Short- and Long-term Changes in Myocardial Perfusion After Percutaneous Transluminal Coronary Angioplasty Assessed by Thallium-201 Exercise Scintigraphy

HEINZ O. HIRZEL, M.D., KARL NUESCH, M.D., ANDREAS R. GRUENTZIG, M.D., AND URS M. LUETOLF, M.D.

SUMMARY Forty-nine patients in whom percutaneous transluminal coronary angioplasty (PTCA) was attempted were evaluated by thallium-201 myocardial scintigraphy after exercise and at rest before the intervention. After successful PTCA of a single stenosis in a native vessel (30 of 44 patients) and of a stenosis in an aortocoronary bypass graft (three of five patients), scintigraphy was repeated within 3 weeks in 30 patients. Long-term follow-up studies by scintigraphy at 5-6-month intervals up to more than 2 years (mean follow-up 18 months) were performed in 16 patients.

Before PTCA, clear-cut regions of decreased thallium-201 activity were observed in 43 of 49 patients. Thallium-201 activity within this zone was reduced to 74 ± 1% (SEM) of maximal myocardial thallium-201 activity after exercise, but returned to normal (> 80%) at rest (88 ± 1%, p < 0.001). After PTCA, no distinct defects were recognizable in the region of previously decreased thallium-201 activity, and the respective values were 89 ± 1% after exercise at identical work loads (p < 0.001 compared with the corresponding values before PTCA) and 94 ± 1% (p < 0.01) at rest. These results paralleled the angiographic findings, which showed an increase in luminal diameter in the stenotic segment of the treated vessel from an average of 15 ± 2% of the pre- and poststenotic vessel diameter before PTCA to 67 ± 3% (p < 0.001) after PTCA. During long-term follow-up, thallium-201 activity remained normal after exercise in the entire heart in 13 of 16 patients. In three patients, a new defect in the same location as before treatment reappeared 4½, 6 and 29½ months after PTCA because the stenosis recurred, as documented by angiography.

We conclude that thallium-201 exercise scintigraphy permits the best documentation of the ongoing changes in myocardial perfusion after PTCA.

THE FEASIBILITY of instrumental exploration of the coronary arterial tree through a transaortic approach and its implications for removal of atheromatous tissue by retrograde curettage was first studied in dogs and human cadavers by May et al. Eight years later, Dotter and Judkins described a new nonoperative technique to dilate atherosclerotic obstructions of the femoral arteries by means of tapered catheters of different outer diameters. In 1976, Gruentzig reported encouraging results in the treatment of femoropopliteal and iliac artery obstructions using a double-lumen catheter with a nonelastic balloon at its tip. Once placed in the stenotic lesion, high pressure inflation of the balloon compressed the obstructing atheromatous material against the vascular wall, thereby enlarging the lumen. With miniaturization of the dilating catheter and with the development of appropriate guiding catheters adapted from the Judkins-type catheters for selective coronary arteriography, the system became suitable for the treatment of coronary artery stenoses.

The first successful percutaneous transluminal angioplasty (PTCA) of a severe proximal lesion of the left anterior descending coronary artery was performed in 1977. Since then, many patients have undergone PTCA at various institutions, and good results have been reported concerning the immediate arteriographic results. However, little is known about the evolution of dilated coronary artery stenoses. Whereas repeated arteriographic studies permit direct visualization of the ongoing changes in the treated vessels, the invasive character of PTCA, combined with a certain risk and discomfort for the patient, limits its serial use. Even though thallium-201 myocardial scintigraphy does not reveal morphologic changes in the vascular wall, it can be used to assess the functional capacity of the vessel and to demonstrate changes in myocardial perfusion after PTCA.

We analyzed the scintigraphic images in a subgroup of patients who underwent PTCA at our institution. Specifically, we examined the patterns obtained before PTCA, within 3 weeks after PTCA, and at 5-6-month intervals after PTCA in a subgroup of patients.

Methods

Patient Population

Forty-nine patients, 43 men and six women, scheduled for PTCA were studied by thallium-201 scintigraphy within 3 weeks before the dilation procedure. They ranged in age from 31-67 years (mean 49 years).

All patients presented with disabling effort-dependent angina. None of them had a history of
myocardial infarction. Selective coronary arteriography revealed a single vascular lesion of >70% narrowing of the luminal diameter in the proximal portion of the left anterior descending coronary artery (LAD) in 36 patients and of the left circumflex artery (LCX) in one patient. In seven patients a lesion of similar severity was found in the middle portion of the right coronary artery (RCA). Some patients had unstable angina pectoris. In other patients the severity of angina was increasing progressively. All these patients were poorly controlled by medical treatment alone and were therefore considered candidates for aortocoronary bypass surgery. As the lesions in these patients were ideal for dilation, a trial with PTCA was undertaken. Five patients had undergone aortocoronary bypass surgery that was not completely successful. The recurrence of angina required arteriographic reevaluation, which showed a localized stenosis of the bypass graft to the LAD at the site of graft implantation in one patient, localized stenosis of grafts to a posterolateral branch of the LCX in two patients and to the RCA in the last two patients.

PTCA was initially successful in 30 of 44 patients with a stenosis in a native coronary vessel and in three of five patients with a stenotic aortocoronary bypass graft. Success was assessed by the reduction of the pressure gradient across the narrowing measured during the pullback of the dilating catheter and by arteriography immediately after dilation. In 16 of 49 patients, the stenotic lesion could not be dilated, either because the catheter could not be passed across the stenotic segment or because the lesion resisted the pressure of the dilating balloon, probably due to calcification or fibrosis.

Thirty of the 33 patients with initially successful PTCA were restudied scintigraphically within 3 weeks after the procedure and repeated scintigraphic follow-up studies at 5–6-month intervals could be obtained in 16 of them.

Thallium-201 Myocardial Scintigraphy

To perform myocardial imaging after exercise, the fasting patients exercised on a bicycle ergometer in the upright position until the appearance of angina or pathologic changes in the three-lead ECG (leads V₂, V₄, and V₆) recorded continuously during the stress test or until submaximal heart rate was achieved under steady-state conditions. At this point, 1.5 mCi of thallium-201 chloride (New England Nuclear) were injected i.v. and the patient continued to exercise for another 2 minutes. Imaging was started 5 minutes after exercise.

Scintigrams were obtained in the 45° and 60° left anterior oblique, anterior and left lateral positions by rotation of the gamma camera head over the supine patient. Using a Picker Dyna camera (model 4/12) with a parallel-hole collimator peaked at 69–83 keV, 250,000-count analog images were recorded on Polaroid prints or CRT x-ray film. Data were accumulated with a PDP-11 computer (Digital Equipment) using the gamma-11 program. In addition, the images were digitized on an Elscint-CTP-system, enhanced by a five-point smoothing procedure and displayed in a single frame of 96 × 96 matrix elements (zooming) in eight colors with an additional color to indicate overrange. This preset color count range, comprising 32 or 64 counts/cell, was set by adjusting the base of the color count range such that only one cell within the myocardial wall showed overrange activity. Comparing the number of counts/cell as indicated by its color with the number of counts in cells with maximal activity (i.e., the cells whose color was second to the color indicating overrange activity), the relative activities within each cell overlaying the myocardial wall could be calculated whereby constant background activity was assumed (fig. 1). This assumption was necessary because true retromyocardial background cannot be determined in vivo, but it also appeared to be a reasonable one on the basis of the experimental work of Narahara and colleagues.¹¹

The images were printed in life-size on paper using a nine-color printer. Based upon earlier observations, a perfusion defect was defined as a transmural segment with a circumferential length at least equal to wall thickness showing less than 80% of maximal myocardial thallium-201 activity. To identify exactly the nature of perfusion defects on the exercise scintigrams, imaging was repeated after a 4-hour rest.

The scintigraphic evaluation was repeated 3 weeks after PTCA. Care was taken to record the exercise scintigrams at the same work load and duration of exercise as before PTCA. All subsequent exercise studies were performed after more strenuous, but still submaximal, exercise.

Evaluation of the Severity of Coronary Artery Stenosis

The degree of coronary artery or bypass graft narrowing was expressed as a percentage of the pre- and poststenotic luminal diameter. For this purpose the diameters of the vessel within the stenosis at its narrowest portion and of the unaltered vessel just proximal and distal to the stenosis were measured in at least three oblique projections in the selective arteriograms performed before and after PTCA.¹³ The individual values were averaged.

Statistics

The results were expressed as mean ± SEM. The paired t test was used to evaluate the statistical significance of differences between groups.

Results

The focuses of the scintigraphic examination were (1) documentation of ischemia before PTCA, i.e., the detection of a significant exercise-induced reduction of myocardial thallium-201 activity within a circumscribed region; (2) detection of immediate changes in the distribution of thallium-201 activity after successful PTCA; and (3) long-term follow-up.

Scintigraphic Findings Before PTCA

Whereas all 49 patients evaluated before the intervention complained about disabling angina on ex-
tion, thallium-201 scintigraphy disclosed typical isolated zones of reduced activity after exercise that filled in as redistribution occurred in at least one projection in 43 patients (88% sensitivity). The location of this exercise-induced defect corresponded closely to the arteriographic findings. None of the patients exhibited a constant defect that indicated scarred tissue. In six patients, however, no distinct abnormality was found on either the exercise or the resting scintigram. The reason for this was probably insufficient stress in four patients, as the exercise heart rate did not exceed the resting heart rate by more than 15 beats/min. In the other two patients, the scintigrams showed inhomogenous thallium-201 uptake in all regions, which did not permit the diagnosis of a distinct defect according to the given definition. In the entire group, thallium-201 activity in the region supplied by the stenotic artery averaged 74 ± 1% of maximal activity after exercise which returned to normal at rest, i.e., to 88 ± 1% (p < 0.001) (fig. 2).

Scintigraphic Findings Immediately After PTCA

Within 3 weeks after successful PTCA, 31 thallium scans were obtained in 30 patients. (In one patient, a second dilation was performed when the stenosis recurred 6 months after the first PTCA documented by scintigraphy and by selective arteriography [fig. 3]). The scintigrams repeated under exercise conditions identical to those before PTCA revealed a significant increase in thallium-201 activity in the previously ischemic region in 28 cases; in the three successful cases without a clear-cut, exercise-induced defect in the scintigrams obtained before PTCA, the activity in the suspected region was either identical (one case) or only slightly less but still normal (two cases) after PTCA. Thus, thallium-201 activity after exercise in the region supplied by the treated artery (in which a marked reduction in thallium-201 activity after exercise with normalization at rest was noted before PTCA) averaged 89 ± 1% of maximal activity after exercise (p < 0.001 compared with the corresponding values before PTCA) and 94 ± 1% at rest (p < 0.01 compared with the exercise values).

The success of PTCA was documented arteriographically by the increase in luminal diameter in the stenotic portion of the artery. This change corresponded to the increase in thallium-201 activity after exercise (fig. 4). Although relative thallium-201 activity increased on the average from 74 ± 2% to 89 ± 1% (p < 0.001) of maximal thallium-201 activity after exercise in the region supplied by the treated artery after PTCA, the dilation procedure had caused an increase in luminal diameter of the vessel within the stenotic segment from an average of 15 ± 2% to 67 ± 3% (p < 0.001) of the pre- and poststenotic vessel diameter.
Scintigraphic Findings in the Long-term Follow-up

Sixteen patients were followed by repeated exercise scintigraphy at 5-6-month intervals up to 30 months (mean follow-up 18 months) after PTCA (fig. 2). After PTCA, the relative thallium-201 activity, which was reduced in the region of interest before treatment, had returned to normal. In four patients, the relative thallium-201 activity in this region increased further, and the shape of the scintographic image increasingly resembled a well-proportioned horseshoe figure, suggesting further improvement in perfusion with time (fig. 5). In four patients, the relative thallium-201 activity in the region of interest was again slightly diminished in the third or fourth scintigram, compared with the one after successful PTCA, but remained normal. These small differences may be explained by slightly different concentrations of the tracer accumulated each time in the heart. In three patients, the third or fourth scintigram again showed a limited reduction in thallium-201 activity in the same location as before PTCA and of similar magnitude. These patients were reexamined by arteriography, which disclosed a new stenosis of the LAD at the site of dilation. Therefore, PTCA was undertaken a second time in one patient, which again was successful. Both subsequent scintigraphic examinations showed normal relative thallium-201 activity (fig. 3). Selective coronary arteriography 6 months after the second dilation confirmed the scintigraphic findings. The other two patients received medical therapy.

Discussion

Since the first successful nonoperative transluminal coronary angioplasty in man performed in 1977,7 dilation of proximal coronary artery stenoses by means of a special catheter technique has received worldwide attention.14 Much technical experience has been gained in the past 2 years in the more than 200 patients who have undergone this procedure.18 However, little is known about the long-term benefits of PTCA. Although follow-up studies performed 4-6 years after dilation of peripheral artery stenoses yielded encouraging results,8 far more information about the long-term course of dilated coronary stenoses is needed before the method can be accepted as one form of treatment in coronary artery disease.

To visualize the primary effect of dilation and the ongoing changes in the dilated segment of the coronary vessel, selective coronary arteriography is the most direct approach. It is invasive, however, and so
Figure 3. Immediate and long-term follow-up scintigrams of a 42-year-old inspector in heavy industry who complained of severe angina on exertion for 3 months. The exercise scintigram disclosed a large region of diminished thallium-201 activity in the anteroseptal wall and fair redistribution at rest. Arteriography revealed a severe single stenosis of the left anterior descending coronary artery (LAD) before the branching off of the first diagonal vessel. Percutaneous transluminal coronary angioplasty (PTCA) was undertaken with excellent arteriographic and clinical results, and the scintigram performed 7 days after dilation showed a significant increase in thallium-201 activity in the region of the previous defect. The scintigraphic reevaluation 4½ months later again showed a defect after exercise that was identical in location and size to that present before PTCA. Arteriography disclosed the reappearance of the stenosis in the LAD. A second dilation was again successful. Consistent with the arteriographic appearance of the vessel after the second PTCA, the scintigrams performed 7 days later showed uniform thallium-201 activity in all regions of the myocardial wall after exercise and at rest. Similar results were obtained 5 months after the second PTCA.

Figure 4. Luminal diameter in the stenotic lesion relative to the pre- and poststenotic vessel diameter and relative thallium-201 activity in the region supplied by the affected artery after exercise before (black dot) and after (open circle) successful percutaneous transluminal coronary angioplasty in 31 instances (mean ± SEM). The shaded region indicates the range of normal thallium activity. The arrow connecting the two points intersects the 80% limit of relative thallium-201 activity at about 40% luminal diameter in the stenosis, indicating that a vascular lesion of more than 60% narrowing will lead to a significant reduction of thallium-201 activity in the region supplied by this artery after exercise.

has limited use for serial studies. Specific information about regional myocardial perfusion even during exercise can also be gained from noninvasive isotope studies. Among the many methods and tracers in use, exercise myocardial scintigraphy with thallium-201 is the most popular technique.

The findings of this study clearly show that thallium-201 exercise scintigraphy permits documentation of changes in regional myocardial activity after PTCA and prove its usefulness in documenting the success of the intervention. Moreover, the method
promises to be a reliable diagnostic tool in the long-term follow-up of these patients. Even though our experience was limited, the scintigraphic results parallel the arteriographic findings precisely.

Our results from more than 2 years of follow-up suggest that the beneficial effect of the dilation of coronary artery stenoses may last for years. The further increase in thallium-201 activity after exercise in the region supplied by the treated artery as time goes on, combined with a progressively more homogenous aspect of the restored wall segment, implies further improvement in perfusion, which is compatible with the arteriographic findings of greater vessel patency and wall smoothness. Early (within 6 months after dilation) and late recurrence of the stenosis at the site of dilation, however, may occur.

We questioned whether substantial peripheral embolization in the course of the compression of the atheromatous material against the vascular wall might cause microinfarctions. In none of the scintigraphic examinations performed after PTCA did we detect small, persistent zones of reduced thallium-201 activity in the region supplied by the treated artery suggesting small areas of necrosis.

The fact that PTCA was limited in this patient group to patients with one-vessel disease facilitated the interpretation of the scintigrams, because the reduction in myocardial thallium-201 activity was directly related to the one major coronary lesion present. Thus, this represents an ideal model to study the localization of thallium-201 defects in the ischemic ventricle of man and the relationship between vessel patency and regional thallium-201 uptake.

The semiquantitative scintigraphic approach used in this study provided an improvement in image analysis. Especially for serial examinations, this method is superior to visual estimation, and only quantification allows respective comparisons and graphic display. The wide variation of thallium-201 activity in different regions of the wall implies a wide range of normal, which therefore was defined as 80–100% of maximal myocardial thallium-201 activity. Based on this assumption and the relation of the changes in thallium-201 activity after exercise before and after PTCA to the increase in luminal diameter after dilation, it is evident that a coronary stenosis of 50–60% narrowing of the luminal diameter manifests itself scintigraphically after exercise.

We conclude that thallium-201 exercise scintigraphy, a completely noninvasive technique, clearly provides the best documentation of ongoing changes in myocardial perfusion after coronary artery dilation.

**Figure 5.** Immediate and long-term follow-up scintigrams of a 38-year-old football player who first presented in 1977 with intractable exercise-dependent angina. The exercise scintigram disclosed a large perfusion defect in the anteroseptal wall that filled in during the redistribution period. This suggested a significant lesion of the left anterior descending coronary artery, which was later documented by selective coronary arteriography. Percutaneous transluminal angioplasty (PTCA) successfully increased the diameter in the narrowing from 15 to 71% of the original vessel size. Scintigraphy performed 4 days after dilation showed a marked increase in thallium-201 activity in the anteroseptal wall after exercise. Repeated scintigraphic evaluations up to 27 months after PTCA revealed uniform thallium-201 activity in all regions of the myocardial wall. RAO = right anterior oblique, LAO = left anterior oblique.
Acknowledgment

We thank Alfred Pfeiffer for his help in recording the thallium scintigrams and Ruth Wegmueller for her skillful secretarial assistance.

References

13. Gruentzig A: Clinical experience with percutaneous transluminal coronary angioplasty (PTCA). In Steering Committee Report, Public Health Service, NIH, DHEW publication no (NIH) 80-0000, 1979
Short- and long-term changes in myocardial perfusion after percutaneous transluminal coronary angioplasty assessed by thallium-201 exercise scintigraphy.

H O Hirzel, K Nuesch, A R Gruentzig and U M Luetolf

_Circulation_. 1981;63:1001-1007
doi: 10.1161/01.CIR.63.5.1001

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1981 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/63/5/1001.citation

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/