Failure to Improve Left Ventricular Function After Coronary Revascularization for Ischemic Cardiomyopathy Is Not Associated With Worse Outcome

Habib Samady, MD; John A. Elefteriades, MD; Brian G. Abbott, MD; Jennifer A. Mattera, MPH; Craig A. McPherson, MD; Frans J. Th. Wackers, MD

Background—Preoperative identification of viable myocardium in patients with ischemic cardiomyopathy is considered important because CABG can result in recovery of left ventricular (LV) function. However, the hypothesis that lack of improvement of LV function after CABG is associated with poorer patient outcome is untested.

Methods and Results—Outcome was compared in patients with ischemic LV dysfunction (LVEF ≤0.30) with and without improvement in LVEF after CABG. Of 135 consecutive patients, 128 (95%) survived CABG and 104 (77%) had pre- and post-CABG LVEF assessment. Of these 104 patients, 68 (65%) had \(0.05\) increase in LVEF (group A) and 36 (35%) had no significant change, or \(≤0.05\) decrease in LVEF (group B) compared with pre-CABG LVEF. No significant differences existed in age, gender, comorbidities, baseline symptoms, baseline LVEF, or intraoperative variables between groups A and B. Group A increased LVEF from 0.24±0.05 to 0.39±0.1 \((P<0.005)\). In Group B, LVEF did not change significantly postoperatively, 0.24±0.05 to 0.23±0.06 \((P=NS)\). Postoperative improvement in angina and heart failure scores were similar between the 2 groups. Survival free of cardiac death was similar for both groups (93% in group A and 94% in group B, \(P=NS\)) at a mean follow-up of 32±23 months.

Conclusions—Lack of improvement of global LVEF after CABG is not associated with poorer outcome compared with that of patients with improved LVEF, presumably because effective revascularization of ischemic myocardium, even without improvement in ventricular function, protects against future infarction and death. *(Circulation. 1999;100:1298-1304.)*

Key Words: ischemia ■ cardiomyopathy ■ revascularization ■ survival
analysis. These 135 patients represent 13.2% of the 1023 patients who had CABG by the same surgeon during the same time period. The patients included 113 males and 22 females, with a mean age of 66.5 years (range 42 to 87 years). Eighty-four percent had prior myocardial infarction, documented either by clinical history or Q waves on the resting ECG; 63% had angina, 61% had heart failure, and 26% had severe ventricular arrhythmias, for which they had simultaneous placement of an implantable cardiac defibrillator (ICD). A general report on the effect of CABG on postoperative survival and LVEF in these patients has been published previously.13

Seven (5%) of the 135 patients died during the perioperative period. Twenty-four (19%) of the 128 CABG survivors did not undergo postoperative assessment of LVEF. The study population, therefore, consisted of 104 patients (81%) who survived the perioperative period and had both pre- and postoperative assessment of LVEF (Figure 1). The patients were divided into 4 groups: Group A: 68 patients (65%) who had >0.05 LVEF units increase of postoperative LVEF, and Group B: 36 patients (35%) who had either a ≤0.05 LVEF units increase or a decrease in postoperative LVEF compared with preoperative LVEF. Twenty-four patients who survived CABG but did not undergo postoperative assessment of LVEF comprised Group C, and the 7 patients who died in the perioperative period are referred to as Group D.

Operative Technique

All patients underwent CABG by a single surgeon (J.A.E.) using standard operative techniques. Myocardial preservation was performed by means of systemic and topical hypothermia and cold crystalloid cardioplegia administered into the ascending aorta before each graft. An average of 2.7 grafts (range 1 to 5) were placed per patient. The internal mammary artery was used in 76% of patients. Intra-aortic balloon pumps were placed in 69 patients before surgery, prophylactically in 55 patients (80%) and emergently in 14 patients (20%). ICDs were placed in 20 patients.

LVEF Assessment

Preoperative LVEF was assessed by contrast ventriculography (CV) in 65 patients and by equilibrium radionuclide angiocardiology (ERNA) in 39 patients. Postoperative LVEF was assessed by ERNA in 102 patients and by CV in only 2 patients.

ERNA was performed by modified in vivo labeling of patients’ own red blood cells with technetium-99 m pertechnetate. Images were acquired in 3 planar views (left anterior oblique, anterior, and lateral views) using a gamma camera equipped with a general, all purpose, parallel hole collimator interfaced with a dedicated computer. LVEF was determined using a previously validated automated computer software package.17

Contrast ventriculography was performed in the RAO projection. LVEF was determined by Simpson’s method, after manual or automated drawing of contours around the left ventricle in diastole and systole. A regression equation (radionuclide LVEF = 0.86 × CV LVEF + 2.90), developed for the TIMI trial,18 was used to relate CV LVEFs to ERNA-derived LVEF. This formula changes the absolute value of the LVEF between the 2 methods by <0.02 points.

Classification of Symptoms

Chart review and telephone conversations with patients were used to assess angina and heart failure classification. The Canadian Cardiovascular Society Functional Classification was used to stratify the degree of angina. Heart failure status was assessed using the New York Heart Association Functional Classification. The investigators acquiring the data were blinded to the values of LVEF after revascularization.

Follow-Up

Follow-up was obtained from office charts, hospital records, and by interviews with primary physicians and/or the patients and was complete in all 104 patients. Mean follow-up was 32±23 months (median, 32 months). Cardiac death was defined as unwitnessed sudden death, death within 1 hour of new symptoms of cardiac ischemia, or death due to heart failure. Noncardiac death was defined as death due to all other causes (stroke, renal failure, diabetes, or cancer). Results of electrophysiology interrogation were available in 15 of 20 patients with ICD placement during the follow-up period.

Statistical Analysis

Continuous data are expressed as mean±1 SD and as median when appropriate. Categorical data are expressed as frequencies. Discrete variables were compared in each ejection fraction group by χ² analysis and continuous variables were compared using Student’s t test. The paired Student’s t test was used to compare continuous variables before and after surgery. P<0.05 was considered statistically significant. Event-free survival was evaluated by Kaplan Meier product-limit method. Differences between survival curves were compared using the generalized Wilcoxon test.

Results

Baseline Characteristics

No significant differences were present in preoperative characteristics and comorbidity between patients in groups A and B (Table 1). Mean age in group A was 66±2.9 years and in group B, 66±10 years (P=NS). Males comprised 83% of patients in group A and 84% of patients in group B (P=NS). The 2 groups were similar with respect to preoperative angina score, heart failure score, and mean preoperative LVEF. The prevalence of prior myocardial infarction was similar in both groups.

Characteristics of patients in groups C and D are included for comparison. Six of 7 patients who died postoperatively (group D) were in cardiogenic shock and required emergent intra-aortic balloon pump placement and revascularization. Because of their extreme high-risk presentation and almost inevitable death without immediate revascularization, we feel justified in excluding them from our analysis. Obviously, postoperative LVEF could not be obtained in this subgroup.

Intraoperative Variables

Intraoperative variables are shown in Table 2. Group A had a trend toward greater use of left internal mammary grafts (83% versus 69%, P=0.09) and longer cross clamp times (50±15 versus 44±13, P=0.10), but neither variable achieved statistical significance. More ICDs were placed in group B than in Group A (25% versus 16%, P=0.41), however, this did not achieve statistical significance. The use of intra-aortic balloon pumps, pump times, and numbers of grafts placed were similar in both groups. No intra-aortic balloon pumps were placed after surgery.
Postoperative LVEF
In 104 patients, the mean time interval between CABG and postoperative assessment of LVEF was 16.6 ± 33 days (median 7 days, range 3 to 214 days). The postoperative time interval for LVEF assessment was not significantly different between group A, 18.6 ± 37 days, and B, 12.6 ± 24 days (P = 0.38). Sixty-two (91%) patients in group A and 35 (97%) in group B had postoperative LVEF assessed within 6 weeks of CABG (P = 0.45).

By study design, mean LVEF improved in group A from 0.24 ± 0.05 before surgery to 0.39 ± 0.10 after CABG and did not change in group B (0.24 ± 0.05 preoperatively to 0.23 ± 0.06 postoperatively, Figure 2).

Postoperative Symptoms
Heart failure and angina class improved in both groups. Angina class improved from 2.6 ± 1.2 to 1.2 ± 0.3 in group A and from 2.6 ± 1.2 to 1.2 ± 0.5 in group B, (Figure 3). Heart failure class improved from 2.3 ± 1.0 to 1.5 ± 0.7 in group A and from 2.4 ± 1.0 to 1.5 ± 0.7 in group B (Figure 4). Of 15 patients who underwent postoperative interrogation of the ICD devices, 4 of 8 patients in group A and 5 of 7 patients in group B had recorded discharges (P = NS).

Postoperative Survival
Figure 5 shows the actuarial survival curves for patients free of cardiac death in groups A and B. Mean duration of follow-up was similar in both groups, 30 ± 21 months in group A and 36 ± 27 months in group B, P = NS. There was no significant difference in survival free of cardiac death between the 2 groups: 93% in Group A and 94% in Group B, P = NS. Figure 6 compares the actuarial survival curves for patients free of cardiac death in Groups A, B (the study population), and C (patients who survived surgery but did not have postoperative assessment of LVEF). There were no significant differences in survival between the 3 groups.

### TABLE 1. Clinical Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group A (ΔLVEF&gt;0.05)</th>
<th>Group B (ΔLVEF≤0.05)</th>
<th>Group C (No Postoperative LVEF)</th>
<th>Group D (Perioperative Death)</th>
<th>P, A vs B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>66 ± 9</td>
<td>66 ± 10</td>
<td>67 ± 8</td>
<td>67 ± 6</td>
<td>0.89</td>
</tr>
<tr>
<td>Men</td>
<td>56 (83)</td>
<td>30 (84)</td>
<td>19 (79)</td>
<td>7 (100)</td>
<td>0.75</td>
</tr>
<tr>
<td>Pre-op LVEF</td>
<td>0.24 ± 0.05</td>
<td>0.24 ± 0.05</td>
<td>0.23 ± 0.05</td>
<td>0.21 ± 0.05</td>
<td>1.00</td>
</tr>
<tr>
<td>Pre-op angina score (CCS)</td>
<td>2.6 ± 1.2</td>
<td>2.6 ± 1.2</td>
<td>2.4 ± 1.2</td>
<td>2.9 ± 1.3</td>
<td>0.94</td>
</tr>
<tr>
<td>Pre-op CHF score (NYHA)</td>
<td>2.3 ± 1.0</td>
<td>2.4 ± 1.0</td>
<td>2.4 ± 1.4</td>
<td>3.6 ± 1.1</td>
<td>0.76</td>
</tr>
<tr>
<td>Prior MI</td>
<td>31 (86)</td>
<td>13 (54)</td>
<td>19 (79)</td>
<td>6 (86)</td>
<td>0.76</td>
</tr>
<tr>
<td>Q waves</td>
<td>48 (71)</td>
<td>13 (54)</td>
<td>19 (79)</td>
<td>6 (86)</td>
<td>0.13</td>
</tr>
<tr>
<td>LBBB</td>
<td>4 (6)</td>
<td>5 (21)</td>
<td>5 (21)</td>
<td>3 (43)</td>
<td>0.35</td>
</tr>
<tr>
<td>Diabetes</td>
<td>20 (29)</td>
<td>10 (42)</td>
<td>10 (42)</td>
<td>2 (29)</td>
<td>0.15</td>
</tr>
<tr>
<td>Hypertension</td>
<td>39 (57)</td>
<td>15 (63)</td>
<td>4 (57)</td>
<td>4 (57)</td>
<td>0.57</td>
</tr>
<tr>
<td>Renal disease</td>
<td>5 (7)</td>
<td>4 (13)</td>
<td>4 (13)</td>
<td>1 (14)</td>
<td>0.49</td>
</tr>
<tr>
<td>Stroke/TIA</td>
<td>6 (9)</td>
<td>4 (13)</td>
<td>4 (13)</td>
<td>0 (0)</td>
<td>0.42</td>
</tr>
<tr>
<td>Tobacco use</td>
<td>27 (40)</td>
<td>10 (42)</td>
<td>10 (42)</td>
<td>4 (57)</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Pre-op LVEF indicates preoperative left ventricular function; CCS, Canadian Cardiovascular Society; CHF, chronic heart failure; NYHA, New York Heart Association; MI, myocardial infarction; LBBB, left bundle branch block; TIA, transient ischemic attack; and Δ, change.

Values in parentheses are percentages.

### TABLE 2. Intraoperative Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group A (ΔLVEF&gt;0.05)</th>
<th>Group B (ΔLVEF≤0.05)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>IABP</td>
<td>43 (65)</td>
<td>27 (75)</td>
<td>0.30</td>
</tr>
<tr>
<td>Pump time, min</td>
<td>96 ± 25</td>
<td>91 ± 20</td>
<td>0.43</td>
</tr>
<tr>
<td>Cross clamp time, min</td>
<td>50 ± 15</td>
<td>44 ± 13</td>
<td>0.10</td>
</tr>
<tr>
<td>ICD</td>
<td>11 (16)</td>
<td>9 (25)</td>
<td>0.41</td>
</tr>
<tr>
<td>LIMA graft</td>
<td>55 (83)</td>
<td>24 (69)</td>
<td>0.09</td>
</tr>
<tr>
<td>Number of grafts</td>
<td>2.8 ± 0.9</td>
<td>2.6 ± 0.8</td>
<td>0.23</td>
</tr>
</tbody>
</table>

IABP indicates intra-aortic balloon pump; ICD, implantable cardiac defibrillator; LIMA, left internal mammary artery; and Δ, change.

Values in parentheses are percentages.
Survival free of cardiac death in a subgroup of 39 patients who underwent both pre- and postoperative ERNA for assessment of LVEF revealed no differences between those who improved LVEF and those who failed to do so after surgery.

Discussion

Patients in whom LV dysfunction is predominantly due to hibernating or stunned myocardium have been shown to improve function and survival following surgical revascularization. However, many patients with ischemic cardiomyopathy have a mixture of scar and viable myocardium and may therefore exhibit a variable degree of improvement in ventricular function after revascularization. Whether such patients, who do not completely recover ventricular function early after revascularization, enjoy benefit from CABG surgery similar to those who improve ventricular function had thus far not been established.

Our study shows that patients with ischemic cardiomyopathy who fail to improve LVEF early after surgical revascularization nevertheless have similar symptomatic benefit and survival compared with patients who recover ventricular function early after surgery.

Relationship Between Myocardial Viability and Improvement of Ventricular Function

Current modalities used to assess myocardial viability are based on the premise that dysfunctional viable myocardium will recover function after revascularization. A threshold of radiotracer uptake (eg, >50% of normal uptake) is often adopted to simplify myocardial viability into a binary concept: either viable or nonviable. This threshold, which corresponds to the likelihood that regional LV function will ...

Figure 3. Pre- and postoperative angina score (Canadian Cardiovascular Society Functional Classification). Top, Mean preoperative angina score improved significantly and similarly in both groups. Bottom, individual change in angina class for each patient in both groups.

Figure 4. Pre- and postoperative New York Heart Association heart failure classification. Top, Mean preoperative heart failure score improved significantly and similarly in both groups. Bottom, individual change in heart failure class for each patient in both groups.

Figure 5. Actuarial survival free of cardiac death in group with increased LVEF (group A) and group that did not change LVEF (group B). There were no statistically significant differences in survival free of cardiac death between the 2 groups. Inc indicates increase.
recover after revascularization, has become synonymous with myocardial viability. Myocardium which does not meet this threshold value will usually not recover function after revascularization and is therefore assumed to be nonviable scar which will not benefit from revascularization.

Our study demonstrates that patients who do not recover LV function early after revascularization and who therefore might have been considered to have nonviable myocardium by the conventional definition, derive symptomatic and survival benefit similar to patients who do recover LV function after CABG.

This finding supports the concept that myocardial viability should be considered a continuum, from full-thickness viability without any scar to full-thickness scarring without viable cells. Indeed, we believe that group B represents a subgroup of patients who possess an intermediate degree of viability as exemplified by an improvement in outcome independent of recovery in ventricular function.

Several other studies lend further support to the concept of myocardial viability being a continuum. Zimmerman et al\(^{23}\) demonstrated a linear relationship between Thallium-201 redistribution defect size and the histopathologic extent of myocardial fibrosis. Several investigators\(^{6,24}\) have demonstrated a relationship between continuous measures of myocardial radiopharmaceutical uptake and the probability of functional recovery among dysfunctional myocardial segments. Baumgartner et al\(^{25}\) using quantitative histological characterization of myocardium from explanted hearts, demonstrated an excellent correlation between the amount of PET metabolic evidence for viability, the degree of resting TI-201 uptake, and the presence of $\geq25\%$ viable myocytes on histopathology.

Furthermore, recent studies suggest that the degree and timing of recovery of LV function after revascularization may be a continuum, depending on the underlying pathophysiologic substrate, i.e., preoperative ratio of viable-to-scarded myocardium. Elsasser et al\(^{26}\) showed a direct correlation between the degree of recovery of LV function after revascularization and the severity of histopathologic changes in hibernating myocardium in biopsies obtained during CABG surgery. Shivalkar et al\(^{27}\) demonstrated that both the degree and timing of recovery in regional LV function were related to the extent of transmural myocardial fibrosis. Patients with only small amounts of viable myocardium had markedly delayed (6-month) improvement in regional LV function after CABG, compared with patients with more extensive amounts of viable myocardium.

**Implications for Noninvasive Assessment of Myocardial Viability**

Postoperative recovery of ventricular function has been used as the bench mark against which modalities for assessment of myocardial viability are evaluated. Comparative studies have suggested that resting Thallium-201 SPECT imaging provided similar sensitivity but less specificity than Dobutamine echocardiography and PET imaging in predicting myocardial viability.\(^{28,29}\) Our study is the first to provide support for the concept that there may be a degree of myocardial viability that, although not capable of generating an early improvement in resting contractile function, is sufficient to elicit favorable outcomes in symptoms and survival. This implies that postoperative recovery of ventricular function may not be the most appropriate variable against which to validate the preoperative assessment of myocardial viability. Although recovery of wall motion obviously indicates the presence of viable myocardium, lack of improvement in function does not exclude the presence a lesser amounts of viable myocardium.

Further support for the concept that revascularization provides clinical benefits beyond improvement of LV function is found in observations by other investigators. Patients with only modest amounts of preoperative myocardial viability on PET imaging, nevertheless improved functional status significantly after revascularization.\(^{30}\) Furthermore, Ragosta et al\(^{31}\) observed that whereas only 19% of myocardial segments with severely reduced preoperative Thallium-201 uptake recovered systolic function after surgical revascularization, 58% showed improvement in Thallium-201 uptake after surgery.

Several recent studies\(^{31–33}\) have investigated the role of preoperative viability assessment in determining clinical outcome after revascularization. Pagley et al\(^{31}\) in a retrospective study, showed that patients with a larger myocardial viability index, determined by Thallium-201 imaging, had improved short- and long-term outcomes compared with patients with lower viability index. However, even the group with a lower viability index had a 2-year survival rate of 75% after CABG. This survival rate is substantially better than the reported 30% to 50% survival for similar patients treated medically,\(^{1,3}\) suggesting substantial benefit from revascularization. Meluzin et al\(^{32}\) arrived at similar conclusions on the basis of the results of preoperative dobutamine 2D echocardiography. Haas et al\(^{33}\) reported in a retrospective study that patients with LV dysfunction who had preoperative PET viability assessment had better perioperative and 1-year survival than patients who had no viability assessment. Although mean LVEF improved modestly in both groups and was only significant in the patients with preoperative PET viability assessment, in both groups there were individual patients who failed to have improvement of LVEF. Furthermore, it is conceivable that results of preoperative PET imaging introduced an unintentional bias in the referral of patients for surgery.
Our findings and those of other investigators suggest that the focus on predicting recovery of ventricular function after surgical revascularization is at least partially misdirected and may underestimate the full beneficial effects of myocardial revascularization in the wide spectrum of patients with ischemic cardiomyopathy.

Potential Mechanisms of Benefit of Revascularization Without Recovery of Ventricular Function

Several pathophysiological mechanisms may be responsible for the clinical benefits of CABG observed despite recovery in LV function. First, restoration of blood flow to ischemic myocardium adjacent to endocardial scar relieves resting ischemia, enhances the reparative process of the myocyte contractile machinery, and may protect against future infarction. Second, the revascularized myocardial bed may limit infarct expansion and ventricular dilation by providing a scaffolding which supports the surrounding necrotic myocardium and reduces myocardial compliance. These mechanisms may also improve diastolic function and even reduce dynamic mitral regurgitation, culminating in further symptomatic improvement. Finally, by reducing LV remodeling and the ischemic burden, revascularization of ischemic myocardium bordering endocardial scar may reduce the incidence of ventricular arrhythmias.

Study Limitations

The most important limitation of this study is its retrospective design. Retrospectively, it is not possible to retrieve the number of patients with severe ischemic cardiomyopathy who were not considered to be appropriate candidates for surgery. The importance of this bias in the selection of patients remains unclear.

Another limitation is the use of 2 different modalities for the preoperative assessment of LVEF. However, using a previously established regression equation to convert CV LVEF to ERNA LVEF resulted in a maximal difference of only 0.02 between the modalities. Furthermore, a subgroup analysis in 39 patients who underwent both pre- and postoperative ERNA assessment of LVEF confirmed no difference in survival free of cardiac death between patients who did and did not improve LVEF after CABG.

Regional LVEF was not measured. It is conceivable that some patients had improvement in regional function, without an increase in global LVEF. In >90% of our patients, the postoperative LVEF was assessed within 6 weeks of surgery. It is possible that if the interval had been longer, some patients might have been categorized differently.

All surgery was performed by a single surgeon. This may potentially limit the general applicability of our findings. On the other hand, this could be considered a favorable aspect of the study because it eliminates additional variables which relate to differences in surgeons’ expertise.

Despite similarity in demographics, comorbidity, preoperative symptoms, and intraoperative variables of groups A and B, minor differences did exist. These included greater use of left internal mammary conduits and greater numbers of diabetics in patients in group A. As stated, these differences did not achieve statistical significance.

A most important limitation of this study is that preoperative myocardial viability studies were not routinely performed. Retrospectively, we identified only 23 (22%) of 104 patients who had resting myocardial perfusion imaging to assess myocardial viability. This small cohort did not warrant meaningful subgroup analysis.

Although not statistically different, more patients in group B received ICD devices than in the group A. When adjusted for ICD implantation, no significant differences existed in survival free of cardiac death between the 2 groups. Furthermore, electrophysiology follow-up did not reveal any difference in ICD discharges between the 2 groups (4 of 8 patients in group A and 5 of 7 patients in group B, P=NS).

Although the median duration of follow-up was substantial (32 months), it is conceivable that with a longer follow-up, differences in survival would become apparent between groups A and B. However, for a cohort of patients as critically ill as those included in our analysis, a survival benefit over a 32-month period is of substantial clinical importance.

Clinical Implications

The selection of patients with severe ischemic cardiomyopathy for surgical revascularization is complex and involves the consideration of many clinical variables. In addition to assessment of myocardial viability, appropriate target vessels and comorbidity are of importance. The implication of the present study is not that assessment of myocardial viability is superfluous. Noninvasive preoperative assessment of myocardial viability allows for risk stratification and identification of optimal candidates for revascularization, in whom the greatest benefit can be expected. However, we believe that a subgroup of patients with intermediate amounts of myocardial viability may be denied the benefits of myocardial revascularization and improved survival, if conventional threshold criteria for preoperative viability assessment are too rigidly applied.

Conclusion

Our study demonstrates that in patients with severe coronary artery disease and depressed LV function who survive CABG surgery, lack of improvement of global ventricular function is associated with a similar survival and similar improvement of angina and heart failure as for patients who improve global ventricular function. These findings suggest that in patients with LV dysfunction, methods for assessment of myocardial viability that focus on predicting improvement of ventricular function after revascularization may underestimate the potential for symptomatic and survival benefit achieved by CABG surgery. Randomized, prospective studies comparing optimal medical therapy with surgical revascularization are warranted in patients with LV dysfunction and intermediate amounts of myocardial viability.

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