Prediction of global left ventricular function after bypass surgery in patients with severe left ventricular dysfunction

Impact of pre-operative myocardial function, perfusion, and metabolism

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Aims Previous studies have compared the accuracy of various tests of viability for the prediction of recovery of regional left ventricular function; global left ventricular recovery has been less well studied, although it has important prognostic and functional ramifications. We sought to identify the relative contribution of ischaemia, regional and global contractile reserve, perfusion and metabolic function to changes in left ventricular volumes and global function after coronary artery bypass surgery in patients with severe left ventricular dysfunction.

Methods and Results Dipyridamole stress Rb-82, fluordeoxyglucose positron emission tomography and low and high-dose dobutamine-atropine stress echocardiography were obtained in 66 patients with left ventricular impairment. Myocardial segments were considered viable if ischaemia or either metabolic or contractile reserve were present, on positron emission tomography or dobutamine echocardiography. Resting left ventricular function was reassessed after surgery (mean 10 ± 3 weeks) in the 59 patients who had not suffered a major peri-operative event; functional improvement was defined by a 5% increment of ejection fraction. Myocardial viability was found in 37 (63%) patients using positron emission tomography and in 42 (71%) patients using dobutamine echocardiography; post-operative functional improvement was noted in 28 (47%) patients. In univariate analyses, predictors of global post-operative functional recovery included: the extent of viability according to positron emission tomography (OR (odds ratio): 2.08 for each additional viable segment, 95% CI (confidence interval): 1.33–3.25, P = 0.001) or dobutamine echocardiography (OR: 2.06 for each additional viable segment, 95% CI 1.28–3.30, P = 0.003) and the increase in ejection fraction with low-dose dobutamine (OR: 1.9 for each 1% increase in ejection fraction with low dose dobutamine, 95% CI 1.39–2.61, P < 0.0001). In a multivariate model which included evidence of viability by either technique, and change in ejection fraction with low-dose dobutamine echocardiography, only change in ejection fraction with a low-dose dobutamine infusion was predictive of post-operative left ventricular functional recovery (adjusted OR: 1.81, 95% CI 1.30–2.52, P = 0.0005).

Conclusion Among patients with severe left ventricular dysfunction who are referred for surgical revascularization, the overall accuracies of positron emission tomography and dobutamine echocardiography for the prediction of post-operative myocardial recovery are comparable. However, the strongest predictor of overall improvement of post-operative left ventricular function is an increase of ejection fraction with a low-dose dobutamine infusion. (Eur Heart J 2000; 21: 125–136) © 2000 The European Society of Cardiology

Key Words: Myocardial viability, positron emission tomography, dobutamine echocardiography, left ventricular dysfunction, coronary artery disease.

See page 101 for the Editorial comment on this article
**Introduction**

The identification of viable myocardium among patients with severe left ventricular dysfunction has important prognostic implications, but the contribution of the extent of myocardial viability to this process is unclear. As overall improvement in left ventricular function is likely to be a major contributor to the prognostic benefits of revascularization, prediction of this recovery is important. However, although previous studies have documented the accuracy of various imaging techniques for the prediction of regional functional recovery, few data are available regarding the prediction of recovery of global left ventricular function.

The commonly performed imaging tests applied for the diagnosis of viable myocardium may also be used to identify myocardial ischaemia. These tests examine perfusion, metabolic reserve or functional reserve, the extent to which these physiological parameters determine recovery is unclear. Existing data on segmental function suggest that contractile reserve is a less sensitive, but more specific, predictor of regional left ventricular improvement post-operatively than metabolic or perfusion evidence of viability. Thus, we sought to determine the relative contribution of these variables to the prediction of global left ventricular functional recovery following surgical revascularization.

**Methods**

**Study design**

Over a 4 year period, we studied 66 patients (56 men, age 63 ± 11 years) with stable, isolated coronary artery disease and impaired left ventricular systolic function (left ventricular ejection fraction <35%, mean 28 ± 5%) who underwent surgical revascularization. Before surgery, all patients underwent positron emission tomography assessment of myocardial perfusion (using Rb-82 before and after dipyridamole stress) and metabolism (using F-18 fluorodeoxyglucose), as well as dobutamine echocardiography for assessment of ischaemic and viable myocardium. Both tests were performed within 1 week, usually on consecutive days, in random order, and decisions to revascularize the patients were undertaken using the available clinical data, including the results of each test. The pre-operative physiological parameters were correlated with the results of resting 2D echocardiography post-operatively, after exclusion of six patients in whom left ventricular assessment was influenced by peri-operative infarction (evidenced by new wall motion abnormalities after surgery) and one patient who required cardiac transplant. The study sample therefore comprised the remaining 59 patients.

**Positron emission tomography**

Positron emission tomography myocardial perfusion imaging was undertaken with a standard acquisition system. Rubidium-82 (40–60 mCi) was injected intravenously at rest, and perfusion data were obtained approximately 75 s later. The process was repeated after injection of dipyridamole (0.56 mg . kg⁻¹), used with handgrip stress in a standard protocol. Following perfusion imaging, a standard glucose-loaded fluorodeoxyglucose protocol was used to identify myocardium with residual metabolic activity. Fasting patients were given a 75 g glucose load prior to i.v. administration of 5–10 mCi of F-18 deoxyglucose, at least 30 min post-stress; for diabetic patients, the blood glucose level was stabilized with insulin administration. Images were acquired approximately 60 min after glucose ingestion.

A seven-segment model was used to compare segmental findings with those of dobutamine echocardiography. These segments comprised the posterior, anteroseptal, lateral, septal, inferior and anterior walls and the apex. Studies were analysed by two observers blinded to the results of echocardiography, using a quantitative colour scale to classify segments as normal, showing a stress-induced defect (>15% relative reduction of Rb-82 activity post stress), or a fixed perfusion defect (>20% reduction of Rb-82 activity relative to maximum counts). In segments with abnormal wall motion demonstrating fixed defects, viability was identified by fluorodeoxyglucose activity >60% maximum activity in a segment with low resting flow ('perfusion–metabolism mismatch'). Segments with normal relative flow at positron emission tomography without evidence of ischaemia (consistent with myocardial stunning) or abnormal resting function showing abnormal flow reserve (consistent with ischaemia) were also considered to be viable.

**Dobutamine echocardiography**

Dobutamine stress echocardiography was performed using a standard protocol, with commercially available equipment. The ‘low-dose’ stages comprised 5 μg . kg⁻¹ . min⁻¹ for 3 min and then 10 μg . kg⁻¹ . min⁻¹ for a further 3 min. These were followed by incremental doses to 40 μg . kg⁻¹ . min⁻¹, with the use of atropine (1–2 mg i.v.) to attain 85% age predicted maximal heart rate in patients developing a submaximal heart-rate response to dobutamine alone. Standard haemodynamic and electrocardiographic monitoring were performed in all patients in conjunction with the dobutamine infusion. Test end-points were the end of the infusion protocol, the occurrence of significant ischaemia, serious arrhythmia, symtomatic hypotension or other major side-effects. Images were acquired from standard parasternal and apical views and all studies were digitized in a quad-screen format (Nova Microsonics, Allendale, NJ, U.S.A.) utilizing rest, 5 μg, 10 μg and peak images, and each stage was recorded on VHS videotape for subsequent review. Left ventricular ejection fraction was calculated using Simpson’s rule from the apical views utilizing both two- and four-chamber views at rest, low dose and peak
dose dobutamine infusion. At least two tracings in each view were analysed with the left ventricular ejection fraction calculated from an average of all values.

Echocardiograms were analysed by two observers blinded to the results of positron emission tomography imaging. Study quality was assessed subjectively as excellent (all endocardium visualized), good (all segments visualized), adequate (all walls visualized), or poor (failure to visualize one or more walls). Left ventricular volumes and ejection fraction were assessed at rest, and at low- and peak dose using Simpson’s method in the apical four- and two-chamber views. To minimize orientation problems when comparing both techniques, the previously described seven-segment model was used for segmental comparison with positron emission tomography[18]. Wall motion in each segment was scored as normal, mildly hypokinetic, moderate to severely hypokinetic, akinetic, or dyskinetic to create a modified wall motion score. Segments with severely hypokinetic or worse function were deemed viable if they demonstrated an improvement in thickening at low dose (5 or 10 μg . kg⁻¹ . min⁻¹) sufficient to improve the wall motion score by at least one point. Segments with mild hypokinesis at rest were considered as normal (if there was no peak dose ischaemia), given the difficulty assigning normality or mild hypokinesis to a segment in a ventricle with diffuse wall motion abnormalities. Ischaemia was identified in the presence of deterioration of regional function either after an initial improvement (biphasic response) or in isolation, unless this involved dyskinesia in an akinetic segment.

Coronary anatomy and coronary artery bypass surgery

All patients had coronary angiography performed in the usual manner and the results analysed by caliper estimation of stenosis severity by readers without any knowledge of the results of the viability studies. A lesion was considered significant if there was a >70% luminal narrowing of a major epicardial coronary artery. Multivessel disease was identified if there was significant disease in ≥2 coronary arteries or significant disease in the left main coronary artery.

Coronary bypass surgery was performed using standard techniques. An attempt was made to revascularize as much myocardium as possible. Particular attention was paid to myocardial protection, and cold blood cardioplegia was delivered using antegrade and retrograde techniques.

Follow-up

After surgery, all patients had a prospectively planned 2D echocardiogram after an interval of 10 ± 3 weeks to evaluate resting left ventricular function. Segmental analysis of wall motion and left ventricular ejection fraction was performed by consensus of two observers blinded to pre-operative viability data. The gold standards of viability were recovery of segmental or global function. Segmental improvement was defined as an increase in wall motion score from the pre-surgical study by at least one grade in more than one segment of the seven segment model. On a ‘per patient’ analysis, global functional recovery was defined by an improvement in left ventricular ejection fraction of >5% post-revascularization.

Statistical analyses

Baseline clinical and echocardiographic characteristics were described as mean ± one standard deviation, or median with 25th–75th percentile for continuous variables and as numbers (percentages) for categorical variables. Variables were compared between patients with and without peri-operative events and patients with or without post-surgical functional improvement. Differences in continuous variables were compared using the Student t-test and Wilcoxon rank sum tests, while differences of categorical variables were compared using the chi-square test.

The primary end-point was confirmation of viability, as manifested by a post-operative improvement of regional function (segmental analysis) or global function (improvement of ejection fraction >5%). Sensitivity, specificity, and accuracy of positron emission tomography and dobutamine echocardiography for predicting viability were calculated using standard definitions. Receiver–operator characteristic curves[20] were constructed to determine the best discriminant criteria for positron emission tomography and dobutamine echocardiography associations with global functional improvement. In other analyses, subjects were divided into tertiles of number of improved segments, preoperative end-diastolic volume, and number of predicted viable segments according to positron emission tomography and dobutamine echocardiography and improvement in ejection fraction with low-dose dobutamine; trend-type associations of these variables with viability were tested using the Mantel–Haenszel extension test[21]. Logistic regression analyses were performed relating these continuously defined variables to viability after adjustment for pre-operative ejection fraction and diabetes. Linear regression analyses were used to examine the relationship between increase in ejection fraction with low-dose dobutamine and post-operative increase in ejection fraction. Regression diagnostics were done to assure absence of outliers, excessively influential observations, and significant collinearity, as well as to confirm the appropriateness of the linear model. All tests were two-sided and a probability value less than 0.05 was considered significant. Analyses were performed using the SAS 6.12 statistical package (SAS, Inc, Cary, NC, U.S.A.).

Eur Heart J, Vol. 21, issue 2, January 2000
Table 1  Clinical characteristics in all patients, with comparison between patients excluded for peri-operative event or additional surgery (event) and the remaining patients (no event)

<table>
<thead>
<tr>
<th></th>
<th>All patients</th>
<th>Event</th>
<th>No event</th>
<th>P (event vs none)</th>
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<td>61±9</td>
<td>62±6</td>
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<td>6M, 1F</td>
<td>50M, 9F</td>
<td>ns</td>
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<td>Hypertension</td>
<td>28</td>
<td>2</td>
<td>26</td>
<td>ns</td>
</tr>
<tr>
<td>Diabetes</td>
<td>30</td>
<td>4</td>
<td>26</td>
<td>ns</td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>49</td>
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<td>44</td>
<td>ns</td>
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<tr>
<td>Number of diseased vessels</td>
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<td>2 (2–3)</td>
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</tr>
<tr>
<td>Beta-blocker therapy</td>
<td>14</td>
<td>2</td>
<td>12</td>
<td>ns</td>
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<tr>
<td>Ca antagonist therapy</td>
<td>19</td>
<td>2</td>
<td>17</td>
<td>ns</td>
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<td>ACE inhibitor therapy</td>
<td>42</td>
<td>3</td>
<td>39</td>
<td>ns</td>
</tr>
<tr>
<td>Left ventricular ejection fraction (%)</td>
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<td>30±10</td>
<td>28±5</td>
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<td>Left ventricular end-diastolic volume (ml)</td>
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<td>Systolic blood pressure (mmHg)</td>
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<td>Diastolic blood pressure (mmHg)</td>
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<td>73±7</td>
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<tr>
<td>RPP (mmHg . beats⁻¹ . min⁻¹)</td>
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<td>9368±2480</td>
<td>10 177±2574</td>
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<tr>
<td>Number of maximal stress test</td>
<td>51</td>
<td>3</td>
<td>49</td>
<td>&lt;0.05</td>
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<td>Dobutamine echocardiography viable segments</td>
<td>4 (2–5)</td>
<td>4 (3–5)</td>
<td>3 (2–4)</td>
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</tr>
<tr>
<td>Positron emission tomography viable segments</td>
<td>4 (3–5)</td>
<td>3 (4–5)</td>
<td>4 (3–6)</td>
<td>ns</td>
</tr>
</tbody>
</table>

RPP = rate-pressure product.

Results

Clinical characteristics

Baseline clinical characteristics of the study sample are summarized in Table 1. The majority had suffered a prior myocardial infarction and had symptoms of heart failure. There were no deaths in the peri-operative period or during the hospital stay. Nevertheless, six patients sustained a significant post-operative deterioration of left ventricular function, and a seventh patient required implantation of a left ventricular assistance device and subsequently underwent heart transplantation. There were no marked differences in clinical characteristics and positron emission tomography or dobutamine echocardiography results noted between the 59 patients who did not suffer a peri-operative cardiac event and the seven who did.

Positron emission tomography

Positron emission tomography imaging, including rest rubidium-82 perfusion scanning and 18-fluorodeoxyglucose metabolic studies, was successfully performed in all patients; dipyridamole stress images were obtained in 54 patients. Chest discomfort occurred in 19 patients (32%), interpretable ST segment change in 22 (37%) with these patients distributed evenly between viable and non-viable groups. Because of adverse effects during infusion, aminophylline was required in 19 patients.

Among the dysfunctional segments, 143 (42%) had normal rest and stress perfusion. A total of 94 (28%) segments had either a perfusion metabolism mismatch or an ischaemic response or both and 102 (30%) segments were classified as scar. Among these patients a median of four segments (25th–75th percentile: 3–5 segments) appeared viable.

Dobutamine echocardiography

Resting echocardiographic dimensions showed a left ventricular end-diastolic volume of 164 ± 48 ml and a left ventricular end-systolic volume of 120 ± 41 ml. The resting ejection fraction was 28 ± 5%. Inter- and intra-observer concordance were high (correlation coefficients respectively 0·80 and 0·77).

Dobutamine stress echocardiography was performed in all patients without major complications; two patients had non-sustained ventricular tachycardia and one had a supraventricular tachycardia which required cardioversion. The protocol was completed to 40 µg . kg⁻¹ . min⁻¹ in 47 patients (80%), and 25 patients (42%) reached 85% of age-predicted heart rate. The test was terminated early in 12 (18%) because of chest pain, or other side effects. The haemodynamic response showed an average rise in heart rate from 79 ± 13 to 130 ± 20 beats . min⁻¹ at peak dose, and a change in systolic blood pressure from 129 ± 25 to 133 ± 32 mmHg, the variance of the latter reflecting dobutamine-induced hypotension in some patients. Overall the study quality was of adequate or better quality in 85% of patients.
Improvement of regional function consistent with viability was noted in 154 (37%) segments, and ischaemia was noted in 44 (11%). Evidence of contractile reserve, defined as an increase in ejection fraction of at least 5% at low-dose dobutamine infusion, was present in 34 (58%) patients.

Prediction of postoperative improvement of left ventricular function

An improvement in left ventricular ejection fraction of at least 5% was noted in 28 (47%) patients; there were two (3%) patients in whom the ejection fraction fell by at least 5%, while eight (14%) had more than a 10% increase. Not surprisingly, patients who had a larger number of improved segments after surgery were more likely to manifest an improvement in global left ventricular systolic function (Fig. 1).

Predictors of viability

In the 59 patients with post-operative left ventricular ejection fraction data, various potential predictors of functional recovery were compared between the 28 demonstrating a >5% improvement of left ventricular ejection fraction (‘viable’) and the 31 patients failing to reach this level of improvement (Table 2). Clinical features, resting left ventricular ejection fraction and left ventricular volumes were not markedly different between these groups, although no patient with a left ventricular end-diastolic volume >220 ml had a >5% improvement of left ventricular ejection fraction. There was no relationship with the number of segments showing echocardiographic evidence of scar and the pre-operative left ventricular end-diastolic volume. There was a highly significant relationship between number of viable segments at positron emission tomography and

Table 2 Clinical and test correlates of patients with global functional recovery (A ejection fraction ≥5%)

<table>
<thead>
<tr>
<th></th>
<th>Non viable</th>
<th>Viable</th>
<th>P (non viable vs viable)</th>
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<tr>
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<tr>
<td>Age (years)</td>
<td>64 ± 10</td>
<td>61 ± 12</td>
<td>ns</td>
</tr>
<tr>
<td>Gender</td>
<td>27M, 4F</td>
<td>23M, 5F</td>
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<tr>
<td>Hypertension</td>
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<td>Previous myocardial infarction</td>
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<td>Number of diseased vessels</td>
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<td>Improvement in ejection fraction post surgery</td>
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<td>9 ± 3</td>
<td>&lt;0.0001</td>
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<tr>
<td>Heart rate (beats. min⁻¹)</td>
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<td>SBP (mmHg)</td>
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<td>129 ± 22</td>
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<tr>
<td>DBP (mmHg)</td>
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<td>74 ± 14</td>
<td>ns</td>
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<tr>
<td>RPP</td>
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<td>ns</td>
</tr>
<tr>
<td>Number of maximal stress test</td>
<td>17</td>
<td>18</td>
<td>ns</td>
</tr>
<tr>
<td>Dobutamine echocardiography viable segments</td>
<td>2 (2–4)</td>
<td>4 (3–5)</td>
<td>=0.0001</td>
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<tr>
<td>Positron emission tomography viable segments</td>
<td>3 (2–5)</td>
<td>5 (4–6)</td>
<td>=0.03</td>
</tr>
<tr>
<td>Segments improved post surgery</td>
<td>1 (1–2)</td>
<td>4 (2–5)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

RPP=rate-pressure product; SBP, DBP=systolic/diastolic blood pressure.

Mantel Haenszel $\chi^2 = 25.3$, $P < 0.001$

**Figure 1** Relationship between the proportion of patients showing global functional improvement (defined by a ≥5% improvement in left ventricular ejection fraction post-revascularization), and tertiles of segments showing improved function. More extensive areas of tissue improving after surgery were associated with a greater likelihood of global functional recovery.
subsequent functional improvement ($P=0.03$) (Table 2). Similarly, there was the same segmental relationship with the number of viable segments at dobutamine echocardiography ($P=0.0001$).

**Prediction from regional evaluation of viability studies**

Receiver–operator characteristic curves were constructed to determine the optimal criteria for predicting a functional improvement of 5% ejection fraction (Fig. 1). Using cut-off values of 4/7 segments by positron emission tomography imaging and 3/7 segments by dobutamine echocardiography, the sensitivities, specificities, and accuracies of the two imaging techniques were similar (Fig. 3). Using these criteria (three viable segments for dobutamine echocardiography and four segments for positron emission tomography) to define evidence of viable myocardium, 42 patients were deemed viable by dobutamine echocardiography and 37 by positron emission tomography. The concordance for prediction of global functional recovery was 44%. Both techniques labelled 26 patients as likely to recover global function and seven as unlikely to recover. The remaining 26 patients had discrepant test results, 15 having a positive dobutamine echocardiography and negative positron emission tomography and 11 having a negative dobutamine echocardiography and a positive positron emission tomography. There was no relationship between dobutamine echocardiography study quality and concordance, with an even distribution of excellent, good, adequate, and poor quality studies in both the concordant and discordant groups.

**Prediction from global left ventricular response to dobutamine**

*Figure 2* illustrates receiver–operator characteristic curves relating to the prediction of post-operative

![Graph](image)

*Figure 2* Receiver operator characteristic curves to determinate the best cut-off for dobutamine echocardiography and positron emission tomography for prediction of global functional improvement of 5% in left ventricular ejection fraction post surgery.

![Graph](image)

*Figure 3* This bar chart demonstrates the per patient sensitivity, specificity and accuracy of dobutamine echocardiography (□) and positron emission tomography (■), in the 59 patients among whom pre- and post-operative left ventricular ejection fraction was evaluated. Global functional improvement was defined as >5% improvement in ejection fraction.
improvement in left ventricular systolic function. The global change in ejection fraction with low-dose dobutamine was the best discriminator of functional improvement (areas under the curve = 0.77 for viability by dobutamine echocardiography, 0.65 for viability by positron emission tomography, and 0.93 for increase in ejection fraction with low dose dobutamine).

The likelihood of post-operative improvement in global left ventricular systolic function according to tertiles of pre-operative left ventricular volume, segment-specific viability by positron emission tomography and dobutamine, and increase in left ventricular ejection fraction with low-dose dobutamine infusion are shown in Fig. 4. As discussed above, there was no relationship between resting left ventricular volumes and outcome; approximately 40% of patients with end-diastolic volumes <140 ml improved ejection fraction by >5%, compared with 70% of patients with volumes of 140–180 ml and 35% of patients with volumes >180 ml.

Again, augmentation of left ventricular ejection fraction with low-dose dobutamine was the strongest discriminator. Similarly when change in left ventricular ejection fraction with low-dose dobutamine was examined as a continuous variable, a strong correlation was noted with post-operative left ventricular function improvement (Fig. 5).

**Multivariable analyses**

In a logistic regression model which included the number of segments viable according to positron emission tomography and dobutamine echocardiography, and the change in global ejection fraction with low dose dobutamine, only the last variable was predictive of a post-operative functional improvement (adjusted OR 1.81 CI 1.30–2.52, P=0.0005). After adjustment for diabetes and pre-operative ejection fraction, variables which were predictive of functional improvement included the number of segments viable by positron emission tomography, dobutamine echocardiography, and the change in ejection fraction with low dose dobutamine (Table 3).
Finally, a multivariable linear regression was obtained to relate change in ejection fraction after surgery to pre-operative variables. These included change in ejection fraction with low dose dobutamine, number of viable segments by positron emission tomography or dobutamine echocardiography, age, sex, hypertension, diabetes, smoking status, history of myocardial infarction, congestive heart failure, prior CABG, number of diseased coronary arteries and resting heart rate. Only the change in ejection fraction with low dose dobutamine was a significant predictor ($F=16$, $P=0.0004$).

**Discussion**

A large literature now supports the use of markers of perfusion, metabolism or contractile reserve for the detection of viable myocardium. In separate studies, these have been shown to have comparable ability to predict regional functional recovery\[13\], although head-to-head comparisons have indicated that the presence of contractile reserve is a more specific predictor than the other indices\[14–16\]. Generally, the previous studies have had two important limitations — they have largely examined viability alone (whereas clinicians are concerned with all jeopardized myocardium, including ischaemic tissue), and they dealt with recovery of individual segments rather than patients. However, given the risk of bypass surgery in this setting\[22\], the likelihood of left ventricular recovery after surgery may be a useful guide to the prognostic and functional benefit of surgery. We therefore sought to compare the ability of different physiological indices of both ischaemia and viability to predict improvement of global left ventricular function. Our findings show that the examination of...
perfusion and metabolic function (by positron emission tomography) and contractile reserve and ischaemia (by dobutamine echocardiography) have similar ability to predict global recovery of left ventricular function (defined as improvement in ejection fraction >5%) after bypass surgery in patients with severe chronic left ventricular dysfunction. Although the extent of viable tissue identified by positron emission tomography or dobutamine echocardiography is significantly related to functional improvement after surgery, the strongest predictor of improvement in ejection fraction is the ejection fraction response to low dose dobutamine.

**Use of conventional indices for predicting recovery of global left ventricular function**

Improvement of left ventricular function after revascularization is dependent on the pre-operative severity of left ventricular dilation and impairment, the extent of recoverable myocardium and scar, the presence of compensatory hyperkinesia pre-operatively, the presence (and treatment of) mitral regurgitation, co-morbidities (i.e. non-coronary causes of left ventricular impairment), and the occurrence of peri-operative cardiac events. We studied patients undergoing pure myocardial revascularization (excluding those undergoing mitral surgery), and also excluded patients with peri-operative cardiac events. While very dilated ventricles (end-diastolic volume >220 ml) did not recover in this study, resting left ventricular volumes and ejection fraction were not predictive of recovery. Likewise, clinical and stress variables were not predictive.

Positron emission tomography and dobutamine echocardiography are usually interpreted on a segmental basis, so selection of patients for surgery based on likely functional recovery requires designation of optimal criteria for predicting global left ventricular functional improvement (defined as a 5% enhancement of ejection fraction). Using receiver-operator characteristic curves with the seven-segment model, we identified this threshold as at least three viable segments by dobutamine echocardiography, and four viable segments by positron emission tomography (Fig. 2). This difference in the proportion of viable myocardium by dobutamine echocardiography and positron emission tomography has been reported previously[23]; these and other data suggest that a substantial extent of viable tissue is required in order to predict global left ventricular recovery. Similar data have been reported using thallium imaging[12].

Using these criteria, the sensitivity for predicting global left ventricular recovery was 94% for dobutamine echocardiography and 56% for positron emission tomography, with a specificity of 59% for dobutamine echocardiography and 64% for positron emission tomography. These findings are concordant with the wide reported range of sensitivity for prediction of regional functional recovery by positron emission tomography (59–100%)[7,24–26] and dobutamine echocardiography (74–91%)[12,24–26]. Both positron emission tomography and dobutamine echocardiography showed relatively low specificity (around 60%) using the above cut-off, a value that is lower than the specificity for regional functional recovery usually reported[27–29] for dobutamine echocardiography (78–92%) and positron emission tomography (50%–92%). There are several potential explanations for this. First, ischaemia was included in this study as an index of viability, and resting function of ischaemic segments may not be improved by revascularization. Second, a uniphase dobutamine response was considered to be consistent with myocardial viability — and this is known to be an ambiguous signal which can be caused by either non-transmural infarction or viable tissue. Finally, the global response of the left ventricle to revascularization is dependent not only on the response of the viable segments, but also the response of other segments. Thus, even when the cut-off leads to prediction of no recovery in hearts with two or three viable segments out of seven — this may be adequate to permit left ventricular recovery depending on the quality of the other segments. This response may also be influenced by the completeness of revascularization (especially in the presence of distal disease), adequacy of myocardial protection during the surgery, and the presence of co-existing primary myocardial dysfunction due to diabetes, hypertension or alcohol.

**Use of global response to dobutamine echocardiography to predict recovery of ejection fraction after revascularization**

The finding that a larger amount of viable myocardium is associated with a greater improvement in post-operative ejection fraction is concordant with the existing literature for positron emission tomography[30] and dobutamine echocardiography[31], both of which have also shown a better long-term prognosis with more viable tissue. However, the best criterion for prediction of recovery of global left ventricular function was not the extent of viable tissue, but rather the improvement of ejection fraction with low dose dobutamine, shown by receiver-operator characteristic analysis (Fig. 2) and linear regression (Fig. 5). Indeed, although the extent of viable myocardium by positron emission tomography or dobutamine echocardiography correlate with functional recovery by univariate analysis, only improvement in ejection fraction with low dose dobutamine remained a significant predictor of improvement of ejection fraction in a multivariate model.

Numerous factors influence the response of myocardial function to dobutamine stimulation or revascularization[30,31], and may explain the difference in predictive power between the number of dobutamine echocardiography responsive segments and the ejection fraction response. Improvement of global function with low dose dobutamine reflects not only the response of
dysfunctional segments but also the ability of normal or less dysfunctional myocardium to improve contractility under inotropic stimulation. Indeed, failure to reduce end-diastolic volume at peak dose has been used as a marker of multivessel disease \[32\]. This global evaluation of the ventricular contractile reserve is analogous with assessment of ejection fraction in response to postextrasystolic potentiation \[33\]. Regional functional responses depend on the extent of transmural necrosis; subendocardial necrosis precludes a regional response to dobutamine echocardiography or revascularization, but the presence of viable sub-epicardium may prevent dyskinesis when the other segments improve, thus preserving global function.

The ability to predict the likelihood of improvement of ejection fraction has important clinical implications for management of patients with severe left ventricular dysfunction. Despite recent progress in anaesthesiology and operative care, the operative mortality in this group \[32\] mandates that selection of patients most likely to benefit is critical. In patients without significant angina, surgery may be performed to improve functional capacity and improve prognosis — both of which are likely to be dependent on improvement of ejection fraction.

**Concordance between physiologic indices of viability and ischaemia**

Some discordances in the identification of viability with different imaging strategies reflect the evaluation of different pathophysiological aspects of the viable myocardium (perfusion and metabolism for positron emission tomography, and presence of contractile reserve and ischaemia for dobutamine echocardiography). For example, the pattern of regional dysfunction with preserved flow (stunning) would typically be associated with a functional augmentation response to dobutamine echocardiography (viability), but would be classified as normal by positron emission tomography. However, other differences are due to imaging differences between positron emission tomography and dobutamine echocardiography. We sought to minimize this by use of a seven (rather than 16) segment model, and correlating studies on a per patient basis rather than a segmental basis. Nonetheless, different artifacts are obtained from each test: technical difficulties in the visualization of some segments are more applicable to echocardiography, but dipyridamole unresponsiveness may be an important limitation of the positron emission tomography protocol \[34\]. Finally, primary myocardial disease independent of coronary disease may have contributed to left ventricular dysfunction in some patients with diabetes or hypertension.

**Limitations**

The hypothesis underlying the use of left ventricular function as an end-point of treatment for viability has been questioned. There are important shortcomings to using regional functional recovery as the ‘gold standard’ of viability because physiology of the myocardial contraction at rest and stress are quite different \[35\]. Even in the absence of systolic improvement, there may be some benefit in revascularization of the dysfunctional area, with respect to improvement of left ventricular diastolic compliance \[35\] and attenuation of left ventricular remodeling \[36,37\]. These subtle benefits of revascularization may not be identified by a relatively gross evaluation of regional or global function. Improved myocardial perfusion, albeit at a reduced level, may reduce the likelihood of electrical excitability and lessen the potential for serious life threatening arrhythmias \[38\]. Nonetheless, these benefits continue to be theoretical, and we believe that ejection fraction will continue to be the most important determinant of exercise capacity and prognosis.

The exclusion of patients with peri-operative infarction is critical to the design of this study, as loss of viable tissue with such an event may erroneously influence the accuracy of pre-operative testing for prediction of viable muscle. Unfortunately, peri-operative enzyme criteria may be ambiguous, and do not identify episodes related to graft closure within weeks of surgery. We therefore designed the study to use deterioration of regional left ventricular function (based on reduction of regional wall motion score by ≥ 1 grade) as a marker of peri-operative infarction. This may have had the consequence of missing some patients with small non-Q wave infarcts, which may have reduced the accuracy of all tests.

**Conclusion**

Positron emission tomography and dobutamine echocardiography have similar accuracy for the prediction of global left ventricular functional recovery in patients with viable myocardium and severe left ventricular dysfunction. Nevertheless the best predictor of postoperative functional improvement is the increase in ejection fraction in response to low-dose dobutamine infusion.

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**References**


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