Effect of Myocardial Viability Assessed by Technetium-99m-Sestamibi SPECT and Fluorine-18-FDG PET on Clinical Outcome in Coronary Artery Disease

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PET imaging of myocardial perfusion and metabolism identifies regional viability as well as patients at high risk for future cardiac events. This study evaluated a combined "hybrid" imaging approach using ^{99m}Tc-sestamibi SPECT and [^{18}F]fluoro-2-deoxy-D-glucose (FDG) PET with regard to reversibility of regional dysfunction and to patient clinical outcome during a 2-yr follow-up. **Methods:** In this study, 161 consecutive patients underwent baseline viability imaging. All had regional wall motion (RWM) abnormalities and 88% had a history of previous myocardial infarction. Regions were classified by semiquantitative analysis of sestamibi and FDG uptake as normal, mild match, mismatch or scar. For clinical outcome, patients were divided into three groups: predominantly scar tissue (Group A, n = 90), mild match (Group B, n = 26) and mismatch (Group C, n = 45). Treatment was performed with the knowledge of nuclear results. Cardiac events during follow-up were defined as death, myocardial infarction, unstable angina requiring revascularization, heart transplantation and survived resuscitation. **Results:** Patients were followed for 29 ± 6 mo. Revascularization rate was 30% in Group A, 81% in Group B and 80% in Group C, whereas the other patients were treated by medication. Only Group C demonstrated a significant reduction of cardiac events after revascularization, whereas, particularly in Group A, revascularization did not influence the frequency of events. Subjective assessment of angina pectoris and heart failure revealed more patients with improvement after revascularization as compared with conservative treatment. Of the 84 revascularized patients, 61 underwent follow-up angiography at 5 ± 2 mo with RWM analysis using the centerline method. RWM improved only in mismatch regions from −2.2 ± 1.0 s.d. to −1.0 ± 1.4 s.d. ($p < 0.01$), whereas regions with a mild match or scar did not change. **Conclusion:** Nuclear imaging using ^{99m}Tc-sestamibi SPECT and [^{18}F]FDG PET allows diagnosis of viability in regions with reduced perfusion and function with prognostic implications for functional outcome as well as for identification of patients who benefit most from revascularization.

Key Words: PET; SPECT; coronary artery disease; myocardial viability

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With recent improvements in the treatment of acute myocardial infarction (MI), more patients with advanced coronary artery disease (CAD) and reduced left ventricular function survive the acute event and may be present in the postinfarct period with symptoms of either angina pectoris or heart failure. Furthermore, thrombolytic therapy or acute angioplasty (PTCA) is now more frequent and successful in older patients. In these patient subgroups, preoperative risk/benefit assessment for subsequent elective revascularization procedures is important and has created an increasing interest in preoperative assessment of myocardial viability.

PET imaging allows for the detection of changes on the cellular level in regions with reduced perfusion and contractility, which occur with either reversible myocardial ischemia or irreversible necrosis (*1–4*). Normal or elevated uptake of [^{18}F]fluoro-2-deoxy-D-glucose (FDG) in regions with reduced resting blood flow has been proposed as a metabolic marker of "hibernating" myocardium, representing a reversible myocardial dysfunction, which improves after coronary revascularization (*5–11*). Furthermore, recent studies using PET indicated that elevated FDG uptake identifies patients at high risk for future cardiac events if subsequent revascularization is not performed and that other patient subpopulations do not benefit from coronary revascularization with regard to subsequent cardiac events (*12–15*).

However, an onsite cyclotron for production of short-life PET perfusion tracers is cost-intensive and not widely available. Therefore, alternatives are of interest when combining metabolic imaging using FDG, produced at a central cyclotron with delivery to several distant scanners ("satellite concept"), with either generator-produced PET perfusion tracers or scintigraphic perfusion markers such as ^{99m}Tc-sestamibi (*16–19*). Recent studies evaluating the predictive value of this "hybrid" approach for functional outcome of regional wall motion (RWM) after coronary revascularization demonstrated comparable results to PET assessment of perfusion and metabolism (*16,20,21*).

The aim of this study was to evaluate the impact of a combined nuclear imaging approach using ^{99m}Tc-sestamibi SPECT and [^{18}F]FDG PET on changes of regional function after coronary revascularization and on clinical outcome and prognosis of patients in relation to different nuclear viability patterns and subsequent treatment.

MATERIALS AND METHODS

Patient Selection and Subsequent Therapy

Nuclear imaging for assessment of myocardial viability was performed from March 1990 until October 1992 in patients with CAD and ischemic RWM abnormalities considered for coronary revascularization. Patients were included in this prospective study if they fulfilled the following inclusion criteria:

1. Significant CAD (diameter stenosis ≥70%) in at least one major vessel proven by recent coronary angiography.

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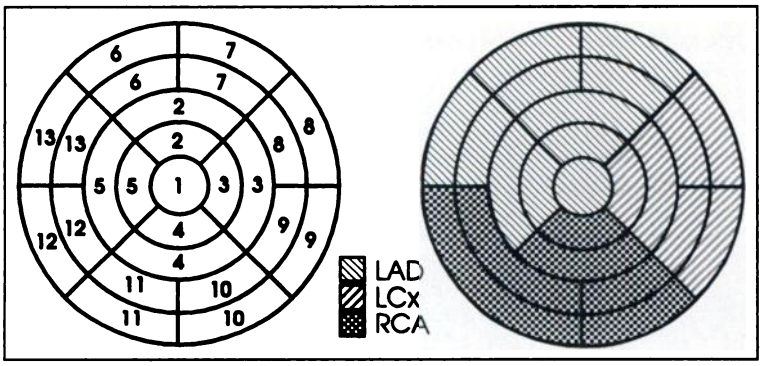

FIGURE 1. Schematic plot of the short-axis slices of the left ventricle indicating the 25 regions. The apex is in the center, and the circumferential regions represent the most basal planes. Combination of 25 regions to 13 segments and their assignment to the coronary artery territories is indicated.

2. Reduced contractility (severe hypokinesis or akinesis) in the region perfused by a vessel considered for revascularization.
3. Angina pectoris despite medical therapy.
4. Abnormal stress test or scintigraphic ischemia (optional).

Baseline exclusion criteria were recent myocardial infarction (<6 wk) or unstable angina pectoris and concomitant heart disease (cardiomyopathy, valve disease).

For angiographic follow-up, patients with a cardiac event between baseline studies and planned revascularization, patients with left bundle branch block, atrial fibrillatione or permanent pacemaker were excluded, since these factors would have influenced quantitative assessment of RWM. Beta-receptor blocking agents had to be withdrawn for ≥48 hr before angiography.

Physicians were not restricted from assessing the nuclear data for treatment decisions. PTCA was attempted in patients with single-vessel disease. In patients with multivessel disease undergoing PTCA, only stenoses with evidence for ischemia or preserved viability were dilated. In cases with several viable or ischemic regions supplied by ≥2 stenosed vessels, patients were revascularized surgically. Bypass surgery (CABG) was performed with complete revascularization if technically feasible. Thus, in the case of multivessel disease, regions with evidence for maintained tissue viability, as well as those identified as scar, were revascularized.

The protocol was approved by the local institutional ethical board and patients gave informed consent before participation.

Technetium-99m-Sestamibi SPECT

Perfusion imaging was performed using standard protocols at our institution (*22,23*). Patients were studied under anti-anginal therapy at rest 2 hr after injection of 10 mCi ^{99m}Tc-sestamibi with a light meal after tracer application. Data were acquired using a Gammasonics ROTA double-head camera equipped with a low-energy, all-purpose collimator allowing a simultaneous 360° rotation (180° for each camera head) with 2 × 30 steps of 6°. Transaxial slices of 6.25 mm thickness were reconstructed using a Butterworth filter third order and a cutoff frequency of 0.5.

Fluorine-18-FDG PET

After transmission imaging and glucose loading with 50 g dextrose p.o., 6–8 mCi [^{18}F]FDG were injected. Static imaging was initiated 30–45 min after tracer injection for 30–40 min. Transaxial images were reconstructed with a Hanning filter (cutoff frequency 0.4) on a 128 × 128 matrix using a defined zoom factor to obtain the same in-plane pixel size as the SPECT images, and consecutive pairs of PET slices were combined to achieve an identical axial pixel size for both imaging techniques (*17,24*).

Coronary and Left Ventricular Angiography

Cardiac catheterization was performed using the Judkins technique and recorded on cinefilm at 50 frames/sec. Left ventricular angiography was obtained in the 30° right anterior oblique and 60° left anterior oblique view during deep inspiration. Vessels were documented in ≥2 identical orthogonal projections at baseline and at follow-up.

Data Analysis: Nuclear Data and Viability Definitions

The transaxial PET files were converted to the structure of SPECT files. Short- and long-axis cuts of the isotropic transaxial slices were rearranged to achieve corresponding tomograms using a previously published method (*17,24*). Six short-axis slices were divided into 25 regions, which were then combined to 13 myocardial segments (Fig. 1). Sestamibi and FDG uptake in each segment was expressed as the percent of the uptake in the region with the maximal sestamibi uptake (reference region). If perfusion was reduced (sestamibi ≤70%), sestamibi and FDG uptake values covering the perfusion defect were used for tissue characterization. The following definitions of regional viability were applied: normal, sestamibi uptake >70% of the reference region; "mismatch," sestamibi uptake ≤70%, FDG minus sestamibi uptake >20%, and FDG uptake >70%; mild match, mild reduction of sestamibi uptake of 51%–70% without evidence for a mismatch (FDG minus sestamibi uptake ≤20%); and scar, marked reduction of sestamibi ≤50%, without evidence for a mismatch (FDG minus sestamibi uptake ≤20%).

In the case of several tissue types within one artery territory, the type covering most segments within the coronary distribution territory was chosen for viability definition.

For clinical outcome analysis, the artery territory in question for baseline viability assessment was chosen for further categorization of the individual patient. For example, a patient submitted for viability imaging of the akinetic anterior wall was categorized as scar if he had a nuclear scar pattern in the anterior wall, even if other regions displayed different viability patterns.

Ventriculograms

Quantitative analysis of ventriculography was performed without the knowledge of clinical, angiographic or nuclear data. Ejection fraction (EF) was calculated by the area length method. RWM was analyzed by the centerline method in the distribution territories of the three major coronary arteries and the deviation from normal motion was expressed in units of s.d. of normal mean derived from a reference population. Negative values indicate hypokinetic RWM. Within each vessel territory, RWM was computed as mean motion in the most abnormally contracting region (*25–28*).

Follow-Up Assessment

All hospital records were checked as the primary source, particularly for the acute success of revascularization and for hospital readmissions. Additionally, patients were contacted by questionnaire after approximately 2 yr (22–44 mo) to assess cardiac events defined as MI, unstable angina requiring revascularization, heart transplantation or survived cardiopulmonary resuscitation since baseline assessment. For statistical analysis, only one event (the most severe one) was counted per patient. Patients

TABLE 1
Clinical and Angiographic Data of All Patients and Subgroups

	Group						
	All	A1	A2	B1	B2	C1	C2
Number	161	63	27	5	21	9	36
Men	89	87	89	80	100	89	89
Women	11	13	11	20	0	11	11
Age (yr)	57 ± 9	58 ± 9	59 ± 7	55 ± 9	55 ± 9	55 ± 8	57 ± 9
Previous MI	88	100	100	40	62	67	83
CCS (class)	2.4 ± 1.1	2.2 ± 1.0	2.8 ± 0.8*	2.0 ± 1.0	2.9 ± 1.1	1.8 ± 1.1	2.2 ± 1.1
NYHA (class)	1.8 ± 0.9	1.8 ± 0.8	2.1 ± 1.1	1.4 ± 1.0	1.5 ± 1.1	2.2 ± 1.2	1.6 ± 1.1
EF (%)	45 ± 12	44 ± 13	41 ± 12	48 ± 1	47 ± 10	50 ± 14†	49 ± 10‡
1-vessel disease	31	43	12*	20	24	22	30
2-vessel disease	30	33	30	40	33	22	25
3-vessel disease	39	24	59*	40	43	56	45

*$p < 0.05$ vs. group A1.
†$p < 0.05$ vs. group A1.
‡$p < 0.05$ vs. group A2.
Results are expressed in percent or as mean ± s.d.
CCS = angina pectoris symptoms according to the classification of the Canadian Cardiovascular Society (29); NYHA = heart failure symptoms according to the classification of the New York Heart Association (30); EF = left ventricular ejection fraction; MI = myocardial infarction.

reported their subjective judgment of anginal symptoms according to the Canadian Cardiovascular Society (CCS) classification (*29*) and heart failure symptoms according to the New York Heart Association (NYHA) classification (*30*) and their overall impression of clinical outcome since baseline evaluation. If this questionnaire indicated further hospital admissions, the records of this hospital were checked, particularly for evidence of a cardiac event. If patients did not respond to the first questionnaire, a second "reminder" was sent to them. If patients did not respond (this was the case in 18%), they were contacted by phone. Finally, if patients could not be contacted, relatives or the patients' physician were asked for further information.

Statistical Analysis

Values are presented as mean ± 1 s.d. Comparisons between two datasets with continuous variables were made by Student's t-test using the software StatView 4.02 (Abacus Concepts Inc., Berkeley, CA). Comparisons of continuous variables between more than two groups defined by categorical variables were performed by Kruskall–Wallis test. Probability values (p) <0.05 were considered significant.

RESULTS

Patient Baseline Data and Subsequent Therapy

Overall, 161 consecutive patients (144 men, 57 ± 9 yr) were recruited prospectively. Clinical and angiographic data are summarized in Table 1. Of these patients, 142 (88%) had a history of chronic (≥6 wk) MI, with 46 patients having thrombolytic therapy or PTCA during the acute phase. Thirty-four patients (21%) had a history of several infarcts. The interval between baseline catheterization and baseline nuclear imaging was 3 ± 2 wk. The interval between baseline viability imaging and subsequent revascularization was 4 ± 3 wk finally resulting in an overall interval of 7 ± 3 wk between recruitment and revascularization.

Follow-up data were available for all patients (except for those who died during hospital stay) with a mean follow-up interval of 29 ± 6 (22–44) mo. Of the 161 patients, 77 (48%) were treated conservatively and 84 patients (52%) underwent elective revascularization, with 52% of them undergoing CABG and 48% receiving PTCA.

According to the above criteria, 90 patients were categorized as having predominantly scar in the target region for viability imaging (Group A). Of these 90 patients, 63 (70%) were treated conservatively (Group A1), while 27 patients (30%) underwent revascularization (Group A2). Patients in Group A2 had preoperatively more severe angina and more often multivessel disease but no difference with regard to heart failure symptoms (Table 1, Fig. 2).

Twenty-six patients displayed a predominantly mild match pattern without evidence for a perfusion/metabolism mismatch in the target region (Group B). Five (19%) were treated conservatively (Group B1), and 21 patients (81%) were revascularized (Group B2). Clinical and angiographic baseline data are outlined in Table 1 and Figure 2. Similar to Group A, there were differences with regard to preoperative angina. Due to the small number of patients in Group B1, no statistical comparison was performed.

Group C consisted of 45 patients with a mismatch pattern. Nine of the 45 patients (20%) were treated by medication only (Group C1) and 36 patients (80%, Group C2) underwent CABG or PTCA. As presented in Table 1, there was no significant symptom-related

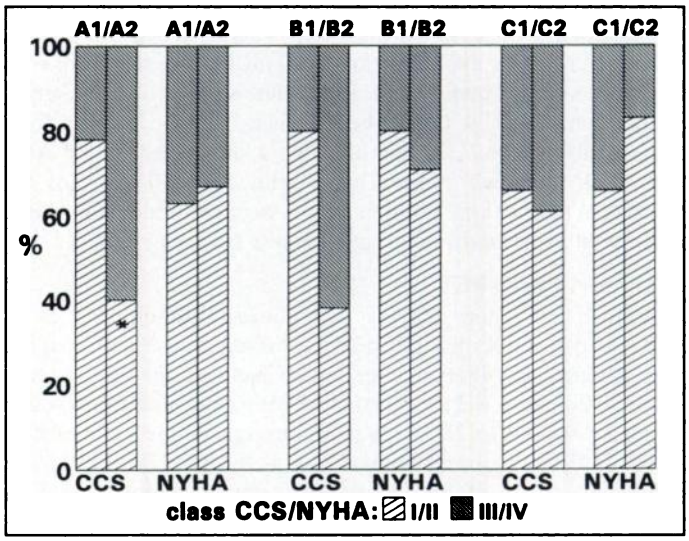

FIGURE 2. Angina pectoris symptoms and heart failure symptoms in a percentage of patients at baseline within the patient subgroups defined by myocardial viability criteria (see Materials and Methods). CCS = angina pectoris class according to the definition of the Canadian Cardiovascular Society (*29*); NYHA = heart failure symptoms according to the definition of the New York Heart Association (*30*).

TABLE 2
Rate of Cardiac Events and Subjective Improvement of Cardiac Symptoms Improvement ≥ 1 Grade According to the NYHA (30) and CCS (29) Classification

Group	n	Cardiac event	Improvement NYHA	Improvement CCS
A1 (scar, medical treatment)	63	12 (19)	2 (3)	16 (25)
A2 (scar, revascularized)	27	6 (22)	4 (15)*	17 (63)*
B1 (mild match, medical treatment)	5	1 (20)	1 (20)	0
B2 (mild match, revascularized)	21	3 (14)	7 (33)	16 (76)
C1 (mismatch, medical treatment)	9	2 (22)	1 (11)	1 (11)
C2 (mismatch, revascularized)	36	0	11 (31)†	25 (69)‡
All medical treatment	77	16 (21)	4 (5)	17 (22)
All revascularized	84	8 (10)	22 (26)§	58 (69)‖

*$p < 0.05$ vs. A1.
†$p < 0.05$ vs. C1.
‡$p < 0.01$ vs. C1.
§$p < 0.05$ vs. medical treatment.
‖$p < 0.01$ vs. medicl treatment.
Presented are the absolute patient numbers and percent within each subgroup (in parentheses).
n = number of patients; NYHA = New York Heart Association; CCS = Canadian Cardiovascular Society.

difference between these two groups. Patients with a mismatch had a higher baseline EF (Table 1) and a lower proportion of patients with heart failure NYHA class III or IV as compared with patients with scar (Fig. 2).

Clinical Outcome and Cardiac Events During Follow-Up

Many patients in Group A reported improved quality of life by subjective assessment. At follow-up, 56% of patients in Group A2 and 31% in Group A1 reported overall subjective improvement. In Group A1 72% were in class I/II CCS and 86% in class I/II NYHA at follow-up. The corresponding numbers were 73% and 81% in Group A2, respectively. The rate of cardiac events did not change with revascularization in this group. Seven out 63 patients (11%) in Group A1 died from cardiac events; 6 during a MI and 1 patient suffered a sudden cardiac death. Four patients (6%) survived a nonfatal MI or cardiopulmonary resuscitation, and one patient underwent heart transplantation. Two patients in Group A2 (7%) died during an acute myocardial infarction, and four patients (15%) survived a cardiac event. The overall event rate was 19% in Group A1 and 22% in Group A2.

In Group B, two patients died; both were in Group B2. One patient in Group B1 survived a sudden cardiac death. The overall rate of cardiac events was 20% in Group B1 and 11% in Group B2. Development of clinical symptoms is presented in Table 2. As in Group A, revascularized patients demonstrated substantial improvement. In Group B2, 58% showed overall improvement of clinical symptoms, whereas none of the five patients in Group B1 reported benefit at follow-up.

Two patients in Group C died during an acute MI. Both were in Group C1 (22%); one of them was waiting for a planned but delayed CABG (because he did not have revascularization at this time and was treated conservatively for the 9 mo since his baseline studies, he was assigned for the analysis to Group C1). Overall, cardiac events in Group C2 were significantly lower when compared with Group C1 and with Group A. Subjective improvement was seen more frequently in patients being revascularized. In Group C2, 94% of the patients were in CCS class I/II and 100% were in NYHA class I/II. Nearly 70% percent of the patients in Group C2 reported subjective improvement of angina and 100% reported improvement or unchanged symptoms with regard to heart failure.

Angiography

In 23 of 84 revascularized patients, no angiographic follow-up was available: four patients had valve replacement or aneurysmectomy during surgery, and four patients died between surgical revascularization and repeat angiography. In four patients, angiography seemed not indicated due to a complicated course after revascularization or as a result of new noncardiac diseases. Eleven patients refused follow-up angiography. These 15 patients were asymptomatic and had no noninvasive evidence of recurrent ischemia.

Thus, 61 of 84 patients underwent follow-up angiography at 5 ± 2 mo (2–20 mo) after revascularization. In 16 of the 61 patients, at least one film was unsuitable for centerline analysis. This was either due to insufficient contrast of the left ventricular contour or to arrhythmias. Those 45 patients with analyzable paired angiograms (23 with PTCA, 22 with CABG) were the final source for quantitative RWM analysis.

Nuclear Tissue Characterization and Functional Changes at Follow-Up

In this study, 135 coronary territories (45 patients with three territories each) were analyzed. Of these 135 regions, 82 (61%) were revascularized and 53 (39%) were not revascularized. Baseline tracer uptake values are presented in Table 3. FDG uptake of hypoperfused regions differed (by definition) significantly between mild match, mismatch, and scar regions. The 53 nonrevascularized regions displayed normal tracer uptake indicating no critical stenoses and no evidence for previous MI.

The results of serial RWM measurements are presented in Table 2. RWM improved in all revascularized regions from -1.5 ± 1.1 to -1.1 ± 1.3 s.d. ($p < 0.01$). This was due to changes in mismatch regions (an example is illustrated in Fig. 3) since they improved from -2.2 ± 1.0 to -1.1 ± 1.4 s.d. ($p < 0.001$) and differed from all other groups ($p < 0.01$). If only successfully revascularized mismatch regions (sestamibi 52% ± 10%, FDG 92% ± 11%) without restenosis or graft failure (defined as ≥50% diameter stenosis) were analyzed, RWM improved from -2.3 ± 1.0 to -0.8 ± 1.5 s.d. ($p < 0.001$), whereas regions with a mismatch (sestamibi 56% ± 8%, FDG 105% ± 30%) but evidence for recurrent hypoperfusion did not change (-2.0 ± 0.6 and -2.0 ± 0.4 s.d.).

In contrast, regions with a mild match pattern (-1.5 ± 0.7 and

TABLE 3
Preoperative Regional Sestamibi and FDG Uptake Values and RWM at Baseline and at Follow-up Angiography

Regions	No. of Patients	Sestamibi (%)	FDG (%)	RWM baseline	RWM follow-up
All revascularized	82	64 ± 16	81 ± 21	−1.5 ± 1.1	−1.1 ± 1.3*
Normal	25	88 ± 4	92 ± 9	−0.3 ± 0.9	−0.4 ± 1.2
Mild match	11	60 ± 7	58 ± 6	−1.7 ± 0.7	−1.5 ± 0.7
Mismatch	33	57 ± 10	98 ± 15	−2.2 ± 1.0	−1.0 ± 1.4†
Scar	13	37 ± 8	35 ± 13	−2.1 ± 1.1	−2.2 ± 0.8
Nonrevascularized	53	79 ± 15	84 ± 20	−0.5 ± 1.0	−0.8 ± 0.9

*$p < 0.05$ vs. RWM baseline.
†$p < 0.001$ vs. RWM baseline.
For definitions of tissue categorization by ^{99m}Tc-sestamibi and FDG uptake see Materials and Methods. FDG and MIBI uptake are mean ± s.d. in percent of the individual reference region. RWM values are s.d. ± s.d.

−1.7 ± 0.7 s.d., respectively) and those with scar (−2.1 ± 1.1 and −2.2 ± 0.8 s.d., respectively) did not improve. As expected, there was no RWM change in nonrevascularized regions (−0.5 ± 1.0 and −0.8 ± 0.9 s.d., respectively).

Overall, the EF improved from 47% ± 10% to 52% ± 11% ($p < 0.01$). With respect to preoperative viability, global EF improved in patients with revascularization of ≥1 mismatch territory from 46% ± 9% to 54% ± 11% ($p < 0.01$). If patients without any mismatch were revascularized, there was no change of global function (EF of 47% ± 11%, and 42% ± 14%, respectively).

DISCUSSION

In this study, patients with angiographically proven CAD and reduced regional and global left ventricular function were followed for a mean of 2.5 yr and the clinical outcome as well as the change of regional function was analyzed with regard to baseline hybrid viability imaging and to subsequent therapy. Subjective assessment of symptoms demonstrated improvement after revascularization regardless of preoperative tissue categorization. Patients treated medically reported less benefit despite similar baseline values for heart failure and ventricular function as those being revascularized. With regard to the frequency of cardiac events during follow-up, only patients with a preoperative mismatch followed by revascularization showed a significant prognostic benefit, whereas in patients with scar tissue revascularization did not alter the clinical outcome. Serial analysis of RWM revealed improvement if regions displayed a preoperative mismatch. In contrast, regions with slightly reduced perfusion and maintained FDG uptake but without a mismatch (mild match) and those categorized as scar did not improve.

Prognostic and Clinical Implications of Viability Imaging

The identification of ischemically compromised regions allows not only detection of principally reversible myocardial dysfunction but also identification of patients with high risk for future cardiac events and those who will benefit most from coronary revascularization. Several PET studies show that patients with evidence for hibernating myocardium are at high risk for future cardiac events if they are not revascularized (*12–15*). In these studies, the overall rate of cardiac events was 48% in patients with mismatch and without subsequent revascularization, whereas only 13% of revascularized patients with a preoperative mismatch suffered a cardiac event. In contrast, revascularization of patients without evidence for ischemically compromised myocardium did not result in a reduction of cardiac events. The previously reported fact that ventricular arrhythmias after myocardial infarction often occur in regions with a PET perfusion/metabolism mismatch supports this finding (*31*).

In our study, the rate of cardiac events in patients with scar tissue was approximately 20% with or without subsequent coronary revascularization, but revascularization of patients with a mismatch pattern reduced future events significantly. All these studies consistently demonstrate the need for coronary revascularization, if technically feasible, if viability imaging reveals evidence for ischemically jeopardized myocardium. Furthermore, a recent analysis from our laboratory indicated that the duration of hibernation may play a critical role for functional outcome, since global ventricular function of patients revascularized within 30 days improved significantly more compared with those with delayed revascularization (*32*). Therefore, patients with evidence for ischemically compromised myocardium should undergo coronary revascularization as soon as possible.

The fact that the rate of cardiac events was only 22% in this study as compared with 48% pooled from the above-cited reports may be due to the mild reduction of global left ventricular function and the higher rate of patients with single-vessel disease in our study. Most of the previous studies recruited patients with multivessel disease and an EF below 40%. Thus, our patients were in a relatively low risk subpopulation. Patient recruitment in our institution during the first year was aiming at the quantitative analysis of RWM outcome with regard to baseline SPECT/PET imaging. Therefore, patients with single-vessel disease and smaller dyskinetic regions undergoing PTCA were recruited. This does not reflect the typical patient population with advanced CAD and markedly reduced EF where viability imaging is most helpful. The relative preserved global function may explain further, independent of viability patterns, why patients in the mismatch group had the best prognosis after revascularization, since their baseline EF was already higher as compared with Group A and their global function improved even more after revascularization. However, the functional improvement of mismatch regions in contrast to mild match or scar patients may contribute to the prognostic benefit of these mismatch patients, but its definitive role has to be evaluated in studies with larger patient populations.

This study shows that revascularization of patients with a mild match pattern, who have evidence for maintained viability but who lack a mismatch, fails to benefit either prognosis or ventricular function, although there is subjective improvement. This viability pattern may reflect a mixture of subendocardial necrosis and viable tissue, resulting in an imaging signal of a mild match. The amount of truly hibernating myocardium may

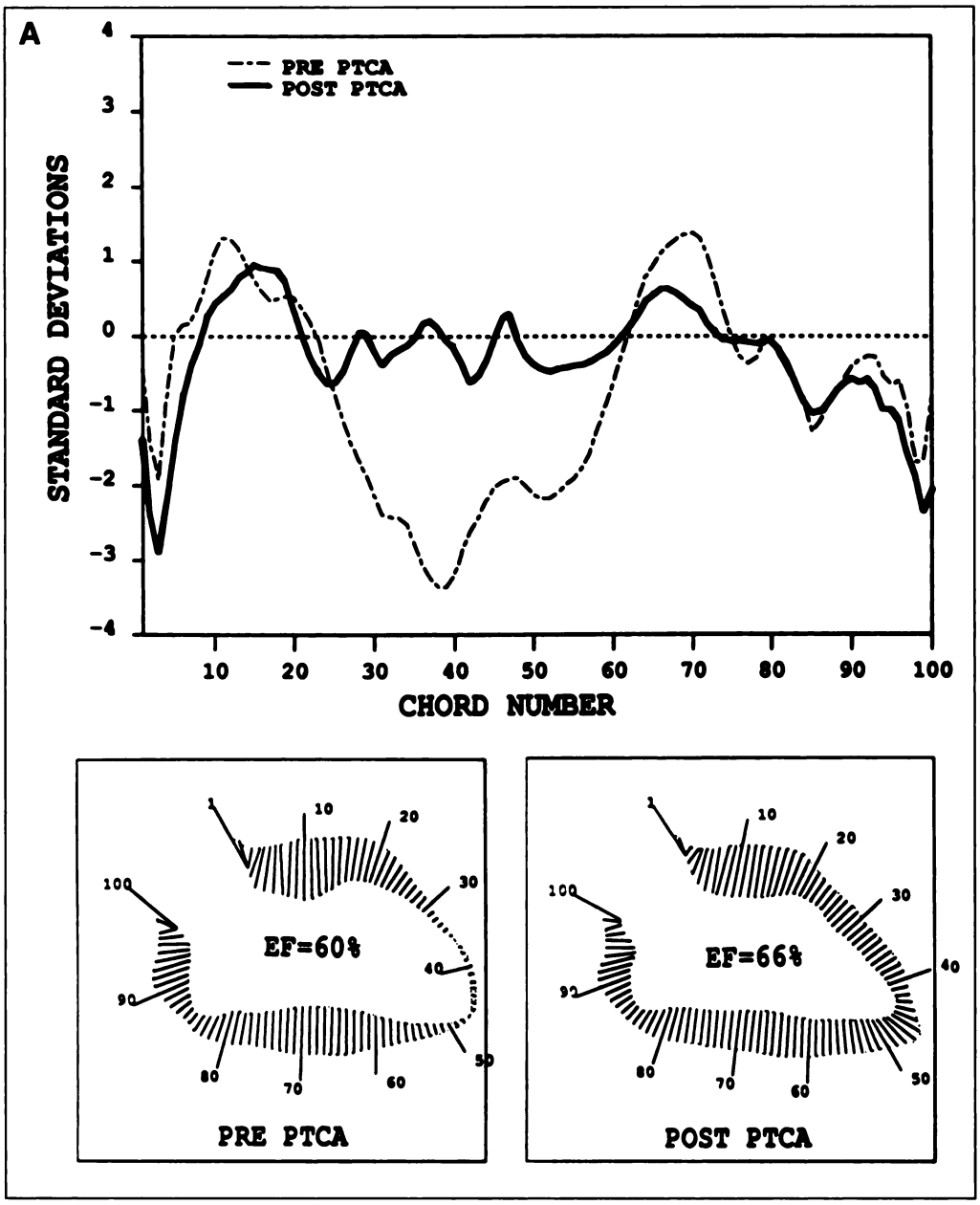

FIGURE 3. Images of a patient with successful PTCA of the LAD and no restenosis at 6 mo follow-up angiography. (A) Analysis of RWM using the centerline method at baseline and at follow-up. End-diastolic and end-systolic contours are illustrated. RWM at baseline and repeat angiography in s.d. of a normal mean is illustrated in the upper figure. There was substantial improvement of the preoperative hypokinetic anterior wall after PTCA with improvement of global EF. (B) Midventricular short-axis images of the baseline sestamibi SPECT (left) and the FDG-PET (right) studies indicating a perfusion/metabolism mismatch in the anterior wall.

be too small to result in a significant improvement of ventricular function, but revascularization of these regions may prevent further ventricular enlargement, preserve functional reserve and reduce stress-induced ischemia and thus lead to subjective improvement of cardiac symptoms.

Similarly, independent of the incidence of future events, the study demonstrates that patients with evidence for scar tissue in the target region may benefit from revascularization with regard to subjective judgment of symptoms. This effect occurred despite missing objective improvement of RWM in scar regions (*9,21*). However, inherent problems of subjective judgment and some bias due to a "placebo effect" of coronary revascularization cannot be ruled out. In addition, patients in Group A2 had more severe angina at baseline as compared with Group A1. This reflects that more patients in Group A2 with multivessel disease were suffering from angina originating from other stenosed vessels. Therefore, revascularization of those remote arteries with relief of symptoms may be important for the subjective improvement.

Limitations and Technical Considerations

Comparison of data acquired by different imaging techniques such as SPECT and PET inherits other technical aspects (*17,33*), such as the higher spatial resolution capacity of PET, particularly in thinned infarcted myocardial regions. Beside "true" sestamibi/FDG mismatches, missing attenuation correction with SPECT may be an important reason for discordant results between both techniques, particularly in the inferior wall (*19,33,34*). In our study, we did not find significant differences

in angiographic or clinical outcome of mismatches in the inferior wall as compared with other regions.

Our approach with large territories to assess regional functional changes limits the sensitivity to detect small mismatch regions and subsequent functional recovery because these regions are not detected by the centerline method. Furthermore, the exact localization and correlation of regions is a challenging problem in combining tomographic studies with two-dimensional angiographic images. However, the large angiographic territories and the subsequent adaptation of nuclear tomographic segments to vessel distribution territories limit this problem, since minor regional misalignments are balanced by the centerline method (*25*).

CONCLUSION

A combined hybrid nuclear imaging approach using ^{99m}Tc-sestamibi SPECT and FDG-PET with quantitative tracer uptake analysis allows identification of myocardial viability in regions with reduced perfusion and contractility. The preoperative identification of perfusion/metabolism mismatch, when followed by timely and successful revascularization, was associated with the greatest reversal of wall motion abnormalities and, more importantly perhaps, with a significant reduction of the cardiac event rate. These data, in combination with previous studies reporting PET assessment of perfusion and metabolism, suggest that evidence of a perfusion/metabolism mismatch should be followed as soon as possible by coronary revascularization, if technically feasible.

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