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Characteristics of Myocardial Perfusion in Patients after Coronary Stent Implantation

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Clinical background

A review of the literature

Regulation of myocardial blood flow

The myocardium is almost totally dependent on the aerobic metabolism. The ability of the coronary circulation to autoregulate is essential for the heart to respond to changing metabolic demands [10]. The major epicardial coronary vessels contribute only little to the coronary vascular resistance, but act primarily as conductance vessels [14,88]. Most of the resistance to the coronary blood flow arises from the smaller intramural coronary vessels [115]. Hypoxia, as a physiological stimulus, relaxes the smooth muscle of these arterioles, thereby increasing the coronary blood flow [99] to as much as 3-5-times the resting value [3,7,47,51,78,79,118,129]. This relative change in myocardial blood flow has been referred to as the coronary flow reserve, as proposed by Gould et al.[40]. The principal mediator of this mechanism is thought to be adenosine, resulting from the metabolism of adenosine triphosphate (ATP) [9], but the roles of numerous endothelium-derived vasoactive substances, such as prostacyclin [84], endothelial derived relaxing factor (nitric oxide) [83,93] and endothelial-derived hyperpolarizing factor [25], have also recently been discussed. A similar magnitude of vasodilation can be provoked in healthy young people by external agents such as intravenously administered dipyridamole or dobutamine, or intracoronary papaverine [128,129]. The parameter of coronary flow reserve is widely used to characterize the functional extent and severity of disorders affecting the myocardial blood supply.

Pathophysiology of coronary heart disease

The underlying disease process responsible for coronary artery disease (CAD) is almost exclusively coronary atherosclerosis. Atherosclerosis is a progressive disease that becomes morphologically manifest only decades after its initiation [69]. According to the most widely accepted theory of atherogenesis, the intimal alteration develops as a response to injuries to the vascular endothelium. The first visible alterations are fatty streaks [113]. This subendothelial lesion contains foam cells that accumulate large amounts of intracellular lipid and a small number of T lymphocytes [70]. Fatty streaks may progress to mature plaques.

Platelets adhere to the lesion and secrete growth factors, including platelet-derived growth factor, epidermal growth factor, transforming growth factor-beta and somatomedin c [15,105]. These factors initiate smooth muscle cell migration from the media to the intima and stimulate the production of proteins providing the connective tissue matrix of the plaque. Extracellular cholesterol crystals and cholesterol esters derived directly from low-density lipoproteins (LDL) or extruded by decaying foam cells accumulate within this matrix [17]. The composition of nonruptured atheromatous plaques is highly variable [18]. Lipid-rich plaques are generally less prominent, producing only minimal narrowing of the luminal area as compared with matured, fibrous plaques.

Clinical manifestations of coronary artery disease

Early changes of myocardial blood flow

Numerous recent articles report on a pathological decrease in coronary reserve capacity in regions supplied by angiographically normal epicardial arteries [6,77,106,117]. These moderate changes have been observed in the angiographically normal arteries of patients with severe coronary artery disease in other vessels [6,106,117]. In addition, patients without clinical evidence of myocardial ischemia, but at high risk of the development of CAD on the basis of the risk factor profile have shown an attenuated response to adenosine as assessed by positron emission tomography (PET) [19]. The pathophysiologic mechanism of the reduced coronary flow reserve in angiographically normal vessels is not yet known, but may involve the interplay of vascular alterations and the endothelial dysfunction caused by pharmacologically induced changes in blood flow [77]. Blood flow measurements may therefore serve as a sensitive means of detecting CAD before any angiographic manifestation of the disease process.

Stable effort angina

Patients with chronic stable angina invariably have critical stenoses of one or more coronary arteries [69]. I consequence of the maintained vasoregulation, the enhanced coronary resistance caused by the stenoses of major epicardial coronary arteries is compensated by the vasodilation of small arteries, resulting in a near-normal level of blood flow at rest until a stenosis narrows the lumen by more than 85% [39]. Since this mechanism exploits part of the

vasodilator capacity, the freely available vasodilator capacity (the coronary flow reserve) is considerably reduced in the corresponding vascular territory. The experimental data of Gould, indicate that coronary flow reserve measurement allows the detection of coronary stenoses of about 40-50% [39].

Acute ischemic syndromes

Acute ischemic syndromes are caused predominantly by coronary thrombi initiated by the rupture of an atherosclerotic plaque [16]. The clinical presentation of plaque rupture depends on the extent of the perfusion abnormality induced by the developed thrombus. Unstable angina, acute myocardial infarction or sudden cardiac death are possible consequences, which are related to the extent and the severity of the acute flow reduction in the affected vascular territory [58].

The time of plaque rupture is hardly predictable. It may be related to a systemic inflammatory process, which shows local manifestation at the plaques [74,85,96]. It is known that plaques with high lipid and macrophage contents have the greatest possibility to rupture [17,35,104]. Such plaques, however, tend to cause less severe stenoses than calcified plaques with a higher fibrous and a lower lipid content [42,64,65]. As the currently available noninvasive diagnostic tests are unable to identify such vulnerable plaques, a significant proportion of stenoses considered insignificant on the basis of these tests may be candidates for later abrupt progression. This train of thought seems to be supported by the results of Ambrose et al. and Giroud et al., who found the culprit lesion in more than two-thirds of conservatively treated patients in coronary segments judged earlier as having insignificant stenosis [2,38]. These observations have important consequences for the prognostic evaluation of patients with CAD. Parameters of regional myocardial perfusion may not be able to predict the risk that a given vascular territory will suffer a later acute myocardial infarction [122]. However, as indicated in numerous studies, perfusion imaging characterizes the functional extent and severity of existing CAD, and can therefore determine the prognosis of the patient as concerns future acute coronary syndromes [37,62,94,123].

The only technique allowing an assessment of the plaque morphology and composition is intravascular ultrasonography [4,49,68,126]. Unfortunately, the high time and cost demands of this invasive technique do not permit its routine utilization in the clinical evaluation of CAD patients.

Prolonged ischemic dysfunction

The term "hibernating myocardium" has been introduced to characterize a chronically hypoperfused, dysfunctional myocardium which recovers its function after the restoration of perfusion [12,101]. A hibernating myocardium represents a state of reduced blood flow at rest without evidence of ischemia (electrocardiogram, symptoms and lactate), but with downregulation of the myocardial contractile function. The sine qua non of viable cells in a dysfunctional myocardium is the presence of residual metabolic activity sufficient to support the integrity of the cell membranes [121].

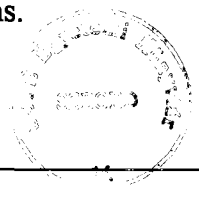
The contractile function of the myocardium can also be absent, however, in areas with a normal resting myocardial blood flow, after periods of transient ischemic injury. The spontaneous restoration of the function with time is characteristic for such areas of "myocardial stunning" [11].

The relation of myocardial stunning and hibernation is a matter of debate. Some authors consider repetitive stunning responsible for the prolonged dysfunction of myocardial areas with a normal resting flow but a severely reduced coronary flow reserve [112]. In such areas repetitive periods of myocardial ischemia induced by a demand-supply imbalance during the everyday physical activity can maintain the permanent stunning.

Methods for assessing myocardial blood flow

Although coronary arteriosclerosis is a disease of the coronary artery wall, the pathological consequences are determined by the degree of regional flow restrictions caused by atherosclerotic plaques. Therefore, the assessment of myocardial blood flow is of great importance in the scientific workup and clinical management of patients with CAD. It should be noted, however, that in clinical practice a number of methods have proved their suitability as regards guidance of the patient management, which evaluate only the ischemic consequences of coronary stenoses, e.g. stress tests using electrocardiogram (ECG) or echocardiographic monitoring [30,36,98].

The methods of myocardial flow assessments can be classified on the basis of the invasiveness and the absolute or relative measures provided by the techniques. While absolute determinations are necessary for an independent characterization of regional blood flow in circumscribed areas under predetermined conditions, relative measures suffice for a comparison of the blood flows in different regions in certain hemodynamic situations.



Invasive methods of myocardial blood flow assessment

Relative flow distribution assessment

Quantitative digital subtraction angiography performed during coronary angiography measures the changes in absorption, transit times and myocardial washout after injection of contrast medium [120]. Such measurements at rest and after maximal vasodilation have been shown to provide indices of coronary vascular reserve without the need to compute the absolute values of rest and stress coronary flow [73].

Absolute coronary flow measurement

Timed venous collections from the sinus coronaries were earlier used to measure coronary flow [102]. Today, coronary sinus thermodilution catheter [31] and intracoronary Doppler flow measurements [128] are the preferred invasive methods for the quantification of coronary flow and flow velocity in humans. The use of inert gases [13], such as helium, xenon-133 and krypton-85, with determination of the arterial and coronary sinus gas concentrations, have only limited applications because of the necessity of intracoronary application accompanied by radioactivity measurement.

Noninvasive methods of myocardial blood flow assessment

Relative flow distribution assessment in nuclear cardiology

Tracer approaches were introduced in the early 1970s to image the distribution of myocardial blood flow [114]. Myocardial perfusion scintigraphy with thallium-201 (^{201}Tl) or technetium-99m (^{99m}Tc)-labeled radiopharmaceuticals is currently the most widely used imaging method for clinical evaluation of the myocardial blood supply [59,60]. Modern tomographic imaging approaches, such as single photon emission computed tomography (SPECT) and static positron emission tomography (PET), visualize the relative tracer accumulation in myocardial regions as compared with a reference region with maximal tracer accumulation. Such techniques have been shown to provide high accuracy in the detection of CAD and in the evaluation of coronary interventions, and to deliver prognostic information on patients with known or suspected CAD [59,60,80,81].

Absolute coronary flow measurement in nuclear cardiology

PET data acquisition with attenuation correction allows accurate measurements of myocardial radiotracer distribution, independently of the relative location of the activity to the detectors. Current systems with dynamic acquisition generate data with high temporal resolution appropriate for the description of tracer kinetics in myocardial and vascular structures. Such PET measurements can be used for the noninvasive determination of myocardial blood flow in ml/min/g heart tissue units by applying suitable tracer kinetic models. A detailed description of the methods of nuclear medicine can be found in a previous publication of the author [63].

Semi-invasive methods of myocardial blood flow assessment

Following the rapid development of echocardiography, it is now possible to perform Doppler flow measurements in coronary arteries by using a transesophageal approach. When the measurements are performed at rest and during maximal vasodilation, we are able to calculate the coronary flow reserve [61]. Some experimental data are also available regarding absolute flow determinations based on the coronary vessel area and Doppler-measured blood flow of this surface. Recent studies have reported on coronary flow measurements in the left anterior descending artery (LAD) by using a transthoracic approach.

Treatment of coronary artery disease

As CAD is a disorder of the coronary artery wall, the treatment should be directed primarily toward reversing the process of plaque development, plaque rupture and thrombus formation. In circumscribed situations, however, when the stenoses of the coronary tree cause complaints, that are intolerable for the patients during their daily life, or critically jeopardize the ability of the heart to survive acute ischemic syndromes, the elimination of stenoses is of the utmost importance.

Conservative treatment

A review of conservative treatment is beyond the scope of this work. It should be emphasized, however, that a change in life style is the basis of the therapy. The well-known risk factors, such as smoking, the lack of physical activity, overweight, hypertension, diabetes mellitus and hypercholesterolemia, should be addressed. Drugs play a role in helping to control the blood

pressure (BP), serum glucose and cholesterol level, inhibiting platelet adhesion and reducing the myocardial oxygen consumption.

Invasive treatment

It has been proved that the complaints of patients with effort angina can be resolved by the elimination of stenoses of epicardial coronary arteries. It has also been demonstrated that multiple stenoses of coronary arteries (triple-vessel-disease, double-vessel-disease with proximal LAD stenosis or stenosis of the left main coronary artery) denote a high risk for the patient, and revascularization of the coronary arteries results in a significant risk reduction [23].

Coronary bypass operation

The pioneering technique of coronary artery revascularization was coronary artery bypass grafting (CABG). Garrett, Dennis, and DeBakey performed the first procedure in 1964 on "bailout" indication [32]. The method rapidly spread and in 1966 already the first revascularization was performed using an internal mammary artery as graft conduct [41,57]. The development of the technique resulted in improved short and long-time results. The perioperative mortality is nowadays around 1-5%, depending on the risk profile of the patients. As regards the long-term prognosis, a recent metaanalysis demonstrated a mortality rate of 10% at 5 years and of 26% at 10 years [23]. The use of the internal mammary artery leads to an improved long-term survival, as the 10-year patency rate appears to be nearly 90% for the internal mammary artery, while the corresponding figure is only 40-60% for venous grafts.

Percutaneous revascularization

Although coronary bypass surgery has a favorable late outcome, the perioperative mortality rate requires consideration by both the patient and the physician. This prompted the search for less invasive revascularization techniques. The earliest percutaneous procedure, percutaneous balloon angioplasty, was performed by Gruentzig in 1977 in Zurich. Following the rapid development, percutaneous transluminal coronary angioplasty (PTCA) is practised nowadays in very high volume throughout the world, with a favorable success rate. According to recently published data [43], the periprocedural mortality rate is below 1%. This benefit,

however, is compromised by the relatively high frequency of restenosis after PTCA, which results in a similar overall survival as for patients treated by CABG and PTCA.

Coronary stents

Coronary stents were originally utilized to treat acute complications of balloon angioplasty such as the dissection of vascular wall layers or elastic recoil of the vessel wall. The beneficial effect of stents on the late success rate assisted its widespread utilization. The recent review of the European Society of Cardiology revealed that stents are implanted in about 50-70% of percutaneous coronary interventions.

Scope of the problem

As CAD is a progressive disease of the arterial wall resulting in significant stenoses of vessel lumen, the treatment of vessel stenoses does not stop the atherosclerotic process. The restenosis rate for implanted stents is still as high as 20-30% during the first 6 months [28,50,89,107,109,111], and patients after stent implantation therefore require reevaluation of the status of the coronary vasculature several times during their life, to determine the prognosis and guide further therapy.

Since stent implantation may induce special flow changes in the myocardium, the information afforded by perfusion studies may differ from that gained in patients with native coronary arteries.

It has been demonstrated that after coronary angioplasty, a discrepancy may exist between the changes in the lumen area of the epicardial coronary arteries and the perfusion of the distal myocardium [66,75,116,127,130]. The results in the published studies indicate that the coronary flow reserve is reduced during the first day after the procedure, and its improvement can be expected only 1 week to 3 months later. The pathophysiology of this slow alteration is still unclear. The effect of distal microembolization or local release of vasoactive agents at the site of dilation has been considered as a possible etiology [5], as has a transient defect in distal resistance vessel autoregulation [116,127]. Other studies have discussed the role of local spasm, or the dynamic recoil of the artery wall at the site of earlier stenosis [48,100], suggesting the dominant role of the anatomical integrity of epicardial arteries at the site of previous stenosis.

The implantation of stents may influence some of these proposed mechanisms. The supplementary procedure of stent positioning may induce the additional release of vasoactive agents. On the other hand, the metallic frame can prevent changes in artery diameter at the site of previous dilation.

Furthermore, the regional microcirculation may be affected because of the obstruction of side-branch arteries by the stent. The reported frequency of side-branch stenoses at the time of implantation of stents varies from 5% to 27% [29,52,95]. The available data are diverse as regards the functional significance of side-branch stenoses, and also the evolution of side-branch stenoses with time [29,95].

The role of perfusion scintigraphy in the management of patients after other revascularization procedures has been defined by several studies [46,76,103,110,124]. However, few data are

available concerning the effects of the above-mentioned factors on the pattern of myocardial perfusion, and the performance of perfusion scintigraphy in this patient population.

Aims

Our aims were to assess the myocardial microcirculation early after coronary stent implantation and to evaluate the value of stress-myocardial perfusion SPECT in the management of stent-implanted patients.

Methods

For the evaluation of myocardial blood flow early after stent implantation, dynamic N-13-ammonia PET was performed at rest and during maximal vasodilation in 14 patients. To evaluate the value of perfusion studies in the management of patients after stent implantation, the results of 93 perfusion scintigraphy were analyzed with reference to the control coronary angiographic finding.

Positron emission tomographic studies

Patient population

Dynamic N-13-ammonia PET was performed at rest and during maximal vasodilation in 14 patients after stent implantation. The 13 men and 1 woman underwent the revascularization procedure 1 to 3 days (average 1.6 ± 0.6 days) before the scintigraphic investigation. Exclusion criteria included a previous myocardial infarction, myocardial hypertrophy or triple-vessel-disease. The mean age of the patients was 59.1 ± 8.4 years (range 39 to 72 years). In 4 cases, the indication for stent implantation was dissection or threatening dissection, while in 10 cases, unsatisfactory results after balloon dilation.

Coronary angiography and interventional procedure

Selective right and left coronary angiography was performed according to the Judkins method with a digital angiography system; images were stored digitally (Hicor; Siemens, Erlangen, Germany). The angiograms were analyzed off-line on a digital angiographic workstation (AWOS; Siemens). For quantitative analysis of the luminal diameter at the culprit lesion, the projection was chosen that showed the highest grade of stenosis. The details of this automated computer-based analysis system were described earlier [55]. The percentage diameter stenosis was calculated by using the minimal diameter and interpolated reference diameter.

PTCA and the placement of Palmaz-Schatz stents (Johnson & Johnson Interventional Systems, Warren, NJ) were performed via a femoral approach, using 7 French sheaths. The stents were hand-crimped onto the angioplasty balloon and deployed as previously described in detail [108]. To improve stent expansion, additional balloon inflations were performed at high pressure (> 15 atm), using a 10-mm balloon (high energy, Boston Scientific, Natwick, Massachusetts).

Positron emission tomography

Nitrogen-13-ammonia was produced via the reaction ^{16}O-(p, alfa)-^{13}N reaction [34] in a local medical cyclotron (Figure 1a). Patients were instructed to discontinue cardiac medication the evening before the PET study. Each subject was positioned in the Siemens ECAT 951R/31 whole-body scanner, which has 16 circular detector rings yielding 31 reconstructed transaxial planes (slice separation 3.4 mm) (Figure 1b). A 15-minute transmission scan was acquired and used to determine attenuation correction factors.

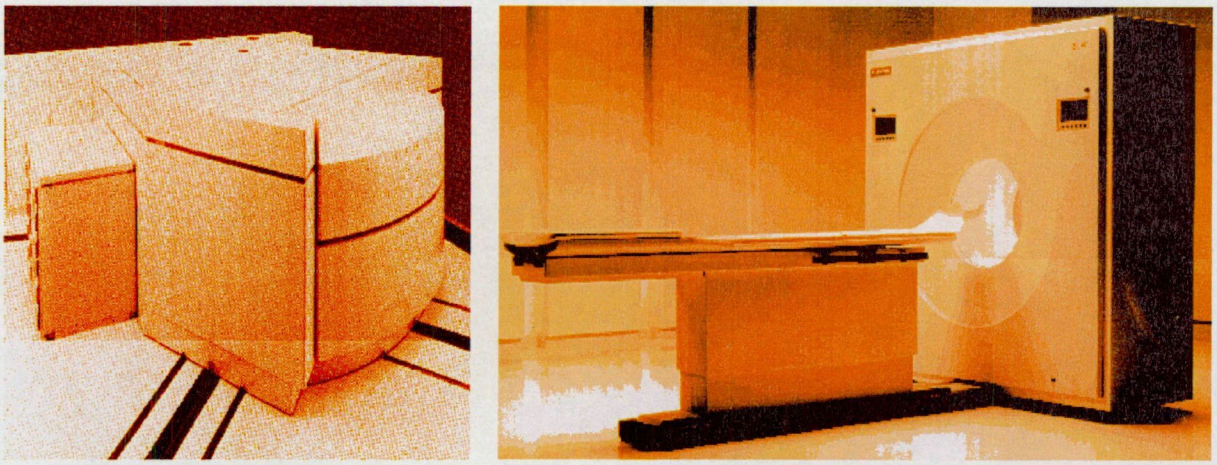


Figure 1

a) Siemens RDS-112 medical cyclotron b) Siemens ECAT 951 PET scanner

After the transmission data acquisition, 20 mCi of N-13-ammonia was injected intravenously and a 20-minute 21-frame dynamic PET acquisition was initiated (12 x 10 s, 6 x 30 s, 3 x 300 s). An additional period of 30 minutes was allowed for the decay of N-13-ammonia, at which time adenosine (0.14 mg/kg/min) was infused intravenously for 5 minutes. After 2 minutes, a second injection of 20 mCi of N-13-ammonia was administered. The dynamic PET acquisition was then repeated.

The transaxial data were reconstructed by using a Hanning filter with a cutoff frequency of 0.4 cycles/pixel. The reconstructed images were reoriented along the long axis of the heart to yield images in the short-axis plane of the left ventricle by using a SUN workstation (SUN Microsystems Inc., Palo Alto, California) and commercial image analysis software (CTI, Knoxville, Tennessee).

Based on the short-axis planes, myocardial time-activity curves were generated by an automated sampling routine previously developed and validated [86]. According to the described algorithm, 12 myocardial sectors were defined in each of 6 planes encompassing nearly the entire left ventricle. The regions were defined by the image planes of the last time frame of the dynamic study sequence and then copied to all other time frames of the dynamic sequence. Before time-activity curves were generated, the dynamic image set was corrected for patient motion with a semi-automated program. The dynamic image set was sampled and 72 (6 planes x 12 sectors) time-activity curves were stored (Figure 2). From this data set, the average time-activity curves of the basal and distal portions of the anterior, lateral and inferior walls and the septum were generated and used for further analysis.

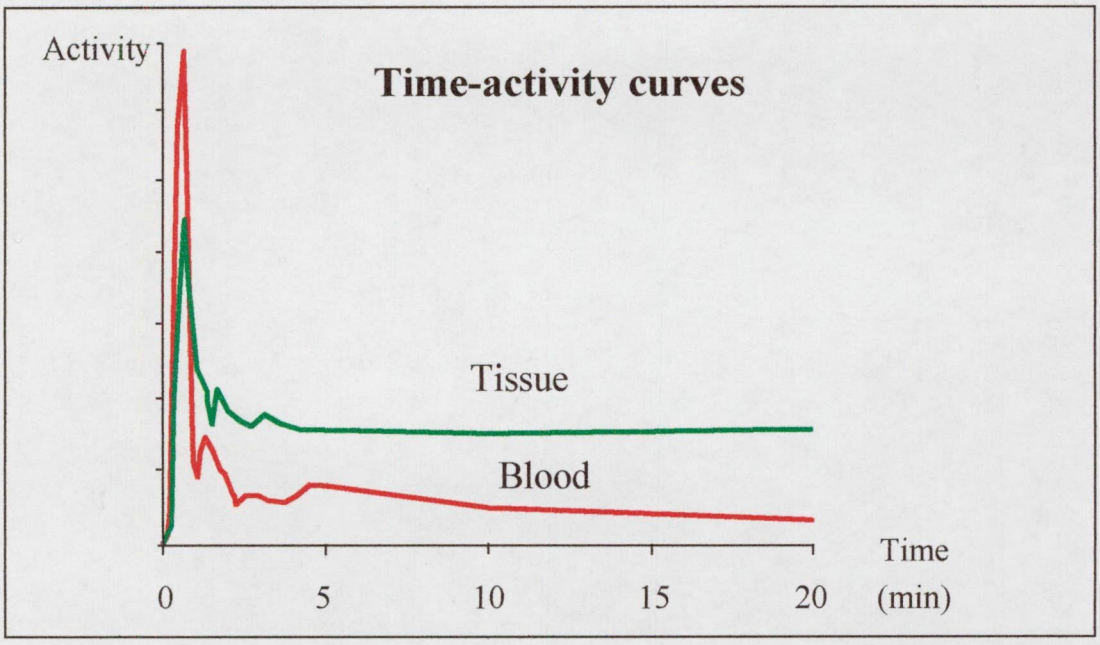


Figure 2 Time-activity curves from the middle of the left ventricle (denoted "Blood": input function) and from a myocardial segment (denoted "Tissue") used for curve fitting in the three-compartment model

The input activity was derived from the central ventricular area of the basal midventricular planes. A three-compartment model described by Hutchins et al. [51] was fitted to the averaged time-activity data (Figure 3.). The K_1 variable of the model provides a direct estimate of myocardial blood flow. The model also corrects for partial volume effect and spillover of activity from blood pool to myocardium using a variable for the total blood volume in the region of interest [51]. Baseline K_1 and adenosine K_1 values were determined as measures of rest and maximal blood flow, respectively. The ratio of maximal flow to rest flow was calculated as myocardial flow reserve.

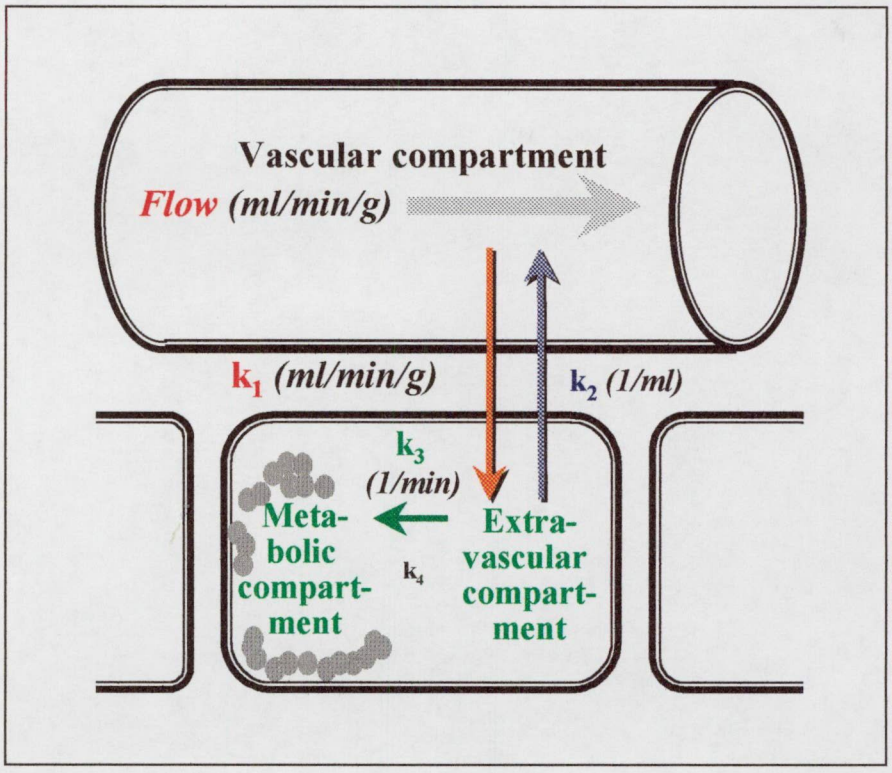


Figure 3 The three-compartment model

To match the coronary artery anatomy to the myocardial regions analyzed by this program, the data from the basal-anterior, distal-anterior, basal-septal and distal-septal regions were assigned to the left anterior descending artery (LAD), the data from the basal-lateral and distal-lateral regions to the left circumflex artery (LCX), and those from the basal-inferior and distal-inferior regions to the right coronary artery (RCA). Additionally, data from vascular territories of stented arteries were compared with those of reference arteries (remote areas). A

coronary artery was considered suitable for use as reference if it did not have a discrete stenosis. If two such vascular territories were present in a patient, the averaged myocardial blood flow of these territories was used in the calculation.

Statistical analysis

Values were reported as means ± standard deviation. Data from stented and remote areas, and also the hemodynamic parameters at baseline and during vasodilation, were analyzed with the paired Student t test. A p value of <0.05 was considered statistically significant.

Single photon emission computed tomographic studies

Patient population

Between January 1993 and August 1995 at the Technische Universität (Munich, Germany), 93 perfusion scintigraphic studies were performed on 82 patients with coronary stents, during the chronic phase after intervention (more than 31 days after stent placement). Coronary angiography was available within 31 days of the scintigraphic studies in all cases. Perfusion scintigraphy and 6-month coronary angiography formed parts of the prospective routine follow-up of the patients in most cases (60 cases). The additional investigations were performed because of the clinical suspicion of restenosis (14 cases) or remote stenosis (19 cases). In 11 patients, 2 stress perfusion studies and 2 coronary angiographies were performed, in consequence of the clinical indications. There were no data suggesting changes in clinical status during the time interval between the scintigraphic and the angiographic evaluation. The results of all of the coronary angiographic investigations were matched with those of the corresponding perfusion scintigraphic examinations. In 6 patients coronary stent implants were present in 2 vascular territories, and therefore 99 stented vascular territories were included in the evaluation. The characteristics of the patient population are listed in Table 1.

Age (average±SD years)	59.9±10.2
Gender (male/female)	61/21
Vessels with ≥50% stenosis	
0	21
1	32
2	21
3	8
Previous	
coronary bypass operation	10
number of bypass grafts	26
myocardial infarction	48

Table 1. Characteristics of patient population at first investigation (n=82)

The coronary stent placements were performed a mean of 210.5 ± 129.6 days (35 to 875 days) before the scintigraphic studies. The mean time interval between the scintigraphic and coronary angiographic investigations was 0.9 ± 9.8 days (range -31 to 31 days).

In 34 cases, the stents were positioned in the RCA, in 50 cases in the LAD, in 10 cases in the LCX, and in 5 cases in a saphenous venous aorto-coronary graft. Previous myocardial infarctions in the stented vascular territory were present in 47 cases, as documented by the clinical history of the patients or by their ECGs. Data regarding any previous posterior wall myocardial infarction were matched to the RCA or LCX on the basis of the results of coronary angiography.

Coronary angiography

Selective right and left coronary angiography and the visualization of bypass grafts, if present, were performed according to the Judkins method. To determine the luminal diameter at the location of the stent and the adjacent reference regions, the projection was chosen that exhibited the highest grade of stenosis. Because of the inability to visualize the Palmaz-Schatz stent clearly by radiography, no attempts were made to distinguish whether the restenosis lay within or in the proximal or distal segments adjacent to the stent. The percentage diameter of the stenosis was graded as a wall surface irregularity, ≥25%, ≥50%, ≥75%, ≥90% or ≥99% stenosis or total occlusion. Restenosis was defined as a stenosis diameter ≥50%.

Stress testing

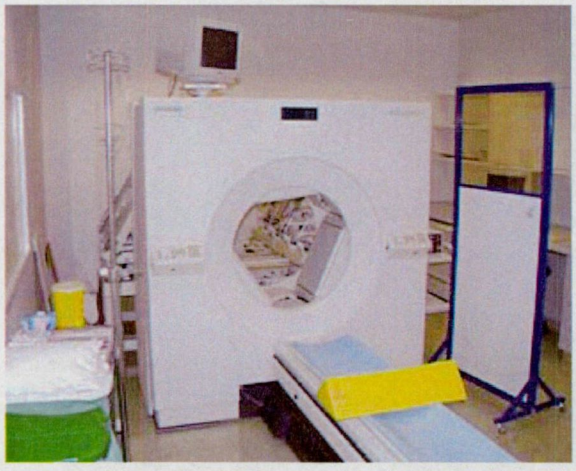
Eighty-three studies were performed after treadmill exercise using a standard Bruce protocol to a symptom-limited endpoint or to >85% of the age-predicted maximal heart rate of the patients. The radiotracer was injected intravenously at peak exercise, and the patients were asked to continue the exercise for an 1-2 additional minutes.

In 10 patients who were unable to exercise, dipyridamole stress tests were performed with a 4-minute infusion of 0.14 mg/kg/min dipyridamole [67]. The radiotracer was administered 4 minutes after the end of the dipyridamole infusion.

Clinical symptoms, e.g. the appearance of dyspnea or angina, were documented during the tests. A horizontal or downsloping ST-depression of $\geq$1 mm in the standard leads and of $\geq$2 mm in the precordial leads was considered a significant change indicating the presence of myocardial ischemia.

Scintigraphy

In 28 patients studied before June 1994, a ^{201}Tl stress-reinjection imaging protocol was used [22,91]. The stress acquisitions were started within 15 minutes of the stress injection of 3 mCi ^{201}Tl, using a Siemens MultiSPECT (Knoxville, TN) triple-head (Figure 4/a) or Siemens Diacam single-head camera (Figure 4/b) equipped with high-resolution, low-energy collimators. Three hours after the stress injection of the tracer, an additional 1-mCi dose of ^{201}Tl was injected at rest and the acquisition was repeated 30 minutes later.



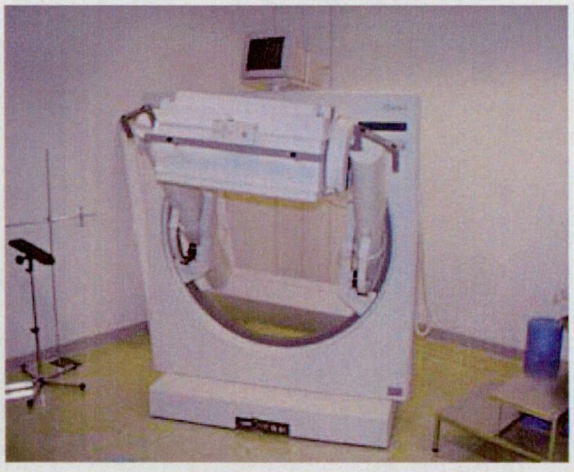


Figure 4

a) Siemens MultiSPECT triple-head camera b) Siemens Diacam single-head camera

After June 1994, 65 studies were performed using the rest ^{201}Tl + stress ^{99m}Tc-MIBI protocol proposed by Berman et al. [8]. The doses of ^{201}Tl and ^{99m}Tc-MIBI were 3 and 25 mCi, respectively. The acquisitions were started at least 30 minutes after the injections of the tracers. The images were acquired for 40 seconds in 32 steps between the right anterior 45° and left posterior 45° positions, and then stored in a 64x64 matrix. For all cases, a Butterworth filter was used for filtered backprojection with a cutoff frequency of 0.45, order 5. The reconstructed transaxial slices were reoriented according to the long axis of the heart. Paired images of stress and rest short-axis, and vertical and horizontal long-axis slices were generated for visual analysis. Through the consensus of three experienced readers the tracer distributions in the vascular territory of stented arteries were classified in individual cases as: (a) normal; (b) a stress-induced perfusion defect with complete normalization at rest (a reversible defect); (c) a stress-induced perfusion defect with incomplete normalization at rest (a partially reversible defect); and (d) a perfusion defect at stress without a significant improvement at rest (a persistent defect). The observers knew the coronary angiography result at the time of stent implantation but were unaware of the results of the control coronary angiography. The assignment of the myocardial segments to individual vessels was guided by the coronary anatomy obtained from angiograms recorded at the time of stent implantation. Either a reversible defect or a partially reversible defect was considered a sign of stent restenosis.

Statistical analysis

Values were reported as mean ± standard deviation. Comparisons of proportions were performed by the chi-square test. A p value of <0.05 was considered statistically significant. The sensitivity and specificity values were calculated as follows: sensitivity (%) = 100 * (true positives)/(true positives + false negatives); specificity (%) = 100 * (true negatives)/(true negatives + false positives).

Results

Positron emission tomographic studies

Coronary angiography

The culprit lesions treated by stent implantation were located in the RCA in 5 cases, in the LAD in 8 cases and in the LCX in 1 case. On the basis of the criterion of ≥50% stenosis, only 1 of the 14 patients had a significant stenosis in a nonstented artery. In 8 cases, however, minor stenoses (≤50%) were present in one of the nonstented arteries. As reference territory, only the 19 arteries without minor stenoses were considered. All patients had at least one such vascular territory (Table 2).

Before the intervention, the mean minimal luminal diameter at the culprit lesion was 0.85 ± 0.25 mm and the stenosis grade was 72.1 ± 7.3%. After stent implantation the corresponding values were 3.18 ± 0.17 mm and 3.7 ± 6.7%, respectively.

Adenosine response

The systolic BP did not change significantly between the start of adenosine infusion and the time of N-13-ammonia injection (128.9 ± 14.1 vs. 128.9 ± 15.9 mmHg) (Table 3.). However, diastolic blood pressure decreased (76.8 ± 6.3 vs. 70.7 ± 6.6 mmHg, p=0.018), while the heart rate increased significantly during this period (64.1 ± 10.4 vs. 80.8 ± 7.8, p=0.001).

Myocardial blood flow and flow reserve

The mean blood myocardial blood flow at rest in the reference region was 76.1 ± 18.5 ml/min/100 g which increased o 179.4 ± 47.4 ml/min/100 during maximal vasodilation (Table 4). The myocardial blood flow did not differ significantly in the territories supplied by stented arteries, neither at rest nor during vasodilation, with values of 75.7 ± 17.7 ml/min/100 g (p = 0.89) and 205.5 ± 59.9 ml/min/100 g (p= 0.119), respectively (Figure 5).

The coronary flow reserve was 2.43 ± 0.55 in the reference region and 2.74 ± 0.64 in the areas supplied by stented arteries (p=0.129) (Figure 6).

Patient	Age	Stented artery	Reference artery	Artery not involved in the evaluation	Before stenting MLD (mm)	Before stenting Sten. (%)	After stenting MLD (mm)	After stenting Stenosis (%)
1	39	LAD	LCX	RCA	0.9	73	2.7	18
2	59	RCA	LAD, LCX	-	0.6	74	3.2	-3
3	66	RCA	LAD	LCX	0.4	86	3.2	-10
4	56	LAD	LCX	RCA	0.7	79	3.2	11
5	50	LAD	RCA	LCX	0.5	83	3.0	3
6	70	LAD	LCX	RCA	1.2	65	3.2	6
7	49	RCA	LAD, LCX	-	0.7	77	3.3	-3
8	72	RCA	LAD	LCX	1.2	63	3.8	12
9	50	LAD	RCA	LCX	1.3	59	3.0	3
10	72	LCX	LAD, RCA	-	0.5	83	3.1	-3
11	67	LAD	RCA, LCX	-	1.0	64	3.2	9
12	56	RCA	LCX	LAD	1.1	62	3.5	0
13	66	LAD	RCA, LCX	-	1.0	68	3.1	3
14	55	LAD	LCX	LAD	0.8	73	3.0	6
Mean	59.1				0.85	72.1	3.18	3.7
SD	8.4				0.25	7.3	0.17	6.7
p values versus before stenting							<0.0001	<0.0001

Table 2. Clinical and coronary angiographic data on 14 patients in the PET study (MLD = minimal luminal diametes)

Patient	Rest			Adenosine		
	Systolic BP	Diastolic BP	Heart rate	Systolic BP	Diastolic BP	Heart rate
1	110	80	47	110	60	78
2	130	80	47	110	60	78
3	110	60	76	110	60	97
4	160	80	74	160	80	86
5	100	80	57	120	70	106
6	140	85	73	160	80	82
7	150	80	64	130	70	82
8	140	70	58	145	80	65
9	120	70	62	110	60	72
10	140	90	82	140	80	82
11	115	70	50	120	70	79
12	140	80	55	150	70	63
13	130	80	80	120	80	85
14	120	70	72	120	70	76
Mean	128.9	76.8	64.1	128.9	70.7	80.8
SD	14.1	6.3	10.4	15.9	6.6	7.8
p values versus Rest data					1.000	0.018
0.001						

Table 3. Hemodynamic parameters at the time of rest and adenosine PET acquisitions (BP= blood pressure)

Patient	Remote area			Stented area		
	Rest flow	Adenosine flow	CFR	Rest flow	Adenosine flow	CFR
1	62	199	3.2	68	226	3.3
2	64	212	3.3	64	208	3.2
3	78	196	2.5	96	218	2.3
4	65	200	3.1	66	187	2.8
5	65	204	3.1	63	283	4.5
6	89	151	1.7	88	343	3.9
7	95	209	2.2	96	156	1.6
8	87	142	1.6	79	160	2.0
9	43	100	2.3	54	150	2.8
10	155	368	2.4	134	374	2.8
11	86	149	1.7	85	203	2.4
12	43	137	3.2	50	153	3.1
13	54	88	1.6	52	85	1.6
14	79	157	2.0	65	131	2.0
Mean	76.1	179.4	2.43	75.7	205.5	2.74
SD	18.5	47.4	0.55	17.7	59.9	0.64
p values versus Remote area data				0.89	0.119	0.1292

Table 4. Myocardial blood flow (ml/min/100 g) and coronary flow reserve (CFR) as determined by PET

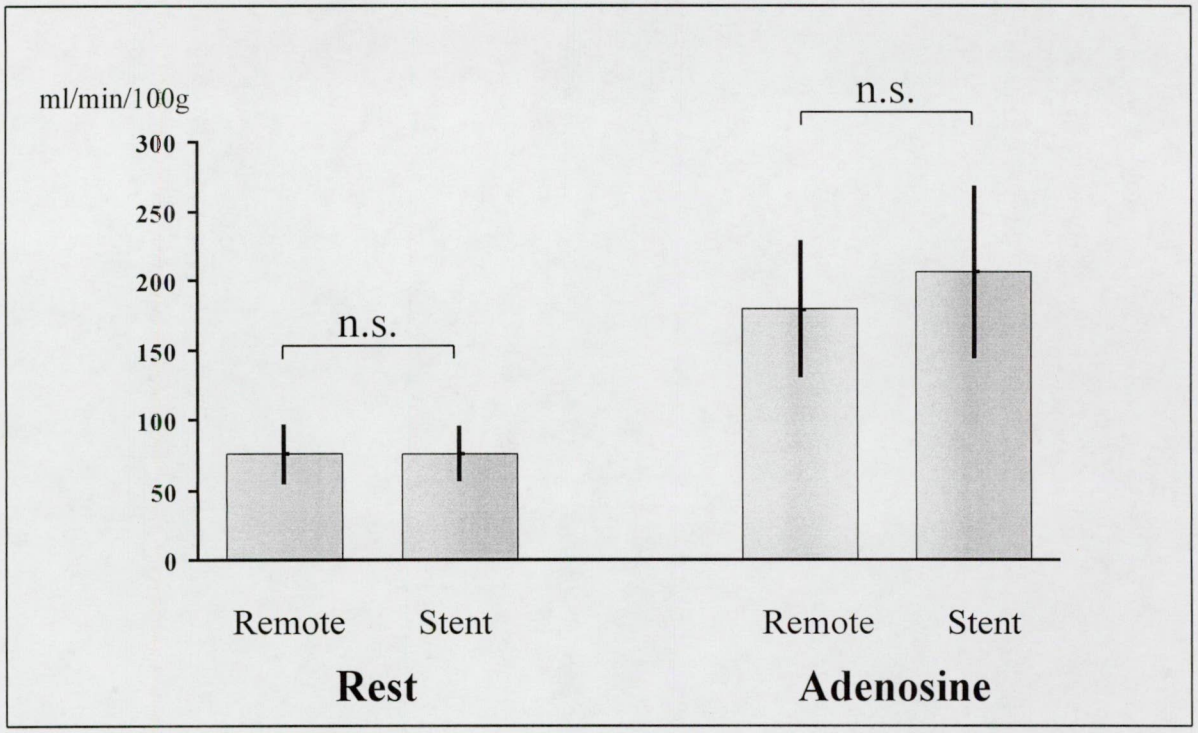


Figure 5. Bar graph of myocardial blood flow data determined by PET in stented vascular territories and remote areas.

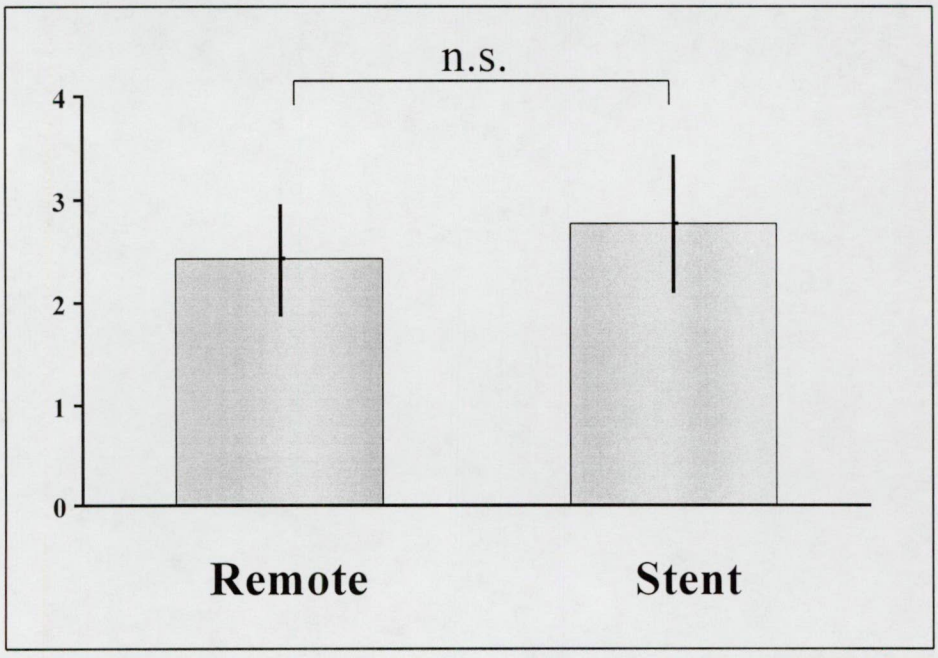


Figure 6. Bar graph of coronary flow reserve determined by PET in stented vascular territories and remote areas.

Single photon emission computed tomographic studies

Coronary arteriography

Nineteen of 99 investigated arteries displayed ≥50% stenosis at the site of the coronary stent on control coronary angiography. The restenosed stents were located in the RCA (5), the LAD (10), the LCX (3) or in a coronary bypass graft to the LCX (1). Eleven stent restenoses were observed in the 47 stented regions with a previous myocardial infarction. There was no significant correlation between the stent restenosis and the documented previous myocardial infarction.

Stress perfusion imaging

The characteristics of exercise performance and the results of perfusion scintigraphic studies are summarized in Tables 4 and 5. A persistent or only partially reversible perfusion defect was present in 35 of 47 (74%) vascular territories with a previous myocardial infarction, while 47 of 52 (90%) territories without myocardial infarction showed no defect at rest.

Table 4. Characteristic of exercise performance (n=83)

	Baseline	Maximum
Heart rate (beats/min)	70.8±14.7	140.1±20.4
RR systolic (mm Hg)	134.1±19.2	184.6±25.4
RR diastolic (mm Hg)	79.9±10.7	94.3±12.1
Double product (mm Hg/min*100)		257.4±62.0
85% of age-predicted maximal heart rate not achieved		22

Table 5. Scintigraphic pattern of stented vascular territories (n=99)

Scintigraphic pattern	Total population	Territories with AMI	Territories without AMI
Number	99	47	52
Normal	44 (44%)	9 (19%)	35 (67%)
Reversible defect	15 (15%)	3 (6%)	12 (23%)
Partially reversible defect	18 (18%)	14 (30%)	4 (8%)
Persistent defect	22 (22%)	21 (45%)	1 (2%)

The sensitivity, specificity and accuracy indices of the clinical parameters of the stress tests and the perfusion scintigraphic studies are listed in Table 6. The transient perfusion pattern observed by means of scintigraphy identified 15 of 19 territories with stent restenosis (sensitivity 79%), while 62 of 80 territories without stent restenosis showed either the normal distribution of the tracer or a perfusion defect without redistribution (specificity 78%). In the subpopulation of patients with a previous myocardial infarction, stent restenosis was detected with a sensitivity of 7/11 (64%) and a specificity of 26/36 (72%). In patients without a previous myocardial infarction, the sensitivity and specificity values were 8/8 (100%) and 36/44 (82%), respectively. The accuracy of the scintigraphic parameters was higher than that of the appearance of angina or a significant ECG abnormality during the stress tests.

	All territories	Territories with AMI	Territories without AMI	Territories evaluated prospectively
Number	99	47	52	65
Angina in stress test				
Number	16	7	9	11
Sensitivity (%)	5/19 (26%)	1/11 (9%)	4/ 8 (50%)	4/15 (27%)
Specificity (%)	69/80 (86%)	30/36 (83%)	39/44 (89%)	43/50 (86%)
Accuracy (%)	74/99 (75%)	31/47 (66%)	43/52 (83%)	47/65 (72%)
Significant ECG change during stress test				
Number	30	17	13	20
Sensitivity (%)	4/19 (21%)	2/11 (18%)	2 / 8 (25%)	4/15 (27%)
Specificity (%)	54/80 (68%)	21/36 (58%)	33/44 (75%)	34/50 (68%)
Accuracy (%)	58/99 (59%)	23/47 (49%)	35/52 (67%)	38/65 (58%)
Transient perfusion pattern in the scintigram				
Number	29	15	14	22
Sensitivity (%)	15/19 (79%)	7/11 (64%)	8/8 (100%)	12/15 (80%)
Specificity (%)	62/80 (78%)	26/36 (72%)	36/44 (82%)	40/50 (80%)
Accuracy (%)	77/99 (79%)	33/47 (70%)	44/52 (85%)	52/65 (80%)

Table 6. Sensitivity, specificity and accuracy values of stress tests and perfusion SPECT for the evaluation of stent restenosis in different patient subpopulations

To evaluate the effectiveness of perfusion scintigraphy in a population less affected by referral bias, we separately analyzed the data on 65 territories in 60 patients who underwent perfusion scintigraphy prospectively as part of a 6-month follow-up. The observed 80% sensitivity and 80% specificity values did not differ significantly from those for the total population.

The effect of side-branch stenoses on the scintigraphic findings was analyzed on the basis of 18 cases without stent restenosis, but with a transient perfusion pattern on scintigraphy. Stenoses of the side-branch arteries were detected in 8 of these 18 cases, including the first diagonal artery of the LAD in 6 cases, the septal branch of the LAD in 1 case, and the ramus posterolateralis of the RCX in 1 case. The development of side-branch stenosis was documented angiographically at the time of the stent implantation in 3 cases (2 first diagonal and 1 septal branch stenoses), while in 5 other cases it existed before stent implantation. The perfusion abnormality on scintigraphy was typical for the first diagonal stenosis, including only the basal anterolateral area of the left ventricle in 2 of the 8 cases. It was also clear that a small, reversible perfusion abnormality, located in the basal area of the anterior septum, was associated with severe stenosis of the septal branch of the LAD (Figure 7). In 4 cases with first diagonal stenosis, however, we were not able to distinguish the induced perfusion abnormality from the expected vascular territory of the stented LAD. Similarly, in the patient with the stenosed ramus posterolateralis, the induced perfusion defect did not differ significantly from the expected vascular territory of the ramus circumflexus.

In addition to the 8 cases with side-branch stenosis, there was a discrepancy between the coronary angiographic findings regarding stent restenosis and the presence or absence of a defect reversibility on scintigraphy in 14 cases. In 4 of these 14 cases, a stenosis was detected in other regions of the stented arteries, which were responsible for the transient pattern on scintigraphy in the absence of restenosis of the stent. In 6 cases, the coronary angiographic findings did not give a reasonable explanation for the transient perfusion abnormality on scintigraphy. In 4 cases, the reason for the discrepancy was the lack of defect reversibility in the presence of the stent restenosis. All of these cases were in vascular territories with a previous myocardial infarction. The severity of luminal stenosis in the area of the stent was 50% in 2 cases and 75% in the other 2 cases.

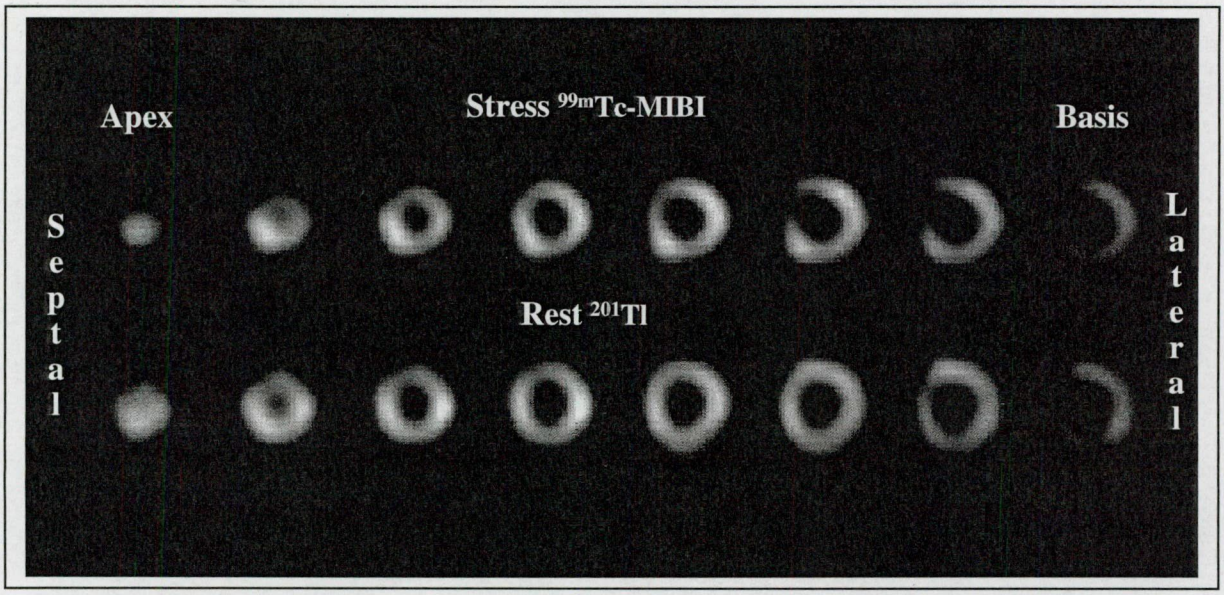


Figure 7 Short-axis SPECT images of a patient with sequential coronary stents in the proximal portion of the LAD. At the time of stent implantation, a significant stenosis developed at the origin of the septal branch artery in this patient. The ^{99m}Tc-MIBI stress images reveal a small area with hypoperfusion in the basal, anteroseptal region. The ^{201}Tl rest images indicate a normal tracer distribution. Coronary angiography demonstrated no significant restenosis in the region of the implanted stents. The reversible perfusion abnormality on stress scintigraphy corresponds to the stenosis of a side-branch artery.

Discussion

The results of our PET study demonstrate that the myocardial blood flow at rest and during maximal vasodilation, and also the coronary flow reserve, are similar in the territory of stented arteries as compared with remote areas within the first 3 days following stent implantation.

Flow changes after PTCA

A number of studies performed in the first few days after PTCA have demonstrated a relative decrease in coronary flow reserve in comparison with remote areas [56,66,87,116,125,127]. The cause of this slow recovery, however, is unclear. The possible role of flow-limiting residual stenosis after the intervention has been demonstrated only by Zijstra et al. [130]. Most authors considered factors involving the distal vasoregulation, resulting in an increase of the resting flow [56,87,116,119], or restricting stress flow [87,116].

Flow changes after stent implantation

Studies to determine flow changes after stent implantation are rare, but recent results obtained by using quantitative angiography and Doppler flow wire techniques have been published [33,44]. These indicate that the moderate improvement in coronary reserve after balloon dilation, and its normalization after stent implantation, correlate well with the changes in minimal luminal diameter during the procedures. These authors did not find a significant change in the resting blood flow, so the alteration in the coronary flow reserve was a consequence of the improved myocardial flow at maximal vasodilation [44]. Their data point to the stress flow reaching a similar level in the stented vascular territory as in remote areas. These reported data are in agreement with the present results.

Angiographic result of PTCA

In most clinical centers, PTCA is considered successful if the residual stenosis is <50%. Consequently, the average residual stenosis in the studies mentioned above ranged between 18 and 37%. Additionally, the minimal luminal diameter is a dynamically changing index after this intervention. The treated segments are prone to spasm and elastic recoil of the vessel

wall. An increased susceptibility of dilated segments to a coronary spasm has been observed in several studies after PTCA [24,27,100]. According to El-Tamimi et al., an average 30% decrease in minimal luminal diameter can be demonstrated 4 hours after PTCA, which is reversible after the administration of intracoronary nitroglycerine. This study also revealed that the basal tone of dilated segments decreases with time, as assessed by repeated investigation at 8 days. The time course of the basal coronary tone change is similar to that of coronary flow impairment reported after PTCA [66,75,116,127,130]. A second recently discussed factor altering the luminal diameter is the remodeling of coronary arteries. The importance of this mechanism has been suggested in the development of restenosis after PTCA [54,82,97]. Recently, De Franco and Topol also postolated its pathophysiological role in the late restoration of coronary reserve [20].

Macroscopic result after stent implantation

In contrast with PTCA, the implantation of stents in most cases normalizes the contour of treated vessels. A difference in angiographic results between PTCA and stent implantation has been found in several studies [28,55,109,111]. Accordingly, the value of residual stenosis in our stented population was only $3.5 \pm 8.0\%$. Furthermore, the luminal diameter is expected to be stable after this intervention. Serial intravascular ultrasound studies have failed to provide evidence of chronic stent recoil early after intervention [45,92]. The restoration of the coronary flow reserve in our patient population, where residual stenoses were practically absent, supports the theory that the minimal luminal diameter is determinant as regards the distal coronary reserve.

However, the stress flow and coronary reserve tended toward higher values in the stented vascular territories as compared with the control areas. This interesting observation may reflect chronic vascular adaptation in the poststenotic vascular bed. The long-standing reduction of perfusion pressure in these areas may induce an increased perfusion capacity, but not hypersensitivity of the vascular bed toward normal perfusion pressure, as suggested earlier by several authors [56,87,116]. The normal resting blood flow rather supports the notion of an intact vasoregulation in these areas. The presumed enhanced vasodilatory capacity of poststenotic areas may have been masked by local restriction of the epicardial vessel segments after PTCA in earlier studies.

Limitations of PET study

In our PET study, the myocardial blood flow was quantified in stented vascular territories and the data were compared with the results on remote areas in the same patient. A direct comparison with a healthy population using the same technique was not performed. Previous studies have demonstrated that patients with proven CAD have an abnormal coronary flow reserve in angiographically normal arteries [6,117], as do patients without angiographic evidence of CAD, but with risk factors for CAD [19]. Therefore, the comparison of various vascular territories within a given patient appeared to be more appropriate than relating the results to a healthy control population. The patients were evaluated only early after intervention: no late follow-up was performed. However, the preliminary analysis of the first 6 patients suggested full restoration of the coronary flow reserve at the time of the early investigation. The follow-up results on 3 patients (1 to 3 days and 2 weeks after the intervention), where similar coronary flow reserve values were found (rest flows of 70.8 and 65.7 ml/min/100 g, stress flows of 244.7 and 226.3, and coronary reserves of 3.5 and 3.5, respectively, in the control and stented territories) led to the subsequent follow-up studies being discontinued to reduce the logistic complexity of the study and to minimize the radiation exposure to the patients.

An additional limitation of our PET study is that it did not include flow measurement data before the intervention. This was due to the logistics of stent implantation. The decision to implant stents was made only during the revascularization procedure, and therefore prior PET measurements could not be performed electively. However, the coronary angiographic data on our population and the results of previous studies demonstrating the close correlation between the severity of coronary stenosis and the distal coronary flow reserve [21,118] indicate that it is reasonable to assume a significantly reduced flow reserve before the interventions.

Diagnostic accuracy of SPECT in stented patients

The results of our SPECT study show that stress myocardial perfusion imaging using the criterion of defect reversibility has a good diagnostic performance for the detection of restenosis in patients after coronary stent implantation. Sensitivity and specificity values are higher in territories without a previous myocardial infarction.

Using the defect reversibility criterion, we identified 79% of vascular territories with and 78% of those without restenosis in the region of the implanted coronary stents. These values are

comparable with those reported for SPECT in the primary detection of CAD in individual native arteries (sensitivity 73% and 79%, specificity 83% and 84%, respectively) [26,72]. For the identification of restenosis in individual arteries after PTCA, the reported sensitivity values range between 75% and 94%, while the specificity ranges between 84% and 93% [46,76,103,110]. However, most of these data are based on a selected population of patients with a low prevalence of either multivessel disease or a previous myocardial infarction [76,103,110].

Effect of previous myocardial infarction on SPECT accuracy

The effect of a previous myocardial infarction on the accuracy of the test results was documented in our study by comparing the subgroups with and without previous myocardial infarctions. We found the sensitivity and specificity values for the detection of stent restenosis to be very high in territories without a previous myocardial infarction (100% and 82%, respectively), and somewhat lower in territories with a previous myocardial infarction (64% and 72%, respectively).

The evaluation criterion in most of the earlier studies was the detection of any coronary stenosis in a vascular tree [71,72]. Use of this method, i.e. the inclusion of territories with a myocardial infarction, which may be detected more reliably due to the severe perfusion abnormalities, increased the overall effectiveness of the test. The clinical question in patients with regional revascularization, however, is the detailed analysis of the regional myocardial perfusion distribution rather than the overall evaluation of the three main vascular territories. Our study population also included territories with a previous myocardial infarction in which the coronary stent was implanted to treat a residual stenosis. The scintigraphic evaluation of stent restenosis in such cases is limited due to the pre-existing perfusion abnormalities. The reduced accuracy of perfusion scintigraphy was reported in a previous study analyzing vascular territories with a previous myocardial infarction and a subsequent revascularization procedure. The sensitivity and specificity for the planar imaging method were only 50% and 79%, respectively [124].

Cause of transient SPECT defect in patients with patent stents

Reversible perfusion defects also appeared without stent restenosis. We found 18 such cases in our population. The most frequent anatomical abnormality observed, inducing a reversible defect without stent restenosis, was stenosis of the side-branch arteries (8 cases). The development of the side-branch stenoses is a known complication of stent implantation. Its reported frequency at the time of implantation varies from 5% to 27%. The available data are uneven as regards the eventual evolution of side-branch stenoses. In our population, 3 of the 8 side-branch-stenosed cases involved patients enrolled prospectively in the study and 2 were revealed on scintigraphy that evaluated the hemodynamic significance of known stenoses in other vascular territories. In 3 cases, the perfusion studies were indicated clinically by the patient complaints. The development of ostial stenosis in the side-branches at the time of stent implantation was documented in 3 of the 8 cases (2 at the origin of the first diagonal and 1 at the origin of the septal branch of the LAD). Two of these patients were enrolled in our study because of chest pain. The scintigscans of these patients, however, revealed only small perfusion abnormalities located in the basal area of the left ventricle, which were considered to be a consequence of side-branch stenosis rather than stent restenosis. The "true" false-positive rate of perfusion defects was very low in the studied patients (10). The data highlight the fact that careful correlation of the scintigraphic and angiographic information is necessary to maximize the diagnostic test performance.

Perfusion pattern in borderline restenosis

There were 4 cases in our population with a stent restenosis between 50% and 75%, but with no reversible pattern of tracer distribution in the corresponding vascular territory. In 4 patients with a similar severity of stent restenosis, a reversible perfusion abnormality was detected by scintigraphy. The appropriate choice of cutoff values for defining hemodynamically significant restenosis remains a subject of controversy. For compatibility with the findings of recently published coronary angiographic studies evaluating stent restenosis, we used 50% instead of 75% for the definition of stent restenosis.

Effect of referral bias on the calculated value of accuracy

The evaluation of any diagnostic test used in the clinical routine may be influenced by referral bias. This is due to a higher frequency of invasive controls after abnormal test results than after normal results. To reduce this effect in our study, we included most patients prospectively as part of the routine follow-up. The analysis of this subpopulation did not reveal any difference as compared with the overall population.

Limitations of SPECT study

One limitation of the SPECT study was the use of different stress methods. However, the parallel application of exercise and pharmacological stresses to evaluate the myocardial perfusion reserve is widely accepted [53,67]. For patients who cannot exercise, pharmacological stress provides more reliable test results than does ineffective exercise [53,67]. In our population, the most appropriate test was selected for each patient.

All images in this study were analyzed by qualitative evaluation, which may be considered a study limitation. The main advantage of quantitative analysis over the qualitative interpretation of experienced observers is the reduced intra- and interobserver variability [1,90], which allows the better detection of small changes in myocardial perfusion (i.e. the effectiveness of therapy). In this study, our aim was to determine the effectiveness of the most commonly applied clinical approach, which is visual interpretation.

Conclusions and new findings

1. In accordance with the literature data, the coronary flow reserve of myocardial areas supplied by angiographically normal coronary arteries is reduced in patients with proved CAD.
2. Early after stent implantation, the coronary flow reserve in myocardial areas perfused through the stent is similar to those of areas supplied by angiographically normal coronary arteries.
3. The early restoration of the coronary flow reserve after stent implantation affords indirect evidence for the role of local factors (elastic recoil and vascular remodeling) in the early changes in coronary flow reserve after PTCA.
4. Stress-induced perfusion defects with reversibility at rest as the criterion in stress perfusion SPECT is an accurate criterion for the detection of chronic restenosis of coronary artery stents.
5. The sensitivity of the above-mentioned criterion is limited in vascular territories with a previous myocardial infarction.
6. The perfusion abnormalities induced by stenoses of the side-branch arteries should be considered in the evaluation; however, perfusion abnormalities seen on perfusion SPECT that are due to stent-induced side-branch stenoses are relatively infrequent.

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Abbreviations

^{201}Tl	thallium-201
^{99m}Tc	technetium-99m
ATP	adenosine triphosphate
BP	blood pressure
CABG	coronary artery bypass grafting
CAD	coronary artery disease
ECG	electrocardiogram
LAD	left anterior descending artery
LCX	left circumflex artery
MIBI	methoxy-isobutyl-isonitrile
PET	positron emission tomography
PTCA	percutaneous transluminal coronary angioplasty
RCA	right coronary artery
SPECT	single photon emission computed tomography

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