Sequential thallium-201 myocardial perfusion studies after successful percutaneous transluminal coronary artery angioplasty: delayed resolution of exercise-induced scintigraphic abnormalities

DANTE E. MANYARI, M.D., MERRIL KNUDTSON, M.D., REINHARD KLOIBER, M.D., AND DAVID ROTH, M.D.

With the technical assistance of Kathryn Reynolds, R.T.N.M., and Janice Spragg, R.T.N.M.

ABSTRACT To characterize the sequential changes of myocardial perfusion scintigraphy in patients with coronary artery disease (CAD) after complete revascularization, 43 patients underwent exercise thallium-201 (201Tl) myocardial perfusion scintigraphy before and at 9 ± 5 days, 3.3 ± 0.6, and 6.8 ± 1.2 months after percutaneous transluminal coronary angioplasty (PTCA). Only patients with single-vessel CAD, without previous myocardial infarction, and without evidence of restenosis at 6 to 9 months after PTCA were included. Perfusion scans were analyzed blindly with the use of a new quantitative method to define regional myocardial perfusion in the topographic distribution of each coronary artery, which was shown to be reproducible (r = .94 or higher and SEE of 7% or less, between repeated measures by one and two operators). At 4 to 18 days after PTCA, the mean treadmill walking time increased by 123 ± 42 sec, mean exercise-induced ST segment depression decreased by 0.6 ± 0.3 mm, group maximal heart rate increased by 20 ± 9 beats/min, and group systolic blood pressure at peak exercise increased by 24 ± 10 mm Hg, compared with pre-PTCA values (p < .001). However, no group differences were noted in these variables between the three post-PTCA stages. Myocardial perfusion in the distribution of the affected (dilated) coronary artery, on the other hand, improved progressively. In the 45 degree left anterior oblique view for instance, myocardial perfusion increased at 9 days after PTCA (from 68 ± 24% before PTCA to 91 ± 9%, p < .001) and at 3.3 months after PTCA (101 ± 8%, p < .05 vs 9 days after PTCA), but no further significant changes were seen at 6.8 months after PTCA (102 ± 8%). Similar changes were noted in the other two views. No relationship between minor complications during PTCA and delayed improvement on the 201Tl was observed. Myocardial ischemia was diagnosed in 12 of the 43 scans recorded a few days after PTCA, but in none recorded at later stages. We conclude that 201Tl scans after PTCA often show delayed improvement and therefore, an abnormal myocardial perfusion scan soon after PTCA does not necessarily reflect residual coronary stenosis or recurrence.


PERCUTANEOUS transluminal coronary artery angioplasty (PTCA) has been shown to improve exercise tolerance and to prevent stress-induced myocardial ischemia in selected patients with coronary artery dis- ease (CAD).1-9 In most patients myocardial perfusion, as measured by stress thallium-201 (201Tl) myocardial scintigraphy, improves or becomes normal after PTCA.2, 6, 9 However, limited information is available regarding the time sequence of such changes in myocardial perfusion. The objective of this study was thus to sequentially assess quantitative myocardial perfusion scintigraphy in selected patients undergoing complete revascularization with PTCA.

Methods

Patient population. Forty-three patients undergoing PTCA at our institution, 30 men and 13 women 37 to 70 years of age (mean 56 ± 8), were prospectively selected for this investiga-
tion if they met the following criteria: (1) single-vessel CAD without prior myocardial infarction, (2) stable clinical condition allowing exercise studies before elective PTCA, (3) successful PTCA, (4) no major complication during PTCA, and (5) no clinical or angiographic evidence of recurrence up to 6 to 9 months after PTCA. In each patient chronic stable angina was present for periods ranging from 4 months to 5 years; 11 patients were in New York Heart Association class I, 19 patients were in class II, and 13 patients belonged to class III. Coronary cineangiography disclosed a single significant atherosclerotic lesion in the left anterior descending coronary artery in 29 patients, the right coronary artery in nine patients, and the left circumflex coronary artery in the remaining five patients. Left ventricular cineangiography was normal in all participants.

Study design. Since the aim of this study was to sequentially assess myocardial perfusion changes, stress 201Tl myocardial perfusion imaging was performed within 15 days before PTCA, within a few days after PTCA, and 6 months after PTCA. When possible, some patients underwent an additional study at 3 months after PTCA, but this was not necessary for their admission into this investigation.

Patients were generally treated with nitrates, β-adrenergic receptor-blocking agents, or calcium-channel blockers, alone or in combination, before PTCA and these drugs were not routinely discontinued to perform exercise studies. After successful PTCA antianginal agents were discontinued and patients were placed on platelet aggregation inhibitors (an oral combination of 75 mg dipyridamole plus 330 mg aspirin every 8 hr), which were continued for the duration of this investigation. The study protocol was approved by our Institutional Ethics Committee. A signed informed consent was obtained from each patient.

Exercise testing and myocardial perfusion studies. Standard equipment and techniques were used to perform both exercise testing and myocardial perfusion imaging. Briefly, all exercise studies were performed in the morning hours on a treadmill machine according to the Bruce protocol. The exercise end points were symptoms of moderate and progressive intensity or fatigue. A three-lead electrocardiogram was continuously monitored and a 12-lead electrocardiogram was recorded every 3 min, at peak exercise, and at 1 and 2 min after exercise. The ST segment displacement was quantitated as the vertical distance from the baseline (TP segment) 80 msec after the J point. Measurements represented the average value of 5 beats in the electrocardiogram lead showing maximal displacement in the first exercise test; thereafter individual observations were made in the same electrocardiographic lead.

At peak exercise 2 mCi (74 MBq) of 201Tl was injected in a peripheral arm vein and the patient exercised for an additional 30 to 60 sec. Stress imaging began 3 to 4 min after stopping exercise. Each planar image contained 300,000 counts that were recorded successively in the 45 degree left anterior oblique (LAO), anterior, and 75 degree LAO projections, with the exact acquisition time (in seconds) being noted. Redistribution images were recorded 180 min later, with the acquisition time being exactly the same, in each view, as the initial images. Scintigrams were recorded with a conventional Anger type scintillation camera equipped with a low-energy, all-purpose, parallel-hole collimator, and interfaced to a nuclear medicine computer system. A 20% energy window centered on the 80 keV x-ray peak and another independent 20% window centered on the 167 keV photopake were used. Data were collected in 128 x 128 matrix and stored on floppy disks.

Quantitative analysis of 201Tl myocardial perfusion images. A new computer-assisted method for analyzing 201Tl myocardial perfusion images was used to comparatively assess the sequential perfusion studies.10 With this method (figure 1), first, each raw image underwent a standard nine-point weighted smoothing followed by a modified interpolative background subtraction.11 Then, an ellipse, defined by its short and long axes, was created around the preprocessed images with the use of an in-house algorithm. In each view the long axis of the ellipse was always aligned with the apex of the left ventricle. The two axes were manually defined as many times as necessary (usually two or three times), until the resultant ellipse was located one pixel away from the edge of the actual myocardial activity (exception taken at the level of the valve plane). Finally, the program automatically divided the ellipse by several radii 30 degrees apart, starting at the apex of each image (zero degrees), and progressing in a counterclockwise manner.

The functional status of each coronary artery was assessed according to the topographic distribution noted in figure 2. 201Tl activity in the segments included between 30 and 120 degrees (septal) in the 45 degree LAO view, 240 and 330 degrees (anterolateral) in the anterior projection, and 30 and 120 degrees (anterior) in the 75 degree LAO projection was ascribed to perfusion territory of the left anterior descending coronary artery. Those segments included between 30 and 120 degrees (inferior) in the anterior view and between 240 and 330 degrees.
FIGURE 2. Schematic representation of the topographic distribution assigned to each coronary artery during quantitative analysis of $^{201}$TI myocardial perfusion images. The septal (SEPT), postero- lateral (POST-LAT), anterolateral (ANT-LAT), inferior (INF), anterior (ANT), and inferoposterior (INF-POST) segments were 90 degree ellipsoid sectors that represented specific coronary arteries (see text). INF-AP = infero-apical.

(inferoposterior) in the 75 degree LAO projection were considered to represent perfusion territory of the right coronary artery. The segment between 240 and 330 degrees (posterolateral) in the 45 degree LAO view was ascribed to the circumflex coronary artery. The apical segment in each view (330-0-30 degrees) was not considered to represent the territory of any given coronary artery since the coronary distribution overlaps in this region.

Regional myocardial perfusion. Mean count per pixel in the segmental distribution of the normal coronary arteries was considered to represent myocardial perfusion of 100% (normal myocardial perfusion). Perfusion of the myocardium in the topographic distribution of the diseased (dilated) coronary artery was quantitated as the mean count per pixel in those segments and it was expressed (in percent units) relative to the segments perfused by normal coronary arteries. This process was repeated in each of the three views. For purposes of this investigation, emphasis was placed on the stress images (those recorded immediately after exercise) since the degree of myocardial ischemia (degree of myocardial perfusion) induced by the stress of exercise is accurately reflected in stress images. The reperfusion (rest) images were useful to determine the degree of reversibility of underperfused segments.

To avoid observer bias, determinations of regional mean count rates in each planar image were carried out by two observers unaware of the patients’ clinical status, results of coronary cineangiography, or date of PTCA. Furthermore, scans were analyzed individually in random order. Only after this stage of analysis was completed, were observers unblinded as to the diseased vessel (dilated) so that they could express the myocardial perfusion of the respective segmental distribution in percent units, as noted above. The results from the two observers were averaged to obtain a single quantitative interpretation of each segmental myocardial perfusion.

Intraobserver and interobserver variability of quantitative thallium-$^{201}$ regional myocardial perfusion. To assess the intraobserver and interobserver variability of this new quantitative method, the scans of 20 patients were analyzed by two independent observers. Each scan was analyzed twice by each observer in sessions separated by at least 2 weeks. There were 10 normal subjects and 10 patients with CAD. The former group included patients with atypical chest pain who were found to have normal coronary cineangiograms at cardiac catheterization. The latter group consisted of patients with documented CAD by coronary cineangiography, including five patients with previous myocardial infarction. The variability of the results was quantitated by: (1) the intraobserver and interobserver correlation coefficients calculated by linear regression analysis, and (2) the SEE calculated for each correlation. In addition, the 95% confidence interval, used to define a significant change in seg-

mental myocardial perfusion during consecutive studies in the individual subject, was determined by calculation of the pooled variance as applied to sequential quantitative radionuclide cardiac studies.12, 13

Coronary artery cineangiography and PTCA. Coronary cineangiography was performed by use of standard procedures and equipment during left heart catheterization. The Judkin’s technique was employed; multiple views, including cranio-caudal angulations, were recorded at 30 frames/sec. The severity of the coronary artery stenosis was expressed as a percentage of the luminal diameter of the unaltered vessel just proximal and distal to the stenosis. Measurements were made in at least three oblique projections and the individual values were averaged. Only lesions producing a diameter stenosis of 50% or more were considered significant. Standard equipment and techniques14 were used to perform PTCA. Successful PTCA was defined as that producing at least a 20% reduction in percent stenosis (diameter of stenosis) and persisted while the patient was in the laboratory.3 Recurrence of disease (restenosis) was considered to be present if there was an increase in percent diameter stenosis equal or greater than 50% of the initial gain achieved at PTCA or if diameter stenosis at follow-up angiography was more severe by at least 30% compared with the immediate post-PTCA diameter stenosis.13 For the purposes of this investigation, a major complication of PTCA was considered to be present if a long (8 mm or more) spiral dissection associated with slow distal filling was seen at the end of the procedure, or an acute myocardial infarction developed (diagnosed by the presence of at least two of the three standard criteria — clinical, electrocardiographic, and enzymatic). A short (less than 8 mm) and tenuous line of coronary artery dissection at the site of PTCA noted at the end of the procedure was considered a minor complication when this was not associated with slow distal filling or acute myocardial infarction.

Statistical analysis. Two-way analysis of variance was used to define the group differences in myocardial perfusion, coronary artery stenosis, and exercise variables before PTCA, and immediately and 6 months after PTCA. Group data at 3 months after PTCA were compared with those at 6 months with use of the t test for unpaired observations, since only part of our study group had measurements performed at 3 months after PTCA. A p value of .05 or less was considered indicative of a statistically significant difference.

Results

Clinical and angiographic results. From 394 patients who underwent PTCA from July 1983 to March 1985, a total of 108 patients had single-vessel CAD and no clinical, electrocardiographic, or angiographic evidence of prior myocardial infarction. Exercise studies were not performed before PTCA in 39 patients because of their unstable clinical condition, a decision made by the patients’ own cardiologists. Among the remaining 69 patients, successful PTCA without major complications was accomplished in 67 patients. Follow-up serial myocardial perfusion studies or coronary cineangiograms after PTCA were not available in 10 patients because of refusal (eight patients) or loss to follow-up (two patients). Thus, the remaining 57 patients with primary successful PTCA underwent pre- and post-PTCA perfusion and angiographic studies according to our study protocol. This population was

CIRCULATION
divided into two groups according to the final outcome: one group consisted of 14 patients with recurrence of CAD and the other of 43 patients without evidence of recurrence of CAD. The latter group constituted the study group proper. In 20 of these 43 patients a minor complication, as defined earlier, was present.

All 43 patients in the study group underwent follow-up cardiac catheterization between 6 to 9 months after PTCA, with mean of 203 ± 35 days after PTCA. There was significant improvement in mean coronary artery diameter stenosis from 76 ± 11% before PTCA to 23 ± 10% immediately after PTCA (p < .001), but it did not significantly change further at 6 to 9 months after PTCA (19 ± 14%, p > .05). The mean pressure gradient across the stenotic lesions fell from 50 ± 11 mm Hg before PTCA to 9 ± 4% mm Hg immediately after PTCA (p < .001). Pressure gradient was not measured during follow-up cardiac catheterization.

Exercise results. Patients in the study group proper remained asymptomatic up to the time of last follow-up. According to the study design, exercise and 201TI myocardial perfusion studies were performed 10 ± 4 (range 1 to 15) days before PTCA and 9 ± 5 (range 4 to 18) days, 3.3 ± 0.6 (range 2 to 4) months, and 6.8 ± 1.2 (range 6 to 9) months after PTCA. As noted in table 1, the mean treadmill walking times and the average maximal rate-pressure products attained during exercise were significantly higher (p < .001) at all stages after PTCA when compared with the respective values before PTCA. The mean exercise-induced ST segment depression on the electrocardiogram was significantly lesser (p < .001) during all post-PTCA measurements, in spite of the higher workloads attained, than that before PTCA.

Variability of quantitative regional myocardial perfusion analysis. With the use of the method of analysis of 201TI myocardial scintigrams described in this study, the intraobserver variability was minimal (r = .98 for one operator and r = .96 for the second operator). Likewise, there was a close correlation between the interpretations of both observers (r = .94 to r = .90). The SEE varied between 3% and 7% units. The pooled variance of repeated (twice) measurements of regional myocardial perfusion in 180 myocardial segments was 7.6% for one observer and 9.3% for the second observer. Thus, by this quantitative method an individual 201TI regional myocardial perfusion difference of 10% or more in two different studies was considered significant (p < .05). Changes of less than 10% in an individual patient can be considered to represent physiologic variation or statistical noise.

Sequential regional myocardial perfusion. Group values for regional myocardial perfusion before and after PTCA are listed in table 2. Before PTCA, myocardial perfusion in the segments corresponding to the dilated coronary artery (affected segments) was markedly reduced relative to that in the regions supplied by normal coronary arteries (normal segments) in each of the three views. Immediately (4 to 18 days) after PTCA, perfusion in the affected segments improved significantly (p < .001) without, however, resulting in complete normalization. At 2 to 4 months after PTCA, further improvement in regional myocardial perfusion was observed in the affected segments (p < .05). At 6 to 9 months after PTCA, myocardial perfusion in the affected segment remained normal, with quantitative group values similar to those at 2 to 4 months after PTCA. Myocardial perfusion in the apical region also improved progressively after PTCA, with no significant group change taking place between 2 to 4 months and 6 to 9 months after PTCA. Illustrations of the typical sequential regional myocardial perfusion pattern before and after PTCA showing progressive, not

| TABLE 1 | Exercise test results in 43 patients with single-vessel CAD before and after successful PTCA and no evidence of restenosis |
|-----------------------------------------------|-------------------|-------------------|-------------------|-------------------|
|                                             | 1–15 days          | 4–18 days     | 2–4 months      | 6–9 months      |
|                                             | before PTCA (n=43) | (n=43)         | (n=31)           | (n=43)           |
| Treadmill walking time (sec)                | 443 ± 133a         | 546 ± 116     | 598 ± 135       | 603 ± 152       |
| Peak heart rate (beats/min)                 | 127 ± 25a          | 147 ± 24      | 153 ± 23        | 148 ± 25        |
| Peak systolic blood pressure (mm Hg)        | 163 ± 18a          | 187 ± 19      | 189 ± 22        | 190 ± 22        |
| Peak rate-pressure product (mm Hg*beats/min) | 206 ± 18a          | 275 ± 32      | 289 ± 29        | 282 ± 31        |
| Maximal ST segment depression (mm)           | 1.7 ± 0.9a         | 0.9 ± 0.9     | 0.9 ± 0.8       | 0.9 ± 0.8       |

Group results are expressed as the mean ± SD.

*p < .001 vs each post-PTCA stage. No significant differences were noted between post-PTCA stages.
immediate, improvement are presented in figures 3 and 4.

In 17 of the 43 patients, stress myocardial perfusion in the affected segment improved in the interval between 3 to 18 days and 2 to 9 months after PTCA by 10% or more. This subgroup of patients had clinical, electrocardiographic, exercise, and angiographic characteristics similar to those of the entire group during each stage, including 3 to 18 days after PTCA. During blind interpretation of perfusion scans, “myocardial ischemia” was diagnosed or suspected in 12 of the 43 patients, as determined by qualitative and widely used commercially available quantitative techniques used routinely in our laboratory for diagnostic purposes.16–18 All 12 patients belonged to the subgroup of 17 patients with significant scintigraphic improvement at later stages (figure 5).

The possible role of trauma at the site of angioplasty on sequential regional 201TI myocardial perfusion images was investigated by dividing our patient population into two subgroups according to the presence or absence of recognizable trauma and comparing their results. There were 20 patients in whom mild intimal dissection was observed at the end of the procedure. Sequential quantitative stress segmental myocardial perfusion in this group of patients was not significantly different from that observed in the remaining 23 patients in whom coronary artery dissection was not observed after PTCA, as noted in table 3.

Additional analyses were performed to assess whether segmental stress 201TI myocardial perfusion 4 to 18 days after PTCA correlated with: (1) the severity of disease given by the percent coronary artery stenosis before PTCA, (2) the severity of disease given by the pressure gradient across the coronary lesion before PTCA, (3) the duration of angina before PTCA (in months), (4) the total (cumulative) time of balloon inflation (in seconds), (5) the residual coronary artery stenosis immediately after PTCA, and (6) the residual pressure gradient across the dilated lesion immediately after the procedure. Because the data on all these variables are continuous, correlation with quantitative myocardial perfusion was assessed by regression analysis. The correlation coefficients were .28, .16, .31, .23, .39, and .19, respectively (p > .05).

For completeness, the group results of the redistribution scans are also shown in tables 2 and 3. Group redistribution 201TI activity in the affected segments and the apex in each view was significantly less before PTCA than during each post-PTCA stage. In addition, 201TI activity was consistently less at 4 to 18 days after PTCA than at 2 to 4 or 6 to 9 months after PTCA, although the differences did not reach statistical significance except in the affected segment in the 45 degree LAO view (table 2). When examining individual results, the number of myocardial segments with perfusion of 90% or less was 146 of 258 before PTCA, 68 of 258 4 to 18 days after PTCA, 16 of 186 2 to 4 months after PTCA, and 29 of 258 segments 6 to 9 months after PTCA (57%, 26%, 9%, and 11%, respectively). Each of the 17 patients whose stress myocardial perfusion scans showed progressive improvement had at least one segment with perfusion quantitated at 90% or less in the redistribution scans at 4 to 18 days after PTCA.
significant differences in the redistribution segmental $^{201}$TI myocardial activity between patients with and without minor trauma during PTCA were noted (table 3).

Discussion

The results of this study demonstrate that myocardial perfusion, as measured by exercise $^{201}$TI cardiac scintigraphy, does not return to normal immediately after successful revascularization in up to one-third of patients. Several mechanisms could account for these findings: local trauma at the site of PTCA or persistent distal vasoconstriction, metabolic abnormalities secondary to chronic repeated episodes of myocardial ischemia ("hibernating myocardial perfusion state"), metabolic abnormalities secondary to acute myocardial ischemia produced by balloon inflation during PTCA ("stunned myocardial perfusion state"), or a combination of these mechanisms. An abnormal stress $^{201}$TI myocardial scan soon after PTCA does not necessarily reflect residual coronary stenosis or recurrence of coronary artery disease.

Quantitative computer method to assess myocardial perfusion in patients with single-vessel CAD. The method described in this study allows sequential quantitative assessment of regional myocardial perfusion in patients with single-vessel CAD. It is best suited for serial follow-up studies after interventions such as medical therapy or coronary artery revascularization. The potential advantages of this technique include the assessment of transmural rather than peak pixel activity, the use of an ellipse rather than a circle to define the myocardial region of interest, and its simplicity. The intraobserver and interoperator variabilities are comparable to those for other quantitative techniques for assessment of $^{201}$TI perfusion scans.\(^{16}\)

FIGURE 3. Changes on stress myocardial perfusion scintigram (45 degree LAO view) and coronary cineangiogram of a patient with successful and uncomplicated PTCA to the left anterior descending coronary artery. Note the gradual, not immediate, improvement in stress myocardial $^{201}$TI activity in the septal segment (arrows). Myocardial perfusion in the septum was 43% before PTCA, 82% immediate (7 days) after PTCA, 101% at 3 months after PTCA, and 103% at 6 months after PTCA. Coronary cineangiography showed a proximal (arrows) 90% diameter stenosis before PTCA, 20% stenosis immediately after PTCA, and 15% stenosis at 6 months after PTCA.

FIGURE 4. Sequential stress $^{201}$TI myocardial images, 45 degree LAO projection, in a patient with single-vessel CAD (proximal left anterior descending coronary artery) who underwent successful PTCA. This vessel had a proximal lesion quantitated at 90% diameter stenosis before PTCA, 15% immediately after PTCA, and 25% at 6 months after PTCA. Note the progressive, not immediate, improvement in septal $^{201}$TI uptake (arrows) after PTCA. Regional septal radiotracer uptake was quantitated at 52% before PTCA (PRE), 72% at 5 days after PTCA (IMM), 101% at 3 months after PTCA (3-Mo), and 98% at 6 months after PTCA (6-Mo). Likewise, apical $^{201}$TI uptake was 56%, 78%, 94%, and 91%, respectively.
Most quantitative techniques used to analyze 201Tl myocardial perfusion scans use “circumferential profiles” and the “hottest pixel” in each radius several degrees apart.16,17 From a theoretical point of view, segmental myocardial perfusion should be best reflected by the average count rate of all pixels in that segment rather than by the hottest pixel in radii several degrees apart. In a previous study, Lim et al.9 described a technique that used both an ellipse and a bandlike myocardial region of interest (transmural activity) rather than peak pixel activity to decrease position-dependent errors. We expanded the concept of assessment of regional perfusion by count rate measurements in larger, more representative regions of interest. By

TABLE 3
Comparative sequential stress (and reperfusion) regional 201Tl myocardial activity in the affected segments before and after PTCA in 20 patients with and 23 patients without mild intimal dissection

<table>
<thead>
<tr>
<th></th>
<th>45 degrees LAO</th>
<th>Anterior</th>
<th>75 degrees LAO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before PTCA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dissection present</td>
<td>69.1 ± 24.1^a (82.8 ± 15.3)^a</td>
<td>91.9 ± 21.3^a (94.5 ± 12.0)^a</td>
<td>72.0 ± 22.5^a (83.3 ± 13.5)^a</td>
</tr>
<tr>
<td>Dissection absent</td>
<td>66.7 ± 21.3 (86.0 ± 13.3)</td>
<td>91.5 ± 16.7 (96.7 ± 11.2)</td>
<td>69.9 ± 23.2 (84.5 ± 12.8)</td>
</tr>
<tr>
<td>4–18 days after PTCA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dissection present</td>
<td>90.2 ± 8.5^a (93.9 ± 9.6)^a</td>
<td>99.5 ± 10.2^a (100.3 ± 6.1)^a</td>
<td>96.1 ± 9.1^a (96.3 ± 7.9)^a</td>
</tr>
<tr>
<td>Dissection absent</td>
<td>89.9 ± 10.4 (95.5 ± 7.8)</td>
<td>98.6 ± 8.6 (99.3 ± 5.3)</td>
<td>92.9 ± 8.2 (95.7 ± 8.1)</td>
</tr>
<tr>
<td>6–9 months after PTCA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dissection present</td>
<td>100.7 ± 9.6^a (101.0 ± 6.0)^a</td>
<td>109.4 ± 8.8^a (103.6 ± 5.1)^a</td>
<td>102.8 ± 7.1^a (100.9 ± 6.4)^a</td>
</tr>
<tr>
<td>Dissection absent</td>
<td>104.4 ± 7.9 (100.0 ± 5.1)</td>
<td>109.5 ± 10.1 (103.9 ± 5.6)^a</td>
<td>103.8 ± 6.9 (99.3 ± 6.9)</td>
</tr>
</tbody>
</table>

Perfusion of the region supplied by the dilated vessel is expressed as a percentage of the perfusion in segments supplied by normal coronary arteries (see text).

Group values represent the mean ± SD.
^p > .05 vs the group with dissection absent.
using a pie-shaped segment limited by two radii 30 degrees apart and the ellipse, our method includes myocardial segments that are parallel instead of only those that are perpendicular to the gamma camera detector, as is the case with other quantitative techniques.9, 16, 17

Clinical and angiographic effects of PTCA. It was not surprising that patients in the study group proper showed significant clinical improvement, as reflected by improved exercise tolerance and diminished exercise-induced ST segment depression, after PTCA since only those with a successful procedure and without recurrence or progression of disease were included. This information is not new. Clinical improvement after successful PTCA has been repeatedly demonstrated.1–9 What is new is that clinical improvement was apparent soon after PTCA (within a few days) and that no further changes in treadmill walking time or ST segment depression were noted at 2 to 4 and 6 to 9 months after PTCA. Clinical improvement was concordant with angiographic improvement, i.e., quantitative angiographic improvement was similar immediately and 6 to 9 months after PTCA.

Sequential myocardial perfusion after PTCA. In this study we documented the sequential changes in myocardial perfusion as assessed by 201Tl myocardial scintigraphy after successful uncomplicated revascularization with PTCA. All patients with major complications, those with unsuccessful PTCA, and those with recurrence of CAD or with progression of the disease elsewhere in the coronary tree were excluded. In addition, a relatively large number of patients were excluded because of our inability to perform all the investigations scheduled. The 43 patients studied represent 40% of the 108 candidates who met the initial entry criteria for the study.

Myocardial 201Tl uptake is dependent on both delivery of the radiotracer (myocardial blood flow) and myocardial cell uptake.19 Before PTCA, markedly abnormal perfusion scintigrams during exercise were the result of both diminished regional coronary blood flow and diminished cellular uptake of 201Tl. Two possible mechanisms may explain the persistently abnormal stress 201Tl myocardial scintigrams observed a few days after successful PTCA but not that at 2 to 4 or 6 to 9 months after PTCA. These mechanisms include a reduced regional blood flow or an impaired regional myocardial uptake of 201Tl. In support of the first mechanism, regional myocardial blood flow has been reported to remain diminished for some time after brief periods of experimental myocardial ischemia, despite total release of the coronary artery occluder used to produce temporary ischemia.20, 21 Although blood flow in those studies was only measured at rest, it remains possible that regional blood flow during exercise in our patients may have remained depressed for several days after successful PTCA. More relevant to our findings, in a recent clinical study Johnson et al.22 were able to show that in one-third of patients undergoing successful PTCA, coronary luminal area measured at 6 to 7 months after the procedure was significantly greater than that measured immediately after PTCA. They measured coronary luminal area by quantitative coronary angiography, with absolute area measurements, and by videodensitometry (based on integrated optical contrast density not dependent on edge identification). In the present study we did not confirm those findings. Furthermore, clinical and electrocardiographic markers of myocardial ischemia were absent during all post-PTCA stages, including a few days after PTCA at the time abnormal stress 201Tl myocardial scans were observed. In spite of our results suggesting that trauma/dissection was not an important factor, it is conceivable that transient and mild trauma, thrombosis, or spasm of the dilated coronary artery could have been present at the time of 201Tl scans (4 to 18 days after PTCA) but not at the time of angiography immediately after PTCA (the day PTCA was performed).

In support of the second mechanism to explain the delayed improvement of stress 201Tl myocardial scans, repeated episodes of transient myocardial ischemia have been shown to produce transient structural, biochemical, and functional abnormalities that may persist for variable periods of time up to 2 to 4 weeks after the ischemic insult.20, 23–28 Prolonged myocardial dysfunction has been produced by intermittent brief periods of coronary artery occlusion21, 29 and by subtotal coronary artery occlusion.30, 31 Although species differences in coronary anatomy make it inappropriate to extrapolate these data from animals to humans with chronic angina, there is ample evidence to support the existence of persistent functional abnormalities in human hearts at times when myocardial ischemia is no longer present.7, 32–38 This phenomenon has been referred in the literature as stunned or hibernating myocardium.38–40 In the present study, patients with chronic intermittent episodes of myocardial ischemia due to critical coronary artery stenosis, and with acute ischemia due to brief episodes of total coronary artery occlusion during PTCA, might have developed biochemical/metabolic abnormalities that persisted for several days after complete revascularization. An insufficient pool of energy precursors, shown to occur...
after experimental myocardial ischemia\textsuperscript{25–27} could be the intimate mechanism by which the active energy-dependent cellular uptake of \textsuperscript{201}TI (extraction) remained impaired for several days after successful PTCA in one-third of our patients. This biochemical/metabolic hypothesis is supported by the fact that there was a trend toward a subnormal \textsuperscript{201}TI segmental activity in the redistribution scans in a significant number of patients at 4 to 18 days after PTCA but not at later stages.

The results of the present investigation failed to give any insight into the pathophysiology of our scintigraphic findings. Local trauma (defined by the presence of a mild dissection) during PTCA, cumulative balloon inflation time, duration of angina before PTCA, severity of coronary artery disease before PTCA, and residual pressure gradient and coronary artery stenosis after PTCA correlated poorly with delayed improvement documented by quantitative \textsuperscript{201}TI perfusion scans.

\textbf{Potential limitations.} First, the fact that patients were taking various types of antianginal medications during pre-PTCA exercise tests should not affect our results, except perhaps in attenuating the effects of exercise-induced myocardial ischemia. Exercise duration may have been shorter and ST segment depression and regional myocardial hypoperfusion more marked if pre-PTCA exercise studies had been done after discontinuation of antianginal medications.\textsuperscript{18} This would not have affected our post-PTCA results or our conclusions. Second, routine administration of oral dipyridamole after PTCA, on the other hand, could have caused abnormal perfusion scans in the presence of residual coronary artery stenosis. It is unlikely that this took place selectively only immediately after PTCA and not at 2 to 4 or 6 to 9 months after PTCA, given that dipyridamole was administered to all patients at all stages after PTCA. Finally, the techniques we used to measure coronary artery stenosis were not sophisticated but had the virtue of being applied blindly and any errors would have been distributed equally in both immediate and 6 to 9 month post-PTCA angiographic data.

\textbf{Clinical relevance.} In patients with long-term successful PTCA, stress \textsuperscript{201}TI myocardial perfusion scintigraphy immediately (3 to 18 days) after the procedure showed a bimodal response. In approximately two-thirds of the patients tested, perfusion in the topographic distribution of the dilated vessel became normal, while in approximately one-third of patients an “ischemic” scintigraphic pattern was observed. In these patients, scans became normal during follow-up studies 2 to 9 months after PTCA. Isolated examples published previously\textsuperscript{2, 6,10} are in agreement with our findings. Thus, an abnormal stress \textsuperscript{201}TI myocardial perfusion study recorded a few days after PTCA does not necessarily reflect residual coronary artery stenosis or recurrence of coronary disease. These “abnormal” scans soon after PTCA may in fact simply represent a stunned or hibernating myocardial perfusion state, or reflect the transient effects of local trauma at the site of angioplasty, and not early restenosis.

We gratefully acknowledge the skillful assistance of Perry Anderson, RTNM, David McDougall, RTNM, Virginia Flintoft, BN, Christine Hall, RN, Diane Galbraith BN and Bonnie Spindler, RN, and the secretarial assistance of Sue Denyar.

\textbf{References}


33. Atkins CW, Pohost GM, Desanctis RW, Block PC: Selection of angina-free patients with severe left ventricular dysfunction for myocardial revascularization. Am J Cardiol 46: 695, 1980


40. Braunwald E, Rutherford JD: Reversible ischemic left ventricular dysfunction: Evidence for the "hibernating myocardium." J Am Coll Cardiol 8: 1467, 1986
Sequential thallium-201 myocardial perfusion studies after successful percutaneous transluminal coronary artery angioplasty: delayed resolution of exercise-induced scintigraphic abnormalities.

D E Manyari, M Knudtson, R Kloiber and D Roth

Circulation. 1988;77:86-95
doi: 10.1161/01.CIR.77.1.86

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1988 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/77/1/86

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/