20. Brown M, Marshall DR, Sobel BE, Bergmann SR. Delineation of myocardial oxygen utilization with carbon-11-labeled acetate. *Circulation* 1987;76:687–696.
21. Buxton DB, Nienaber CA, Luxen A, Ratib O, Hansen H, et al. Noninvasive quantitation of regional myocardial oxygen consumption in vivo with [1-^{11}C]acetate and dynamic positron emission tomography. *Circulation* 1989;79:134–142.
22. Buxton DB, Schwaiger M, Nguyen A, Phelps ME, Schelbert HR. Radiolabeled acetate as a tracer of myocardial tricarboxylic acid cycle flux. *Circ Res* 1988;63:628–634.
23. Armbrecht JJ, Buxton DB, Brunken RC, Phelps ME, Schelbert HR. Regional myocardial oxygen consumption determined noninvasively in humans with [1-^{11}C]acetate and dynamic positron tomography. *Circulation* 1989;80:863–872.
24. Adler LP, Blair HF, Makley JT, Williams RP, Joyce MJ, et al. Noninvasive grading of musculoskeletal tumors using PET. *J Nucl Med* 1991;32:1508–1512.
25. Haberkorn U, Strauss LG, Dimitrakopoulou A, Engenhart R, Oberdorfer F, et al. PET studies of fluorodeoxyglucose metabolism in patients with recurrent colorectal tumors receiving radiotherapy. *J Nucl Med* 1991;32:1485–1490.
26. Gambhir SS, Schwaiger M, Huang SC, Krivokapich J, Schelbert HR, et al. Simple noninvasive quantification method for measuring myocardial glucose utilization in humans employing positron emission tomography and fluorine-18-deoxyglucose. *J Nucl Med* 1989;30:359–366.
27. Tamaki N, Kawamoto M, Yonekura Y, Fujibayashi Y, Takahashi N, et al. Regional metabolic abnormality in relation to perfusion and wall motion in patients with myocardial infarction: assessment with emission tomography using an iodinated branched fatty acid analog. *J Nucl Med* 1992;33:659–667.
28. Nishimura T, Sago M, Kihara K, Oka H, Shimonagata T, et al. Fatty acid myocardial imaging using ^{123}I-beta-methyl-iodophenyl pentadecanoic acid (BMIPP): comparison of myocardial perfusion and fatty acid utilization in canine myocardial infarction (occlusion and reperfusion model). *Eur J Nucl Med* 1989;15:341–345.
29. De-Geeter F, Franken PR, Knapp F Jr, Bossuyt A. Relationship between blood flow and fatty acid metabolism in subacute myocardial infarction: a study by means of ^{99m}Tc-sestamibi and ^{123}I-beta-methyl-iodo-phenyl pentadecanoic acid. *Eur J Nucl Med* 1994;21:283–291.
30. Franken PR, De-Geeter F, Dendale P, Demoor D, Block P, et al. Abnormal free fatty acid uptake in subacute myocardial infarction after coronary thrombolysis: correlation with wall motion and inotropic reserve. *J Nucl Med* 1994;35:1758–1765.
31. Lerch RA, Bergmann SR, Ambos HD, Welch MJ, Ter-Pogossian MM, et al. Effect of flow-independent reduction of metabolism on regional myocardial clearance of ^{11}C-palmitate. *Circulation* 1982;65:731–738.
32. Kawamoto M, Tamaki N, Yonekura Y, Magata Y, Tadamura E, et al. Significance of myocardial uptake of ^{123}I-labeled beta-methyl iodophenyl pentadecanoic acid: comparison with kinetics of ^{11}C-labeled palmitate in positron emission tomography. *J Nucl Cardiol* 1994;1:522–528.
33. Wyns W, Schwaiger M, Huang SC, Buxton DB, Hansen H, et al. Effects of inhibition of fatty acid oxidation on myocardial kinetics of ^{11}C-labeled palmitate. *Circ Res* 1989;65:1787–1797.
34. Fox KA, Abendschein DR, Ambos HD, Sobel BE, Bergmann SR. Efflux of metabolized and nonmetabolized fatty acid from canine myocardium. Implications for quantifying myocardial metabolism tomographically. *Circ Res* 1985;57:232–243.
35. Samuel D, Paris S, Ailhaud G. Uptake and metabolism of fatty acids and analogues by cultured cardiac cells from chick embryo. *Eur J Biochem* 1976;64:583–595.
36. Gloster J, Harris P. Fatty acid binding to cytoplasmic proteins of myocardium and red and white skeletal muscle in the rat. A possible new role for myoglobin. *Biochem Biophys Res Commun* 1977;74:506–513.
37. Schelbert HR, Henze E, Phelps ME, Kuhl DE. Assessment of regional myocardial ischemia by positron-emission computed tomography. *Am Heart J* 1982;103:588–597.
38. Marshall RC, Tillisch JH, Phelps ME, Huang SC, Carson R, et al. Identification and differentiation of resting myocardial ischemia and infarction in man with positron computed tomography, ^{18}F-labeled fluorodeoxyglucose and ^{13}N-ammonia. *Circulation* 1983;67:766–778.
39. Schwaiger M, Schelbert HR, Ellison D, Hansen H, Yeatman L, et al. Sustained regional abnormalities in cardiac metabolism after transient ischemia in the chronic dog model. *J Am Coll Cardiol* 1985;6:336–347.
40. El Alaoui-Talibi Z, Moravec J. Carnitine transport and exogenous palmitate oxidation in chronically volume-overloaded rat hearts. *Biochim Biophys Acta* 1989;1003:109–114.

Dipyridamole Scintigraphy and Intravascular Ultrasound After Successful Coronary Intervention

Rainald Bachmann, Udo Sechtem, Eberhard Voth, Jörg Schröder, Hans W. Höpp and Harald Schicha
Departments of Nuclear Medicine and Internal Medicine, University of Cologne, Cologne, Germany

Despite angiographically successful interventions, perfusion defects are not uncommonly observed in postinterventional perfusion scintigrams. The aim of this study was to test the hypothesis that perfusion defects after coronary intervention are associated with a significant residual stenosis in the treated vessel segment detectable by intravascular ultrasound but not by angiography. **Methods:** Forty consecutive patients with angiographically successful coronary interventions were prospectively studied by intravascular ultrasound immediately after the intervention. Within 48 hr after the intervention all patients had myocardial scintigraphy using ^{99m}Tc-methoxyisobutyl-isonitrile SPECT after dipyridamole stress. Myocardial perfusion defects in the scintigram were assigned to a segmental left ventricular model and compared to the perfusion territory of the treated vessel estimated from the coronary angiogram **Results:** Twenty of 40 patients had reversible myocardial perfusion defects. Mean ultrasound area stenosis was 50% in these patients and 33% in patients without perfusion defects ($p < 0.002$); ultrasound percent plaque area was 75% versus 63% ($p < 0.0001$), respectively. The best concordance between residual area stenosis and perfusion defects was found for an ultrasound area stenosis ≥40%. **Conclusion:** Patients with stress-induced myocardial perfusion defects immediately after successful coronary intervention show high-grade residual stenoses that are more pronounced in patients with perfusion defects than in patients with normal postinterventional scintigrams. In addition, vessels serving myocardial regions with perfusion defects showed a significantly higher plaque burden indicating diffuse atherosclerotic changes in the vessel. The evaluation of the postprocedural result by intravascular ultrasound contributes to a better understanding of the discrepancy between the angiographic finding of a widely patent vessel but scintigraphic evidence of impaired perfusion.

Key Words: intravascular ultrasound; coronary intervention; dipyridamole; technetium-99m-MIBI; SPECT

J Nucl Med 1997; 38:553–558

Despite angiographically successful interventions, residual ischemia in the perfusion territory of the treated coronary artery is not uncommonly observed in postinterventional perfusion scintigrams. Reversible perfusion defects have been demonstrated by thallium scintigraphy in up to 40% of the patients after angioplasty (*1–4*). These patients seem to have a higher risk of developing restenosis within the next 6 mo. The pathophysiology underlying such persisting ischemia is not fully understood. Different explanations have been put forward: some authors claim a vascular dysregulation and an impaired coronary flow reserve to be responsible (*5,6*), whereas others suggest an impaired uptake of the radiotracer due to persisting metabolic abnormalities in the dependent left ventricular region (*2,7*). Still others suppose that abnormal thallium results after coronary intervention are due to inadequate dilatation of the target vessel or associated lesions (*8*).

Intravascular ultrasound is a relatively new method with the capability to clearly delineate the structure of the arterial wall and the extent of atherosclerotic plaque, allowing a more

Received Mar. 22, 1996; revision accepted Aug. 2, 1996.
For correspondence or reprints contact: Udo Sechtem, MD, Klinik III für Innere Medizin, Universität zu Köln, Joseph-Stelzmann-Str. 9, D-50924 Köln, Germany.

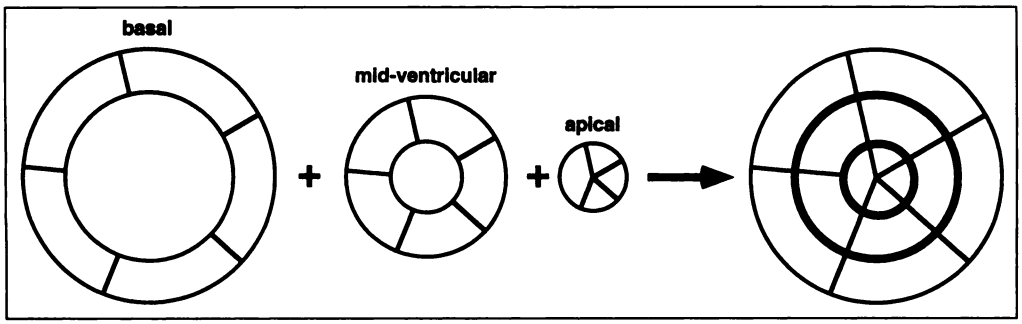

FIGURE 1. Segmental model of the left ventricle which consists of 14 regions. The free wall of the left ventricle is divided into an anterior, lateral and inferior segment, whereas the septum is divided into an anterior and inferior segment. These segments again are divided into a basal, middle and apical third, but the apical segment of the septum is combined into one region.

detailed evaluation of stenoses with complex morphology (*9,10*). By providing a cross-sectional image of the vessel, the method permits reliable measurements of luminal diameters and areas with a low intra- and interobserver variability, leading to a more precise quantification of the effective degree of vessel obstruction (*11,12*). Intracoronary ultrasound studies have demonstrated that the extent of residual intracoronary plaque and obstruction may be underestimated by angiography (*9,13*). A persistent reduction of the cross-sectional area after coronary intervention, not identifiable by angiography, could contribute to a reversible perfusion defect. Aim of this study was to test the hypothesis that perfusion defects after coronary intervention are associated with a larger plaque burden and a smaller cross-sectional area as defined by intravascular ultrasound.

MATERIALS AND METHODS

Patients

Forty consecutive patients (32 men, 8 women; ages 43–76 yr, mean 57.5 yr) with angiographically successful coronary interventions were prospectively studied. Sixteen patients had a history of prior myocardial infarction, but none was related to the localization of the treated coronary artery lesion. Coronary intervention was done as clinically indicated, based on the spontaneous or induced evidence of myocardial ischemia. All patients gave informed consent. The study protocol was approved by the ethics committee of the hospital. Vessels treated included 21 left anterior descending arteries, 16 right coronary arteries and 3 circumflex arteries. Twenty-three patients had single-vessel disease, 13 double-vessel disease and 4 triple-vessel disease. Interventional techniques included 21 conventional coronary balloon angioplasties, 14 stent implantations, 3 directional and 2 rotational atherectomies. Successful coronary intervention was defined as reduction in luminal narrowing $\geq$30% and a remaining stenosis $\leq$50% of the luminal diameter as determined by angiography.

Procedures

Coronary interventions were performed using the femoral approach. Patients were selected for stenting because of significant restenosis after previous conventional balloon angioplasty. Alternative methods (directional and rotational atherectomy) were used in selected patients with lesions felt to be treated by these techniques (*14,15*). Standard coronary angioplasty was performed leaving type and size of the balloon catheter as well as number of balloon inflations and pressure exerted to the discretion of the operator. All coronary stents implanted were Palmaz-Schatz stents with a nominal diameter ranging from 3.0 mm to 4.0 mm. The intervention was terminated if the lesional narrowing was less than 50%, as visually assessed by the operator, and the angiographic appearance of the lesion was satisfactory.

Angiography

Selective coronary angiography was performed in multiple projections before and after intervention. End-diastolic frames with identical radiographic angulations that clearly visualized the target lesion and showed the most severe residual narrowing were selected for measurement by one observer unaware of the scintigraphic and ultrasound findings. Minimal lumen diameters were measured in the diseased and adjacent normal proximal and distal segments using an operator-defined electronic caliper. Angiographic percent diameter stenosis was calculated from the minimal lumen diameter and the mean value of normal proximal and distal segments. The diameter of the angioplasty guiding catheter was used as a calibration reference. The severity of coronary narrowing before and after intervention was expressed as percent diameter stenosis.

Intravascular Ultrasound

All patients were examined by intravascular ultrasound immediately after the intervention. A 3.5 French ultrasound catheter with a 20-MHz transducer interfaced to an imaging console was used. After positioning the catheter within the target lesion, as identified by multiple contrast injections under fluroscopy, the catheter was slowly pulled backwards and continuous ultrasound images were recorded on videotape. Injection of the contrast medium was used repeatedly to define the position of the transducer along the length of the artery and to improve the visibility of the lumen/vessel wall interface.

Quantitative measurements were made as described previously (*16*) by one observer unaware of the angiographic measurements and scintigraphic findings, using off-line computer analysis of images proximal to the target lesion and from the target lesion itself. Care was taken to select images with a good visibility of the outer border of the media. If parts of the vessel wall were obscured by distal shadowing in the presence of calcium, the shape of the wall in the cross section was estimated. Vessel area was defined as the area within the outer border of the media, lumen area as the area confined within the leading edge echo and residual plaque burden was calculated as vessel area minus lumen area. The percent plaque area was calculated as plaque area divided by vessel area. As a measure of the relative luminal narrowing in the lesion, with regard to the proximal reference segment, percent area stenosis was determined as lumen area of the proximal reference segment minus lumen area of the treated vessel segment divided by lumen area of the proximal reference segment per 100.

Myocardial Scintigraphy

Within 48 hr after the intervention, all patients underwent myocardial scintigraphy with ^{99m}Tc-methoxyisobutyl-isonitrile (MIBI) after dipyridamole stress. A rest study was done on the following day. No antianginal medication was given after the intervention. All patients refrained from oral intake of methylxanthines on the day of the stress test. Patients were fasted and received a fatty meal 30 min prior to imaging. A 12-lead electrocardiogram, blood pressure and heart rate were recorded at baseline and then every 2 min during dipyridamole stress until all values had returned to normal. Dipyridamole (0.75 mg/kg) was infused intravenously at a rate of 5 mg/min. The infusion was stopped if patients experienced typical anginal chest pain or had horizontal

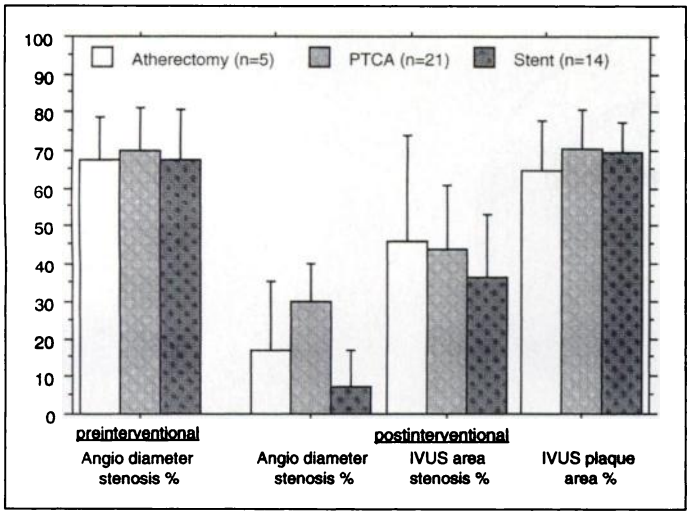

FIGURE 2. Bar graphs representing angiographic diameter stenosis before and after intervention and ultrasound area stenosis and percent plaque area in the target lesion after intervention. Stenosis reduction as assessed by angiography was significantly higher by stenting than by angioplasty ($p < 0.0001$), whereas the differences between all other groups did not reach statistically significant values. Angio = angiographic; IVUS = intravascular ultrasound.

ST-segment depression of ≥0.2 mV. At peak stress, 740 MBq ^{99m}Tc-MIBI were injected into a cubital vein. Three min later the stress test was ended by slow intravenous administration of 240 mg aminophylline. Image acquisition was started 90 min later using a triple-head SPECT camera equipped with low-energy, high-resolution, parallel-hole collimators and interfaced with a computer system. The camera was rotated at 3° increments, collecting 120 views for 40 sec each over an elliptical 360° arch of acquisition. Acquisition data were reconstructed by filtered backprojection using a low-pass filter. An identical acquisition protocol was used for the rest study.

After reconstruction of short, horizontal long and vertical long-axis tomograms, a qualitative comparison of rest and stress images was made by two experienced observers on a segmental basis. Segments were then interpreted by consensus as showing normal perfusion, a stress-induced perfusion defect or a fixed perfusion defect and assigned to the segmental left ventricular model described below.

Regional Comparison of Angiographic and Scintigraphic Data

The perfusion territory of each target vessel was estimated from the coronary angiogram by two observers and assigned by consensus to a segmental left ventricular model taking into consideration the individual coronary anatomy of the patient and the localization of the stenosis (*17*). Regions with reversible myocardial perfusion defects were assigned to the same model by two observers blinded to the angiographic results. Patients were only classified positive if the malperfused segment corresponded to the angiographically defined perfusion territory (Fig. 1).

Statistical Analysis

Data were compared using a Wilcoxon signed rank test for discrete variables and chi-square test for categorical variables. A p value of <0.05 was considered significant. Data are expressed as mean values ±1 s.d. To compare and visualize specificity and sensitivity of ultrasound area stenosis for the presence of perfusion defects over the entire range of measurements, a ROC-analysis was generated.

RESULTS

Dipyridamole Stress Test

Seventeen patients developed anginal chest pain during the stress test (nine with single-vessel disease, eight with multivessel disease), and in three patients the dipyridamole infusion had to be terminated before reaching the target dose; four of the 17 patients also showed significant ST-segment depression. Chest pain resolved in all patients after intravenous aminophylline administration. Out of the 17 symptomatic patients, 11 demonstrated a reversible perfusion defect in the following scintigraphy, whereas six patients had normal scintigrams.

Angiographic Data

Angiographic percent diameter stenosis was reduced from 68.2% ± 10.5% before intervention to 20.5% ± 14.6% after intervention (Fig. 2). There was no significant difference in preinterventional percent diameter stenosis between patients scheduled for angioplasty, stent implantation or alternative methods. Stenosis reduction was larger after stenting than after balloon angioplasty (67.5–7.5% versus 69.8–30.1%, respectively, $p < 0.0001$).

Intravascular Ultrasound

Ultrasound images of the proximal reference segment that was not directly involved in the intervention showed a percent plaque area of 46.2% ± 9.8%, whereas the percent plaque area in the dilated segment was 69.5% ± 9.7%. Total vessel area remained virtually unchanged between proximal and dilated segment (17.4 ± 6.0 mm^2 versus 17.8 ± 7.3 mm^2, p = ns), but residual plaque burden increased (8.0 ± 3.9 mm^2 versus 12.8 ± 6.6 mm^2, $p < 0.0001$), and lumen area decreased (9.0 ± 3.0 mm^2 versus 5.1 ± 2.0 mm^2, $p < 0.0001$). Percent area stenosis was 41.4% ± 18.2%.

Absolute vessel dimensions showed a significant difference between lesions treated by balloon angioplasty and stented lesions due to the more proximal localization of the latter (vessel area: 15.8 ± 7.3 mm^2 versus 22.2 ± 6.4 mm^2, $p < 0.01$; free lumen area: 4.1 ± 1.1 mm^2 versus 6.6 ± 2.0 mm^2, $p < 0.0001$), but relative values as percent plaque area and lumen stenosis were independent of the kind of intervention performed.

Correlation Between Quantitative Angiography and Intravascular Ultrasound

No correlation was found for ultrasound percent area stenosis and percent diameter stenosis as determined by quantitative angiography. The minimal lumen diameter as assessed by both methods showed only a loose correlation (r = 0.46).

MIBI Scintigraphy

Of the 40 patients studied, 20 showed a reversible perfusion defect after intervention in the vascular territory of the dilated artery (Fig. 3A-E). In two patients the perfusion defect extended beyond the angiographically defined perfusion territory of the dilated artery. No fixed defects were present in the respective territories. The prevalence of a perfusion defect was independent of the kind of intervention performed (Fig. 4) and did not depend on the number of diseased vessels.

Perfusion Defect versus Residual Stenosis

Mean ultrasound percent area stenosis of the treated vessel segment was 50.0% ± 17.3% in patients with and 33.0% ± 15.2% in patients without perfusion defect ($p = 0.002$), whereas the angiographic percent diameter stenosis did not differ significantly for both groups (defect versus no defect 22.7% ± 16.5% versus 20.2% ± 13.0%, p = ns) (Fig. 5). The ultrasound percent plaque area was 75.7% ± 7.6% in patients with and

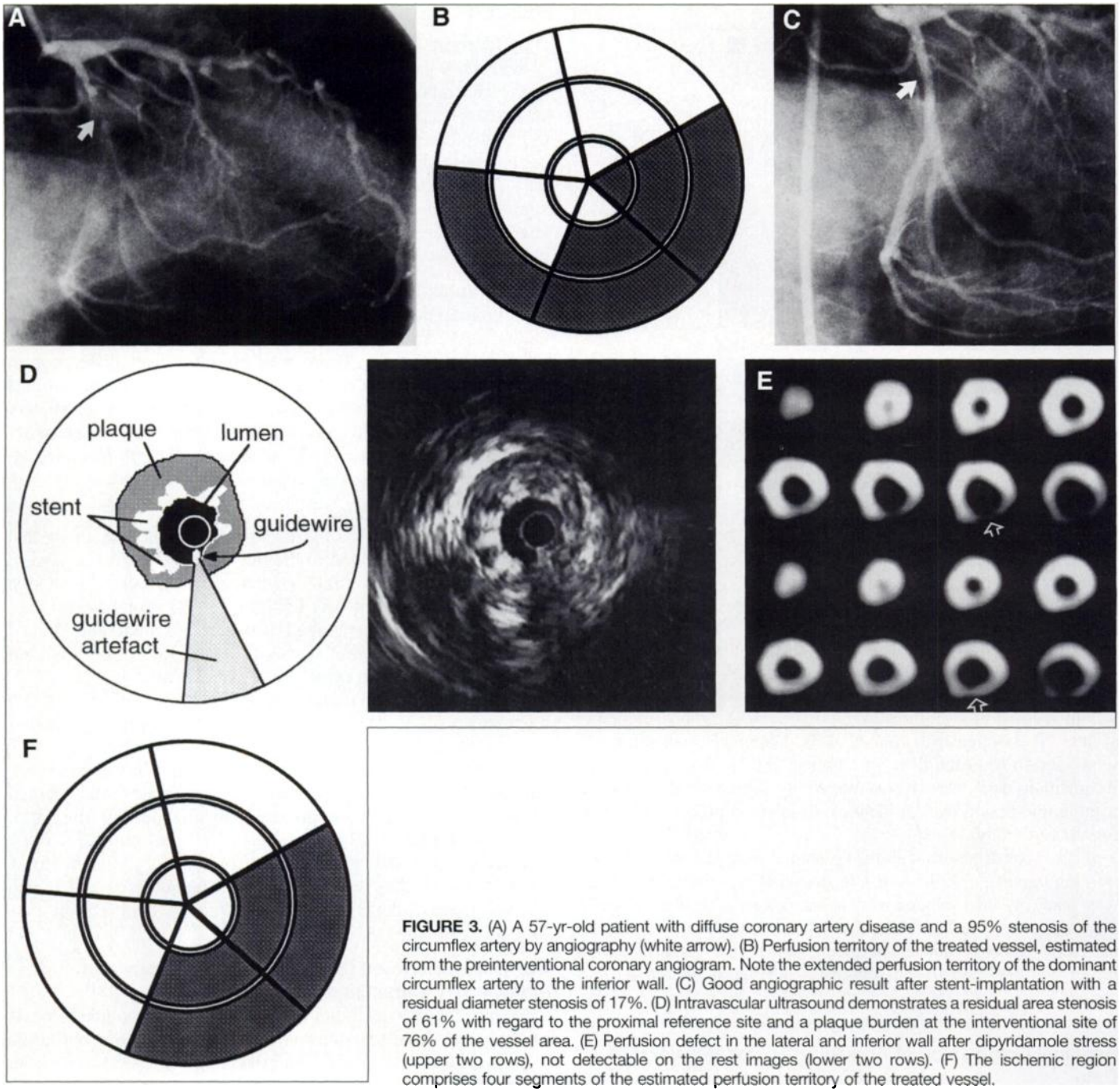

FIGURE 3. (A) A 57-yr-old patient with diffuse coronary artery disease and a 95% stenosis of the circumflex artery by angiography (white arrow). (B) Perfusion territory of the treated vessel, estimated from the preinterventional coronary angiogram. Note the extended perfusion territory of the dominant circumflex artery to the inferior wall. (C) Good angiographic result after stent-implantation with a residual diameter stenosis of 17%. (D) Intravascular ultrasound demonstrates a residual area stenosis of 61% with regard to the proximal reference site and a plaque burden at the interventional site of 76% of the vessel area. (E) Perfusion defect in the lateral and inferior wall after dipyridamole stress (upper two rows), not detectable on the rest images (lower two rows). (F) The ischemic region comprises four segments of the estimated perfusion territory of the treated vessel.

63.2% ± 7.2% in patients without perfusion defect ($p < 0.0001$). Ultrasound lumen area was significantly smaller in the presence of a perfusion defect (4.4 ± 1.9 mm^2 versus 5.8 ± 1.8 mm^2, $p = 0.02$) and cross-sectional plaque area was increased (15.3 ± 8.0 mm^2 versus 10.2 ± 3.4 mm^2, $p = 0.01$), whereas total vessel area did not differ significantly between both groups (19.7 ± 8.9 mm^2 versus 16.0 ± 4.7 mm^2, p = ns).

	type of coronary intervention		
perfusion defect	PTCA	Stent	Other
yes	12	6	2
no	9	8	3
	p = ns		

FIGURE 4. Frequency distribution of perfusion defects grouped by interventions. Incidence of perfusion defects was independent of the kind of intervention.

In the proximal reference segment, the ultrasound cross-sectional plaque area and the percent plaque area were increased in patients with a perfusion defect but failed to reach statistically significant values (9.0 ± 4.3 mm^2 versus 6.9 ± 3.0 mm^2, $p = 0.08$, and 48.9% ± 8.8% versus 43.5% ± 10.2%, $p = 0.08$, respectively). No relevant difference was found between both groups for the lumen area and the vessel area (9.1 ± 3.2 mm^2 versus 8.9 ± 8.0 mm^2, p = ns; 18.2 ± 6.8 mm^2 versus 15.8 ± 4.9 mm^2, p = ns).

The best specificity and sensitivity of ultrasound area stenosis for the presence of perfusion defects was found for a residual stenosis of 43% with a specificity of 80% and sensitivity of 75% (Fig. 6).

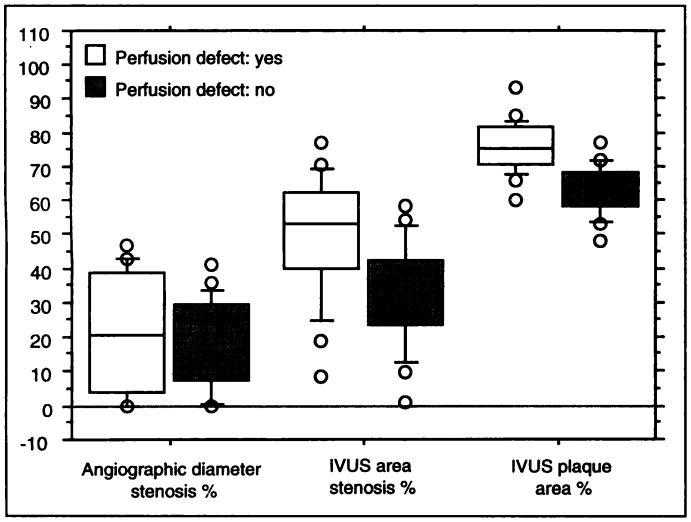

FIGURE 5. Box plots representing: median, 25th and 75th percentiles (box); 10th and 90th percentiles (error bars); and outliers (data points in extreme 20% of observed values) for angiographic diameter stenosis, ultrasound area stenosis and percent plaque area for patients with and without perfusion defect. A significant difference was found for the ultrasound derived parameters but not for the angiographic values.

DISCUSSION

Although it is well known that reversible perfusion defects may persist after successful coronary intervention, the pathophysiological mechanisms and the clinical significance of this observation continue to be a matter of discussion. The aim of this study was to test the hypothesis that lesions associated with a reversible perfusion defect after coronary intervention show a larger residual stenosis in the treated vessel segment than lesions without perfusion defect. It was further hypothesized that this difference was not detectable by angiography but by intravascular ultrasound. A reference segment proximal to the intervention site and the dilated vessel segment were examined by intravascular ultrasound in 40 patients after angiographically successful intervention, and the perfusion of the dependent left ventricular region was assessed very early after the intervention by myocardial scintigraphy after dipyridamole stress testing.

Half of our study patients demonstrated a reversible perfusion defect by dipyridamole stress scintigraphy. This is similar to the incidence of 40% reported for exercise-redistribution ^{201}Tl scintigraphy by various investigators in similar clinical settings

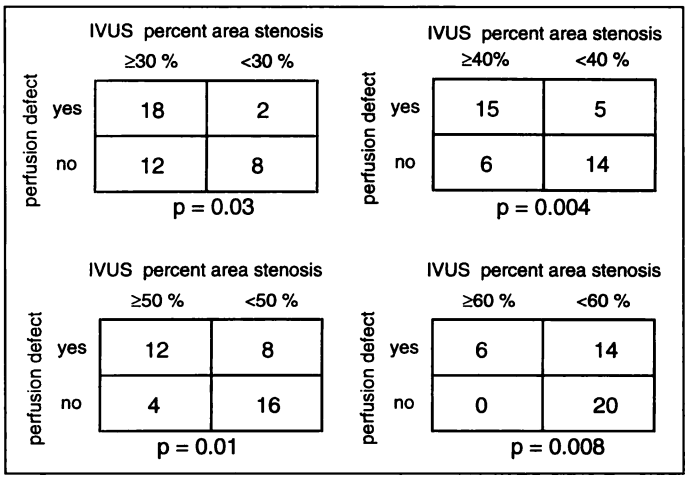

FIGURE 6. ROC analysis representing specificity and sensitivity of intravascular ultrasound area stenosis for the presence of a perfusion defect. Selected percent values for intravascular ultrasound area stenosis are given in the diagram.

(*1–4,18*). Analysis of our data according to the presence or absence of a perfusion defect did not reveal differences with respect to the angiographic diameter stenosis. However, there was a significant difference in the ultrasound area stenosis (50% versus 33%). Moreover, in the group with reversible perfusion defects the dilated coronary segment bore a larger burden of atherosclerotic plaque, and the absolute ultrasound luminal area was decreased with respect to the group without perfusion defects.

Several investigators have reported that the residual ultrasound percent plaque area after successful angioplasty amounts up to 60% and more of the vessel lumen (*13,16,19*). In our study the mean residual plaque area was 69% at the dilated site, indicating a significant luminal narrowing despite the angiographically successful intervention. Our finding of a mean ultrasound plaque area in the angiographic normal proximal reference segment of 46% is in good concordance with previously published data (*12,16,19*). The poor correlation of minimal lumen diameter between angiography and intravascular ultrasound ($r = 0.46$) was not unexpected (*11,20*). It reflects the differences between a silhouette imaging method such as angiography and a tomographic modality such as ultrasound, which are most profound in imaging of postinterventional arteries and depend highly on the irregularity of lumen shape. A lumen gain derived from complex cracks in the atheroma may appear angiographically satisfying, whereas ultrasound will show the large residual plaque albeit cracked and a much smaller effective cross-sectional area. For this reason, Topol deducts that "fundamentally, angiography cannot accurately depict the true size of the complex luminal shapes commonly encountered after interventions" (*21*).

The hemodynamic significance of a coronary stenosis is judged mainly by the angiographic percent diameter stenosis. In our study, postinterventional angiographic and ultrasound residual stenosis showed no correlation. We know of no quantitative data on the hemodynamic significance of coronary stenosis determined by intravascular ultrasound. However, our findings suggest that ultrasound narrowing of more than 40% of the lumen within the treated vessel segment as compared to the proximal segment should be considered hemodynamically relevant.

Nevertheless, the relatively wide overlap in our study for ultrasound area stenosis values between the groups with and without perfusion defects indicates the presence of additional mechanisms capable of impairing myocardial blood flow after coronary intervention. It is important to keep in mind that the mechanism of action of dipyridamole does not require the induction of ischemia. Rather the drug tests the coronary flow reserve by inducing maximal dilatation of the precapillary and arteriolar capillary beds, causing a heterogenous myocardial blood flow in the presence of a flow-limiting stenosis of an epicardial vessel (*22,23*). However, a similar flow pattern also will result in the absence of a stenosis if the microvasculature fails to dilate in one particular region. Such a mechanism has been proposed by Uren et al. (*5*) to be present immediately after percutaneous transluminal coronary angioplasty. They found that the dipyridamole-induced increase in blood flow velocity and myocardial perfusion was lower in the region perfused by the previously stenosed artery as compared to a remote control region. An altered vasomotor response after coronary intervention also has been described for acetylcholine, serotonin and papaverine (*6,24,25*). However, the efficacy of dilatation in these studies was only proven by angiographic evidence. Nonetheless, besides the presence of a flow-obstructing stenosis, endothelial dysfunction may be an additional factor that

determines the occurrence of perfusion defects after angioplasty. Moreover, endothelial dysfunction is supposed to be more pronounced in patients with a high degree of diffuse atherosclerotic changes (*24,25*). Indeed, a significantly higher residual plaque burden was observed in our patients with a perfusion defect as compared to the group without such a defect (75% versus 63%). This also was true for the subgroup of patients (n = 5) with an ultrasound area stenosis of <40% but a perfusion defect. In these five patients plaque burden was 72% as compared to 62% in the remaining 14 patients with an ultrasound area stenosis <40% but no perfusion defect (p = 0.01).

The prognostic value of a pathologic MIBI scan immediately after intervention is still unclear. The experience with thallium scintigraphy indicates an elevated risk of restenosis in about 2 of 3 patients with a pathologic thallium scan very early after intervention, whereas in the remaining 1/3 of the patients the perfusion would normalize without evidence of restenosis up to 9 mo after the intervention (*1–3*). To our knowledge, only one study used ^{99m}Tc-MIBI to assess regional blood flow early after coronary intervention (*26*). The results of this preliminary study with nine patients indicate an elevated risk to develop restenosis for patients with a reduced MIBI uptake on stress images.

Patients with multivessel disease (17 of 23 patients) present a particular problem in this study, since it cannot be definitely excluded that perfusion defects might be caused by a lesion in a nontreated coronary artery. We tried to address this problem by restricting our analysis to perfusion territories related to the treated vessel by visual correlation of scintigram and angiogram. Only two patients had perfusion defects outside the predefined area, which we judged to be due to an underestimation of the perfusion territory, since the segments were directly adjacent.

In summary, despite a good angiographic result after coronary intervention, intravascular ultrasound is able to identify in the treated vessel segment a relevant degree of residual stenosis. The degree of stenosis is more pronounced in patients with perfusion defects than in patients with normal postinterventional scintigrams, rendering the presence of a perfusion defect plausible. Thus, the evaluation of the postprocedural result by intravascular ultrasound contributes to a better understanding of the discrepancy between the angiographic finding of a widely patent vessel but scintigraphic evidence of impaired perfusion. Recent efforts to improve the results of coronary interventions guided by intravascular ultrasound (*27*), which were successful in further decreasing postinterventional area stenosis, may ultimately reduce the number of perfusion defects observed after coronary intervention.

REFERENCES

1. Jain A, Mahmarian JJ, Borges NS, et al. Clinical significance of perfusion defects by thallium-201 single-photon emission tomography following oral dipyridamole early after coronary angioplasty. *J Am Coll Cardiol* 1988;11:970–976.
2. Manyari DE, Knudtson M, Kloiber R, Roth D. Sequential thallium-201 myocardial perfusion studies after successful percutaneous transluminal coronary artery angioplasty: delayed resolution of exercise-induced scintigraphic abnormalities. *Circulation* 1988;77:86–95.
3. Hardoff R, Shefer A, Gips S, et al. Predicting late restenosis after coronary angioplasty by very early (12 to 24 hr) thallium-201 scintigraphy: implications with regard to mechanisms of late coronary restenosis. *J Am Coll Cardiol* 1990;15:1486–1492.
4. Wijns W, Serruys PW, Reiber JH, et al. Early detection of restenosis after successful percutaneous transluminal coronary angioplasty by exercise-redistribution thallium scintigraphy. *Am J Cardiol* 1985;55:357–361.
5. Uren NG, Crake T, Lefroy DC, et al. Delayed recovery of coronary resistive vessel function after coronary angioplasty. *J Am Coll Cardiol* 1993;21:612–621.
6. El Tamimi H, Davies GJ, Crea F, Maseri A. Response of human coronary arteries to acetylcholine after injury by coronary angioplasty. *J Am Coll Cardiol* 1993;21:1152–1157.
7. Nienaber CA, Brunken RC, Sherman CT, et al. Metabolic and functional recovery of ischemic human myocardium after coronary angioplasty. *J Am Coll Cardiol* 1991;18:966–978.
8. Iskandrian AS, Lemlek J, Ogilby JD, et al. Early thallium imaging after percutaneous transluminal coronary angioplasty: tomographic evaluation during adenosine-induced coronary hyperemia. *J Nucl Med* 1992;33:2086–2089.
9. Liebson PR, Klein LW. Intravascular ultrasound in coronary atherosclerosis: a new approach to clinical assessment. *Am Heart J* 1992;123:1643–1660.
10. White CJ, Ramee SR, Collins TJ, Jain A, Mesa JE. Ambiguous coronary angiography: clinical utility of intravascular ultrasound. *Cathet Cardiovasc Diagn* 1992;26:200–203.
11. Tobis JM, Mahon DJ, Moriuchi M, Honye J, McRae M. Intravascular ultrasound imaging following balloon angioplasty. *Int J Card Imaging* 1991;6:191–205.
12. Porter TR, Sears T, Xie F, et al. Intravascular ultrasound study of angiographically mildly diseased coronary arteries. *J Am Coll Cardiol* 1993;22:1858–1865.
13. Honye J, Mahon DJ, Jain A, et al. Morphological effects of coronary balloon angioplasty in vivo assessed by intravascular ultrasound imaging. *Circulation* 1992;85:1012–1025.
14. Foley JB, Penn IM, Brown RI, et al. Safety, success and restenosis after elective coronary implantation of the Palmaz-Schatz stent in 100 patients at a single center. *Am Heart J* 1993;125:686–694.
15. Kimball BP, Bui S, Cohen EA, Carere RG, Adelman AG. Comparison of acute elastic recoil after directional coronary atherectomy versus standard balloon angioplasty. *Am Heart J* 1992;124:1459–1466.
16. Hodgson JM, Reddy KG, Suneja R, et al. Intracoronary ultrasound imaging: correlation of plaque morphology with angiography, clinical syndrome and procedural results in patients undergoing coronary angioplasty. *J Am Coll Cardiol* 1993;21:35–44.
17. Edwards WD, Tajik AJ, Seward JB. Standardized nomenclature and anatomic basis for regional tomographic analysis of the heart. *Mayo Clin Proc* 1981;56:479–497.
18. Okada RD, Lim YL, Boucher CA, et al. Clinical, angiographic, hemodynamic, perfusional and functional changes after one-vessel left anterior descending coronary angioplasty. *Am J Cardiol* 1985;55:347–356.
19. Tobis JM, Mallery J, Mahon D, et al. Intravascular ultrasound imaging of human coronary arteries in vivo. Analysis of tissue characterizations with comparison to in vitro histological specimens. *Circulation* 1991;83:913–926.
20. De Scheerder I, De Man F, Herregods MC, et al. Intravascular ultrasound versus angiography for measurements of luminal diameters in normal and diseased coronary arteries. *Am Heart J* 1994;127:243–251.
21. Topol EJ, Nissen SE. Our preoccupation with coronary luminology. The dissociation between clinical and angiographic findings in ischemic heart disease. *Circulation* 1995;92:2333–2342.
22. Botvinick EH, Dae MW. Dipyridamole perfusion scintigraphy. *Semin Nucl Med* 1991;21:242–265.
23. Penell DJ. Pharmacological cardiac stress: when and how? *Nucl Med Commun* 1994;15:578–585.
24. Sambuceti G, Parodi O, Giorgetti A, et al. Global alteration in perfusion response to increasing oxygen consumption in patients with single-vessel coronary artery disease. *Circulation* 1994;90:1696–1705.
25. Sambuceti G, Parodi O. Role of coronary microvascular abnormalities in coronary artery disease-implications for perfusion imaging. *J Nucl Cardiol* 1995;2:78–84.
26. Carvalho PA, Vekshtein VI, Tumeh SS, et al. Technetium-99m-MIBI SPECT in the assessment of myocardial reperfusion after percutaneous transluminal coronary angioplasty. *Clin Nucl Med* 1991;16:819–825.
27. Colombo A, Hall P, Nakamura S, et al. Intracoronary stenting without anticoagulation accomplished with intravascular ultrasound guidance. *Circulation* 1995;6:1676–1688.