Results of coronary artery surgery in patients with poor left ventricular function (CASS)

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ABSTRACT We identified 420 medically treated and 231 surgically treated patients (coronary graft plus myocardial surgery in 30%) who had severe left ventricular dysfunction manifest by an ejection fraction below 0.36 and markedly abnormal wall motion. Compared with medically treated patients, those treated surgically had more severe angina (56.7% vs 29.0% class III or IV; p < .001), less heart failure as predominant symptom (11.1% vs 18.8%; p < .003), more severe coronary disease (66.7% vs 50.2% three-vessel disease; p < .001), a greater concentration of left main coronary artery lesions > 70% (12.6% vs 3.8%; p < .001), and a greater estimated extent of jeopardized myocardium (p < .001). Multivariate regression analysis of survival, which adjusts for the above covariates, showed that surgical treatment prolonged survival (p < .05), although it ranked below severity of heart failure symptoms, age, ejection fraction, and left main stenosis > 70% in determining prognosis. Surgical benefit was most apparent for patients with ejection fractions below 0.26 who had a 43% 5 year survival with medical treatment vs 63% with surgery. Surgically treated patients experienced substantial symptomatic benefit compared with medically treated patients if their presenting symptoms were predominantly angina; however, there was no relief of symptoms caused primarily by heart failure. We conclude that patients with predominantly ischemic pain symptoms, despite poor left ventricular function, benefit from surgery; however, operative mortality in this high-risk subset must equal or better the 6.9% obtained in this study. 

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MANY STUDIES have examined the role of coronary surgery in patients with disabling symptoms, advanced coronary vascular lesions, and relatively well-retained myocardial function. However, for patients who have significant left ventricular dysfunction, concerns about increased operative mortality, diminished long-term survival, and irreversibility of myocardial scar have made it difficult to assess the role of coronary surgery in these patients. The NHLBI-sponsored Coronary Artery Surgery Study (CASS) Registry, which enrolled patients from 1974 to 1979, includes many patients with left ventricular dysfunction whose management varied according to local physicians' preferences based on their assessment of patient symptoms and angiographic findings. We retrospectively reviewed those patients who fell below a specific threshold of left ventricular dysfunction and sought to evaluate those variables that determine survival, coronary events, and symptomatic status.

Methods

CASS is a multi-institutional research program consisting of a randomized trial of the medical vs surgical treatment of coronary artery disease and a substantially larger registry of patients undergoing diagnostic evaluation, including coronary arteriography for the presence of proven or suspected coronary artery disease. Extensive history, physical examination, and laboratory data were collected for each patient at the time of entry into CASS. The details of quality control and the data entry have been reported.1

Patient selection. From August 1975 through May 1979, a total of 18,894 men and 6065 women underwent coronary arteriography for proven or suspected coronary disease at one of the 15 CASS clinics. From this pool of patients, those meeting specific selection criteria were randomized into medical and surgical treatment groups. Because randomization excluded patients with poor left ventricular function (usually ejection fractions below 36%), this study focuses on nonrandomized registry patients who had left ventricular dysfunction defined as a combination of an ejection fraction less than or equal to 35% and a left ventricular wall motion score greater than or equal to 12 (definition given in next section). We imposed this simultaneous requirement for an abnormal ejection fraction and abnormal wall motion score to ensure concurrence of an objective measurement usually made by a technician (ejection fraction) and a qualitative assessment of wall motion made by the angiographer. We also required that patients have no history of prior coronary surgery or mitral regurgitation of moderate or severe degree; our patients were not included within the subset of
randomized CASS patients. Patients were required to have a coronary lesion of 70% or greater in at least one major artery and to have completed a minimum of 1 year follow-up.

**Variables included in the study.** Table 1 is a complete list of the variables included in this study. The severity of angina was categorized according to the Canadian Heart Association classification. Class I angina occurs only with strenuous, rapid, or prolonged exertion, whereas angina of class IV severity prevents the patient from doing any activity without developing angina. The distinction between intermediate classes II and III depends on whether the patient can walk two blocks or climb one flight of stairs under ordinary temperature or wind conditions. Congestive heart failure (CHF) symptoms were categorized by four levels of severity in accordance with the extent of functional limitation of the patient (none, mild, moderate, or severe). Other clinical variables included angina as the primary symptom, CHF as the primary symptom, and use of digitalis or diuretics. In addition, a CHF score was used, which included the number of positive responses to history of CHF, digitalis use, diuretic use, and the presence of rales (total possible score: 0 to 4).

The number of diseased arteries (one to three) was based on whether the right coronary artery, left anterior descending artery, or circumflex vessel in their major segments or major branches contained lesions greater than or equal to 70% or whether the left main segment contained a lesion of 50% or more. Determination of the number of operable arteries (range zero to three) depended on both the location of lesions and the morphologic appearance of vessels distal to the lesions, with the requirement that the distal vessel be sufficiently well visualized and of adequate size to be a graft recipient. The presence or absence of left main coronary artery lesions greater or equal to 70% was coded as a separate variable.

Ejection fraction was measured by the area-length method.

Left ventricular cineangiography was performed in the 30-degree right anterior oblique view and five segments were identified: anterobasal, anterolateral, apical, diaphragmatic, and posterobasal. The systolic motion of each of these segments was scored as follows: normal = 1, moderate hypokinesia = 2, severe hypokinesia = 3, akinesia = 4, dyskinesia = 5, and aneurysm = 6. The left ventricular wall motion score is the sum of the segmental scores for the five segments. Left ventricular end-diastolic pressures were available in 646 of the 651 patients included in this study.

A composite variable, myocardial jeopardy, was used to evaluate whether there were severely diseased coronary vessels leading to "viable" anterior left ventricular segments, to "viable" inferior left ventricular segments, or to both. Anterior segmental jeopardy was defined as the condition in which the three anterior ventriculographic segments had either normal or hypokinetic motion jeopardized by a significant left main or left anterior descending artery lesion. Inferior segmental jeopardy was defined as the condition in which the inferobasal and diaphragmatic ventriculographic segments had normal or hypokinetic wall motion jeopardized by significant lesions in the proximal or middle right coronary artery, or alternatively, by lesions in the left main or proximal circumflex vessels of left dominant anatomy.

**Statistical analyses.** Tabular results comparing different groups of patients were analyzed by F-test statistics for continuous variables and chi-square statistics for discrete variables. Survival analysis was based on a Cox model using multivariate regression with censoring at the point of loss of follow-up information. Comparison of survival between the medical and surgical patients uses two different statistical approaches. In method A, the medical group comprised all patients in the study, including those who ultimately had surgery (an event that censored their membership in the medical group and added them to the surgical group). The surgical group included all patients from the time they underwent surgery, irrespective of time between enrollment and surgery. Method B defined surgical patients as those who underwent surgery within 90 days or within a site-specific time window, which included 95% of the patients operated on at each site within the first year. Any other patient belonged to the medical group. To compensate for the fact that medically treated patients are at risk for cardiac events before the surgically treated patients, medically treated patients start their exposure at the average number of days from enrollment to surgery in the surgical group.

**Results**

The distribution of clinical characteristics of the 420 medically treated and 231 surgically treated patients is shown in tables 2 and 3. Significant differences between the two groups were based on chi-square statistics for discrete variables and F-test statistics for continuous variables. There were no significant differences between the two groups with regard to age, functional impairment caused by heart failure, digitalis use, diuretic use, left ventricular end-diastolic pressure, or presence of left ventricular aneurysm on angiography.

There was, however, a distinct concentration of patients with angina as the primary symptom in the surgical group as compared with the medical group. Conversely, patients with predominant heart failure symptoms were concentrated in the medical group. Moreover, surgically treated patients tended to have more severe coronary vascular disease, with 66.7% having three-vessel disease vs 50.2% in the medical group (p < .001). Similarly, 12.6% of the 231 surgically treated patients had left main lesions greater or equal to 70% vs 3.8% in the medical group (p < .001). The medically treated patients had somewhat lower ejection fractions and worse wall motion scores compared with surgically treated patients. The medically treated patients also had significantly fewer myocardi-
TABLE 2
Distribution of clinical characteristics in medically and surgically treated patients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Medical (%)</th>
<th>Surgical (%)</th>
<th>Chi square</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>54.4</td>
<td>55.5</td>
<td>2.4^A</td>
<td>NS</td>
</tr>
<tr>
<td>Sex ratio (M/F)</td>
<td>6.5/1</td>
<td>12.6/1</td>
<td>5.3</td>
<td>.021</td>
</tr>
<tr>
<td>Primary symptom</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Angina</td>
<td>56.2</td>
<td>76.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CHF</td>
<td>18.8</td>
<td>10.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>5.7</td>
<td>4.3</td>
<td>27.0</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Asymptomatic post-MI</td>
<td>11.7</td>
<td>4.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>7.6</td>
<td>4.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Angina: class III or IV severity</td>
<td>29.0</td>
<td>56.7</td>
<td>61.2</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Predominant symptom</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CHF</td>
<td>18.8</td>
<td>11.1</td>
<td>8.8</td>
<td>.003</td>
</tr>
<tr>
<td>Impairment due to CHF: mild, moderate, severe</td>
<td>37.6</td>
<td>35.5</td>
<td>4.26</td>
<td>NS</td>
</tr>
<tr>
<td>Digitalis use</td>
<td>51.9</td>
<td>45.5</td>
<td>2.5</td>
<td>NS</td>
</tr>
<tr>
<td>Diuretic use</td>
<td>45.5</td>
<td>45.9</td>
<td>0.1</td>
<td>NS</td>
</tr>
</tbody>
</table>

MI = myocardial infarction.
^A = test for continuous variable.

TABLE 3
Distribution of angiographic characteristics in medically and surgically treated patients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Medical (%)</th>
<th>Surgical (%)</th>
<th>Chi square</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of diseased coronary arteries (≥ 70% stenosis)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>One</td>
<td>18.8</td>
<td>6.1</td>
<td>24.8</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Two</td>
<td>31.0</td>
<td>27.3</td>
<td>17.7</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Three</td>
<td>50.2</td>
<td>66.7</td>
<td>0.8</td>
<td>NS</td>
</tr>
<tr>
<td>Left main lesion ≥ 70%</td>
<td>3.8</td>
<td>12.6</td>
<td>17.7</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>LV aneurysm present</td>
<td>30.9</td>
<td>29.9</td>
<td>0.8</td>
<td>NS</td>
</tr>
<tr>
<td>LV ejection fraction</td>
<td>0.260</td>
<td>0.271</td>
<td>3.87^A</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>LV wall motion score</td>
<td>16.0</td>
<td>15.5</td>
<td>6.74^A</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>LV end-diastolic pressure</td>
<td>20.2</td>
<td>19.7</td>
<td>3.53^A</td>
<td>NS</td>
</tr>
<tr>
<td>Myocardial jeopardy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>67.6</td>
<td>49.4</td>
<td>21.9</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Inferior</td>
<td>19.8</td>
<td>29.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior</td>
<td>9.0</td>
<td>16.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inferior &amp; anterior</td>
<td>3.6</td>
<td>4.3</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

LV = left ventricular.
^A = test for continuous variable.

had three or more bypass grafts, with 68.0% having grafts placed into the distributions of both the right and left coronary circulations. Myocardial resection or plication was performed in 30.3% of surgically treated patients. The right anterior oblique angiographic segmental descriptors for all surgically treated patients included a discrete aneurysm in 29.4%, dyskinesia in 22.5%, and akinesia in 43.7%. Conversely, 59.4% of patients who had an angiographic segment coded as discrete aneurysm actually had operative resection or plication of myocardium. Death during hospitalization occurred in 6.9% of patients. The prevalence of definite myocardial infarction during hospitalization was 5.6%, and that of probable infarction was 5.2%. The average duration of hospitalization after initial surgery was 12 days.

Cox regression analysis with survival as the dependent variable was assessed by multiple analyses (table 5). Analysis 1 included all patients (646) studied by method B, which identified the medically and surgically treated patients as mutually exclusive groups. All of the variables listed in table 1 were considered in this analysis, including the treatment variable. The numeric rank order and the p value associated with each of the variables that reached statistical significance (p < .05) are listed. In analysis 1, severity of functional impairment caused by heart failure symptoms ranked first, followed by advanced age, number of diseased vessels, surgical treatment, depressed ejection fraction, elevated left ventricular end-diastolic pressure, and the presence of a left main lesion greater than or equal to 70%. In all subsequent Cox regression analyses, essentially the same variables were identified as significant (p < .05), although the particular
TABLE 5
Cox regression analysis of survival

<table>
<thead>
<tr>
<th>Analysis No.</th>
<th>Patient group (n)</th>
<th>Analysis method(a)</th>
<th>Variables restricted (R) or open (O)(b)</th>
<th>Treatment variable: med or surg</th>
<th>Functional impairment due to CHF</th>
<th>Advanced age</th>
<th>No. of vessels diseased</th>
<th>Ejection fraction</th>
<th>LV end-diastolic pressure</th>
<th>LMCA (\geq 70)%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 All patients</td>
<td>646 B O</td>
<td>4(e) 1(e) 2(e) 3(e) 5(d) 6(c) 7(c)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 Patients with LV aneurysm</td>
<td>199 B O</td>
<td>1(e) 2(d) 4(c) 3(d) (_)(f) (_)(f)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 Patients without LV aneurysm</td>
<td>447 B O</td>
<td>2(e) 1(e) 3(c) (_)(o) (_)(o) 5(c) 4(c)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>4 All patients</td>
<td>646 B O</td>
<td>Excluded 1(e) 2(e) 3(e) 4(d) 5(c) 6(c)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 All patients</td>
<td>646 B R</td>
<td>3(e) 1(e) 2(e) 4(d) 6(d) 7(c) 5(d)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 All patients</td>
<td>930 A O</td>
<td>Excluded 1(e) 2(e) 4(d) 3(e) 5(c) 6(c)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7 All patients</td>
<td>930 A R</td>
<td>5(d) 1(e) 2(e) 6(d) 3(e) 7(d) 4(d)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8 All patients</td>
<td>646 B R</td>
<td>4(e) 1(e) 2(e) (_) 5(d) 6(d) 3(e)</td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>

\(a\)Method A: all patients considered medically treated until surgery; method B: mutually exclusive groups defined by surgery within a specific time after enrollment.

\(b\)Restricted to those ranked in previous analysis or open to all variables in table 1.

Statistical comparisons: \(c\) \(p < .05\); \(d\) \(p < .01\); \(e\) \(p < .001\).

\(f\)Other predominant symptom ranked fifth \(p < .05\).

\(g\)Diuretic use entered sixth \(p < .05\) and absence of angina as predominant symptom entered seventh \(p < .05\).

Because 30.3% of patients had left ventricular aneurysmectomy or plication, separate regression analyses (Nos. 2 and 3, table 5) were performed to compare rank ordering of variables in patients who had or did not have left ventricular aneurysm surgery. For each group of patients the functional impairment caused by heart failure symptoms ranked first. Surgical treatment ranked second \(p < .001\) as a determinant of survival in the analysis of patients without left ventricular aneurysm but did not rank in survival analysis of patients who had a left ventricular aneurysm (analysis 2, table 5).

To corroborate the statistical ranking of surgical treatment in the regression analysis, analyses 4 and 6 (table 5) were performed by methods B and A, respectively, but excluded the treatment variable. These analyses yielded the same ranked variables as independent predictors of survival. Analyses 5, 7, and 8 were then performed with the treatment variable added but were constrained to include only those variables that had ranked as significant determinants of survival in analyses 4 and 6. In all three of these analyses, surgical treatment ranked from third to fifth, with \(p\) values ranging from .01 to .001.

Figures 1A to 1D compare percent survival of patients with medical or surgical treatment. Figure 1A shows a comparison of survival for all 651 patients adjusted for ejection fraction terciles, whereas figures 1B, 1C, and 1D show survival curves for patients in the upper, middle, and lower terciles of ejection fractions at or below 35%. The 5 year survival of medically treated patients ranged from 64% for patients in the upper tercile (ejection fraction between 31% and 35%) to 41% for patients with ejection fractions at or below 25%. A statistically significant difference determined by the log rank method between surgical and medical treatment was present for the combination of all three terciles \(p = .0007\), figure 1A) and for the lowest tercile \(p = .0056\), figure 1D).

All patients have been followed up at annual intervals for a mean follow-up time of 3.7 years. Twenty-tenths of 1% of patients have been lost to follow-up and 9.3% of the medically treated patients have had coronary surgery more than 90 days after angiography.
At the time of annual patient follow-up examinations, subsequent hospitalizations for cardiac symptoms were noted. Hospitalizations for myocardial infarction have occurred in 10.7% of medically treated patients vs 7.8% of surgically treated patients (NS). Hospitalizations for CHF have occurred in 25.2% of the medically treated patients vs 19.5% for the surgically treated patients (NS). Hospitalizations for arrhythmia have occurred in 17.9% of medically treated patients vs 21.2% of surgically treated patients (NS). In all three instances there was no significant difference between the frequency of the hospitalizations for cardiac events subsequent to treatment.

Table 6 illustrates the symptomatic status of patients at the time of initial enrollment and at the time of 3 year follow-up. Detailed clinical data were available for 89.7% of patients. The upper portion of table 6 shows the severity of limitation and the lower portion shows the major factor responsible for any limitation, if present. Although there were similar degrees of functional limitation at baseline for medically and surgically treated patients, the primary limiting factor was weighted toward angina in the surgically treated patients and, conversely, weighted toward dyspnea and fatigue in the medically treated patients (p < .001). At the time of 3 year follow-up, however, 27.7% of surgically treated patients had no functional limitation vs 16.0% of medical patients. Moreover, the limiting factor in patients who were experiencing functional limitation was angina in 15% of the surgically treated patients vs 36.9% of the medically treated patients. As previously noted, surgically treated patients had a better survival rate, with only 22.5% dying by the time of the 3 year follow-up vs 33.3% of medically treated patients.

At the time of 3 year follow-up, 30.2% of surgically treated and 9.8% of medically treated patients whose primary presenting symptom was chest pain became free of functional limitation. In those patients who were still experiencing some degree of functional limitation, angina was the responsible factor in 49.3% of the medically treated patients and 19.0% of the surgically treated patients. Thirty-two percent of the medically treated patients had died vs 16% of the surgically treated patients. The three leading clinical syndromes associated with death were, in rank order, sudden death, myocardial infarction, and heart failure for medically treated patients, whereas the ranking for surgery patients was heart failure, shock, and arrhythmia.

For patients whose primary limitation was dyspnea or fatigue, the percentages of patients dead at 3 years were the same for medical and surgical treatment (45.2% medical vs 45.2% surgical). The three leading clinical syndromes associated with death for both medical and surgical patients were, in rank order, heart failure, sudden death, and arrhythmia. Only 5.8% of the medically treated patients and 6.4% of the surgically treated patients were free of functional limitation at the time of 3 year follow-up. Angina and dyspnea were
more prominent as the limiting factor in the medical group (25.6% and 35.9%, respectively), whereas dyspnea and fatigue were more prevalent in the surgical group (30.0% and 40.0%, respectively).

Figure 2A shows the percentage of patients who were alive and free of moderate or severe functional limitation, plotted in a format similar to that of survival analysis. At the time of 5 year follow-up, 38% of medically treated patients were alive and free of moderate or severe limitation compared with 58% of surgically treated patients (p = .0003). Figures 2B and 2C show similar analyses for those patients with angina and those with heart failure as the predominant baseline symptom. The cumulative difference in patients both alive and free of moderate or severe functional limitation was highly significant for patients with angina as the predominant baseline symptom (p = .0006) in contrast to the absence of significant difference for
patients with heart failure as the predominant presenting symptom (NS).

Discussion

The results of this study suggest that coronary surgery is beneficial in patients with severe left ventricular dysfunction, not only in promoting their survival but also in improving their functional status. This benefit of surgery was partially confined to patients who had angina as the predominant symptom. Although it is commonly considered that patients with the lowest ejection fractions are at greater risk for surgical complications and mortality, this study points out that the long-term benefits of surgery outweigh the somewhat increased short-term hazards. The fact that the lowest ejection fraction terciles of patients (figure 1D) showed statistical benefit compared with the other terciles reflects the greater ease of demonstrating a beneficial effect when event frequency in the control group is high. It is possible that a larger number of patients in

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left ventricular dysfunction in this study was 6.9% compared with an operative mortality of 1.55% for patients with ejection fraction above 35%, adjusted for the relative numeric contribution of each site. Despite the fact that multiple reports document increased oper-

FIGURE 2A. Percentage of patients alive and free of moderate or severe limitation (life table analysis and method B).

FIGURE 2B. Percentage of patients with angina as the predominant symptom who are alive and free of moderate or severe limitation.
THERAPY AND PREVENTION—CORONARY ARTERY DISEASE

![Graph showing survival analysis](image)

FIGURE 2C. Percentage of patients with heart failure as the predominant symptom who are alive and free of moderate or severe limitation.

Independent hazard for patients with poor left ventricular function, improved techniques of anesthetic induction, use of postoperative intra-aortic balloon, vasodilator therapy, and addition of cardioplegic infusion have benefited survival of patients in high-risk subtypes. Mean duration of postoperative hospitalization for patients with poor left ventricular function was 12 days, which was moderately elevated over the 7 days for the site-adjusted number of postoperative days for surgical patients with ejection fraction greater than 35%. The quality of surgery is clearly important in high-risk patients if these CASS survival statistics are to be extrapolated to other centers. It should be recognized that 52% of the surgical patients in this study were operated on at four of the 15 CASS sites, three of which had the lowest overall risk-adjusted (observed/expected) mortality rates, with a mortality below 1.0% for all patients who underwent surgery.

This study used conservative statistical techniques in confirming the benefit of surgery on long-term survival. Cox regression analyses used two methods; one assigned medically and surgically treated patients in accordance with a site-specific criterion to surgery, and the other included all patients in the medical group, censoring patients from the medical group when they had surgery. Moreover, subsidiary analyses were carried out by use of only the most important independent prognostic indicators that had been ranked and by including the treatment variable in the analysis. There also was an adjustment to avoid any bias that could result from including medically treated patients in the analysis for a longer period of time than surgically treated patients.

It should be recognized that there were differences in the clinical features of patients referred for medical or surgical therapy. Despite our efforts to adjust for differing prevalence of selection criteria, there may have been clinical or laboratory features affecting survival that were either not coded or not readily quantified and therefore not susceptible to analysis. Such an unidentified patient characteristic might have permitted biased selection of patients for medical vs surgical treatment. It would escape detection in a retrospective, nonrandomized study by not being included within the Cox regression analysis and therefore not being adjusted for.

The strength of this CASS study lies in its completeness of clinical and angiographic characterization and the fact that variables were characterized prospectively, i.e., before a decision regarding surgical or medical management. Follow-up data were collected by telephone interview, and there is no reason to suspect that information regarding symptomatic status was biased by knowledge of the particular therapy that was used.
The patients represent a consecutive series at all participating sites, thus avoiding exclusion biases. Follow-up of patients in this study was 99.8% complete at 3 years.

The presence of left main coronary artery disease is an important adverse determinant not only of prognosis but also of surgical mortality. Surgical benefit for patients with left main disease has been amply documented and in this study there was a strong trend toward surgery in these patients. Although the frequency of 70% left main disease in this patient subset was relatively high (7%), the Cox regression model adjusted for the biased distribution of patients with left main disease to surgery. The analysis documents that there is surgical benefit for patients with left ventricular dysfunction over and above the benefit that was derived as a result of the presence of left main lesions.

Previous analysis of CASS data has documented that the angiographic presence of a left ventricular aneurysm was not of prognostic significance when survival was adjusted for its two most important determinants: functional impairment caused by heart failure symptoms and left ventricular wall motion score. This result implies that therapeutic interventions directed at left ventricular aneurysms would not have important prognostic significance. This indeed is the conclusion that can be derived from the regression analysis noted in table 5 (analysis 2), in which myocardial surgery in patients with left ventricular aneurysm had no beneficial effect on survival. Moreover, the fact that symptomatic benefit was primarily restricted to patients with angina suggests that myocardial resection did not help patients with predominant heart failure symptoms.

The specific criteria that the surgeons used to determine whether resection or plication would be added to the bypass graft procedure were not defined by the CASS protocol. The fact that a substantial portion of patients undergoing aneurysm or plication surgery did not have a discrete aneurysm noted on ventriculography is an indication of the heterogeneity of approaches used in the management of abnormal myocardial segments at the time of surgery. Certainly questions might be raised regarding the extent to which myocardial surgery should be added to coronary bypass (30.3% in this study), particularly when one considers that it constitutes a threefold increase in univariate relative risk for operative mortality. However, left ventricular aneurysmectomy was not an independent operative risk factor by multivariate analysis.

In years past, the elevated operative risk of patients with severe left ventricular dysfunction has led to medical management of such patients, even when considerable angina was the presenting complaint. This approach was questioned by Isom et al., who in 1975 reported a 9.7% mortality and 85% 2 year survival in 62 patients with severe angina and markedly dysfunctional ventricles. Coles et al., in 59 consecutive patients with refractory angina and angiographic criteria similar to those used in this report, noted in 1981 a 1.7% operative mortality, a 5 year actuarial survival rate of 80%, and substantial symptomatic benefit. Our results are also similar to those reported by Manley et al. and Pigott et al. in retrospective comparisons of medically and surgically treated patients. These reports and those of others all suggest that myocardial revascularization in patients with angina as the primary symptom can be accomplished with significant benefit for the patient.

It remains controversial regarding the extent to which silent ischemic left ventricular dysfunction may be present in patients with low ejection fractions, thus accounting for a beneficial effect from revascularization. At the time of the baseline left ventriculogram it is also possible that some patients have active ischemia with accompanying wall motion abnormalities that do not necessarily reflect prior infarction and fibrosis, but rather active ischemia. Radionuclide studies performed 2 weeks postoperatively by Hellman et al. did demonstrate a beneficial effect on ejection fraction; however, increased adrenergic tone, as demonstrated by substantially higher heart rates, probably accounts for these findings. Hung et al. performed radionuclide scans in 18 of 20 survivors at 19 months and showed benefit on ejection fraction only in six patients who had left main coronary lesions. Certainly the fact that operative benefit was more notable in patients with ischemic symptoms, in contrast with heart failure symptoms, supports the hypothesis that myocardial fibrosis underlying heart failure symptoms is not reversible by surgery. However, predominantly ischemic symptoms implies the presence of jeopardized yet potentially viable myocardium and it is these patients who exhibit the most prominent clinical benefit. Moreover, the fact that the leading clinical syndromes associated with death in patients whose major presenting complaint was ischemic pain shifted from sudden death, infarction, and heart failure in medically treated patients to heart failure, shock, and arrhythmia in surgically treated patients implies that benefit in survival resulted from infarct prevention rather than restoration of hemodynamic function.

In conclusion, our results suggest that patients with overt heart failure and the absence of ischemic symp-
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Toms should not receive surgery. However, patients with angina as the predominant symptom, although having poor ventricular function, should not be excluded from coronary surgery despite higher operative risk and prolonged hospitalization. In fact, our results suggest that survival and relief of symptoms will be substantially benefited.

An important caveat regarding these conclusions is that the surgery and associated diagnostic and postoperative care must be of sufficient quality to result in an operative mortality rate at or below the range defined in this study. Cardiac surgery in this group of patients should not be undertaken in centers in which operative mortality statistics are marginal or in which complete facilities for management of complex postoperative problems cannot be provided.

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