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Functional Significance of Recruitable Collaterals During Temporary Coronary Occlusion Evaluated by ^{99m}Tc-Sestamibi Single-Photon Emission Computerized Tomography

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OBJECTIVES The present study evaluated the impact of recruitable collaterals on regional myocardial perfusion measured by ^{99m}technetium (Tc)-sestamibi single-photon emission computerized tomography (SPECT) during temporary coronary occlusion and related these estimates to the coronary wedge pressure and electrocardiographic (ECG) ST-segment changes.

BACKGROUND Clinical variables (angina and ECG changes) and intracoronary flow and pressure recordings have indicated a protective role of recruitable collaterals on myocardial perfusion during percutaneous transluminal coronary angioplasty (PTCA).

METHODS Thirty patients (mean age 55 years, SD 9; 20 men) with stable angina pectoris and proximal nonoccluding single-vessel left anterior descending coronary artery (LAD)-stenosis scheduled for PTCA were included. Visualization of recruitable collaterals by ipsilateral and contralateral contrast injection, registration of coronary wedge pressure and injection of ^{99m}Tc-sestamibi during 90-s LAD occlusions were undertaken. A rest perfusion study was performed within four days before PTCA. As an estimate of the severity of regional hypoperfusion during occlusion, an occlusion/rest count ratio was calculated (mean defect pixel count during occlusion divided by mean pixel count in identical regions at rest).

RESULTS The scintigraphic occlusion/rest count ratio was higher in patients with recruitable collaterals ($n = 16$), $67 \pm 11\%$, compared to patients without collaterals ($n = 14$), $60 \pm 6\%$ ($p < 0.05$). The occlusion/rest count ratio correlated with the coronary wedge pressure ($R^2 = 0.34$; $p < 0.001$). The occlusion/rest count ratio was lower, $61 \pm 6\%$, in patients with ST-segment elevation ($n = 23$) versus $74 \pm 9\%$ in patients without ST-segment elevation ($n = 7$) ($p < 0.0001$).

CONCLUSIONS Using ^{99m}Tc-sestamibi SPECT imaging during brief episodes of coronary occlusion, the severity of regional myocardial hypoperfusion was reduced by the presence of recruitable collaterals in a selected patient population with proximal LAD stenoses. Our results demonstrate a protective effect of recruitable collaterals on myocardial perfusion during temporary coronary occlusion. (J Am Coll Cardiol 2000;35:624–32) © 2000 by the American College of Cardiology

The protective role of coronary collaterals during occlusion of coronary arteries in humans has been debated for years. In infarct patients with angiographically verified collaterals, the extent of myocardial necrosis is smaller compared to patients without collateral supply, evidenced by biochemical (1) and scintigraphic estimates of infarct sizes (2–4), and by less severe regional and global contractile dysfunction (5). Aneurysm formation has been reported to be less frequent in patients with collateral supply to the infarct-related artery (6).

By injecting contrast medium in both the contralateral and the ipsilateral coronary artery during controlled coronary occlusion by percutaneous transluminal coronary angioplasty (PTCA), Rentrop et al. (7) developed a method that enabled visualization of collaterals (recruitable collaterals) that were not visualized during routine angiography

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Abbreviations and Acronyms

AUC	= area under the curve
LAD	= left anterior descending coronary artery
PTCA	= percutaneous transluminal coronary angioplasty
SPECT	= single-photon emission computerized tomography
^{99m}Tc-sestamibi	= ^{99m}-technetium-sestamibi

(spontaneously visible collaterals). The existence of recruitable collaterals has been demonstrated in 30% to 60% of patients with single-vessel disease (8,9) and has shown protective effects during controlled coronary occlusion evidenced by less occurrence of angina and electrocardiographic changes (9,10) in patients with recruitable collaterals compared to patients without. None of these studies included direct estimates of myocardial perfusion.

The primary aim of this study was to evaluate the impact of recruitable collaterals on regional myocardial perfusion by ^{99m}Tc-sestamibi single-photon emission computerized tomography (SPECT) during temporary coronary occlusion in a selected patient population with proximal left anterior descending coronary artery (LAD)-stenosis undergoing PTCA.

METHODS

Patient population. To obtain a population with a high probability of recruitable collaterals, we prospectively included patients with angina pectoris, who were admitted for coronary angioplasty due to angiographically verified proximal (segment 1 or 2) single-vessel nonoccluding LAD stenosis with a grade of stenosis between 50% and 95% and an ejection fraction above 50%, assessed by biplane ventriculography, as the frequency of spontaneously visible collaterals was assumed to be higher in patients with occlusive coronary disease and in patients who had survived Q-wave myocardial infarctions. Excluded were patients with 1) myocardial infarction within three months; 2) previous anterior Q-wave infarction; 3) previous revascularization (coronary bypass surgery or PTCA); 4) hemodynamically significant valvular heart disease; 5) uncontrolled hypertension defined as resting systolic blood pressure >200 mm Hg or resting diastolic blood pressure >100 mm Hg; 6) hypertrophic cardiomyopathy; 7) chronic or paroxysmal atrial fibrillation or flutter; and 8) left bundle branch block.

Patients continued their usual medication throughout the study. The study was approved by the local ethical committee and conducted in accordance with the Helsinki-II declaration. All patients received verbal and written information and gave informed consent before inclusion.

Invasive procedures. COLLATERALS AND GRADE OF STENOSIS. Coronary angioplasty was performed by the percutaneous femoral approach by an over-the-wire system. An 8F guiding catheter was used for guidance of the balloon catheter and a 6F catheter for angiography of the contralateral coronary artery. Before angioplasty, contralateral and ipsilateral contrast injections were performed to visualize spontaneously visible collaterals. Cineangiography was continued until no further opacification of the injected vascular bed was present. After angioplasty, the balloon catheter was reintroduced to the site of the treated lesion and the balloon was reinflated at low pressure (1.5 to 2 bar). After 30 s, repeat angiograms with first contra- and then ipsilateral contrast injections were performed to visualize recruitable collaterals and to ensure total balloon occlusion (7).

Spontaneously visible and recruitable collateral blood flows were assessed in accordance with the classification proposed and validated by Rentrop et al. (7): 0: no contrast filling of the recipient artery; 1: filling of side branches of the recipient artery; 2: partial filling of the recipient artery; 3: complete filling of the recipient artery. Patients with grade 2 or 3 collaterals were classified as having collaterals, whereas patients with grade 0 or 1 were classified as having no collaterals. Grades of stenosis and the occurrence of collaterals were evaluated blindly by one experienced angiographer by visual analysis.

CORONARY WEDGE PRESSURE. Simultaneously with visualization of recruitable collateral flow, the mean distal coronary occlusion pressure was assessed by a dedicated pressure transducer (Baxter, the Netherlands). After positioning of the balloon in the treated lesion, the guide wire was removed, and it was ascertained that the lumen of the catheter was fluid-filled and without any air microbubbles. Balloon inflation at low pressure (1.5 to 2 bars) was undertaken with simultaneous registration of distal intracoronary pressure, which was recorded on graph paper. As soon as the pressure curve leveled off, approximately 30 s after balloon inflation, the mean distal coronary pressure was registered (7,11). Ipsilateral contrast injection was performed to check complete balloon occlusion.

Mean aortic pressure was measured through the guiding catheter and registered simultaneously with the coronary wedge pressure. Heart rate was monitored continuously during the procedure.

Electrocardiographic changes and chest pain. A 12-lead ECG was recorded during balloon occlusion and continued until 30 s after balloon deflation or until disappearance of any significant electrocardiographic changes. The ST-segment elevation equal to or exceeding 0.2 mV measured at the J-point or ST-segment depression equal to or exceeding 0.1 mV measured 80 ms after the J-point were considered as significant markers of myocardial ischemia.

Patients were asked about chest pain during angioplasty at every balloon occlusion according to the Borg scale (12).

A score of 0 indicated no chest pain, and a score of 10 indicated extremely strong chest pain.

Scintigraphy. Studies of regional myocardial perfusion were performed at rest (within four days before the angioplastic procedure) and during low-pressure balloon occlusion of 90 s at the end of the therapeutic procedure. ^{99m}-Technetium-sestamibi (^{99m}Tc-sestamibi; Cardiolite, Dupont, Hertfordshire, UK) was injected as a bolus of 700 MBq ± 10% in an antecubital vein and followed by 10 ml of saline. Image acquisition was performed 1 h after tracer injection. The SPECT acquisition was carried out with patients in the supine position using a single-headed rotating gamma camera (Genesys, ADAC) with a high-resolution, parallel-holed collimator. Sixty-four projections of 20 s each were obtained over a noncircular 180° arc, extending from the 45° right anterior oblique to the 45° left posterior oblique position. A 20% symmetric energy window centered on the 140-keV peak was used. Both the injected dosage of sestamibi and the scintigraphic procedure during the rest scan were identical to the PTCA procedure. All projection images were stored on magneto-optic disks in a 64 × 64 matrix. Filtered backprojection was performed using a Butterworth filter with a cutoff frequency of 0.35 cycles/pixel, order 5, to reconstruct transverse axial tomograms. No attenuation or scatter correction was used. Raw data were checked for patient motion. Reorientation of slices was performed after reconstruction according to the anatomic axis of the heart. Slices were displayed as short axis, vertical, and horizontal long axis slices.

Polar maps were automatically generated, and the size of the PTCA-induced perfusion defects was estimated in accordance with the Cedar's-Sinai program (13), in which the volume-weighted polar maps were compared to gender-specific normal databases of regional myocardial perfusion at rest. The severity of the PTCA-induced perfusion defects was calculated by normalizing pixel counts in the polar maps obtained in the PTCA study and the rest study to maximum pixel count. The blackout from the polar map of the PTCA study was transferred to the polar map obtained at rest, and the average pixel counts in these blackout areas were divided to assess an occlusion/rest count ratio, which was taken as an estimate of the severity of myocardial hypoperfusion induced by the coronary occlusion. All studies were validated by visual assessment of scintigrams and performed blinded to all other patient data.

Arterial plasma profile of ^{99m}Tc-sestamibi. To evaluate the amount of recirculating sestamibi at the time of balloon deflation, arterial blood samples of 1 ml were sampled from the left femoral artery in 11 consecutive patients every 5 s during the first 5 min after ^{99m}Tc-sestamibi injection with a dedicated sample collector (Ole Dich Instruments, Denmark). All samples were counted as 0.5 ml whole blood samples the day after collection (Cobra II, Packard). Radioactivity was corrected for decay and expressed as a percentage of radioactivity in the blood sample with peak activity. The amount of sestamibi available for myocardial uptake was calculated as the area under the curve (AUC) by numeric integration and by exponential fitting and extrapolation to 1-h postinjection (start of imaging).

Statistical analysis. Data were expressed as proportions or as mean with standard deviations (SD) in normal distributed data or by median and range in nonparametric distributions. Either the chi-square test or the Fisher exact test was used for evaluation of differences between proportions. Differences of mean values in normal distributed data were assessed by the Student *t* test and by the Mann-Whitney *U* test in nonparametric distributions. Relations between continuous variables were described by linear regression analyses and expressed as R^2 values. All tests were two-tailed, and p values less than 0.05 were considered significant.

RESULTS

Thirty-six patients were included in the study. Severe coronary spasm during the PTCA procedure occurred in two patients, significant patient movement during SPECT imaging in two patients, progression of the coronary lesion to a total occlusion between diagnostic angiography and PTCA in one patient and unintended occlusion of the balloon in the circumflex territory during sestamibi injection in one patient with an ostium LAD stenosis. The remaining 30 patients (mean age 55 years, SD 9; 20 men) completed the study protocol. No complications were induced by the additional balloon occlusions.

Demographic data. As seen in Table 1, the only significant difference between patients with (n = 16) and without collaterals (n = 14) was a higher proportion of men in the group with collaterals. This difference was not related to the median duration of anginal symptoms, 12 months (5 to 90 months) for women versus 14 months (6 to 60 months) for men (NS), the occurrence of prior myocardial infarction, 30% of women versus 25% of men (NS), or the median grade of stenosis, 85% (55% to 95%) for women versus 80% (70% to 95%) for men (NS). Eight patients had a history of a prior myocardial infarction, five non-Q-wave anterior infarctions, two non-Q-wave infarctions with unknown location, and one Q-wave inferior infarction. Most infarctions were likely to be small as the mean ejection fraction was normal and did not differ from patients without prior myocardial infarction, 72% (57% to 91%) versus 75% (60% to 88%) (NS), respectively.

Invasive procedures. Sixteen patients were treated with PTCA as the only treatment, 12 patients with PTCA and stenting, 1 patient with atherectomy and PTCA, and 1 patient was treated with rotablation and PTCA. A median of four dilations (2 to 7 dilations) were performed per patient. No differences were observed between patients with and without collaterals.

Table 1. Demographic Data in 30 Patients with Nonoccluding LAD Stenosis in Relation to the Occurrence of Recruitable Collaterals

	+Collaterals (n = 16)	−Collaterals (n = 14)	p Value
Age, years, mean ± SD	56 ± 8	55 ± 10	NS
Gender, male, n (%)	88	43	0.02
Prior MI, n (%)	38	14	NS
AP duration, months, median (range)	12 (5–84)	14 (6–90)	NS
AP attacks per week, median (range)	7 (5–25)	10 (5–100)	NS (0.06)
CCS class, n			
1	4	3	
2	7	7	
3	5	4	NS
4	0	0	
Rest AP, n (%)	38	79	NS (0.06)
Smoking, n (%)	75	79	NS
Hypercholesterolemia, n (%)	63	43	NS
Diabetes, n (%)	13	0	NS
Hypertension, n (%)	6	21	NS
Family history of CAD, n (%)	56	43	NS
Long-acting nitrates, n (%)	50	43	NS
Ca-antagonists, n (%)	19	50	NS
Beta-blockers, n (%)	81	57	NS
≥2 antianginal drugs, n (%)	50	50	NS
Acetylsalicylic acid, n (%)	88	79	NS

AP: angina pectoris; CCS: classification of Canadian Cardiological Society; Family history of CAD: ≥1. generation relative with CAD; hypercholesterolemia: total se-cholesterol >6 mmol/liter or cholesterol-lowering therapy; hypertension; based on anamnestic diagnosis; MI: myocardial infarction; smoking: patients who stopped smoking within three years or were currently smoking.

COLLATERALS AND GRADES OF STENOSIS. Baseline angiography of the contralateral vessel (right coronary artery) revealed spontaneously visible collaterals in only one patient (grade 2). During balloon occlusion 11 patients developed grade 3 recruitable collaterals, 5 patients grade 2 collaterals, 4 patients grade 1 collaterals, and 10 patients remained without collateral filling (Fig. 1). Patients with grade 1 or 2 spontaneously visible collaterals during baseline developed a more evident collateral supply during vessel occlusion. Accordingly, 16 patients were classified as having recruitable collaterals (grade 2 or 3) and 14 patients as having no collateral supply during occlusion (grade 0 or 1).

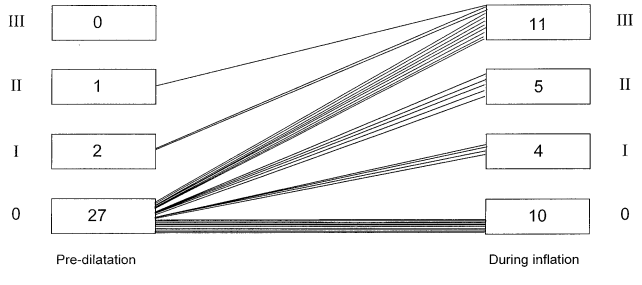

Figure 1. Change of collateral grade during temporary coronary occlusion. The collateral grades pre-dilation and during inflation are given by III: grade 3 collaterals; II: grade 2 collaterals; I: grade 1 collaterals; 0: no collaterals. The number of patients with a certain collateral grade is shown in the boxes.

The median grade of stenosis in vessels receiving recruitable collaterals, 85% (70% to 95%) was significantly higher than in vessels without collaterals, 75% (55% to 90%), ($p < 0.05$). Ejection fractions ranged from 57% to 91%, with a mean value of 73 ± 10% in patients with collaterals and 72 ± 9% in patients without (NS).

COLLATERALS AND CORONARY WEDGE PRESSURE. The mean overall coronary wedge pressure was 27 ± 11 mm Hg, range 8 to 57 mm Hg, being significantly higher, 33 ± 10 mm Hg, in vessels with angiographically demonstrable collateral supply versus 21 ± 7 mm Hg in those without ($p < 0.001$). A coronary wedge pressure above 30 mm Hg was found in 8 of 16 patients with collateral supply as opposed to 1 of 14 patients without collateral supply ($p < 0.01$). The ratio between the coronary wedge pressure and the simultaneously measured mean aortic pressure was 0.34 ± 0.08 in patients with collaterals versus 0.22 ± 0.06 in patients without collaterals ($p < 0.001$).

HEMODYNAMICS. Mean aortic pressure during balloon occlusion, at which the evaluation of collaterals was performed, was 98 ± 15 mm Hg in patients with collaterals versus 92 ± 14 mm Hg in patients without recruitable collaterals (NS). Mean heart rate during occlusion was 67 ±

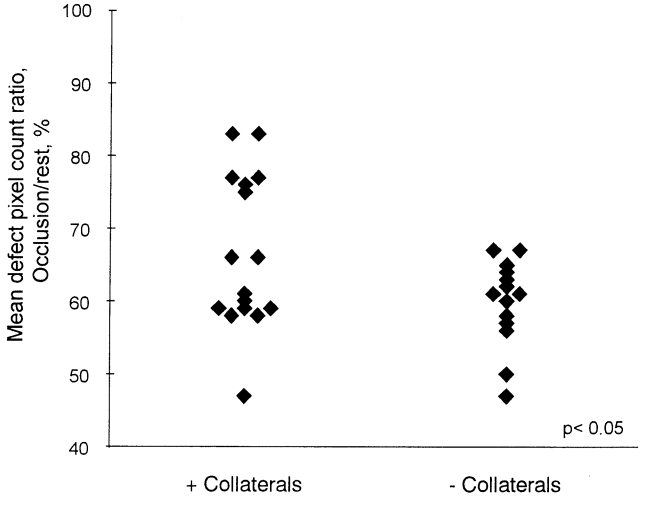

Figure 2. Scintigraphically estimated defect severity during balloon occlusion in patients with and without recruitable collaterals.

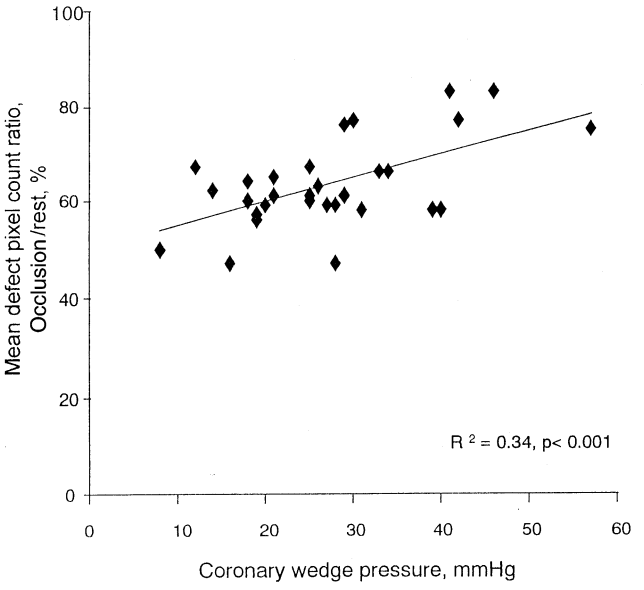

Figure 3. Coronary wedge pressure in relation to scintigraphic defect severity during balloon occlusion.

9 beats/min in patients with collaterals versus 71 ± 14 beats/min in patients without (NS).

Collaterals and ECG changes/chest pain. Two patients had significant Q-waves at rest, in one patient located in leads II, III, aV_F and in one patient in lead III as the only location. During the PTCA procedure, 23 patients developed ST-segment elevation, 3 patients had ST-segment depression, and 4 patients had no ST changes. The ST-segment elevation was observed in 56% of patients with recruitable collaterals versus 100% of patients without collaterals ($p < 0.01$).

Twenty-eight of 30 patients developed angina during the PTCA procedure with no difference between patients with and without collaterals. The mean maximal intensity of chest pain during the procedure as evaluated by the Borg scale was more pronounced in patients without collaterals than in patients with collateral supply, 8 ± 1 versus 6 ± 3 ($p < 0.05$).

Collaterals and scintigraphy. Twenty-eight of 30 patients had completely normal regional myocardial perfusion at rest, of whom 7 patients had a diagnosis of a prior non–Q-wave myocardial infarction. Two patients had small areas, 5.7% and 8.3% of the left ventricle, with significant decrease of regional myocardial perfusion at rest.

By study design the balloon was kept inflated for 90 s during the balloon occlusion, at which sestamibi was administered. In 8 patients the balloon was deflated earlier due to either severe chest pain (5 patients) or multifocal ventricular extrasystoles (3 patients), representing 2 of 16 patients with collaterals and 6 of 14 patients without collateral supply (NS). The mean PTCA-defect size in the entire population was 31 ± 10%, range 16% to 46%, while the mean defect severity estimated as the occlusion/rest count ratio was 63 ± 9%. No differences were found in mean defect sizes and mean defect severities in patients with 90-s occlusions versus patients with less occlusion time.

Scintigraphy, coronary wedge pressure and recruitable collaterals. The defect severity during PTCA, estimated as the mean occlusion/rest count ratio in patients with recruitable collaterals, was 67 ± 11% versus 60 ± 6% in patients without collaterals ($p < 0.05$) (Fig. 2). This difference in the occlusion/rest count ratio was not due to differences between groups in regional perfusion at rest in the LAD territory, as the mean rest/maximum pixel count ratio was 74 ± 6% in patients with collaterals versus 75 ± 7% in patients without ($p = 0.69$), respectively.

An occlusion/rest count ratio above 70% was only found in patients with recruitable collaterals, 6 of 16 patients with collaterals versus 0 of 14 patients without collaterals ($p < 0.05$). All patients with an occlusion/rest count ratio above 70% had grade 3 recruitable collaterals. Furthermore, these 6 patients had a mean coronary wedge pressure that was significantly higher than in 10 patients also demonstrating collaterals with occlusion/rest count ratios below 70%, the figures being 41 ± 10 mm Hg versus 29 ± 8 mm Hg ($p < 0.05$).

A significant positive correlation was observed between the coronary wedge pressure and the severity of hypoperfusion evaluated by the scintigraphic occlusion/rest count ratio ($R^2 = 0.34$, $p < 0.001$) (Fig. 3).

The PTCA-defect size was neither correlated with the coronary wedge pressure nor with the occurrence of recruitable collaterals.

Invasive and noninvasive estimates of myocardial perfusion. The ECG changes were significantly related to the scintigraphic estimates of myocardial hypoperfusion during

Table 2. Relation Between Electrocardiographic Signs of Severe Ischemia During PTCA and Three Variables for Assessing the Recruitable Collateral Extent

	RST Elevation Absent (n = 7)	RST Elevation Present (n = 23)
Occlusion/rest count ratio,‡ (n)		
>70%	5	1
≤70%	2	22
Coronary wedge pressure,* (n)		
>30 mm Hg	5	4
≤30 mm Hg	2	19
Recruitable collaterals,† (n)		
Grade 2 or 3	7	9
Grade 0 or 1	0	14

Three of seven patients with absent RST elevation had ST depression. *$p < 0.05$. †$p < 0.01$. ‡$p < 0.001$.

PTCA, as the mean occlusion/rest count ratio was 61 ± 6% in patients with ST-segment elevation (n = 23) versus 74 ± 9% in patients with no ST-segment elevation (n = 7) ($p < 0.0001$). Also, ECG changes were correlated to the PTCA-defect sizes, the mean defect sizes being 33 ± 9% (ST elevation) versus 24 ± 7% (no ST elevation) ($p < 0.05$).

The ECG changes were significantly related to the coronary wedge pressure, as the mean pressures were 24 ± 8 mm Hg in patients with ST-segment elevation (n = 23) and 39 ± 11 mm Hg in patients without ST-segment elevation (n = 7) ($p < 0.001$).

In Table 2, the relations among ECG changes and the scintigraphic severity of the induced perfusion defects, the coronary wedge pressure, and the occurrence of angiographically visible recruitable collaterals are shown. All three parameters were significantly related to the occurrence of RST elevation, with ^{99m}Tc-sestamibi SPECT as the most accurate method, with an accuracy of 90%, while the coronary wedge pressure and the recruitable collateral status correctly predicted RST elevation in 80% and 70% of cases, respectively.

Maximal severity of chest pain during the PTCA procedure was not correlated to the scintigraphically estimated defect size ($R^2 = 0.06$, $p = 0.22$), the occlusion/rest count ratio ($R^2 = 0.07$, $p = 0.17$), or to the coronary wedge pressure ($R^2 = 0.0001$, $p = 0.96$).

Arterial plasma profile of ^{99m}Tc-sestamibi. Arterial peak concentration was reached in mean 25 s postinjection (Fig. 4). The procentual parts of the AUC during the first 1, 2, 3, 4, and 5 min in relation to the AUC from injection to imaging were as follows: 55%, 76%, 85%, 90% and 93%. At 90 s postinjection, the estimated value was 68%.

DISCUSSION

In this study, we were able to demonstrate an overall protective role of recruitable collaterals on regional myocardial perfusion evaluated by ^{99m}Tc-sestamibi SPECT during controlled coronary occlusion of the LAD. A scintigraphic index, the occlusion/rest count ratio, was used. A ratio above 70% was only seen in patients with recruitable collaterals. This threshold value predicted the occurrence of ECG RST elevation with an accuracy of 90%. In addition, the ratio was significantly correlated to the coronary wedge pressure.

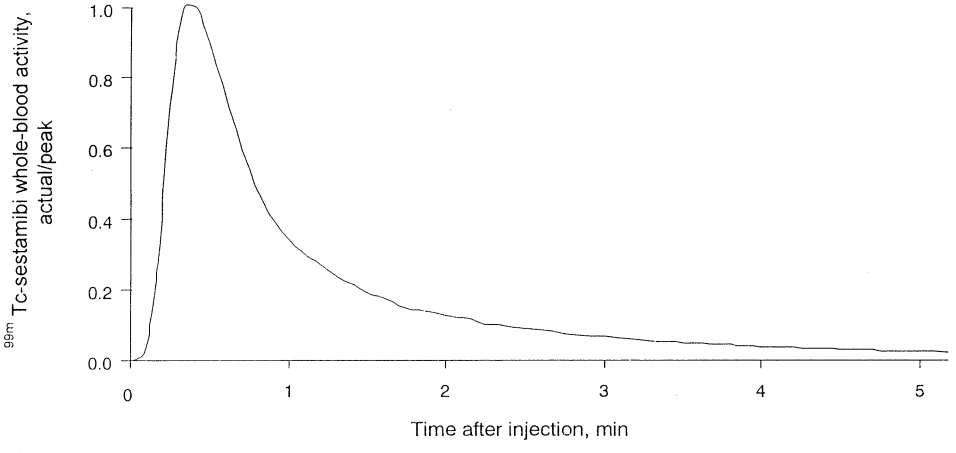

Figure 4. Time-activity curve for ^{99m}Tc-sestamibi in arterial blood after venous bolus injection.

Scintigraphic estimated perfusion and collaterals. Confirming previous studies (14,15) the size of the territory supplied by the LAD varied greatly between patients, which might explain that we found no difference in the mean of perfusion defects in patients with and without recruitable collaterals. The variation in defect sizes is unlikely to be caused by methodological problems of perfusion imaging, as recent studies have found that the area at risk evaluated by scintigraphy was positively correlated with the release of biochemical markers of necrosis in patients with acute myocardial infarction (16) and negatively to the occurrence of spontaneously visible collaterals during PTCA (17). In animal studies (18), close agreement between microsphere-determined collateral flow and the severity of perfusion defects evaluated by sestamibi SPECT during coronary occlusion has been demonstrated.

To evaluate the severity of hypoperfusion within abnormally perfused regions, prior studies used different methods of analysis, employed different ischemic cutoff limits and reference areas (14,19,20), but no consensus has been reached. In this study we applied a scintigraphic estimate that was based on defining the size of the territory with significant abnormal perfusion during balloon occlusion by comparison to a validated rest normal database (13). The activity within that area was compared to the identical area at rest to obtain an occlusion/rest count ratio. The rationale for applying this ratio was that of minimizing interindividual confounding effects of body attenuation of gamma rays.

In this study, performed in selected patients with proximal LAD stenoses and preserved left ventricular function, we demonstrated a protective effect of recruitable collaterals on myocardial perfusion during temporary coronary occlusion by using the described occlusion/rest ratio. To validate these results further, we compared our scintigraphic data to other objective measures of hypoperfusion during balloon occlusion, the coronary wedge pressure and electrocardiographic changes.

Scintigraphic hypoperfusion and coronary wedge pressure. A significant correlation was found between myocardial hypoperfusion estimated by perfusion imaging and the coronary wedge pressure: the latter being an invasive epicardial pressure recording distal to a simultaneous coronary occlusion (7), the former a noninvasive estimate of regional microcirculation, combining injection of the radioactive tracer during balloon occlusion and delayed SPECT imaging.

Recently, the evaluation of the protective effects of recruitable collaterals during temporary coronary occlusion by intracoronary pressure recordings has been further developed by Pijls et al. (21), who introduced the term "recruitable fractional collateral blood flow," defined as a function of the mean arterial pressure, the coronary wedge pressure and the central venous pressure during coronary occlusion. Recruitable fractional collateral blood flow was found to be a more accurate marker of PTCA-induced electrocardiographic changes than the coronary wedge pressure alone. To which extent recruitable fractional collateral blood flow actually was associated with the occurrence of recruitable collaterals during temporary occlusion was not determined in the study by Pijls, as contralateral contrast injection was not undertaken. Although we did not measure right atrial pressure during balloon occlusion, we were able to demonstrate a significant correlation between our scintigraphic estimate of hypoperfusion and the wedge pressure.

Scintigraphic hypoperfusion and electrocardiographic changes. The analyses of ECG changes during coronary occlusion only included the occurrence of ST-segment changes without taking into account the number of leads or the magnitude of ST changes. Nevertheless, we found a significant relation between ST changes and the severity of hypoperfusion by SPECT imaging. Others found no correlation between the number of leads with electrocardiographic changes and the severity of hypoperfusion evaluated by sestamibi SPECT during PTCA of the LAD (22). However, all patients in that study were survivors of an acute anterior myocardial infarction, and 7 of the 11 patients had perfusion defects at rest representing more than 20% of the left ventricle, which might have influenced both the evaluation of electrocardiographic and scintigraphic changes.

In another report (19), performed in 11 patients without prior myocardial infarction and nonoccluding LAD lesions, resembling our population, neither the size nor the severity of perfusion defects was correlated to the number of leads with electrocardiographic changes. In contrast, by applying dynamic vectorcardiographic registrations to the evaluation, a significant correlation was observed between ST changes and scintigraphic estimates of hypoperfusion. Although the registration of electrocardiographic changes in our study only represented a crude estimate of the overall electrocardiographic changes, there seemed to be a fairly good correlation to the scintigraphic occlusion/rest count ratio. The reason might be that both methods reflect changes of perfusion in the microcirculation.

Our results suggest that scintigraphic estimates of myocardial hypoperfusion can be used as an indicator of the protective value of the recruitable collateral circulation during coronary occlusion.

Methodological comments. A most crucial point for evaluating regional myocardial perfusion during brief episodes of total occlusion of coronary arteries is probably related to the amount of recirculating ^{99m}Tc-sestamibi in the blood pool immediately after balloon deflation, at a time characterized by reactive coronary hyperemia. In a previous study, Wackers et al. (23) found that 36% and 23% of the injected dose remained in the circulation 1 and 3 min, respectively, after tracer injection. However, these figures relied on venous blood sampling. According to the arterial plasma profile of ^{99m}Tc-sestamibi (Fig. 4), we estimated the relative

amount of sestamibi available for uptake during the first 90 s following tracer injection to be 68%. Thus, a substantial part of the injected dose was present in the blood pool at the time of balloon deflation. This potential limitation of exact measurements of regional myocardial perfusion in our model might be attenuated by a decreased extraction fraction of sestamibi early after severe myocyte ischemia due to electrochemical changes.

The possible time gap between the arterial peak concentration of the tracer and the fully developed collateral circulation might be of importance for the estimation of the protective role of recruitable collaterals in our model. From previous studies (24–26) it is known that coronary occlusion is followed by a sequential process within the first 20 to 30 s, including alterations of contractility, development of electrocardiographic changes, and angina. The exact time at which collaterals are fully recruited is unknown and may be of critical importance for evaluating the protective role of collaterals by sestamibi perfusion imaging. Arterial peak concentration of ^{99m}Tc-sestamibi appeared approximately 25 s after injection. In one previous study (14) the tracer was injected 20 s within the balloon occlusion and the range of perfusion defect sizes (20% to 82%) during occlusion of the proximal or mid-LAD resembled the values in our study. Therefore, we believe that this is a minor limitation of our study.

Photon scatter and reconstruction algorithms tend to decrease the estimated scintigraphic severity of perfusion defects, resulting in underestimation of truly existing hypoperfusion during balloon occlusion.

The inherent limitation related to the low resolution (100 μm) of the angiographic procedure compared to the size of collaterals might have influenced our results. The classification of patients into those with and without collaterals was based on visible filling of the recipient artery rather than visualization of the collateral circulation itself. Further, all patients with scintigraphically mild hypoperfusion during balloon occlusion had evidence of recruitable collateral supply. Therefore, patients who had a substantial collateral supply were likely not misclassified.

Study limitations. Evident limitations of this study are related to the moderate number of patients with LAD stenoses, which tend to diminish the statistical strength of the study. In addition, ongoing antianginal medication might have altered microcirculatory perfusion including the collateral circulation.

The evaluation of collaterals/coronary wedge pressure and regional hypoperfusion by sestamibi SPECT was performed in two subsequent balloon dilations at the end of angioplasty. These balloon dilations most often represented dilation 4 and 5. In the study by Pijls et al. (21) fractional collateral blood flow was doubled between the first and second inflation, but thereafter remained constant, indicating that no further recruitment of collaterals takes place after the second inflation. Therefore, recruitment would not be expected between inflation 4 and 5, and our estimations of the functional capacity of collaterals probably represented maximal achievable collateral supply. Undetected minor differences in vascular tone of epicardial arteries between subsequent balloon inflations in some patients cannot, however, be excluded.

Study implications. The use of scintigraphy during coronary occlusion should be seen as an additional method to obtain insight about factors modifying regional perfusion during coronary occlusion. The experimental setup used in this study can be applied in most patients undergoing PTCA without significant prolongation of the procedure, and it may be useful for a number of investigational purposes.

In the clinical setting, one previous study has shown that indirect measures of the recruitable collateral status of patients with one-vessel disease undergoing PTCA has prognostic importance (21), and it therefore seems likely that scintigraphic estimates of the functional capacity of the collateral coronary supply might be a prognostic marker in post-PTCA patients.

Conclusions. In a selected population with proximal LAD stenosis, we found that patients with a substantial recruitable collateral supply had significant less hypoperfusion than did patients without collaterals during brief episodes of coronary occlusion evaluated by ^{99m}Tc-sestamibi SPECT. The scintigraphic estimate of hypoperfusion, the occlusion/rest count ratio, was significantly correlated to the coronary wedge pressure and ECG changes. Our results demonstrate a protective role of recruitable collaterals on regional myocardial perfusion during brief episodes of coronary occlusion.

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