Journal of the American College of Cardiology
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Published by Elsevier Science Inc.

Vol. 33, No. 3, 1999
ISSN 0735-1097/99/$20.00
PII S0735-1097(98)00642-1

Functional Status and Quality of Life in Patients With Heart Failure Undergoing Coronary Bypass Surgery After Assessment of Myocardial Viability

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OBJECTIVES The aim of this study was to evaluate whether preoperative clinical and test data could be used to predict the effects of myocardial revascularization on functional status and quality of life in patients with heart failure and ischemic LV dysfunction.

BACKGROUND Revascularization of viable myocardial segments has been shown to improve regional and global LV function. The effects of revascularization on exercise capacity and quality of life (QOL) are not well defined.

METHODS Sixty three patients (51 men, age 66 ± 9 years) with moderate or worse LV dysfunction (LVEF 0.28 ± 0.07) and symptomatic heart failure were studied before and after coronary artery bypass surgery. All patients underwent preoperative positron emission tomography (PET) using FDG and Rb-82 before and after dipyridamole stress; the extent of viable myocardium by PET was defined by the number of segments with metabolism-perfusion mismatch or ischemia. Dobutamine echocardiography (DbE) was performed in 47 patients; viability was defined by augmentation at low dose or the development of new or worsening wall motion abnormalities. Functional class, exercise testing and a QOL score (Nottingham Health Profile) were obtained at baseline and follow-up.

RESULTS Patients had wall motion abnormalities in 83 ± 18% of LV segments. A mismatch pattern was identified in 12 ± 15% of LV segments, and PET evidence of viability was detected in 30 ± 21% of the LV. Viability was reported in 43 ± 18% of the LV by DbE. The difference between pre- and postoperative exercise capacity ranged from a reduction of 2.8 to an augmentation of 5.2 METS. The degree of improvement of exercise capacity correlated with the extent of viability by PET ($r = 0.54$, $p = 0.0001$) but not the extent of viable myocardium by DbE ($r = 0.02$, $p = 0.92$). The area under the ROC curve for PET (0.76) exceeded that for DbE (0.66). In a multiple linear regression, the extent of viability by PET and nitrate use were the only independent predictors of improvement of exercise capacity (model $r = 0.63$, $p = 0.0001$). Change in Functional Class correlated weakly with the change in exercise capacity ($r = 0.25$), extent of viable myocardium by PET ($r = 0.23$) and extent of viability by DbE ($r = 0.31$). Four components of the quality of life score (energy, pain, emotion and mobility status) significantly improved over follow-up, but no correlations could be identified between quality of life scores and the results of preoperative testing or changes in exercise capacity.

CONCLUSIONS In patients with LV dysfunction, improvement of exercise capacity correlates with the extent of viable myocardium. Quality of life improves in most patients undergoing revascularization. However, its measurement by this index does not correlate with changes in other parameters nor is it readily predictable. (J Am Coll Cardiol 1999;33:750–8) © 1999 by the American College of Cardiology

Patients with left ventricular (LV) dysfunction due to coronary artery disease present a difficult dilemma for clinical decision-making. While they stand to gain most benefit from surgical revascularization, they also pose the greatest risk (1–3). Currently, such patients undergo intervention for improvement of anginal symptoms or because of prognostic considerations (4). However, many such patients are symptomatic due to LV dysfunction. As revascularization may lead to recovery of global LV function, an improvement of functional status may be attained by use of this approach in selected patients with viable myocardium (5).

Myocardial viability may be accurately identified using various imaging techniques (6) of which positron emission

From the Department of Cardiology, Cleveland Clinic Foundation, Cleveland, Ohio. Supported in part by a Grant in Aid from the American Heart Association.

Manuscript received June 4, 1998; revised manuscript received September 23, 1998, accepted November 18, 1998.

Abbreviations and Acronyms

CABG	=	coronary artery bypass surgery
CHF	=	congestive heart failure
DbE	=	dobutamine echocardiography
FDG	=	fluorodeoxyglucose
LV	=	left ventricular
mCi	=	milliCuries
METS	=	metabolic equivalents
ROC	=	receiver operating characteristic
PET	=	positron emission tomography
QOL	=	quality of life

tomography (PET) has the longest experience (7,8). Resting regional LV function has been shown to improve postoperatively after revascularization of this viable tissue (6), but these studies have not accounted for the effects of intervention on the development of ischemia (9), and improvement of resting function may not correspond to changes in exercise capacity. However, this analysis is important, as the risk of coronary bypass surgery (CABG) would be more readily justified if improvements in functional capacity and quality of life could be predicted.

Thus, in a group of patients with moderate or worse LV function with predominant symptoms of heart failure, we evaluated the effects of revascularization of viable myocardium on patient outcome, exercise capacity, functional class and quality of life (QOL). We sought to predict postoperative changes on the basis of preoperative clinical and test data.

METHODS

Study design. We prospectively studied 63 patients who underwent CABG between 1993 and 1997. Patients were eligible for recruitment if they had at least moderate LV dysfunction, their main symptoms were related to LV dysfunction rather than angina and they were scheduled for coronary bypass surgery. This prospective cohort study comprised preoperative testing with postoperative follow-up. Preoperative data were gathered from PET imaging using Rb-82 and F-18 deoxyglucose (FDG), resting echocardiography, dobutamine echocardiography, exercise testing, evaluation of functional class and a quality of life assessment. During follow-up after bypass surgery, the exercise test, assessment of functional class and quality of life questionnaire were repeated. The study was approved by the Institutional Review Board and patients gave informed consent.

Clinical evaluation. A preoperative clinical history was obtained, including evaluation of New York Heart Association Functional Class. Assessment of functional class was repeated at follow-up.

Positron emission tomography. All patients underwent PET in the fasting state with standard commercially available equipment (Posicam 6.5, Positron Corporation, Houston, Texas) using a previously described protocol (10,11). First, the patient's position was checked with a 3 min image, obtained 65 s after infusion of 20 milliCuries (mCi) of generator-produced Rb-82 (Cardiogen, Squibb, Stanford, Connecticut). After satisfactory positioning was ensured, a transmission image was obtained for a total of 60 to 70 million counts over 15 to 20 min for attenuation correction, using a Germanium-68 source. Fifty seconds after injection of 60 mCi of Rb-82, resting images were acquired over 6 min (25–40 million counts). Rb-82 was reinjected 6 min following the start of a standard dipyridamole stress (0.57 mg/kg) with isometric hand grip, and stress images were obtained.

After the patient returned to the baseline state, normoglycemia was established. Standard oral glucose loading (50 g) was performed an hour before injection of 5–10 mCi of FDG. In diabetic patients, blood glucose was titrated to the range of 55–110 mg/dl by iv administration of 5–20 units of regular insulin, the dose being titrated by blood glucose paper strip monitoring. After a delay of 45 min to allow clearance from the blood pool, images were acquired over 20 min. Attenuation correction was performed with transmission image data obtained before the Rb-82 imaging.

Images were interpreted by readers blinded to the remainder of the clinical data. Based on previous work (11), the heart was divided into a 24 segment model—eight segments (septal, anteroseptal, anterior, anterolateral, lateral, inferolateral, inferior, inferoseptal) at basal, mid and apical LV levels (excluding the basal septal due to the membranous septum) and the apex. Segments were designated as normal if myocardial perfusion was within 80% of maximum. Ischemia was identified by <15% relative reduction of activity after stress. Hibernation was defined by a metabolism perfusion mismatch, defined by FDG activity within 2 standard deviations (>70%) of normal, within a perfusion defect. Segments were designated "viable" if they demonstrated either a mismatch or ischemic pattern.

Echocardiography. Resting echocardiography was performed using commercially available equipment and in standard views. Images were digitized into cine-loops and ejection fraction was assessed using modified Simpson's rule (12), blinded to the other data. The ejection fraction was calculated in all patients before revascularization.

Dobutamine echocardiography was performed using a standard incremental dose protocol starting at 5 mcg/kg/min, increasing at 3 min intervals to 10, 20, 30 and 40 mcg/kg/min; atropine was added if required (13). Images were digitized into cine-loops and the regional wall motion score, based upon the 16 segment ASE model (12), was assessed at each stage blinded to the other data. Ischemia was identified in the presence of a new or worsening wall motion abnormality. Viable myocardium was identified by augmentation of an abnormal segment at low dose (5–

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10 mcg/kg/min), with or without subsequent deterioration at peak dose. Infarction was identified by severe hypokinesis or akinesis at rest that failed to respond to dobutamine. These data were obtained preoperatively in 47 patients; in the remainder, the test was declined by the patient or referring physician, or could not be scheduled before surgery.

Exercise testing. Symptom-limited exercise testing was performed in 58 patients preoperatively, five being unable to exercise. A standard treadmill protocol (Bruce, modified Bruce) was selected according to the exercise capacity and age of the patient. Standard endpoints were employed, and the usual hemodynamic and ECG monitoring was performed with rate pressure product measured at each stage. Exercise capacity was measured using expired gas analysis (Cardio II, MedGraphics, Minneapolis, Minnesota) in 38 patients, and metabolic equivalents (METS) were derived from the oxygen uptake. In patients in whom expired gas analysis could not be scheduled before surgery, oxygen uptake was estimated from published tables (14). Postoperative exercise testing was performed in the 55 patients who were able to return for follow-up.

Quality of life. The Nottingham Health Profile is a well validated test (15,16), which has been used previously for assessment of quality of life before and after cardiac surgery (17–21). This profile consists of scores for energy, pain, emotion, sleep, social function and mobility which were derived from weighted scores for positive responses to 38 statements regarding each of these categories. The maximum score for each category is 100 which reflects a low quality of life and the minimum score is 0 which reflects a high quality of life. A single observer made the assessment of these symptoms before and after surgery in 56 patients.

Coronary artery bypass surgery. Coronary bypass surgery was accomplished using standard techniques. Cold blood cardioplegia was performed through antegrade and retrograde approaches. Arterial grafting was performed whenever possible, and complete revascularization of all involved territories was attempted (22). Patients were followed perioperatively for evidence of myocardial infarction which was defined on the basis of elevation of the creatine kinase MB fraction to >20 U/liter.

Follow-up. Exercise testing was repeated after an interval of 6 ± 4 months after CABG, reflecting the availability of patients for the test at the time of follow-up. Quality of life evaluation was performed over the telephone by the same observer and was delayed until 11 ± 11 months postoperatively. Finally, to record major adverse events (death, myocardial infarction or cardiac transplantation), all patients were followed by clinic review or telephone contact with the patient or family at an interval of 17 ± 13 months after surgery.

Statistical analysis. The functional class, exercise capacity and QOL were compared at baseline and postoperatively. Subgroups with ischemic and viable myocardium in greater or less than 25% of the left ventricular mass were compared before and after surgery, this threshold being selected on the basis of our previous experience (23). Continuous variables were compared using the paired *t* test and discrete variables using the chi square test. Quality of life scores were compared using the Wilcoxon signed rank test. The univariate associations between preoperative variables (including stress test results) and change in exercise capacity were assessed using Pearson's correlation and significant correlates were entered into multiple linear regression models. Regression diagnostics were performed to assure validity of the linear model and to assure that no excessively influential observations were present. Receiver operating characteristic (ROC) curves were obtained to assess the accuracy of PET and dobutamine echocardiography (DbE) for the prediction of improvement of exercise capacity. The association between preoperative variables (including stress test results) and change in QOL or change in functional class were assessed using Spearman's correlation. Analyses were performed using the SAS 6.12 analysis program (SAS Inc, Cary, North Carolina).

RESULTS

Clinical characteristics. Of the 63 study patients, 51 were men, and their mean age was 66 ± 9 years. All had prior myocardial infarctions and multivessel coronary artery disease; 41 had prior bypass surgery. Diabetes mellitus was present in 32 (14 were insulin dependent). All patients had symptoms of heart failure; the mean New York Heart Association Functional Class was 2.6 ± 0.7; 36 were in Classes III and IV. Patients were on medical therapy for heart failure, and 51 were taking angiotensin converting enzyme inhibitors. Only patients with moderate or worse dysfunction were studied, and the mean EF preoperatively was 0.28 ± 0.07.

Positron emission tomography. Resting perfusion defects were present in a mean of 7.4 ± 3.4 segments per patient (31 ± 14% of LV mass). Ischemia, evidenced by dipyridamole-induced perfusion defects, was detected in 4.4 ± 4.6 segments (18 ± 19% of LV mass). Hibernation, denoted by a metabolism-perfusion mismatch, was present in 2.8 ± 3.6 segments (12 ± 15% of LV mass). Thus, the extent of viable (ischemic and/or hibernating) tissue was 7.2 ± 5.0 segments or 30 ± 21% of LV mass.

Dobutamine echocardiography. Resting wall motion abnormalities were present in a minimum of 6 segments and averaged 13.2 ± 2.8 segments per patient (83 ± 18% of LV mass). Of these, 8.1 ± 3.3 (51 ± 21%) segments were identified as nonviable and 5.2 ± 2.8 (33 ± 18%) showed augmentation at low dose (analogous to "hibernation" by PET) with or without change at peak dose. Ischemia, evidenced by deterioration of regional function without prior improvement, was detected in 1.7 ± 2.3 segments (11 ± 14% of LV mass). Thus, the extent of viable (ischemic and/or hibernating) tissue was 6.9 ± 2.8 segments or 43 ± 18% of LV mass.

Exercise capacity. Patients exercised maximally; in patients undergoing measurement of oxygen uptake, the respiratory exchange ratio was 1.12 ± 0.12 before and 1.18 ± 0.09 after surgery. Exercise was limited by fatigue or dyspnea although 5 patients had anginal symptoms preoperatively. The most common ECG findings were nondiagnostic (in 30 patients) because of resting repolarization abnormalities, elevation or depression of the ST segment was identified in 17 patients, and the remainder showed no ST segment changes with exercise. The tests were performed without complication, apart from one patient developing ventricular tachycardia without hemodynamic compromise. The average exercise capacity preoperatively improved from 5.4 ± 2.3 to 5.9 ± 2.2 METS ($p < 0.00001$), but the change in exercise capacity varied from a decrement of 2.8 to an increment of 5.2 METS. The cardiac work response to exercise improved after revascularization with a baseline rate-pressure product of 21,600 ± 5,700 to 24,600 ± 6,500 bpm.mm Hg ($p = 0.001$).

The extent of viable myocardium by PET correlated significantly with the degree of improvement of exercise capacity ($r = 0.54$, $p = 0.0001$; Fig. 1A), but the extent of hibernating tissue (mismatch pattern) correlated less well ($r = 0.37$, $p = 0.005$; Fig. 1B). However, the extent of viable myocardium by DbE was not correlated with improvement in exercise capacity ($r = 0.005$, $p = 0.92$; Fig. 1C). In a multiple linear regression involving the whole group, the extent of viability by PET ($r = 0.66$, $p = 0.0001$) and nitrate use ($r = 0.17$, $p = 0.005$) were the only independent predictors of improvement of exercise capacity (model $R^2 = 0.40$, $p = 0.0001$). Thus, for every two viable segments identified by PET, there was a 5% improvement of exercise capacity.

In order to further compare PET and DbE before surgery, we reexamined the subgroup of 37 patients who underwent both tests preoperatively, as well as pre and postoperative exercise testing. This group (age 67 ± 9 years, EF 27 ± 7%, 59% functional class 3 and 4) corresponded to the demographics of the larger group. In separate regression models, no clinical variable (age, ejection fraction or Functional Class) or DbE variable (extent of scar, ischemia or viability) was predictive of change of exercise capacity. Moreover, while both ischemia ($p = 0.007$) and viability ($p = 0.03$) by PET were predictive of outcome, these findings interacted so that ischemia was more predictive of outcome in the presence of viability and vice versa.

The area under the ROC curve for PET (0.76, $p = 0.004$) exceeded that under the DbE curve (0.66, $p = 0.08$; Fig. 2). The optimal cut point for prediction of any recovery in exercise capacity with PET was obtained with viability in

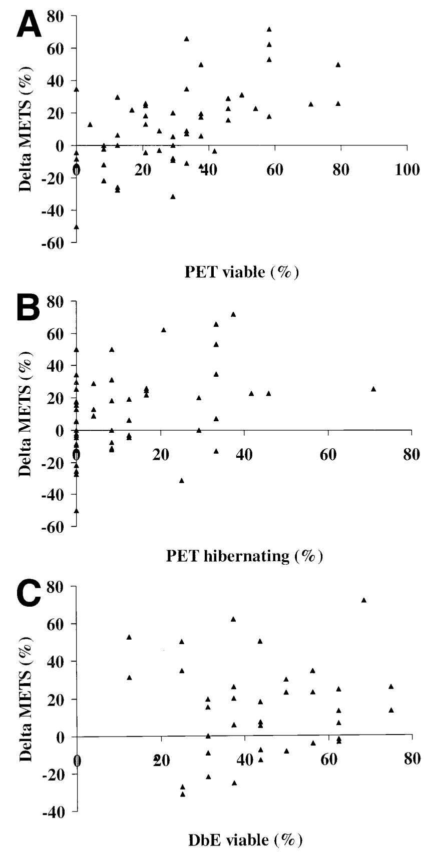

Figure 1. Relationship between extent of viable myocardium by PET **(A)**, hibernating myocardium by PET **(B)** and total viable myocardium by DbE **(C)** and change in exercise capacity.

33% of LV (sensitivity 79%, specificity 68%); with DbE, this was obtained with a cut point of 44% of LV mass (sensitivity 64%, specificity 64%). Previous studies have suggested the presence of viable myocardium in >25% of LV mass to predict a significant likelihood of functional recovery. In our study, this would give a 75% sensitivity for functional improvement using either test; although this is

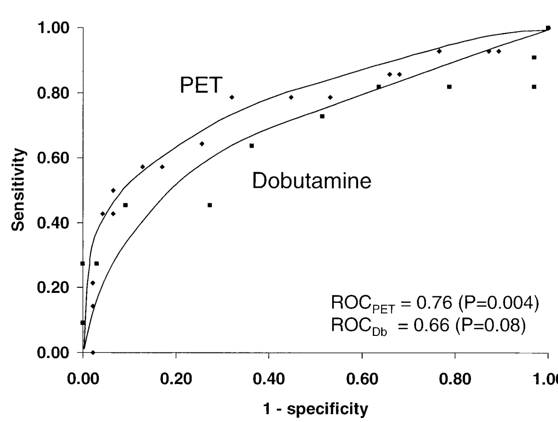

Figure 2. Receiver operating characteristic (ROC) curves of prediction of an improvement of exercise capacity by the extent of viable myocardium by PET and DbE.

Table 1. Improvement of Exercise Capacity According to the Extent of Viable Myocardium by PET

	PET Viability ≤25% LV (n = 30)			PET Viability >25% LV (n = 33)		
	Preoperative	**Postoperative**	**p**	**Preoperative**	**Postoperative**	**p**
Baseline ejection fraction (%)	0.28 ± 0.06	—	—	0.28 ± 0.08	—	p = NS*
Resting wall motion abnorm	14 ± 2	—	—	13 ± 3	—	p = NS*
Rb—reversible segments	1.9 ± 1.9	—	—	6.6 ± 5.3	—	p < 0.001*
FDG—mismatch segments	1.2 ± 1.7	—	—	4.3 ± 4.3	—	p < 0.001*
Exercise capacity (METS)	5.9 ± 2.8	6.3 ± 2.8	p = 0.67	4.6 ± 1.5	5.6 ± 1.4	p = 0.002
Workload (RPP*1000)	22.5 ± 5.1	23.2 ± 7.6	p = 0.84	21.8 ± 5.9	25.8 ± 5.4	p = 0.005

*Comparison of baseline findings in groups with PET viability ≤25% and >25%.

not the "optimal" cutoff in a statistical sense, it represents a level of sensitivity that is clinically desirable. The results of exercise testing before and after surgery using this cut point are summarized in Tables 1 and 2. Exercise capacity and rate pressure product did not improve significantly in patients with <25% of the left ventricle showing viable tissue by either PET (Table 1) or DbE (Table 2) and did improve significantly in patients with more extensive viable tissue.

Functional class. The average functional class improved from 2.6 ± 0.7 preoperatively to 1.9 ± 0.7 after surgery. The number of patients in classes 3 and 4 decreased from 34 patients (56%) to 12 patients (20%) after surgery ($p < 0.0001$). The improvement in functional class correlated weakly with the change in exercise capacity ($r = 0.25$), the extent of viable myocardium by PET ($r = 0.23$) and the extent of viability by DbE ($r = 0.31$).

Quality of life. The changes in QOL score components over follow-up are compared with normal ranges in a reference population in Figure 3. Four components of the QOL score (energy, pain, emotion and mobility status) significantly improved over follow-up. There was no significant change in sleep pattern, and social function deteriorated postoperatively. Table 3 classifies responses as normal and abnormal by comparison of scores with a reference population.

There were no meaningful correlations between QOL scores and the results of preoperative testing (Table 4). Patients with various extents of viable myocardium had comparable levels of health assessment and improved to a similar degree (Fig. 4). Using a categorical analysis of responses as normal or abnormal, only the presence of normal energy levels after surgery was greater in those with extensive (>25%) viable myocardium by PET compared with those with less extensive viability (38% vs. 63%, $p = 0.05$).

Patient outcome. No perioperative deaths or myocardial infarctions occurred in this series of patients with LV dysfunction. Over 17 ± 13 months, three patients (5%) died, of whom two died from cardiac causes, respectively, one and two years after surgery. One patient required heart transplantation due to worsening heart failure after bypass surgery.

DISCUSSION

The results of this study indicate that in patients with ischemic LV dysfunction, improvements in exercise capacity are correlated more with the total extent of jeopardized myocardium than the extent of PET mismatch pattern or the extent of viability by dobutamine echocardiography. Functional class and QOL improved in most patients after myocardial revascularization, but this improvement did not have a predictable association with the extent of viable myocardium.

Exercise capacity. With the increasing survival of patients after postinfarction thrombolysis and the aging of the population, an increasing number of patients are being seen with either no or minimal anginal symptoms in whom surgery for prognostic reasons would not be considered on

Table 2. Improvement of Exercise Capacity According to the Extent of Viable Myocardium by DbE

	DbE Viability ≤25% LV (n = 8)			DbE Viability >25% LV (n = 55)		
	Preoperative	**Postoperative**	**p**	**Preoperative**	**Postoperative**	**p**
Baseline ejection fraction (%)	0.25 ± 0.08	—	—	0.27 ± 0.06	—	p = NS*
Resting wall motion abnorm	14 ± 2	—	—	13 ± 3	—	p = NS*
DbE—ischemic segments	0.3 ± 0.5	—	—	2.0 ± 2.4	—	p < 0.001*
DbE—viable segments	3.8 ± 2.4	—	—	5.5 ± 2.8	—	p < 0.01*
Exercise capacity (METS)	4.6 ± 1.5	5.1 ± 1.5	p = 0.44	4.7 ± 1.3	5.1 ± 1.3	p = 0.01
Workload (RPP*1000)	18.6 ± 4.7	21.1 ± 4.6	p = 0.31	21.8 ± 5.5	25.8 ± 6.3	p = 0.002

*Comparison of baseline findings in groups with DbE viability ≤25% and >25%.

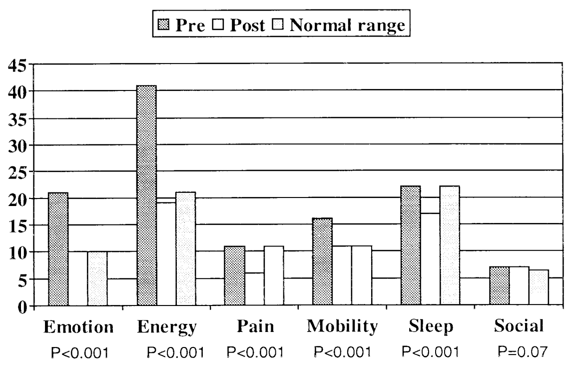

Figure 3. Change of quality of life scores after coronary artery bypass surgery.

the basis of age or comorbidities. However, the functional capacity of these patients is often compromised and, if improvement of function could be predicted, this could become an indication for intervention in selected patients. Studies of viable myocardium that have been performed to date have focused on the recovery of regional LV function after revascularization, and a few studies have shown improvement of global LV function (24–26). However, the correlation of resting indexes of LV function with exercise capacity is poor (27). Moreover, while the severity of LV dysfunction is associated with adverse cardiac outcome, exercise capacity has been shown to provide independent prognostic information in patients with reduced LV ejection fraction (28).

Dyspnea, fatigue or angina may limit exercise capacity. Previous studies of exercise capacity before and after myocardial revascularization have shown improvement following relief of angina (29–31), but angina was either absent or a minor symptom in this group. Fatigue and dyspnea largely reflect the consequences of reduced cardiac output—thus, in the absence of ischemia, exercise capacity reflects LV reserve and peripheral adaptation to exercise. Thus, improvement of functional capacity after CABG will only be evident if the cardiac response to exercise is examined, and resting parameters cannot be used as a surrogate endpoint. The results of this study indicate that, in patients with compromised functional capacity due to LV dysfunction, but with no or limited anginal symptoms, improvement in exercise capacity correlates with the extent of jeopardized myocardium defined by PET.

Previous work by Di Carli et al. has examined the impact of CABG on heart failure symptoms in patients with viable myocardium (5). In 36 patients with severe LV dysfunction, improvement in the Specific Activity Scale correlated with the extent of perfusion-metabolism mismatch identified by PET. There are some important differences between the latter study and our experience. First, we compared exercise capacity directly while Di Carli estimated this from the Specific Activity Scale which loosely correlates with METS. Second, we examined the total extent of tissue which was liable to contribute to an improvement in function—both viable (mismatch) and ischemic. This may account for the use of a different cutoff to optimize the sensitivity and specificity of the test. Third, the extent of viable myocardium (30 ± 21%) was less in our series than in the former study (63 ± 13%). However, the most important findings are concordant—that there is a correlation between improvement of exercise capacity and extent of jeopardized tissue.

Comparison of DbE and PET. Both tests are able to identify both viable and ischemic myocardium, and both have been shown to predict improvement of regional LV function at rest after revascularization (6). However, no data have been gathered to address alteration of regional or global LV function after stress to which changes of exercise capacity are a corollary. There are some important physiologic differences between the tests which might be grounds for anticipating this result. First, metabolic imaging with PET is exquisitely sensitive for the detection of viable myocardium, to the extent that some (perhaps subepicardial) viable regions are unable to contribute to improvement of resting function. If adequately revascularized, these areas may nonetheless be important in the response to exercise. Second, dipyridamole stress PET perfusion imaging is probably the most sensitive marker of myocardial ischemia (10), the accurate quantitation of which is likely to be an important determinant of exercise capacity. Third, the response of viable myocardium to dobutamine is heterogeneous. The uniphasic response is particularly problematic in this respect (32), as the same response may be seen from areas involved in non-Q-wave myocardial infarction which

Table 3. Changes in Quality of Life Responses After Revascularization

	Improved	Normal pre-CABG	No Change	Worsened
Emotional reactions	16 (29%)	24 (43%)	13 (23%)	3 (5%)
Energy	18 (32%)	10 (18%)	23 (41%)	5 (9%)
Pain	15 (27%)	28 (50%)	6 (11%)	7 (12%)
Physical mobility	12 (21%)	23 (41%)	15 (27%)	6 (11%)
Sleep	8 (14%)	31 (55%)	12 (21%)	5 (10%)
Social isolation	4 (7%)	38 (68%)	8 (14%)	6 (11%)

Table 4. Correlation Between Change in Constituent QOL Indices and Extent of Viable Myocardium by PET and DbE

	PET Viability	p	DbE Viability	p	Δ ex Capacity	p
Emotional reactions	r < 0.17	0.23	r = 0.24	0.13	r = −0.15	0.29
Energy	r < 0.1	0.55	r < 0.1	0.83	r = 0.14	0.33
Pain	r < 0.1	0.68	r = 0.2	0.16	r = 0.05	0.74
Physical mobility	r < 0.1	0.56	r < 0.1	0.94	r = −0.14	0.36
Sleep	r < 0.1	0.82	r < 0.1	0.66	r = −0.12	0.41
Social isolation	r = 0.2	0.16	r = 0.17	0.30	r = 0.14	0.31

may not be able to contribute to regional contractile reserve with exercise. Fourth, the segmentation of the LV with DbE is not attuned to subtle gradations of LV dysfunction so that assessment of the extent of jeopardized tissue (which may be very important in prediction of functional recovery) may be less reliable than with PET, the interpretation of which is performed by examination of sequential imaging planes. Finally, we selected the most difficult group to study with DbE; patients with extensive dysfunction present interpretive difficulties that relate to tethering. Nonetheless, the greater expense of PET may be justified in the selection of heart failure patients for surgery.

Functional class. The New York Heart Association Functional Class is the most widely used index of functional capacity in patients with congestive heart failure (CHF). Previous studies have shown a poor correlation between functional class and exercise capacity (33). In this study, most patients improved functional class after surgery ($p < 0.0001$). This improvement correlated weakly with the change in exercise capacity ($r = 0.25$), extent of viable myocardium by PET ($r = 0.23$) and extent of viability by DbE ($r = 0.31$).

Quality of life. Patients undergoing treatments for chronic disease may not feel better despite the "success" of the treatment in achieving endpoints important to their physicians. For example, the presence of neuropsychiatric complications and employment difficulties after CABG lead about 20% of patients undergoing such surgery to believe that their quality of life is worse or no better than it was preoperatively (34). Quality of life scores, which may be generic or disease specific, are being used increasingly to address these issues in the assessment of therapeutic efficacy. The standard criteria for efficacy in the treatment of coronary disease, which center on physiologic measurements (exercise capacity, ejection fraction), have shown limited correlation between the patient's evaluation of health status and other testing (35).

The Nottingham Health Profile is multidimensional and was initially developed as a generic scale, but it has been used previously for the evaluation of patients following

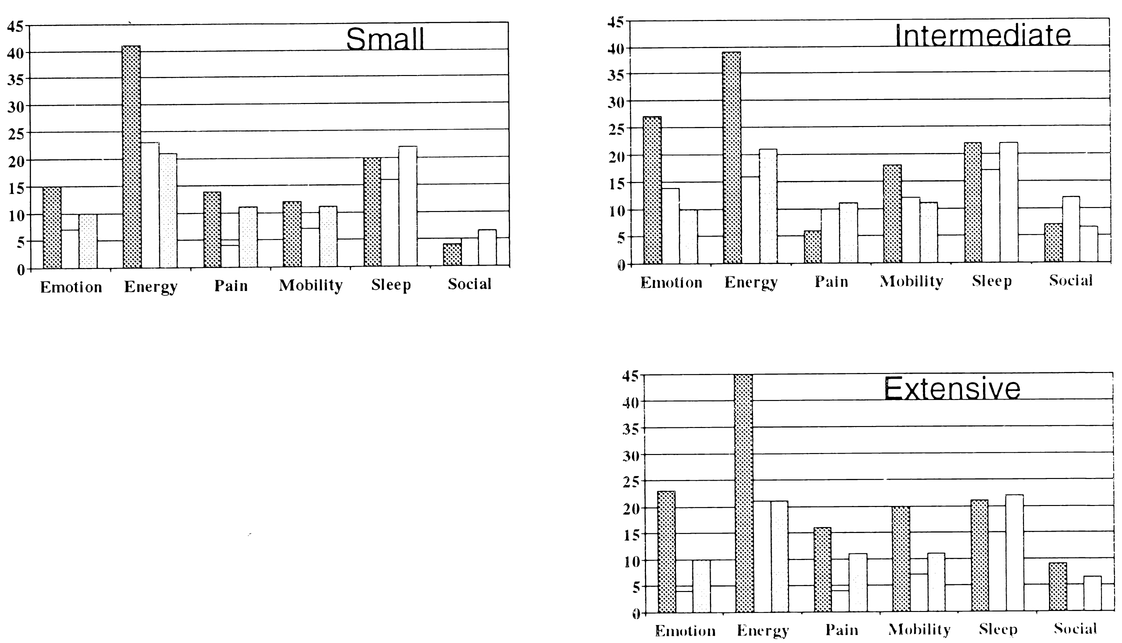

Figure 4. Relationship between quality of life (before and after surgery, and normal range) and the extent of viable myocardium (in tertiles).

cardiac surgery and its categories evaluate dimensions that are commonly influenced by cardiac disease. The questions are standardized and easy to use although the data are extensive. This test has been validated in cardiac patients (36) and is responsive to change (37), but it is reproducible when the clinical status is stable (38). Although QOL may be perceived as a "soft" endpoint, the validation and reproducibility of these scores is comparable to many other measured parameters.

Previous evaluations of QOL with cardiac surgery have focused on patients with angina. Studies of revascularization for angina pectoris have shown only a modest correlation of angina with QOL, and this is specifically limited to the chest pain and physical ability aspects of the QOL evaluation (39). Nonetheless, in the Bypass Angioplasty Revascularization Investigation (BARI), QOL improved to a similar degree in patients undergoing CABG and coronary angioplasty (21). In the Randomized Intervention Treatment of Angina (RITA) study, reduction in QOL correlated with the presence of angina before and after revascularization, and, in patients without ongoing angina, QOL was indistinguishable from that of a normal group (17). In a large Swedish study, improvement of QOL was related to the severity of preoperative angina and was more commonly seen in women while improvements of exercise capacity were more commonly seen in men. The most symptomatic patients with the worst exercise limitation experienced the greatest improvement in QOL, but this did not correlate well with changes in exercise capacity (40).

The efficacy of heart failure therapy for the improvement of QOL is less clear. Despite the efficacy of angiotensin converting enzyme inhibition for the improvement of left ventricular function and survival, substantial benefits in QOL have not been reported on this therapy (41). In surgically treated patients, Chocron et al. (18) reported higher New York Heart Association functional classes to be predictive of less improvement of energy and physical mobility, and segmental left ventricular dysfunction to be predictive of less improvement of pain. Indeed, in that study, higher functional classes were associated with a greater likelihood of deterioration of QOL after surgery. In the context of these findings, it is reassuring that QOL in most patients with severe LV dysfunction but viable myocardium improved after bypass surgery. In the context of previous studies showing the poor correlation of QOL with other indices, it is not surprising that the degree of improvement of QOL is not matched to the extent of recovery of exercise capacity. It is likely that other baseline and operative variables interact with the patient's perception of recovery.

Limitations. The findings of this study reflect the results of CABG in selected patients at an institution with high surgical volume. While we believe that the use of functional testing may have contributed to avoidance of perioperative mortality, the selection of the patients and their treatment at our institution may also be responsible for their favorable perioperative outcome.

The Nottingham Health Profile was selected for this study because of its profile as a test of overall quality of life while also being used in a number of cardiovascular studies. However, this test has not been validated as a correlate of functional capacity, and another index of quality of life might have correlated better with changes in exercise testing.

Clinical implications. Myocardial revascularization improves exercise capacity, functional class and QOL in selected patients with left ventricular dysfunction and viable myocardium. The extent of viable myocardium appears to correlate with improvement of exercise capacity and cardiac workload. Thus, in selected patients, bypass surgery may be indicated to improve functional status. However, despite the previous documentation of equivalence between PET and DbE for the prediction of recovery of regional LV dysfunction, PET appears to be superior as a predictor of improved exercise capacity.

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REFERENCES

1. Bounous EP, Mark DB, Pollock BG, et al. Surgical survival benefits for coronary disease patients with left ventricular dysfunction. Circulation 1988;78:I151–7.
2. Hellman C, Schmidt DH, Kamath ML, Anholm J, Blau F, Johnson WD. Bypass graft surgery in severe left ventricular dysfunction. Circulation 1980;62:I103–10.
3. Shearn DL, Brent BN. Coronary artery bypass surgery in patients with left ventricular dysfunction. Am J Med 1986;80:405–11.
4. Alderman EL, Fisher LD, Litwin P, et al. Results of coronary artery surgery in patients with poor left ventricular function (CASS). Circulation 1983;68:785–95.
5. Di Carli MF, Asgarzadie F, Schelbert HR, et al. Quantitative relation between myocardial viability and improvement in heart failure symptoms after revascularization in patients with ischemic cardiomyopathy. Circulation 1995;92:3436–44.
6. Bonow RO. Identification of viable myocardium. Circulation 1996;94:2674–80.
7. Brunken RC, Mody FV, Hawkins RA, Nienaber C, Phelps ME, Schelbert HR. Positron emission tomography detects metabolic viability in myocardium with persistent 24-hour single-photon emission computed tomography 201Tl defects. Circulation 1992;86:1357–69.
8. Tillisch J, Brunken R, Marshall R, et al. Reversibility of cardiac motion abnormalities predicted by positron emission tomography. New Engl J Med 1986;314:884–8.
9. Kaul S. There may be more to myocardial viability than meets the eye. Circulation 1995;92:2790–3.
10. Go RT, Marwick TH, MacIntyre WJ, Saha GB, Neumann DR, Underwood DA. A prospective comparison of rubidium-82 PET and thallium-201 SPECT myocardial perfusion imaging utilizing a single dipyridamole stress in the

diagnosis of coronary artery disease. J Nucl Med 1990;31: 1899–905.
11. Go RT, MacIntyre WJ, Cook SA, et al. The incidence of scintigraphically viable and nonviable tissue by rubidium-82 and fluorine-18-fluorodeoxyglucose positron emission tomographic imaging in patients with prior infarction and left ventricular dysfunction. J Nucl Cardiol 1996;3:96–104.
12. Schiller NB, Shah PM, Crawford M, et al. Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. American Society of Echocardiography Committee on Standards, Subcommittee on Quantitation of Two-Dimensional Echocardiograms. J Am Soc Echocardio 1989;2:358–67.
13. Secknus M, Marwick TH. Evolution of dobutamine echocardiography protocols and indications: Safety and side-effects in 3011 studies over 5 years. J Am Coll Cardiol 1997;29:1234–40.
14. American College of Sports Medicine. Guidelines for graded exercise testing and exercise prescription. 3rd ed. Philadelphia: Lea & Febinger, 1985.
15. Hunt SM, McKenna SP, McEwen J, Backett EM, Williams J, Papp E. A quantitative approach to perceived health status: a validation study. J Epidem Com Health 1980;34:281–6.
16. Hunt SM, McEwen J, McKenna SP. Measuring health status: a new tool for clinicians and epidemiologists. J Royal College of Gen Pract 1985;35:185–8.
17. Pocock SJ, Henderson RA, Seed P, Treasure T, Hampton JR. Quality of life, employment status, and anginal symptoms after coronary angioplasty or bypass surgery. 3-year follow-up in the Randomized Intervention Treatment of Angina (RITA) Trial. Circulation 1996;94:135–42.
18. Chocron S, Etievent JP, Viel JF, et al. Prospective study of quality of life before and after open heart operations. Annals of Thoracic Surgery 1996;61:153–7.
19. Klersy C, Collarini L, Morellini MC, Cellino F. Heart surgery and quality of life: a prospective study on ischemic patients. Eur J Cardio-Thoracic Surg 1997;12:602–9.
20. Sjoland H, Caidahl K, Wiklund I, et al. Impact of coronary artery bypass grafting on various aspects of quality of life. Eur J Cardio-Thorac Surg 1997;12:612–9.
21. Anonymous. Five-year clinical and functional outcome comparing bypass surgery and angioplasty in patients with multivessel coronary disease. A multicenter randomized trial. Writing Group for the Bypass Angioplasty Revascularization Investigation (BARI) Investigators. JAMA 1997;277:715–21.
22. Jones EL, Craver JM, Guyton RA, Bone DK, Hatcher CR Jr, Riechwald N. Importance of complete revascularization in performance of the coronary bypass operation. Am J Cardiol 1983;51:7–12.
23. Marwick TH, Nemec JJ, Lafont A, Salcedo EE, MacIntyre WJ. Prediction by postexercise fluoro-18 deoxyglucose positron emission tomography of improvement in exercise capacity after revascularization. Am J Cardiol 1992;69:854–9.
24. Tillisch J, Brunken R, Marshall R, et al. Reversibility of cardiac wall-motion abnormalities predicted by positron tomography. N Engl J Med 1986;314:884–8.
25. Depre C, Vanoverschelde JL, Melin JA, et al. Structural and metabolic correlates of the reversibility of chronic left ventricular ischemic dysfunction in humans. Am J Physio 1995;268: H1265–75.
26. Lucignani G, Paolini G, Landoni C, et al. Presurgical identification of hibernating myocardium by combined use of technetium-99m hexakis 2-methoxyisobutylisonitrile single photon emission tomography and fluorine-18 fluoro-2-deoxy-D-glucose positron emission tomography in patients with coronary artery disease. Eur J Nucl Med 1992;19:874–81.
27. Franciosa JA, Ziesche S, Wilen M. Functional capacity of patients with chronic left ventricular failure. Relationship of bicycle exercise performance to clinical and hemodynamic characterization. Am J Med 1979;67:460–6.
28. Pilote L, Silberberg J, Lisbona R, Sniderman A. Prognosis in patients with low left ventricular ejection fraction after myocardial infarction. Importance of exercise capacity. Circulation 1989;80:1636–41.
29. Kent KM, Borer JS, Green MV, et al. Effects of coronary artery bypass on global and regional left ventricular function during exercise. N Engl J Med 1978;298:1434–9.
30. Lapin ES, Murray JA, Bruce RA, Winterscheid L. Changes in maximal exercise performance in the evaluation of saphenous vein bypass surgery. Circulation 1973;47:1164–73.
31. Bode RF, Zajtchuk R. Evaluation of saphenous vein bypass surgery with multistage treadmill test and ventricular function studies. J Thorac & Cardiovasc Surg 1998;74:44–6.
32. Armstrong WF. "Hibernating" myocardium: asleep or part dead? J Am Coll Cardiol 1996;28:530–5.
33. Franciosa JA, Park JA, Levine B, et al. Lack of correlation between exercise capacity and indices of resting left ventricular performance in heart failure. Am J Cardiol 1981;63:856–63.
34. Mayou R, Bryant B. Quality of life after coronary artery surgery. Quart J Medicine 1987;62:239–48.
35. Guyatt GH, Thompson PJ, Berman LB, et al. How should we measure function in patients with chronic heart and lung disease? J Chron Dis 1985;38:517–24.
36. O'Brien BJ, Buxton MJ, Patterson DL. Relationship between functional status and health-related quality-of-life after myocardial infarction. Med Care 1993;31:950–5.
37. Caine N, Harrison SC, Sharples LD, Wallwork J. Prospective study of quality of life before and after coronary artery bypass grafting. BMJ 1991;302:511–6.
38. Hunt SM, McEwen J, McKenna SP. Perceived health: age and sex comparisons in a community. J Epidemiol Com Health 1984;38:156–60.
39. Sjoland H, Wiklund I, Caidahl K, Albertsson P, Herlitz J. Relationship between quality of life and exercise test findings after coronary artery bypass surgery. Int J Cardiol 1995;51: 221–32.
40. Sjoland H, Wiklund I, Caidahl K, Haglid M, Westberg S, Herlitz J. Improvement in quality of life and exercise capacity after coronary bypass surgery. Arch Int Med 1996;156:265–71.
41. Rogers WL, Johnstone DE, Yusuf S, et al. Quality of life among 5,025 patients with left ventricular dysfunction randomized between placebo and enalapril: The studies of left ventricular dysfunction. J Am Coll Cardiol 1993;23:393–400.