Preoperative Positron Emission Tomographic Viability Assessment and Perioperative and Postoperative Risk in Patients With Advanced Ischemic Heart Disease

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Objectives. **This study sought to investigate whether determination of tissue viability by means of positron emission tomography (PET) before coronary artery bypass graft surgery (CABG) affects clinical outcome with respect to both in-hospital mortality and 1-year survival rate.**

Background. **Patients with coronary artery disease (CAD) and severe left ventricular (LV) dysfunction are at higher risk for perioperative complications associated with CABG. Therefore, the selection of patients who will benefit from CABG is an important clinical issue.**

Methods. **This study retrospectively evaluated 76 patients with advanced CAD and LV dysfunction (LV ejection fraction ≤0.35) who were considered candidates for CABG. Thirty-five patients were selected for CABG on the basis of clinical presentation and angiographic data (group A), and 34 of 41 patients were selected according to extent of viable tissue determined by PET (group B) in addition to clinical presentation and angiographic data.**

Results. **There were four in-hospital deaths (11.4%) in group A and none in group B ($p = 0.04$). After 12 months, the survival rate was 79% in group A and 97% in group B ($p = 0.01$). Postoperatively, group B patients had a less complicated recovery ($p = 0.05$). They required lower doses of catecholamines ($p = 0.002$) and demonstrated a significantly decreased incidence of low output syndrome ($p = 0.05$).**

Conclusions. **This retrospective data analysis suggests that selection of patients with impaired LV function on the basis of extent of viability supplementary to clinical and angiographic data may lead to postoperative recovery with a low early mortality and promising short-term survival. Therefore, viability studies permit selection of patients who are at low risk for serious perioperative complications.**

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Previous studies (1–5) have shown that long-term survival after coronary artery bypass graft surgery (CABG) is better than that after medical treatment alone in patients with severe left ventricular (LV) dysfunction. In patients with congestive heart failure due to ischemic heart disease receiving only medical treatment, a 2-year survival rate of only 31% has been reported (6). In contrast, several studies (1–5,7,8) have indicated that patients with a left ventricular ejection fraction (LVEF) <30% benefit most from revascularization. However, perioperative morbidity and mortality are high in the subgroup of patients with advanced three-vessel coronary artery disease (CAD), congestive heart failure and impaired LV function. The in-hospital mortality rate ranges from 5% to 20%, depending on LVEF and severity of congestive heart failure (1,9–12). Therefore, it is important to select patients who are likely to benefit from the long-term effect of CABG.

Noninvasive imaging, such as positron emission tomography (PET), has been reported to be a useful tool for the determination of tissue viability and hence for the prediction of reversibility of regional LV dysfunction. PET using nitrogen-13 (N-13) ammonia and fluorine-18 fluorodeoxyglucose (F-18 FDG) has been shown (13,14) to be highly specific in distinguishing viable from nonviable or scarred myocardium. After successful revascularization, improvement of regional wall motion is expected to occur in 78% to 92% of myocardial segments viable on PET (15–19). In addition, recent studies have indicated that myocardial tissue characterization by PET has prognostic significance. Eitzman et al. (20) showed that the presence of metabolically compromised myocardium identifies patients with a significantly higher rate of cardiac complications in the absence of coronary revascularization. Di Carli et al. (21,22) reported that the magnitude of decrease in heart failure symptoms after CABG is related to the preoperative extent and magnitude of myocardial viability. However, there

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Abbreviations and Acryonyms

AICD	=	automatic implantable cardioverter-defibrillator
CABG	=	coronary artery bypass graft surgery
CAD	=	coronary artery disease
F-18 FDG	=	fluorine-18 fluorodeoxyglucose
ICU	=	intensive care unit
IMA	=	internal mammary artery
LV	=	left ventricular
LVEF	=	left ventricular ejection fraction
PET	=	positron emission tomography (tomographic)
RNV	=	radionuclide ventriculography (ventriculographic)

has been no study to date concerning the impact of myocardial viability assessed by PET on short-term outcome in patients undergoing surgical revascularization.

Therefore, to examine the influence of selection criteria based on "viability testing" on short-term outcome after CABG, patients with significant three-vessel disease and severe LV dysfunction who underwent CABG were retrospectively evaluated. Perioperative morbidity and mortality were compared in patients selected for revascularization on the basis of clinical status and angiographic data alone versus patients who underwent preoperative tissue viability assessment by PET and were selected according to angiographic data, clinical status and extent of tissue viability.

Methods

Study groups. We retrospectively reviewed 76 consecutive patients with advanced three-vessel CAD and severe LV dysfunction (LVEF $\leq$0.35) who were referred for CABG or cardiac transplantation to our institution from January 1994 to November 1995. All patients gave written informed consent for this study. Cardiac catheterization was performed in all patients to assess ventricular function and extent of CAD. Global LVEF was measured by biplane cineangiography. *Advanced three-vessel disease* was defined as a visually estimated lumen narrowing of at least 75% of the diameter of each of the three major vessels or their major branches. Patients with LV aneurysm or concomitant valve disease were excluded from the study. Most patients in group A had angina pectoris, and the angiographic results indicated distal coronary vessels suitable for CABG. In Group B, patients had preoperative tissue viability assessment by PET in addition to cardiac catheterization. PET was requested by the cardiac surgeons for patients in whom the angiographic report showed coronary arteries that were considered technically difficult for revascularization and included arteries in which the estimated target vessel size was considered too small or in which no collateralization was angiographically present in cases of proximal coronary artery occlusion. PET was also performed in patients who were referred as possible candidates for cardiac transplantation and in patients who had symptoms of congestive heart failure primarily, without angina pectoris. PET was also ordered in eight patients who had previously been rejected for CABG at other institutions.

PET studies. All patients without known diabetes mellitus were studied in the postprandial state after additional oral glucose loading with 50 g of glucose. Patients with known diabetes or abnormal glucose tolerance received insulin before and during the imaging sequence, according to a standardized protocol (23). After initial transmission scanning for attenuation correction, rest regional myocardial perfusion imaging with N-13 ammonia (740 MBq) was performed. After sufficient time for N-13 decay, F-18 FDG (370 MBq) was injected, and data acquisition was initiated 40 min after tracer injection. Transaxial planes were obtained using whole-body PET (Siemens CTI 951 or Siemens Exact 47). Attenuation-corrected transaxial PET images were generated from N-13 ammonia and F-18 FDG data. The images were reoriented perpendicular to the long axis of the left ventricle, after which volume-weighted polar maps were calculated from circumferential profiles of the maximal myocardial activity. In addition, the transaxial image data were realigned to generate images in short-axis, vertical and horizontal long-axis views for visual analysis (20). Regional tracer uptake of N-13 ammonia and F-18 FDG was evaluated visually, in blinded manner, by two experienced observers (S.N., M.S.) who had no knowledge of the clinical and angiographic data, to estimate the extent of necrosis and viable tissue.

Viability criteria. Tissue viability by PET was assessed by the combined interpretation of perfusion and metabolism within the vascular territories of the left ventricle. The septal, anterior and anterolateral walls were considered the vascular territory of the left anterior descending coronary artery. The left circumflex coronary artery was considered to supply the lateral and posterolateral walls, whereas the vascular territory of the right coronary artery was the inferior and posterior walls. Two different viability criteria were used: 1) reduced blood flow with preserved or increased F-18 FDG uptake (*mismatch*); 2) normal or near-normal blood flow with normal or increased F-18 FDG uptake (*normal*). Reduced blood flow with reduced F-18 FDG uptake (*matched defect*) was used as the criterion for scar. On the basis of this visual evaluation, three main criteria were used to determine whether an individual patient was a suitable candidate for CABG: 1) The presence of a "normal or mismatch" pattern in akinetic or severely hypokinetic myocardial areas supplied by a stenosed or obstructed artery was required. 2) If viable myocardium was detected in at least two different vascular territories, we considered the patient an adequate candidate for CABG, independent of the estimated target vessel size from the angiographic report. 3) A large area of scar tissue using an approximate threshold of 40% was a deciding factor against CABG. This arbitrary threshold was based on studies of acute myocardial infarction that indicated a high incidence of cardiogenic shock in infarct areas >40% of LV mass (38–40). It was assumed that patients with a large infarct area are more susceptible to hemodynamic complications during CABG.

The visually estimated extent of scar tissue was retrospectively confirmed by semiquantitative analysis. *Scar tissue* was defined as F-18 FDG uptake ≤50% of maximal uptake on "bull's eye" quantitation (24). On the basis of the PET criteria, in association with the angiographic report, seven patients were found to be inappropriate candidates for CABG and either underwent heart transplantation (n = 4) or received only medical treatment (n = 3).

Surgical technique. Complete revascularization was attempted in all patients. For myocardial protection, cold cristalloid cardioplegic solution with topical cooling of the heart and moderate systemic hypothermia (28°C) was used (25). After cessation of cardiopulmonary bypass, the venous grafts were measured with electromagnetic flow probes.

Follow-up. Three- to 28-month ([mean ± SD] group A: 12.0 ± 8.5, group B: 14.5 ± 5.8) postoperative follow-up information was obtained for all patients by telephone interview. Heart failure status was classified according to New York Heart Association criteria. In addition, all patients who underwent postoperative radionuclide ventriculography (RNV) were seen by a physician.

RNV. RNV was performed in both groups for functional follow-up. Red blood cells were labeled with 950 MBq technetium-99m using an in vivo technique, and images were obtained with a scintillation camera (Siemens, Basicam SI plus) equipped with a 140-keV low energy all-purpose collimator. Data acquisition was carried out in three standard projections. Global LVEF was calculated using commercially available software (Siemens). A regression equation (RNV LVEF = 0.86 × Biplane angiographic LVEF + 2.9) was used to compare preoperative biplane cineangiographic LVEF with the results of RNV, according to Wackers et al. (26).

Postoperative outcome and definitions. Perioperative and postoperative complications and mortality were recorded prospectively as part of an ongoing quality assurance program. *In-hospital mortality* was defined as death within 30 days of operation or during hospital stay. *Low output syndrome* was diagnosed when high inotropic medication (dopamine ≥10 μg/kg body weight per min) was required to maintain a systolic blood pressure >80 mm Hg or when intraaortic balloon pumping was used to sustain adequate hemodynamic status. In patients whose cardiac output measurements were available, a cardiac index <2.5 liters/min per m^2 was considered a criterion of low output syndrome. Cardiopulmonary resuscitation was performed in patients with rhythm disturbances, including ventricular tachycardia compromising hemodynamic condition or ventricular fibrillation. *Uncomplicated recovery* was defined as transfer from the intensive care unit within 2 days.

Statistical analysis. The Student *t* test for independent samples for continuous and chi-square analysis for categoric variables were used to evaluate differences between groups. A two-tailed p value <0.05 was considered statistically significant. Multivariate logistic regression analysis was performed to assess the combined impact of several risk factors on outcome by means of a forced-entry model with SPSS for windows version 6.0. Kaplan-Meier curves were calculated to estimate midterm survival; differences between groups were assessed with the log-rank test.

Table 1. Preoperative Patient Characteristics

	Group A (n = 35)	Group B (n = 34)	p Value
LVEF (%)	29.6 ± 5.2	27.7 ± 4.6	0.12
Range	17–35	18–35	
LVEDP (mm/Hg)	18.8 ± 9.0	18.9 ± 10.5	0.99
LVEDVI (ml/m^2)	120.8 ± 33.4	135.5 ± 36.0	0.16
LVESVI (ml/m^2)	85.8 ± 25.0	95.8 ± 29.9	0.22
NYHA III/IV (%)	68.6	73.5	0.65
History of CHF (%)	40	56	0.19
Previous MI (%)	85.7	67.6	0.08
Age (yr)	60.3 ± 10.4	63.2 ± 9.2	0.23
>70 yr	8	9	0.95
Female gender (%)	20	8.8	0.19
Reoperation (%)	0	5.9	0.15
DM (%)	34.3	29.4	0.66
Urgency (%)	51	47	0.30
Left main stenosis (%)	22.9	23.5	0.95
Higgins score	5.9 ± 2.8	6.1 ± 2.8	0.77

Data presented are mean value ± SD or percent of patients. CHF = congestive heart failure; DM = diabetes mellitus; Group A = patients selected for revascularization on the basis of clinical status and angiographic data alone; Group B = patients undergoing additional tissue viability assessment by positron emission tomography; LVEDP = left ventricular end-diastolic pressure; LVEDVI = left ventricular end-diastolic volume index; LVESVI = left ventricular end-systolic volume index; MI = myocardial infarction; Urgency = operation within 14 days of catheterization.

Results

From January 1994 to November 1995, 69 of 76 referred patients with advanced three-vessel disease and marked LV dysfunction underwent CABG at our institution. Thirty-five of these patients (group A) were selected for revascularization on the basis of clinical status and angiographic data alone. The remaining 34 patients (group B) underwent additional tissue viability assessment by PET.

Comparative demographics. Table 1 depicts the main preoperative clinical characteristics of both groups. There were no significant differences in comparative demographics between groups A and B. In addition, multivariate logistic regression analysis showed no difference between the two groups according to their preoperative risk profile. Assessment of preoperative risk according to the Higgins et al. (27) clinical severity score also demonstrated no difference between the two groups.

Operative management. In all cases the same technique was used for myocardial protection. The mean cross-clamp time was similar in both groups. The left internal mammary artery (IMA) was used slightly less often in group A (80% in group A vs. 85.3% in group B), and an average of 3.7 distal anastomoses/patient were performed in the two groups. In group A, one patient required balloon counterpulsation, and two patients developed a low output syndrome intraoperatively. No intraoperative complications occurred in group B.

Table 2. Perioperative Outcome and Complications

	Group A	Group B	p Value
No catecholamine support	0%	29.4%	0.002
Low output syndrome	17.1%	2.9%	0.05
Cardiac arrest (ICU)	14.3%	2.9%	0.09
Uncomplicated recovery	33.3%	66.7%	0.05
Mortality			
30 days	11.4%	0%	0.04
12 mo	14.3%	2.9%	0.02
HTX after CABG	1 Pt	0 Pt	

CABG = coronary artery bypass graft surgery; HTX = heart transplantation; ICU = intensive care unit; Pt = patient.

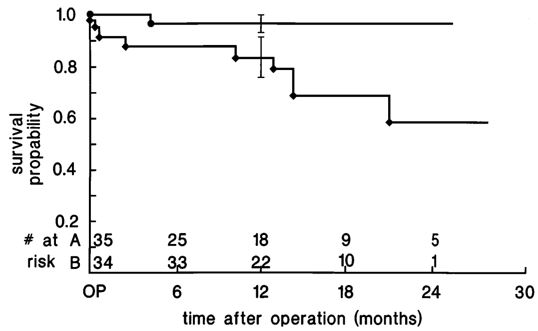


Figure 1. Actuarial survival curve (±SE) with the hospital mortality included. **Diamonds** = group A; **circles** = group B ($p < 0.01$).

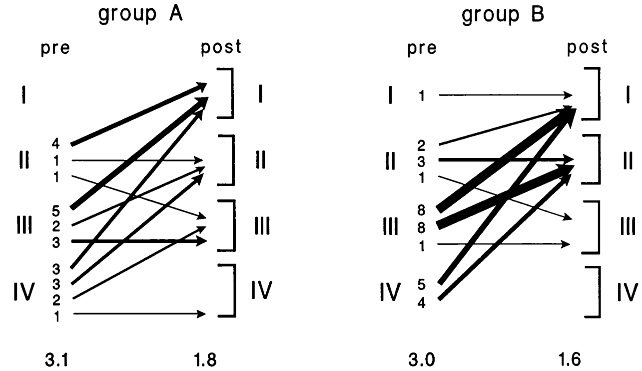
The electromagnetic bypass flow measurements after extracorporeal circulation did not indicate any differences between the two groups (mean blood flow, group A: 187 ± 98 ml/min [range 48 to 490]); mean blood flow, group B: 185 ± 62 ml/min [range 45 to 380]). Mean blood flow in patients who died was 143 ± 72 ml/min; however, there was no statistically significant difference between patients who died in the early postoperative period and survivors. Nine different surgeons performed the operations; no association was found between surgeon and outcome.

Surgical outcome. Table 2 depicts the perioperative outcome of both groups. No patient died during operation. On admission to the intensive care unit (ICU), nearly 30% of group B patients required no catecholamine support ($p = 0.002$) and demonstrated a significantly decreased incidence of low output syndrome ($p = 0.05$), whereas 14% of group A patients ($p = 0.09$) required cardiopulmonary resuscitation because of rhythm disturbances. Seven of 35 group A patients and 14 group B patients had an uncomplicated recovery ($p = 0.05$). Four patients (11.4%) in group A died in the hospital. Death occurred postoperatively on days 2, 8 and 15 and at 2 months, respectively. One patient died of arrhythmia-related causes; one patient had electrocardiographic changes compatible with a postoperative infarction; and two patients died primarily due to worsening heart failure. In contrast, there were no in-hospital deaths in group B ($p = 0.04$). After 3 months, the mortality rate did not change; however, one group A patient underwent heart transplantation because of worsening congestive heart failure after CABG.

Follow-up. The duration of follow-up in the two groups was 913 patient-months. In group A, follow-up ranged from 3 to 28 months (mean 12.0, median 12.3). During this period, five patients in group A (17.2%) died at 8, 12, 13, 14 and 22 months, respectively, after operation. Twenty-five patients attained a 6-month, 18 patients a 12-month, 9 patients an 18-month and 5 patients a 24-month follow-up survival time. The remaining patients had either <6 months of follow-up (four patients), or it was not possible to contact them (one patient). In these patients, the cause of death was cardiac related in four patients and was due to rhythm disturbances and worsening of heart failure; in one patient, the cause of death was cancer. In group B, the follow-up period ranged from 6 to 25 months (mean 14.5, median 14.6). After 4 months, one patient (2.9%) died of worsening of heart failure. In group B, 33 patients attained a 6-month, 22 patients a 12-month, 10 patients an 18-month and 1 patient a 24-month follow-up survival time. The survival curve (Fig. 1) includes in-hospital mortality and mortality during follow-up and shows significantly different survival between the two groups. After 12 months, the survival rate was 79 ± 8% in group A and 97 ± 3% in group B ($p < 0.01$). Figures 2 and 3 compare the preoperative and postoperative functional and symptomatic data. Postoperative functional class was recorded for all patients available for follow-up 3 to 28 months after operation. Most patients showed marked improvement. The majority of patients were asymptomatic or minimally symptomatic and were in functional classes I and II. However, seven patients (28%) in group A were still in functional classes III and IV. One patient in this group underwent heart transplantation because of worsening congestive heart failure 3 months after CABG. In contrast, only two patients in group B were in functional class III, and none were in functional class IV ($p = 0.02$). Mean congestive heart failure class improved from 3.1 preoperatively to 1.8 in group A and from 3.0 to 1.6 in group B.

Follow-up data concerning functional status were evaluated according to preoperative and postoperative LVEF obtained

Figure 2. Change in New York Heart Association functional class in the two groups after revascularization. Mean functional class improved from 3.1 to 1.8 in group A and from 3.0 to 1.6 in group B. post = after CABG; pre = before CABG.



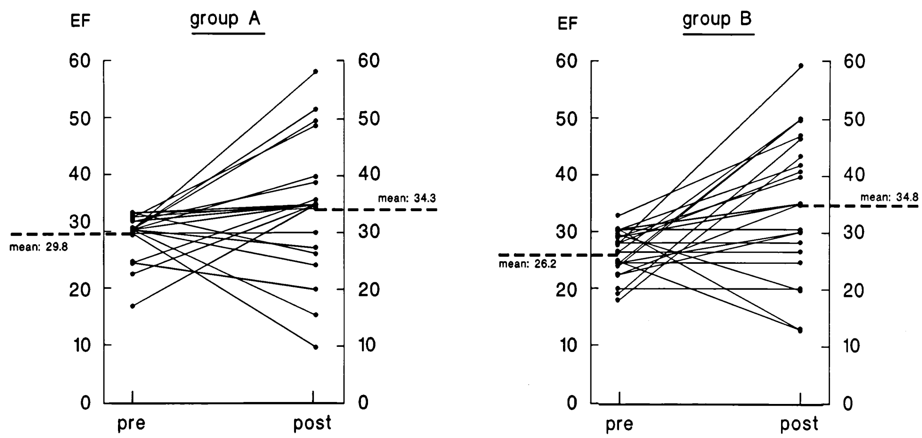


Figure 3. Change in global LV function expressed as LVEF. There is a modest increase from 29.8% to 34.3% in group A and from 26.2% to 34.8% in group B.

by radionuclide ventriculography. Because RNV data were not available preoperatively, a regression equation was used to normalize contrast angiographic LVEF to equilibrium radionuclide LVEF. This normalization shows only minor differences between both techniques (group A: angiographic LVEF 31.6 ± 4.3% vs. LVEF RNV 29.8 ± 3.7%; group B: angiographic LVEF 27.2 ± 4.9% vs. LVEF RNV 26.2 ± 4.3%). Forty-four patients (75%) of the 59 survivors underwent this procedure. Fifteen patients declined the investigation. LVEF was determined at a mean of 12.4 months in group A and a mean of 12.5 months in group B after operation. In group A, mean LVEF increased from 29.8 ± 3.7% to 34.3 ± 12.4% (change in LVEF 16.6%), which was not significant. In group A, LVEF decreased substantially in six patients, with a maximal decrease of 18 percentage points. The largest improvement was 27 percentage points. In four patients, LVEF returned to near-normal values. In contrast, LVEF in group B patients showed a significant increase; mean LVEF improved from 26.2 ± 4.3% to 34.8 ± 12.2% (change in LVEF 36.2%, $p = 0.003$). Only three patients showed a decrease in LV function. The maximal decrease was 18 percentage points, and the largest improvement was 31 percentage points. Of group B patients, six attained nearly normal ventricular function. However, the follow-up LVEF values were not significantly different between the two groups (34.3% [group A] vs. 34.8% [group B]).

Discussion

The results of the present study suggest that selection of patients on the basis of tissue viability assessed by PET supplementary to clinical and angiographic data leads to a postoperative recovery with a low early mortality and promising short-term survival after CABG. In contrast, in patients who were selected for revascularization on the basis of clinical status and angiographic data alone, the outcome confirms previously published high complication and mortality rates.

To our knowledge, this study is the first to examine the effect of preoperative assessment of tissue viability on perioperative and postoperative complications in patients with advanced three vessel CAD and severe LV dysfunction. This subgroup of patients shows the greatest long-term benefit from surgical revascularization (3,4) and has been confirmed by Elefteriades et al. (10) who showed excellent survival in a comparable group of patients up to 3 years after CABG. However, the in-hospital mortality in that study was reported to be 8.4% in the patient group selected for revascularization without preoperative viability assessment. Similarly, in-hospital mortality in the present study was ~11% in patients without preoperative PET, whereas patients with preoperative PET imaging had very low in-hospital mortality. Thus, these data suggest that PET may provide unique information, independent of other established prognostic markers, for identifying patients who are at low risk for early complications associated with coronary revascularization. The identification of viable myocardium using imaging approaches such as PET appears to be clinically relevant in patients with advanced CAD and severely impaired LV function who are being considered for revascularization.

Risk assessment. Several studies concerning risk factors for morbidity and mortality in patients undergoing CABG have been reported. Christakis et al. (9) found that emergency revascularization, LV dysfunction, age and previous bypass operation remain significant predictors of operative mortality; however, improved techniques for heart surgery in recent years have neutralized many traditionally accepted risk factors, such as gender, left main coronary artery stenosis and number of diseased vessels (28,29). In our investigation, all patients in groups A and B had significant three-vessel disease and severely impaired LV dysfunction as assessed by contrast ventriculography, with no difference in preoperative LVEF between the two groups. All other preoperative clinical and demographic data were not significantly different and are therefore comparable in both groups (Table 1). In addition, multivariate logistic regression analysis taking into account the impact of several risk factors simultaneously showed no differences between the two groups. The operative risk of each patient was ranked using the clinical severity score determined by Higgins et al. (27), which is a widely accepted system for preoperative estimates of morbidity and mortality risks. This score also failed to show differences between the two groups. Therefore, differences in patient characteristics, insofar as known risk factors are concerned, can be excluded in accounting for the observed differences in mortality.

Operative methods and treatment in the ICU. All patients underwent surgical revascularization using the same surgical and myocardial protective techniques. The IMA was used in the majority of patients; 80% of group A patients and 85.3% of group B patients received the left IMA as a conduit to the left anterior descending coronary artery. It is unlikely that any differences in postoperative treatment of patients in either group is responsible for the observed differences in complication and mortality rates. The physicians in the ICU were not aware of whether a patient had undergone PET imaging; therefore, treatment bias can be excluded as a source of the observed differences in outcome. Observation bias is equally unlikely because data concerning patient characteristics and perioperative events were collected prospectively as part of our ongoing quality assurance program.

On admission to the ICU, approximately one-third of group B patients required no catecholamine support, which suggests improved LV function after CABG. Topol et al. (30) showed that immediate improvement in regional wall thickening after CABG was most marked in those segments with the most severe preoperative dysfunction. The functional outcome of regional myocardial segments after CABG was not investigated in the present study. However, more rapid functional improvement in viable myocardial segments may be an explanation for the lower need for catecholamine support. Of the patients who were transferred from the ICU within 2 days with uncomplicated recovery, nearly 70% were from group B. All patients (except one) who were treated initially without any catecholamines were discharged within 2 days from the ICU. One may again speculate that the more rapid improvement in regional ventricular function was responsible for faster clinical recovery after operation.

Seventeen percent of group A patients developed low output syndrome, and 14% required cardiopulmonary resuscitation because of malignant arrhythmias. Blakeman et al. (31) showed that the occurrence of malignant arrhythmias is a significant risk factor in patients with severe LV dysfunction undergoing CABG. The use of an automatic implantable cardioverter-defibrillator (AICD) may avoid sudden death after hospital discharge and should improve the intermediate and long-term survival. In the present study, two patients from both groups received an AICD after CABG; therefore, more frequent use of AICDs is not likely to be a reason for the different results among the two groups. In the perioperative period, patients in group A showed a tendency ($p = 0.09$) to be more susceptible to the development of malignant arrhythmias, which may be due to their somewhat higher ($p = 0.08$) rate of previous myocardial infarction. Another explanation may be that group A patients had a greater extent of scar tissue, which may have predisposed them to postoperative arrhythmias. However, this explanation remains speculative because we did not perform assessment of infarct size in group A to assess the extent of scar tissue in these patients.

As the retrospective semiquantitative analysis of PET data have demonstrated, most patients with preoperative tissue viability assessment had areas of scar tissue comprising <20% of the left ventricle. The small infarct size may explain the significant reduction in incidence of low output syndrome and early mortality rate. The functional capacity of the remaining myocardium was probably sufficient to prevent the development of low output syndrome or early mortality due to myocardial failure.

Viability assessment. Viable myocardium in dysfunctional segments was defined as a region with normal blood flow or with reduced blood flow but with preserved or increased F-18 FDG uptake. This definition includes increased glucose uptake in segments with reduced blood flow (flow–metabolism mismatch), which may represent the metabolic expression of hibernating myocardium (13,14). In addition, recent studies have indicated that in patients with myocardial hibernation, the loss of regional contraction is out of proportion to the reduction in myocardial blood flow (perfusion–contraction mismatch). Chronic reversible dysfunction in hibernating myocardium is not only caused by chronic hypoperfusion, but may be the consequence of repeated episodes of ischemia followed by myocardial stunning (32). Normal or increased glucose uptake in regions with normal or near-normal blood flow at rest may also represent the metabolic expression of stunned myocardium, which is characterized by a flow–function mismatch (33). Preliminary results suggest that scintigraphic patterns of "stunning" are more pronounced than that of "hibernation" in patients with marked LV dysfunction (34). The present study did not distinguish between both pathophysiologic representations of dysfunctioning myocardium. Stunned and hibernating myocardium may be associated with severe impairment of contractile function and worsening of heart failure; however, both conditions have shown functional recovery after revascularization (35,36).

Two main viability criteria were used in the selection of patients who were referred for CABG: 1) the presence of viable myocardium in akinetic myocardial areas that were supplied by a stenosed or obstructed artery. 2) If viable myocardium was detected in at least two different vascular territories, then that patient was considered an adequate candidate for CABG. Extent of scar tissue >40% of the left ventricle was a deciding factor against CABG because postmortem studies (37–39) have shown that patients who died of cardiogenic shock after acute myocardial infarction had large infarct areas, averaging 37%, 43% and 51% of LV mass, which may indicate an irreversible and untractable condition. Yoshida and Gould (40) showed that the size of the infarct area and viability in arterial zones at risk assessed by PET are good prognostic indicators of mortality, particularly in patients with LV dysfunction. In their study, 6 of 35 patients had an infarct size between 39% and 77%, as determined by quantitative PET measurements. Four of these patients had died within a

3-year follow-up period, three of them after percutaneous transluminal coronary angioplasty or CABG.

Nevertheless, the criterion of scar extent >40%, which was applied in the present study, represents an arbitrary threshold. As the retrospective semiquantitative analysis in the present study showed, the criterion of scar extent alone is not sufficient for the selection process in some patients. One group B patient had a scar tissue area of 43%. However, in this patient the other main viability criteria and the angiographic report supported the decision that this patient was an adequate candidate for CABG. Therefore, in patients with a scar tissue area ~40%, the criterion of scar tissue area should only be applied in combination with the other viability criteria as well as angiographic results.

Most patients who underwent revascularization had a scar tissue area comprising <20% of the left ventricle, which confirms previous observations that advanced symptoms of heart failure do not exclude the presence of extensive areas of viable myocardium. In addition, all patients who were previously rejected for CABG on the basis of clinical status and angiographic data from other institutions showed a scar tissue area by PET data of <20%, indicating that selection of patients for operation without viability assessment may be insufficient. PET may therefore provide a better selection process that extends the indication for operation to patients who are likely to benefit from revascularization but would have otherwise been rejected.

Study limitations. In interpreting the results of the present study, several limitations should be recognized:

1. The main limitation is that the present study did not involve randomization of patients. The study included patients with severe reduction of LV function who were referred for revascularization. Limited availability of PET and outside referral prohibited prospective randomization of patients in this study. Although a randomization protocol would have been ideal, careful retrospective analysis of risk factors was performed in both groups to identify any selection bias. The incidence of heart failure was slightly higher in the PET group than in the control group, suggesting possibly sicker patients in the PET group. Overall, there was no significant difference detected in preoperative risk factors between the two groups. However, we cannot exclude the possibility that other variables may have contributed to the improved survival in group B. After multivariate statistical adjustment for important clinical differences between the two groups, we observed a significant advantage in early mortality for group B. The unadjusted odds ratio for early mortality (group B vs. group A) was 0.09 compared with the adjusted odds ratio of 0.06 after controlling for age, gender, preoperative functional class, history of congestive heart failure, previous myocardial infarction, LVEF, left main coronary artery stenosis, priority of operation, diabetes mellitus and reoperation. This finding suggests that the observed improved outcome in group B is not attributed to differentially distributed risk factors. Therefore, the statement that PET provides unique information for appropriate selection of patients with LV dysfunction appears to be valid.

2. Symptomatic status was assessed using New York Heart Association functional class, a widely used system for estimating quality of life. In the present study we did not use the Canadian Cardiovascular Society classification (41) because the predominant symptom in the majority of patients was dyspnea on exertion rather than angina pectoris. In both groups, we found improvement in congestive heart failure status after operation; however, in group A significantly more patients remained in functional class III or IV postoperatively. Moreover, in some patients the evaluation of the symptomatic status according to functional class is limited because it remains unclear how much improvement in functional class resulted from decreased angina rather than improvement in dyspnea on exertion. To determine actual improvement in LVEF, postoperative RNV was performed at varying intervals at rest. Consequently, we did not control for physiologic factors that may influence LVEF. However, all patients who underwent RNV did so at least 3 months after operation, at which time surgically induced depression of LV function, residual myocardial stunning or catecholamine-induced functional improvement should no longer be present. Mean rest LVEF rose from 29.8% to 34.3% in group A and from 26.2% to 34.8% in group B, indicating a trend toward improved global LV function after CABG in both groups. However, it should be emphasized that preoperative LVEF was determined by contrast angiography, and postoperative LVEF was determined in all patients by equilibrium RNV. Therefore, a direct comparison between preoperative and postoperative LVEF is limited. For this reason, a regression equation (26) was used to normalize preoperative contrast angiographic LVEF to the equilibrium radionuclide LVEF. The calculation showed a modest enhancement of LV function in both groups. This functional improvement may be responsible for the amelioration of congestive heart failure symptoms.

3. This study did not include a comparison of PET with other imaging modalities for detection of viable myocardium. Further studies are necessary to determine whether the same results may be obtained with conventional scintigraphic techniques, such as thallium-201 imaging or low dose dobutamine echocardiography.

Conclusions. Selection of patients on the basis of tissue viability assessment using PET in combination with F-18 FDG and N-13 ammonia, in addition to clinical status and angiographic data, led to postoperative recovery with fewer complications and a significant decrease in early mortality in patients with severe LV dysfunction undergoing CABG compared with patients selected on the basis of clinical and angiographic results alone. Our results suggest that preoperative assessment of myocardial viability should be considered to identify patients at lower risk of perioperative complications and mortality associated with revascularization. Furthermore, this selection process may extend the indication for operation to patients otherwise excluded. Therefore, viability studies may not only provide prognostic information with regard to recovery of function after revascularization, but also permit selection of patients who are at low risk for serious perioperative complications. Additional studies, preferably randomized trials with a large patient population, are required to confirm the results of the present study.

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