Coronary revascularisation for postischaemic heart failure: how myocardial viability affects survival

D Pagano, M E Lewis, J N Townend, P Davies, P G Camici, R S Bonser

Abstract
Objective—To assess the impact of revascularisation of viable myocardium on survival in patients with postischaemic heart failure.

Methods—35 patients (mean (SD) age 58 (7) years) with severe heart failure (New York Heart Association (NYHA) functional class ≥ III), mean left ventricular ejection fraction (LVEF) 24 (7)% (range 10–35%), and limited exercise capacity (peak oxygen consumption (VO2) 15 (4) ml/kg/min) were studied. 21/35 patients had no angina. Myocardial viability was assessed with quantitative positron emission tomography and the glucose analogue 18F-fluorodeoxyglucose (FDG) (viable segment = FDG uptake ≥ 0.25 µmol/min/g) in all patients before coronary artery bypass grafting. Patients were divided into two groups: group 1, ≥ 8 viable dysfunctional segments (mean 12 (2), range 8–15); and group 2, < 8 viable dysfunctional segments (mean 3.5 (3), range 0–7). The two groups were comparable for age, sex, NYHA class, LVEF, and peak VO2.

Results—Two patients died perioperatively and seven patients died during follow up (mean 33 (14) months). All deaths were from cardiac causes. Kaplan-Meyer survival analysis showed 86% survival for group 1 patients versus 57% for group 2 (p = 0.03). Analysis by Cox proportional hazard model revealed three independent factors for cardiac event free survival: presence of ≥ 8 viable segments (p = 0.006); preoperative LVEF (p = 0.002); and patient age (p = 0.01).

Conclusion—Revascularisation for postischaemic heart failure can be associated with good survival, which is critically dependent upon the amount of viable myocardium.

(Heart 1999;82:684–688)

Methods

PATIENT POPULATION

The patients for this study were recruited from those referred to our hospital for investigation of heart failure, or consideration for CABG or heart transplantation. Inclusion criteria were: chronic (≥ 6 months) heart failure (NYHA class ≥ III); sinus rhythm; multivessel coronary artery disease; and impaired left ventricular systolic function with at least one dysfunctional left ventricular wall subtended by a stenotic coronary artery amenable to surgical revascularisation. Exclusion criteria were: myocardial infarction within six months; decompensation of heart failure within three months; the presence of more than moderate mitral valve regurgitation, as assessed by transthoracic echocardiography; and the presence of left ventricular aneurysm. Over an 18 month period 39 consecutive patients (35 male and four female, mean (SD) age 58 (7) years, range 41–72 years) met the entry criteria. Fourteen patients suffered with symptoms of heart failure and effort angina, and 25 patients had symptoms of heart failure but no angina. CABG was performed in all 14 patients with angina irrespective of the viability study.
findings and in 21/25 patients without angina. Four patients in the latter group, in whom no evidence of viability could be found by positron emission tomography (PET), did not undergo CABG and underwent cardiac transplantation or continued medical treatment. Thus, 35 patients undergoing CABG constituted the population of this study.

All 35 patients had suffered at least one myocardial infarction (range 1–3) and the mean time of the most recent was 30 (14) months (range 12–60 months) before the study period. Eleven patients were diabetic (four insulin dependent) and five patients had a history of hypertension. The preoperative ECG showed Q wave infarction in at least one myocardial territory in all the patients (two territories in nine patients). All patients were receiving maximal medical treatment for heart failure including angiotensin converting enzyme (ACE) inhibitors (35), diuretics (25), and digoxin (7) at the time of recruitment. The patients with angina were also receiving nitrates (14) and calcium channel blockers (3).

The study was approved by the local ethics committee and written informed consent obtained by all patients before the study. The radiation exposure was licensed by the UK administration of radioactive substances advisory committee.

STUDY PROTOCOL

Selective coronary arteriography was performed in all patients. Patients underwent cardiopulmonary exercise testing, transthoracic echocardiography, PET imaging with 18F-fluorodeoxyglucose (FDG), and radionuclide ventriculography (MUGA) within four weeks before CABG.

Cardiopulmonary exercise testing

Symptom limited cardiopulmonary exercise testing was performed using a treadmill according to a modified Naughton protocol. Breath by breath ventilatory and gas exchange data were measured using a Morgan Benchmark system (PK Morgan Ltd, Gillingham, Kent, UK). Peak oxygen consumption (VO₂) was calculated as the mean of the values recorded during 30 seconds before peak exercise.5 Attainment of the anaerobic threshold was assessed as the point at which carbon dioxide (VCO₂) increases disproportionately to VO₂ (v-slope method).7 Exercise tests were supervised by a physician unaware of the patients’ clinical details to avoid bias.

Echocardiography

Segmental left ventricular wall motion was assessed by transthoracic echocardiography (HP Sonos 2500, Hewlett Packard) according to the recommendations of the American Society of Echocardiography.6 The wall motion was graded as 1 (normal), 2 (hypokinetic), 3 (akinetim), and 4 (dyskinetic). The wall motion score index (WMSI) was calculated as the sum of the scores of the left ventricular segments divided by the number of segments evaluated.8 The echo images were analysed by two independent observers blinded to the clinical details and viability details of the patients. In a random subset of 10 patients (160 segments), the interobserver and the intraobserver agreement was assessed using the κ agreement coefficient: interobserver κ = 0.82 (95% confidence interval (CI) 0.69 to 0.95); intraobserver κ = 0.90 (95% CI 0.80 to 1.00).

PET

The study for the measurement of myocardial glucose utilisation was carried out during hyperinsulinaemic euglycaemic clamp with the glucose analogue FDG as described previously.4 Images were resliced in the short axis view and the left ventricle was divided to provide 16 regions of interest comparable to the ones used for echo analysis.4 A dysfunctional segment was considered viable if FDG uptake was ≥ 0.25 µmol/min/g.10

MUGA

All patients underwent radionuclide ventriculography for the assessment of LVEF.9 Analysis was performed by two independent physicians blinded to clinical details including the pre- or postoperative status. The interobserver and intraobserver agreement was assessed in a random subset of 10 patients using a standard method.11 The mean of the differences in LVEF was 0.05 (1.5)% and the 95% limits of agreement were −2.9% to 3%.

Clinical end point

The end point of the study was major cardiac events defined as cardiac death or transplantation. Cardiac mortality was defined as death
8 viable segments indicates the number of viable left ventricular segments revascularised.

**Table 2** Prognostic indicators in survivors and non-survivors before CABG

<table>
<thead>
<tr>
<th>Variable</th>
<th>Survivors</th>
<th>Non-survivors</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>57 (7)</td>
<td>59 (8)</td>
<td>0.5</td>
</tr>
<tr>
<td>NYHA class IV</td>
<td>3/26</td>
<td>4/9</td>
<td>0.05</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>25 (7)</td>
<td>25 (8)</td>
<td>0.02</td>
</tr>
<tr>
<td>Peak VO2 (ml/kg/min)</td>
<td>15 (5)</td>
<td>14 (2)</td>
<td>0.1</td>
</tr>
<tr>
<td>Number of viable segments</td>
<td>10 (5)</td>
<td>6 (5)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

**Table 3** Comparison of prognostic indicators between the two groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group 1</th>
<th>Group 2</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>58 (7)</td>
<td>57 (8)</td>
<td>0.8</td>
</tr>
<tr>
<td>NYHA class IV</td>
<td>6/21</td>
<td>1/14</td>
<td>0.5</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>23 (6)</td>
<td>23 (8)</td>
<td>0.6</td>
</tr>
<tr>
<td>Peak VO2 (ml/kg/min)</td>
<td>14 (5)</td>
<td>15 (3)</td>
<td>0.9</td>
</tr>
</tbody>
</table>

Group 1, ≥ 8 viable segments; Group 2, < 8 viable segments.

**Table 4** Hazard ratios for independent predictors of survival

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hazard ratio</th>
<th>95% CI</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 8 viable segments</td>
<td>17.2</td>
<td>2.2 to 134</td>
<td>0.006</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>0.78</td>
<td>0.7 to 0.9</td>
<td>0.002</td>
</tr>
<tr>
<td>Age (years)</td>
<td>0.83</td>
<td>0.7 to 0.9</td>
<td>0.02</td>
</tr>
</tbody>
</table>

≥ 8 viable segments indicates the number of viable left ventricular segments revascularised.
Discussion

In patients with heart failure caused by coronary artery disease undergoing surgical revascularisation, the amount of viable myocardium is a determinant of survival. The prognostic importance of this factor is equivalent to the LVEF. This corroborates our previous observation that the amount of viable myocardium is related to the improvement in left ventricular function after revascularisation. Viability assessment may allow the identification of a group of patients with postischaemic heart failure who may benefit both symptomatically and prognostically from surgical revascularisation.

The prognostic value of myocardial viability has also been shown in retrospective studies of patients with less severe left ventricular dysfunction and less severe heart failure. In addition to the amount of viable myocardium, our study confirmed the prognostic value of LVEF and to a lesser extent the age of the patients. Peak aerobic capacity, a known powerful prognostic indicator in patients with heart failure, did not add significant information. The latter finding needs further explanation. A relatively high proportion (38%) of patients did not attain anaerobic threshold during the exercise test and therefore maximal aerobic capacity may have been underestimated. This was usually the case in patients with angina, in whom development of chest pain preceded the threshold of maximal exercise, thus limiting the prognostic value of peak VO₂. In addition, peak VO₂ values were similar in the survivors and in the mortality patients indicating that patient groups were homogenous for this variable.

There are a number of potential mechanisms to explain the improved survival detected in patients with large amounts of viable myocardium. Firstly, as we have previously shown, the presence of significant amounts of viable myocardium before CABG is the best discriminator to predict convincing improvements in LVEF, which is a strong prognostic indicator in patients with coronary artery disease and heart failure. In addition, revascularisation of viable myocardium leads to improvements in myocardial contractile reserve, may reduce the risk of fatal arrhythmias, and may have a beneficial effect on left ventricular remodelling.

Although we did not aim to compare CABG to medical treatment, it is noticeable that the survival detected in patients with at least six viable dysfunctional segments revascularised was significantly better than that usually reported for patients with class III or IV heart failure treated medically. This finding acquires more significance in view of the fact that most of the patients in our study had no symptoms of angina or evidence of exercise inducible ischaemia, thus constituting a group of patients who, in the past, were not recommended for CABG.

STUDY LIMITATIONS

We have not compared the effects of CABG with those of continued medical treatment, and although the survival detected in our patients is encouraging, we believe that a prospective randomised study to address this issue is both necessary and justified.

In our study viability was assessed using the most sophisticated technique, PET, which is not widely available, at least in the UK. Although the value of thallium 201 scintigraphy and dobutamine echocardiography in the identification of patients with long term benefit has been described, the potential limitations of dobutamine echocardiography in assessing viability in patients with severe postischaemic heart failure have been underlined previously.

We did not measure LVEF after six months and this could have provided further insight into the potential mechanisms of prolonged survival in patients with more viability.

16 Kaul S. There may be more viability that meets the eye! Circulation 1995;92:2790–3.
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