a three-way stopcock, and the intravenous line was closed to avoid premature delivery of technetium-99m sestamibi to the patient. Balloon position across the stenosis was confirmed by fluoroscopy, and the angiographic equipment was moved away from the patient's chest. The SIM-400 detector was positioned anteriorly with the lateral margin at the left anterior axillary line, the medial margin at the right sternal border and the superior margin just beneath the patient's chin. Approximately 20 s into the balloon inflation, technetium-99m sestamibi was flushed in with a 15- to 20-ml normal saline bolus. The first-pass radionuclide angiographic images were then acquired for 30 s.

After successful completion of the angioplasty procedure, patients underwent single-photon emission computed imaging 2.1 ± 1.7 (mean ± SD) h after the initial sestamibi injection. Technetium-99m sestamibi, 19.5 ± 0.9 (range 18 to 21.3) mCi, was again injected through the femoral vein immediately after the initial tomographic imaging (n = 33) or through an antecubital vein 24 to 48 h after angioplasty (n = 2), with repeat first-pass radionuclide angiography performed at 2.6 to 4.6 h after angioplasty. The second tomographic imaging procedure was performed 3.6 to 5.6 h after angioplasty.

Image processing. The studies were processed by an experienced observer who had no knowledge of the coronary angioplasty or computed tomographic results. After the first-pass study was acquired, frames were displayed showing the transit of technetium-99m sestamibi through the superior vena cava, right ventricle, lung and left ventricle. Superior vena cava and left ventricular regions of interest were selected and outlined. A histogram showing counts versus time was used to select the lung background (lowest valley before the left ventricular phase) and the first and last systolic frames of the left ventricular phase. A representative left ventricular cycle was generated by adding the selected frames. On the basis of previously drawn regions of interest, the count rates within the left ventricular phase histogram were displayed by the computer.

The end-diastolic and end-systolic frames were selected and their corresponding counts and duration (in ms) were displayed. The raw left ventricular ejection fraction for each cardiac cycle was calculated as: (End-diastolic counts – Background) – (End-systolic counts – Background)/(End-diastolic counts – Background). The duration of each cardiac cycle was calculated to establish beat to beat variability. The corrected left ventricular ejection fraction was determined by averaging the raw ejection fractions after excluding the beats showing the greatest deviation from the mean (SD of the RR interval >50 ms or SD of raw left ventricular ejection fraction >5%).

The observer then drew the left ventricular region of interest by using the computer-generated end-diastolic silhouette and marked the center of the aortic valve plane and apex. The left ventricular ejection fraction, ventricular volumes
were acquired a mean of 2.1 ± 1.7 h after the first sestamibi injection and 1 to 2 h after the second injection by techniques previously reported from our laboratory (13-16). Images were obtained by using a large field of view gamma camera equipped with a low energy, high resolution collimator and interfaced to a computer (ADAC 3300). Thirty-two images were obtained over an anterior 180° arc at 6° intervals for 40 s/image. Transaxial reconstruction was performed after filtered back-projection (Butterworth filter, order 5, cutoff 50%). Reconstructed slices were reoriented into the short, horizontal long and vertical long axes.

Image display and regional function analysis. Left ventricular cinemtomographic images during occlusion and recovery were displayed side by side on the computer’s color screen for visual analysis. Analysis of regional left ventricular function was aided by viewing computed color-coded regional maps and the superimposed end-diastolic and end-systolic silhouettes.

Myocardial perfusion tomography. Tomographic images were acquired a mean of 2.1 ± 1.7 h after the first sestamibi injection and 1 to 2 h after the second injection by techniques previously reported from our laboratory (13-16). Images were obtained by using a large field of view gamma camera equipped with a low energy, high resolution collimator and interfaced to a computer (ADAC 3300). Thirty-two images were obtained over an anterior 180° arc at 6° intervals for 40 s/image. Transaxial reconstruction was performed after filtered back-projection (Butterworth filter, order 5, cutoff 50%). Reconstructed slices were reoriented into the short, horizontal long and vertical long axes.

Interpretation of myocardial perfusion tomograms. Myocardial segments were matched to coronary artery territories as previously reported from our laboratory (13-16); septal and anterior segments corresponded to the left anterior descending coronary artery, inferior and posterior segments to the right coronary artery and lateral segments to the left circumflex coronary artery. The apex was not assigned to any one vascular territory because apical defects may correspond to lesions in any of the three major coronary vessels. Perfusion defect severity was visually graded as 3 = normal perfusion and 2 = mildly diminished, 1 = moderately diminished and 0 = severely diminished to absent perfusion. Mildly diminished perfusion was defined as >60% of normal tracer activity, moderately diminished perfusion as 30% to <60% of normal count activity and severely diminished perfusion as <30% of normal activity.

Perfusion defect size was quantified by using polar maps depicting the three-dimensional radionuclide distribution, as previously reported from our laboratory (13-16). Polar maps were statistically compared with a normal data bank of persons undergoing technetium-99m sestamibi single-photon emission computed tomography in our laboratory. Pixels with counts <2.5 SD from the mean values in the normal data bank were considered abnormal. In addition, polar maps depicting the severity and reversibility of perfusion defects were generated as previously described (16). Defect severity and reversibility were also assessed by determining the technetium-99m sestamibi activity in regions of interest (5 × 5 pixels) placed in the center of the hypoperfused area in the polar plots and in the corresponding regions in the subsequent recovery study. The activity in the defects was compared with that of normally perfused regions on both the occlusion and the recovery polar maps.

Statistical analysis. Hemodynamic variables and myocardial perfusion during coronary occlusion and at rest were compared by using the Student paired t test. One-way analysis of variance with the Newman-Keuls multiple comparison test was used to assess differences among left anterior descending, left circumflex and right coronary artery occlusions. Univariate linear regression analysis was used to correlate changes in left ventricular function with perfusion defects. Multivariate linear regression analysis was used to correlate clinical, hemodynamic and perfusion variables with change in left ventricular ejection fraction during coronary occlusion; in this analysis, the left ventricular ejection fraction during occlusion was entered as the independent variable and the perfusion defect size, history of angina, number of diseased vessels, percent stenosis of the artery subjected to angioplasty, history of myocardial infarction and amount of ST segment change during occlusion were sequentially entered into the model as dependent variables provided they improved the overall correlation coefficient. Results are reported as mean value ± SD. For all statistical tests, a p value ≤0.05 was considered significant.

Results

Clinical characteristics. Twenty of the 35 patients had one-vessel, 9 had two-vessel and 6 had three-vessel coronary artery disease. During diagnostic coronary angiography no patient had visible collateral channels to or from the vessel undergoing angioplasty. During coronary occlusion 19 patients (8 during left anterior descending, 5 during left circumflex and 6 during right coronary artery occlusion) had angina pectoris, and 17 had either ST segment elevation (1 during left anterior descending, 2 during left circumflex and 4 during right coronary artery occlusion) or ST segment depression (6 during left anterior descending and 4 during left circumflex coronary artery occlusion). The ST segments were uninterpretable in 8 patients because of a paced rhythm, left ventricular hypertrophy or left bundle branch block and remained normal in 10 patients. During coronary occlusion heart rate increased from 62 ± 8 to 71 ± 13 beats/min (p = 0.0001) and diastolic blood pressure increased from 72 ± 11 to 80 ± 11 mm Hg (p = 0.0003), but systolic blood pressure did not change significantly (131 ± 19 to 132 ± 24 mm Hg). Directionally similar hemodynamic changes occurred during left anterior descending, left circumflex and right coronary artery occlusion (Table 1).

Coronary angioplasty. Studies were obtained during occlusion of the left anterior descending artery in 11 patients. The balloon was inflated in the proximal (before the first diagonal and septal branches) left anterior descending artery in six patients, in the midportion of the vessel (between the first septal and the first diagonal branch) in two and in the distal vessel (after the first diagonal branch) in two. In one patient the inflation was performed in a large first diagonal branch. For purposes of data analysis, this patient was included in the group with angioplasty of the left anterior descending artery. Thirteen patients underwent balloon inflation of the left circumflex artery in an obtuse marginal branch (n = 6), the circumflex trunk (n = 2), a posterior descending branch (n = 2), a posterolateral branch (n = 2) or an obtuse marginal
Table 1. Hemodynamic Variables During Coronary Occlusion and at Rest

<table>
<thead>
<tr>
<th>Occluded Artery</th>
<th>Total Group (n = 29)</th>
<th>LAD (n = 11)</th>
<th>RCA (n = 7)</th>
<th>LCx (n = 11)</th>
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<tbody>
<tr>
<td>Heart rate (beats/min)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Occlusion</td>
<td>71 ± 13*</td>
<td>75 ± 18*</td>
<td>69 ± 9</td>
<td>69 ± 7*</td>
</tr>
<tr>
<td>Recovery</td>
<td>62 ± 8</td>
<td>63 ± 9</td>
<td>63 ± 8</td>
<td>61 ± 8</td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>132 ± 24</td>
<td>131 ± 29</td>
<td>132 ± 22</td>
<td>135 ± 22</td>
</tr>
<tr>
<td>Recovery</td>
<td>131 ± 19</td>
<td>130 ± 26</td>
<td>135 ± 24</td>
<td>137 ± 6</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>80 ± 11*</td>
<td>86 ± 12*</td>
<td>79 ± 7</td>
<td>75 ± 10</td>
</tr>
<tr>
<td>Recovery</td>
<td>72 ± 11</td>
<td>74 ± 14</td>
<td>74 ± 12</td>
<td>69 ± 10</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>48 ± 12*</td>
<td>40 ± 11*</td>
<td>53 ± 8</td>
<td>52 ± 9*</td>
</tr>
<tr>
<td>Occlusion</td>
<td>-17 ± 17</td>
<td>-26 ± 21</td>
<td>-8 ± 10†</td>
<td>-15 ± 11†</td>
</tr>
<tr>
<td>Recovery</td>
<td>104 ± 30</td>
<td>108 ± 36</td>
<td>110 ± 29</td>
<td>96 ± 22</td>
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<td>EDVI (ml/m²)</td>
<td>56 ± 24*</td>
<td>66 ± 30*</td>
<td>53 ± 21</td>
<td>47 ± 15*</td>
</tr>
<tr>
<td>Recovery</td>
<td>43 ± 18</td>
<td>45 ± 19</td>
<td>47 ± 17</td>
<td>35 ± 15</td>
</tr>
<tr>
<td>ESVI (ml/m²)</td>
<td>56 ± 24*</td>
<td>66 ± 30*</td>
<td>53 ± 21</td>
<td>47 ± 15*</td>
</tr>
<tr>
<td>Occlusion</td>
<td>13 ± 3*</td>
<td>41 ± 11*</td>
<td>57 ± 13</td>
<td>49 ± 11</td>
</tr>
<tr>
<td>Recovery</td>
<td>54 ± 13</td>
<td>49 ± 13</td>
<td>59 ± 13</td>
<td>52 ± 13</td>
</tr>
<tr>
<td>SVI (l/min/m²)</td>
<td>3.6 ± 1.1</td>
<td>3.4 ± 1.1</td>
<td>4.1 ± 1.2</td>
<td>3.4 ± 0.9</td>
</tr>
<tr>
<td>Occlusion</td>
<td>3.3 ± 0.9</td>
<td>3.1 ± 1.0</td>
<td>3.8 ± 1.0</td>
<td>3.1 ± 0.6</td>
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</table>

*Analysis of variance, p < 0.05 versus left anterior descending coronary artery (LAD). †p < 0.05 by paired t test. Data are expressed as mean value ± SD. CI = cardiac index; DBP = diastolic blood pressure; EDVI = end-diastolic volume index; ESVI = end-systolic volume index; LAD = left anterior descending artery; LCx = left circumflex coronary artery; LVEF = left ventricular ejection fraction; RCA = right coronary artery; SBP = systolic blood pressure; SVI = stroke volume index.

saphenous vein graft (n = 1). Ten patients underwent right coronary artery inflation proximally (n = 7), distally (n = 1), in a posterior descending branch (n = 1) or in a saphenous vein graft (n = 1).

For the group as a whole, the average lumen diameter stenosis of the dilated vessel decreased from 67 ± 22% before angioplasty to 28 ± 15% after angioplasty (p = 0.0001). For individual arteries, diameter stenosis before versus after angioplasty was 66 ± 24% versus 21 ± 13% (p = 0.0001) for left anterior descending, 68 ± 17% versus 29 ± 12% (p = 0.0001) for left circumflex and 66 ± 28% versus 33 ± 18% (p = 0.001) for right coronary artery lesions. In two cases, angioplasty was complicated by acute closure of the vessel, which was successfully opened by using an intracoronary stent. In all other cases, angioplasty and the early postangioplasty course throughout the duration of the investigation were uncomplicated.

Ventricular function changes during coronary occlusion. Figures 1 to 3 illustrate, respectively, representative first-pass radionuclide angiography during occlusion of the left anterior descending coronary artery, right coronary artery and left circumflex coronary artery and their corresponding images during recovery. Figure 4 summarizes the changes in left ventricular ejection fraction from recovery to occlusion, whereas Figure 5 depicts the percent decrease in ejection fraction categorized by dilated artery. For the entire group, the absolute left ventricular ejection fraction increased from 48 ± 13% during occlusion to 57 ± 8% during recovery (p = 0.0001). The absolute (Fig. 4) and relative (Fig. 5) decreases in ejection fraction during occlusion were artery dependent, in that significant decreases occurred only during occlusions of the left anterior descending and left circumflex arteries but not during occlusion of the right coronary artery.

Changes in regional wall motion were assessed in the 29 patients with technically satisfactory first-pass radionuclide angiograms. Most patients during left anterior descending artery occlusion manifested anterolateral hypokinesia (n = 7), or akinesia (n = 2), although two patients (one each with occlusion in the mid- or distal left anterior descending artery) had normal wall motion. Six patients also had inferior hypokinesia during right coronary artery occlusion, whereas four others had no perceptible change in wall motion. With left circumflex artery occlusion, four patients showed inferior hypokinesia, one patient (undergoing dilation of an obtuse marginal branch) showed anterobasal hypokinesia, and six patients had no detectable wall motion abnormality. Only one patient, who had a prior non-Q wave inferior infarction, had abnormal wall motion in the recovery study.

Hemodynamic changes during coronary occlusion are shown in Table 1. For the entire group, there was a significant increase in end-systolic volume index and a decrease in stroke volume index but no change in end-diastolic volume index. Cardiac index did not change significantly because the decrease in stroke volume index was offset by an increase in heart rate. A significant increase in end-systolic volume index occurred during both left anterior descending and left circumflex artery occlusions, although the stroke volume index only decreased significantly with the former. No significant changes in ventricular volumes or cardiac index occurred during right coronary artery occlusion.

Myocardial perfusion patterns during coronary occlusion. Perfusion defects developed in the vascular territory of the occluded artery in all but one patient. Anterior, septal or apical defects, alone or in combination, developed in all 12 patients with left anterior descending artery occlusion and inferior defects also developed in four. All 10 patients with right coronary artery occlusion had an inferior or posterior defect or both, but only one patient had a lateral defect. During left circumflex artery occlusion 10 of 13 patients showed either a lateral or posterolateral (n = 8) defect or an apical defect; 2 patients with a dominant left circumflex coronary artery had a posterior defect, and 1 patient, who had inflation of a small left circumflex posterolateral branch, had no measurable perfusion defect. Apical perfusion defects always occurred during left anterior descending artery occlusion but were uncommon with
Figure 1. Proximal left anterior descending coronary artery occlusion. **A**, The left panel of each pair depicts the left ventricular first-pass radionuclide angiogram in the anterior view at baseline (Rest) and during occlusion. The outer perimeter depicts end-diastolic and the inner perimeter end-systolic silhouettes. The right panel of each pair depicts the regional ejection fraction images at baseline and during occlusion, with each color corresponding to a certain value of ejection fraction: black = 0% to 10%; green = 11% to 20%; blue = 21% to 30%; gray = 31% to 40%; purple = 41% to 50%; magenta = 51% to 60%; red = 61% to 70%; orange = 71% to 80%; yellow = 81% to 90%; white = 91% to 100%. At baseline (Rest) the left ventricular ejection fraction (LVEF) is 64% and wall motion is normal. During occlusion, the ejection fraction decreases to 41% and there is global hypokinesia. **B**, Corresponding single-photon computed tomographic myocardial perfusion images in the short and vertical and horizontal long axes during occlusion (upper panels) and at recovery (lower panels) and polar maps (right) displaying defect extent, severity and reversibility. Moderate, completely reversible anteroseptal, anterior and apical defects are seen. Polar maps display these defects, which by quantitative analysis involved 51% of the left ventricle.

Figure 2. Right coronary artery occlusion. **A**, Similar format as in Figure 1, illustrating first-pass radionuclide angiograms at baseline (Rest) (left) and during occlusion (right). At baseline, there is normal wall motion and left ventricular ejection fraction (LVEF) of 67%. During occlusion, the ejection fraction decreases to 56% and severe inferior hypokinesia develops. **B**, Similar format as in Figure 1B, showing myocardial perfusion images during right coronary artery occlusion and at recovery. A moderate, and completely reversible perfusion defect involves 30% of the left ventricle.
left circumflex (4 of 13) or right coronary artery (1 of 10) occlusions.

Figures 1B, 2B, and 3B show, respectively, representative single-photon emission computed tomographic images during left anterior descending coronary artery, right coronary artery and left circumflex coronary artery occlusions.

Perfusion defect severity during coronary occlusion was mild in 18 patients, moderate in 14 and severe in 2. There was no difference in defect severity among different coronary arteries.

Twenty-five (74%) of the 34 patients with perfusion defects during coronary occlusion had an entirely normal scan later at rest, although 8 patients had a partially reversible defect and 1 patient had a small fixed defect. However, four of the eight patients with partially reversible defects, had only a small (<4%) fixed component, whereas three patients had a previous non-Q wave infarction. The remaining patients had an acute occlusion of the first diagonal branch of the left anterior descending artery during angioplasty with subsequent successful intracoronary stent placement. The only patient with an exclusively fixed defect had a nondiagnostic ECG (owing to ventricular paced rhythm) but no history of myocardial infarction. In this patient, a 6% posterior perfusion defect was

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**Figure 3.** Left circumflex artery occlusion. A, Similar format as in Figure 1A, showing first-pass radionuclide angiograms at baseline (rest) and during occlusion. There is normal wall motion and the left ventricular ejection fraction (LVEF) is 53% at baseline (left). During occlusion (right), the ejection fraction decreases to 47%. B, Similar format as in Figure 1B, showing myocardial perfusion during occlusion. A moderately severe but reversible lateral perfusion defect involves 22% of the left ventricle.

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**Figure 4.** Left ventricular ejection fraction at baseline (rest) and during coronary occlusion. During occlusion of the left anterior descending coronary artery (LAD), ejection fraction decreased significantly from 54 ± 6% to 40 ± 11%. During right coronary artery (RCA) occlusion, ejection fraction decreased from 58 ± 6% to 53 ± 8% (p = NS). During left circumflex coronary artery (LCX) occlusion, ejection fraction decreased from 61 ± 11% to 52 ± 9% (p = 0.002). OM = obtuse marginal branch; PDA = posterior descending artery; prox. = proximal.
The present study is unique in correlating left ventricular function with myocardial perfusion during coronary occlusion and later during recovery, thus allowing assessment of the integrated physiologic effects of occlusion at various coronary artery sites in humans. Overall, left ventricular ejection fraction and stroke volume index decreased while heart rate, diastolic blood pressure and end-systolic volume index increased with coronary occlusion. Impairment of left ventricular function was most severe during proximal or mid-left anterior descending artery occlusion and was accompanied by large, reversible perfusion defects. No significant changes in left ventricular function occurred during right coronary artery occlusion, whereas intermediate effects were seen during left circumflex artery occlusion. Finally, by regression analysis, we demonstrated a significant correlation between total perfusion defect size and left ventricular ejection fraction during occlusion.

**Discussion**

The present study is unique in correlating left ventricular function with myocardial perfusion during coronary occlusion and later during recovery, thus allowing assessment of the integrated physiologic effects of occlusion at various coronary artery sites in humans. Overall, left ventricular ejection fraction and stroke volume index decreased while heart rate, diastolic blood pressure and end-systolic volume index increased with coronary occlusion. Impairment of left ventricular function was most severe during proximal or mid-left anterior descending artery occlusion and was accompanied by large, reversible perfusion defects. No significant changes in left ventricular function occurred during right coronary artery occlusion, whereas intermediate effects were seen during left circumflex artery occlusion. Finally, by regression analysis, we demonstrated a significant correlation between total perfusion defect size and left ventricular ejection fraction during occlusion.

**Correlations between quantitative perfusion defect size and left ventricular function.** By linear regression analysis, left ventricular ejection fraction during coronary occlusion correlated significantly with size of the total perfusion defect \( r = 0.63, p = 0.0004 \) (Fig. 7A). Similarly, the relative percent change in ejection fraction from occlusion to recovery correlated significantly with the extent of reversibility within the defect \( r = 0.69, p = 0.0001 \) (Fig. 7B).

With respect to the left ventricular hemodynamics, no significant correlation existed between changes in left ventricular volumes and perfusion defect size during occlusion.

By multivariate linear regression analysis, ejection fraction during coronary occlusion correlated significantly with perfusion defect size and a history of unstable angina preceding coronary angioplasty \( r = 0.73, p = 0.007 \). The addition of percent stenosis of the involved artery, number of vessels with coronary stenosis, previous history of myocardial infarction or ST segment changes during coronary angioplasty did not significantly improve the multivariate regression model.

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**Table 2. Perfusion Defect Size During Coronary Occlusion**

<table>
<thead>
<tr>
<th></th>
<th>Total Group (n = 35)</th>
<th>Occluded Artery (n)</th>
<th>LAD (n = 12)</th>
<th>RCAX (n = 10)</th>
<th>LCX (n = 15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perfusion defect size</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>(LV%)</td>
<td>23 ± 18%</td>
<td>39 ± 20%</td>
<td>15 ± 9%*</td>
<td>15 ± 11%*</td>
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<tr>
<td>Range</td>
<td>0 to 82%</td>
<td>9% to 82%</td>
<td>3% to 30%</td>
<td>0 to 42%</td>
<td></td>
</tr>
<tr>
<td>Reversible defect size</td>
<td>21 ± 8%</td>
<td>37 ± 22%</td>
<td>13 ± 10%*</td>
<td>12 ± 2%*</td>
<td></td>
</tr>
<tr>
<td>Fixed defect size</td>
<td>2 ± 5%</td>
<td>2 ± 5%</td>
<td>3 ± 1%</td>
<td>3 ± 2%</td>
<td></td>
</tr>
</tbody>
</table>

\*p < 0.05 versus left anterior descending coronary artery (LAD) by analysis of variance. Data are expressed as mean value ± SD or range. LV = left ventricle; other abbreviations as in Table 1.
sion and between ischemic perfusion defect size and percent change in ejection fraction.

**Left ventricular function during transient coronary occlusion.** Dynamic changes in left ventricular function during coronary occlusion were previously described with contrast angiography (7,8,17) and echocardiography (3,6,18), although these studies did not correlate functional changes with the site of coronary occlusion. Our findings on left ventricular function during transient coronary occlusion are supported by previous studies using nuclear techniques. Hartmann et al. (19), using a nonimaging scintillation probe and technetium-99m pertechnetate, studied 18 patients during balloon inflation and found that left ventricular ejection fraction decreased more with left anterior descending and left circumflex artery occlusions than with right coronary artery occlusions. Using the nuclear VEST technique, Kayden et al. (20) demonstrated a mean decrease in left ventricular ejection fraction from 53 ± 18% to 28 ± 11% during left anterior descending artery occlusion. The larger decrease in ejection fraction in their study than in ours may have been due to their use of a longer inflation time before imaging (70 ± 16 s). Our group (21) recently reported first-pass radionuclide angiographic results using tantalum-178 and a prototype multwire gamma camera during balloon inflation of coronary arteries in 46 patients. In that study, we also observed a large decrease in left ventricular ejection fraction during left anterior descending artery occlusion, in contrast to a moderate decrease during left circumflex artery occlusion and no significant changes during right coronary artery occlusion.

**Left ventricular perfusion during transient coronary occlusion.** The present results are concordant with our previous quantification of jeopardized myocardium (22) in patients with single-vessel coronary artery disease undergoing exercise testing with thallium-201 single-photon emission computed tomography. Although significantly larger defects were noted with severe (≥70% stenosis) proximal left anterior descending artery lesions (29.8 ± 12.9%) than with severe left circumflex (13.6 ± 8.4%), or right coronary artery (17.7 ± 10.2%) coronary artery lesions, individual patients demonstrated enormous heterogeneity in perfusion defect size. A wide range of perfusion defects was observed irrespective of the involved vessel or the location of the stenosis within each vessel.

Assessment of myocardial perfusion during coronary balloon inflation using technetium-99m sestamibi planar imaging was reported by Pfisterer et al. (9) in 25 patients undergoing coronary angioplasty of the left anterior descending coronary artery. Ischemic defects occurred in 84% of their patients and correlated with absence of collateral vessels but not with the time of coronary occlusion. More extensive defects were noted in patients with proximal left anterior descending artery occlusions, although quantitative assessment was not done. In a study of 13 patients undergoing technetium-99m sestamibi single-photon emission computed tomographic imaging during coronary angioplasty, Braat et al. (10) found that perfusion defects were larger during left anterior descending artery inflation, although these investigators did not quantify defect sizes and did not obtain single-photon emission computed tomographic images during recovery. Quantification of perfusion defect size during coronary occlusion using technetium-99m sestamibi planar imaging was done by Haronian et al. (11). Similar to our study, they found larger perfusion defects for left anterior descending (22 ± 15%) versus non-left anterior descending (7 ± 11%) artery occlusions.

**Defect severity during coronary occlusion.** Defects of only moderate severity were observed in 50% of our patients, despite complete coronary artery occlusion and absence of demonstrable collateral channels by contrast angiography. This observation may in part be due to short coronary occlusion times (average 84 s) in our study, with balloon deflation at a time when a substantial fraction of the injected sestamibi probably had not yet been cleared from the blood (23). Moreover, it is possible that reactive hyperemia after balloon deflation led to partial filling in of the perfusion defects. Alternatively, collateral channels that were not visible on baseline angiography may have been present (24,25) and contributed to delivery of technetium-99m sestamibi to the jeopardized territory. Cohen and Rentrop et al. (24–26) have elegantly demonstrated that in a substantial proportion of patients with severe coronary stenosis collateral channels are not visible on baseline angiography but will become recogniz-
able 60 to 90 s after coronary occlusion on contrast injection into the contralateral artery. However, because the percent coronary stenosis in our patients was not particularly severe, it is unlikely that collateral channels enhanced perfusion to the vascular bed of the occluded artery.

**Correlation of ventricular function and perfusion during stress.** Very few studies have attempted to correlate ventricular function and perfusion in humans during acute myocardial ischemia. Our group (27) previously reported on the feasibility of simultaneous first-pass radionuclide angiography using iridium-191m and myocardial perfusion imaging with thallium-201 single-photon emission computed tomography; concordance between regional wall motion abnormalities and hypoperfusion was noted in 12 of 14 patients. Neglia et al. (28) evaluated left ventricular ejection fraction by blood pool radionuclide angiography and ventricular perfusion by thallium-201 planar scintigraphy during spontaneous or ergonovine-induced episodes of coronary spasm in the left anterior descending or right coronary artery. The absolute decrease in ejection fraction in that study concur with our results. Jones et al. (1) simultaneously assessed ventricular function (with first-pass radionuclide angiography) and perfusion (with technetium-99m sestamibi single-photon emission computed tomography) at rest and during exercise. A direct correlation between end-systolic volume and perfusion defect size, as well as an inverse correlation between left ventricular ejection fraction and defect size, was noted, although large discrepancies between function and perfusion occurred in 14% of their patients.

The relatively low (albeit statistically significant) correlation coefficient between the decrease in left ventricular ejection fraction and perfusion defect size in our study and that of Jones et al. (1) indicates that other factors (e.g., heart rate, preload, afterload, effective intravascular volume and compensatory hyperkinesia of adjacent walls) influence the relation between global left ventricular function and extent of myocardial hypoperfusion. This lack of perfect correlation between perfusion and function is also in keeping with our recent observation (16) that the total perfusion defect size and the left ventricular ejection fraction have a complementary role in predicting prognosis after a recent myocardial infarction. Nonetheless, these data suggested that size of the perfusion defect itself is not a particularly good predictor of the left ventricular ejection fraction in a given patient.

Borges-Neto et al. (2) compared changes in perfusion and function during coronary angioplasty with changes during exercise using technetium-99m sestamibi in a group of 20 patients. They observed larger perfusion defects and lower left ventricular ejection fractions during coronary occlusion than during exercise. These investigators did not study the relation between perfusion defect size and changes in ejection fraction and did not evaluate the responses to coronary occlusion on the basis of anatomic location of the occluded artery.

An important finding in our study is the high frequency of perfusion defects that developed in 34 (97%) of 35 patients during coronary occlusion, whereas wall motion abnormalities developed in only 17 (59%) of 29 patients. Even if one excludes patients with angioplasty of the left circumflex artery (because the radionuclide angiograms were obtained in the anterior view, which does not depict the posterolateral wall of the left ventricle), only 12 (67%) of 18 patients whose target artery was either the left anterior descending or the right coronary artery had abnormal wall motion. Thus, cardiac imaging is much more sensitive for depicting hypoperfusion than for depicting wall motion abnormalities during acute ischemia.

**Occlusion-rest imaging sequence for technetium-99m sestamibi imaging.** An important question in our investigation was whether imaging during coronary occlusion, and again after reperfusion, would allow scintigraphic identification of reperfusion. A rest-stress sequence has been considered optimal for sestamibi imaging (29) to avoid the possibility that false defects would be created by inhomogeneous background activity. However, when technetium-99m sestamibi imaging is used to evaluate the effects of acute reperfusion therapy, by necessity the first images are acquired during coronary occlusion, with subsequent images obtained after reperfusion. Thus, our data support the use of imaging during occlusion followed within several hours by rest imaging. With the use of this sequence, the defects were reversible in most of our patients. In fact, the images of only one patient showed no filling-in of the initial defect present during inflation. Of course, in the clinical setting of occlusion-reperfusion, one needs to contend with myocardial stunning, which may by itself produce apparent perfusion defects due to a partial volume effect (30,31). Nevertheless, sestamibi single-photon emission computed tomographic imaging has been shown to be a very effective technique to assess the success of reperfusion and the extent of myocardial salvage within a few days of reperfusion therapy (32,33). Our data suggest that repeat imaging within a few hours of the initial images, in patients without evidence of ongoing ischemia, may allow identifying coronary artery patency.

**Conclusions.** Our study demonstrates a wide range of perfusion defect sizes and changes in left ventricular ejection fraction during transient coronary occlusion. Significantly larger perfusion defects and decreases in ejection fraction occurred during occlusion of the left anterior descending coronary artery than during occlusion of either the left circumflex or the right coronary artery. However, the angiographic severity or location of coronary artery stenosis did not predict the extent of change in left ventricular function or perfusion in individual patients, nor did the extent of the perfusion defect size predict the severity of decrease in ejection fraction.

Finally, our data support the concept that an occlusion-rest sequence with technetium-99m sestamibi imaging is appropriate in evaluating the response of patients with an acute ischemic syndrome to emergency reperfusion therapies.

**References**

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