Left Main Coronary Artery Stenosis

Results of Coronary Bypass Surgery

By Howard J. Zeft, M.D., Jack C. Manley, M.D., John H. Huston, M.D., Alfred J. Tector, M.D., James E. Auer, M.D., and W. Dudley Johnson, M.D.

SUMMARY
Fifty-six patients with severe stenosis of the left main coronary artery underwent coronary bypass surgery between January 1970 and December 1971. All patients had angina pectoris. Seventy-five per cent of the patients had an unstable anginal pattern. There were six perioperative deaths for a surgical mortality of 10.7%. Of the 50 patients surviving surgery, 96% are alive from 12 to 36 months postoperatively, 90% have had a significant reduction in anginal symptoms and 76% are asymptomatic. Postoperative catheterization studies, performed one to 28 months after surgery in 31 patients, showed that 83% of 75 bypass grafts were widely patent. In each patient studied there was at least one widely patent graft to the left coronary artery. Six patients had exercise studies using supine bicycle ergometry during pre- and postoperative cardiac catheterization. These studies demonstrated improvement in exercise tolerance and in left ventricular hemodynamics after coronary surgery.

Additional Indexing Words:
Angina pectoris  Coronary artery disease  Coronary arteriography
Saphenous vein bypass

The left main coronary artery is that short segment of the left coronary artery before its bifurcation to the anterior descending and circumflex branches. The anterior descending and circumflex branches nourish the anterior and lateral surfaces of the left ventricle including the apex and the interventricular septum. Patients with severe stenosis of the left main coronary artery are in jeopardy of massive myocardial infarction and death. Such patients are frequently symptomatic with angina pectoris that is both progressive and poorly responsive to the usual forms of medical management. We have taken an aggressive approach to the management and treatment of patients with this potentially lethal problem. This report presents our experience with direct surgical therapy in the treatment of patients with severe stenosis of the left main coronary artery.

Methods

Patient Population
Fifty-six patients with severe stenosis of the left main coronary artery underwent coronary bypass surgery during a two year period between January 1970 and December 1971. Patients with hemodynamically significant valvular heart disease or with left ventricular aneurysm were excluded from the study.

The age of the patients ranged from 39 to 66 years with an average age for the group of 55 years. Forty-seven patients were males and nine were females.

All patients had typical symptoms of angina pectoris. Forty-two of the 56 patients (75%) had unstable anginal symptoms. Unstable angina pectoris was defined as the recent onset or worsening of angina within a six month period or angina decubitus. Twelve patients (21%) had nocturnal angina. All patients were treated with short and long acting coronary vasodilators (nitrites) and many patients had received propranolol in various dosage schedules. Disabling symptoms of angina pectoris persisted in all patients despite medical therapy. Only three patients (5%) had objective evidence of congestive heart failure, which was readily managed with digitalis and oral diuretics. In two patients, life threatening ventricular arrhythmias were documented preoperatively; in one, ventricular tachycardia was precipitated by a Master's stress test.

From the Sections of Cardiology and Cardiovascular Surgery, St. Luke's Hospital, and The Medical College of Wisconsin, Milwaukee, Wisconsin.


Address for reprints: Howard J. Zeft, M.D., Professional Arts Building, 7635 West Oklahoma Avenue, Milwaukee, Wisconsin 53219.

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Catheterization Studies

Prior to angiography, right and left heart catheterization was performed. An accurate left ventricular end diastolic pressure at rest was recorded in 53 patients. Cardiac output was determined by either Fick or dye dilution technique in 44 patients. Ventriculograms, performed in 55 of the 56 patients, were done in the right anterior oblique projection with 35 to 45 cc of contrast material, containing 50% meglumine diatrizoate and 25% sodium diatrizoate. The right anterior oblique ventriculograms were graded for this study as follows: Class I—normal contractility of both the anterior and posterior-inferior walls of the left ventricle; Class II—areas of mild hypokinesia in one or both walls; Class III—areas of moderate or severe hypokinesia or akinesia in either the anterior or the posterior-inferior wall; Class IV—areas of moderate or severe hypokinesia or akinesia of both walls.

Selective coronary arteriography was performed in all patients, using the Sones technique in 43 patients and the Judkins technique in 13 patients. Multiple injections of both coronary arteries in various degrees of left and right anterior obliquity were performed. All patients in whom left coronary arteriograms showed at least 75% stenosis of the left main coronary artery, irrespective of associated coronary artery disease, were included in the study. No deaths or myocardial infarctions were precipitated by selective coronary arteriography. Thirteen patients had coronary arteriography at other hospitals and were referred to our institution for surgery. The 43 patients who had coronary arteriography at St. Luke's Hospital represented 1.7% of all coronary arteriograms over this 24 month period of time.

Coronary Surgery

All patients underwent direct coronary bypass surgery. In most instances, surgery was performed on the same hospitalization as the diagnostic studies and in many cases was performed within 72 hours of these studies. Prior to surgery, unstable patients were monitored on the Coronary Care Unit and treated with coronary vasodilators, sedation, and antiarrhythmic agents if necessary. Digitalization was carried out in those patients with hemodynamic and angiographic evidence of left ventricular dysfunction. The severity of an individual patient's anginal symptoms on medical therapy and the degree of stenosis of the left main coronary artery dictated the urgency of revascularization therapy. One patient in this series had emergency surgery in the early stages of an acute myocardial infarction, 72 hours after the catheterization studies.

The saphenous vein bypass technique introduced by Johnson et al. and Favaloro et al. was employed. A total of 131 saphenous vein bypass grafts were performed in the 56 patients. In addition, direct anastomosis of the left internal mammary artery to the left anterior descending coronary artery, described by Green et al., was carried out in three instances. Multiple bypass grafts were performed in 54 of the 56 patients. The details of surgical technique including anesthesia have been well described.

Postoperative Evaluation

Clinical follow-up of all patients who survived surgery was obtained from a minimum of 12 months to a maximum of 36 months after surgery. Follow-up was through December 1972. Long-term survival and symptom relief was tabulated.

Thirty-one of the surviving patients had postoperative catheterization studies from one to 28 months after surgery. The average interval from surgery to the postoperative catheterization was nine months. Selective visualization of the vein bypass grafts was performed in these 31 patients at the time of the catheterization studies.

Exercise stress testing using supine bicycle ergometry at the time of cardiac catheterization was performed in six patients before and after surgery. Because of angina decubitus and an unstable anginal pattern, preoperative stress testing was not performed in most patients. Left ventricular end diastolic pressure and cardiac output were recorded at graded work loads in those patients tested. Left ventricular stroke work index (LVSWI) in g-m/m² was calculated from the formula

\[
LVSWI = \frac{SVI \times (MAP - LVEDP \times 1.36)}{100}
\]

where SVI = stroke volume index in ml/m²; MAP = mean aortic pressure (mm Hg); and LVEDP = left ventricular end diastolic pressure (mm Hg).

Results

Severity of Coronary Artery Disease

All 56 patients had greater than 75% stenosis of the left main coronary artery as judged from selective left coronary arteriograms (fig. 1). In 28 patients (50%), the left main stenosis was judged to be greater than 90% of the vessel lumen. Greater
than 75% stenosis in at least one area of the anterior descending and circumflex coronary arteries was present in 34 and 32 patients respectively (table 1). Of the 56 patients, 26 patients had severe associated disease of both the anterior descending and circumflex branches of the left coronary artery. Seventeen additional patients had severe associated disease of either the anterior descending or circumflex branches. Thirty-seven patients had severe disease and greater than 75% stenosis of the right coronary artery. Only three patients had isolated disease of the left main coronary artery.

Preoperative Left Ventricular Function (Table 2)

Twenty-one patients had normal preoperative ventriculograms (Class I) and seven patients had mild impairment of contractility (Class II). Fifteen patients had moderate or severe impairment of contractility of either the anterior or the posterior wall of the left ventricle (Class III) and 12 patients had moderate to severe impairment of both walls (Class IV).

Cardiac index at rest measured in 44 patients was greater than 2.5 L/min/m² in 30 patients (68%) and less than 2.5 L/min/m² in 14 patients. Left ventricular end diastolic pressure recorded in 53 patients was less than 12 mm Hg in 35 patients (66%) and greater than 12 mm Hg in 18 patients. Cardiac index ranged from 1.5 L/min/m² to 5.0 L/min/m² (average, 2.9 L/min/m²) and left ventricular end diastolic pressure ranged from 2 mm Hg to 34 mm Hg (average, 12 mm Hg).

Coronary Surgery

A total of 134 bypass grafts were performed in 56 patients (table 3). Bypass grafts to the left anterior descending coronary artery were performed in 53 patients. In 50 patients, this was carried out with a saphenous vein bypass and in three patients by direct anastomosis of the left internal mammary artery to the anterior descending coronary artery.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Coronary Arteriography</th>
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</thead>
<tbody>
<tr>
<td>&gt;75 percent stenosis</td>
<td>No. patients</td>
</tr>
<tr>
<td>Left main (LM)</td>
<td>56</td>
</tr>
<tr>
<td>Left anterior descending (LAD)</td>
<td>34</td>
</tr>
<tr>
<td>Circumflex (CX)</td>
<td>32</td>
</tr>
<tr>
<td>LM + LAD + CX</td>
<td>26</td>
</tr>
<tr>
<td>LM + LAD</td>
<td>10</td>
</tr>
<tr>
<td>LM + CX</td>
<td>7</td>
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<tr>
<td>Right coronary artery</td>
<td>37</td>
</tr>
<tr>
<td>Isolated LM stenosis</td>
<td>3</td>
</tr>
</tbody>
</table>

In seven patients, a vein bypass to the anterior diagonal branch of the anterior descending coronary artery was performed. Bypass grafts to a branch of the circumflex coronary artery were performed in 39 patients. Forty patients (71%) had multiple bypass grafts to the left coronary artery. The percentage of patients who received multiple grafts to the left coronary artery was higher in 1971 (96%) than in 1970 (62%). Thirty-six of the 56 patients had multiple grafts. The average number of grafts per patient was 2.4.

There were six early deaths within the initial four weeks after surgery for a peri-operative mortality of 10.7%. Two patients died from myocardial infarction, one at surgery and the other on the fourth postoperative day with graft closure. Two patients died of pulmonary infection four and 24 days after surgery. One patient died from a ruptured abdominal aneurysm on the fourth postoperative day, and another from pancreatitis 14 days postoperatively.

Graft Patency

Postoperative cardiac catheterization studies were performed in 31 patients from one to 28 months after surgery. Seventy-five bypass grafts had been performed in these 31 patients. Sixty-two of the 75 grafts (83%) were widely patent, three grafts were

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Left Ventricular Function</th>
</tr>
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<tr>
<td>Parameter</td>
<td>No. patients</td>
</tr>
<tr>
<td>A. Ventriculogram</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>21</td>
</tr>
<tr>
<td>II</td>
<td>7</td>
</tr>
<tr>
<td>III</td>
<td>15</td>
</tr>
<tr>
<td>IV</td>
<td>12</td>
</tr>
<tr>
<td>B. Cardiac index</td>
<td></td>
</tr>
<tr>
<td>&gt;2.5 L/min/m²</td>
<td>30</td>
</tr>
<tr>
<td>&lt;2.5 L/min/m²</td>
<td>14</td>
</tr>
<tr>
<td>C. LVEDP</td>
<td></td>
</tr>
<tr>
<td>&lt;12 mm Hg</td>
<td>35</td>
</tr>
<tr>
<td>&gt;12 mm Hg</td>
<td>18</td>
</tr>
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</table>

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significantly narrowed and 10 grafts were closed (table 4). Thirty-one of 34 grafts (91%) to the anterior descending or its large diagonal branch and 17 of 23 grafts to the circumflex were widely patent. Fourteen of 18 grafts to the right coronary artery were patent. Eighty-four per cent of the 57 grafts to a branch of the left coronary artery were patent. In all patients studied there was at least one widely patent graft to the left coronary artery system, bypassing the severe left main coronary stenosis.

Figure 2 illustrates patent grafts to the left anterior descending and dominant left circumflex coronary arteries in a 53-year-old man one year after bypass surgery. This patient had severe angina pectoris and a 90% left main coronary stenosis preoperatively. The patient is asymptomatic one year after surgery.

Postoperative left coronary arteriograms demonstrated progression of the left main coronary artery disease to virtually total occlusion in three of the 31 patients. In each instance, patent bypass grafts to the anterior descending and circumflex coronary arteries were demonstrated. These three patients were asymptomatic following surgery, and postoperative ventriculograms demonstrated preserva-

<table>
<thead>
<tr>
<th>Coronary artery</th>
<th>No.</th>
<th>Patent (%)</th>
<th>Narrowed</th>
<th>Closed</th>
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</thead>
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<tr>
<td>Anterior descending or diagonal</td>
<td>34</td>
<td>31 (91)</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Circumflex</td>
<td>23</td>
<td>17 (74)</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Right coronary</td>
<td>18</td>
<td>14 (78)</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>75</td>
<td>62 (83)</td>
<td>3</td>
<td>10</td>
</tr>
</tbody>
</table>

Table 4

Figure 2

Left, selective visualization of a vein bypass graft (VG) to the anterior descending coronary artery (LAD) in the RAO view in a 53-year-old man one year after surgery. Right, selective visualization of a vein bypass graft (VG) to the marginal branch of a large circumflex coronary artery (CX) in the RAO view in the same 53-year-old man one year after surgery.
tion of contractility of the anterior myocardium. Figure 3 shows left coronary injections in right and left anterior oblique projections illustrating virtually total left main coronary occlusion in the same patient whose patent bypass grafts are illustrated in figures 2 and 3.

Exercise Studies

Supine bicycle ergometry was performed at the time of pre- and postoperative catheterization studies in six patients. The results of these studies are summarized in figure 4. Prior to surgery, exercise to 150 kpm precipitated typical angina pectoris associated with a marked rise in LVEDP and a fall in LVSWI. LVEDP rose from $8.3 \pm 1.2$ (mean ± SEM) mm Hg to $26.6 \pm 1.3$ mm Hg and LVSWI declined from $46.2 \pm 4.0$ (mean ± SEM) g-m/m$^2$ to $37.7 \pm 6.9$ g-m/m$^2$. After surgery, all six patients exercised to 150 kpm without angina and with more normal hemodynamics. Postoperatively, exercise to 150 kpm produced less of an increase in LVEDP from $10.1 \pm 1.3$ mm Hg to $17.4 \pm 1.2$ mm Hg, and an increase in LVSWI from $44.7 \pm 4.6$ g-m/m$^2$ to $51.0 \pm 5.4$ g-m/m$^2$. Furthermore, five of the six patients could exercise to 450 kpm without angina and with little additional increase in the LVEDP.

Clinical Follow-Up

Of the 50 patients surviving surgery, 48 patients (96%) are alive 12 to 36 months postoperatively with an average interval of clinical follow-up of 24.5 months. Thirty-eight patients (76%) are totally asymptomatic. Seven patients (14%) have angina pectoris but are much improved symptomatically since surgery. Only three patients (6%) continue with severe angina and have had no significant improvement. In these three patients, continued severe angina could be explained by closure of the majority of bypass grafts (three of five grafts

Figure 3

Selective left coronary arteriograms in the RAO and LAO views in a patient with severe left main coronary stenosis (LM) one year after bypass surgery. Figure 2 illustrates patent grafts in this patient.
closed, two patients) or inadequate revascularization because of diffuse coronary artery disease (one patient).

There have been only two late deaths. One patient died seven months after surgery as the result of ventricular arrhythmias. This patient was one of two patients with documented ventricular arrhythmias preoperatively. Postoperative catheterization studies in this patient one month after surgery showed that two of three vein bypass grafts were patent. A second patient died six months after surgery as the direct result of alcoholism. She had a triple vein bypass procedure and had been free of cardiac symptoms until her death. An autopsy was not performed.

**Discussion**

Seventy-five per cent of the 56 patients with severe left main coronary stenosis had an unstable pattern of angina pectoris. In many of these patients, mild symptoms progressed to an incapacitating state within a six month period. The high incidence of nocturnal angina (21%) demonstrated the severity of symptoms in this group. It has been our philosophy to perform selective coronary arteriography on all patients with unstable angina pectoris, who would otherwise be considered candidates for coronary bypass surgery.

Recent studies have reported a high mortality from selective coronary catheterization in patients with left main coronary stenosis. Cohen et al.\(^8\) reported five deaths in 32 patients with left main stenosis directly attributable to catheterization studies. Three of these deaths were related to studies in which the Judkins catheter was used and this pre-formed end-hole catheter was implicated. The authors suggested that nonselective left coronary bypass injections should be done in patients with left main coronary stenosis. Lavine et al.\(^9\) observed a 10% mortality from coronary catheterization (by the Sones technique) in 30 patients with 70% or more obstruction to the left main coronary artery. In contrast, 43 patients included in this report had selective coronary arteriograms at our institution with no deaths. The studies were done in 32 instances by the Sones technique and in 11 instances by the Judkins technique.

Patients with unstable angina pectoris should have coronary catheterization studies performed quickly and by experienced individuals. Any hypotension during the procedure should be quickly corrected. The arterial pressure, through the coronary catheter, should be carefully monitored; any dampening of the pressure tracing requires immediate withdrawal of the catheter from the left coronary ostium. When patients with unstable angina pectoris have had rapid progression of their symptoms or the development of nocturnal angina, our cardiac surgery team is alerted prior to the catheterization studies. Thus, if a patient with left main coronary stenosis should develop prolonged ischemic pain immediately before, during, or after the coronary arteriograms, he can be considered for emergency bypass surgery. Selective coronary arteriograms, as opposed to nonselective left coronary cusp injections, are necessary in the great majority of patients in order to adequately evaluate the distal coronary branches for bypass surgery.

Patients with severe left main coronary stenosis may be subject to hypotension and serious ventricular arrhythmias with induction of anesthesia. Cohen et al.\(^8\) reported one anesthetic death in their small series undergoing bypass surgery. The extra-corporeal pump should be ready for immediate use before anesthesia is attempted. Once the patient is anesthetized, he should be placed on full cardiopulmonary bypass as quickly as possible.

The operative and early postoperative mortality
for the 56 patients with severe left main coronary stenosis was 10.7%. The surgical mortality in this series was similar to that reported by Lavine et al., who found an 11.7% operative mortality in a smaller group of 18 patients with left main coronary stenosis. This surgical mortality is higher than that recently reported for large patient populations undergoing surgery for coronary artery disease without critical left main coronary stenosis.10-12 The higher operative mortality reflects the severity of the coronary artery disease and the unstable clinical status of this population of patients. Furthermore, surgical mortality in patients undergoing coronary bypass surgery is directly related to pre-existing abnormalities in left ventricular function and the degree of myocardial scarring. In this group of patients with severe left main coronary stenosis, the surgical mortality was considerably less in patients with Class I, II or III ventriculograms (7% of 43 patients) than in patients with Class IV ventriculograms (25% of 12 patients).

Multiple bypasses to the left coronary artery in patients with left main coronary stenosis are frequently necessary because of the high incidence of associated disease in either or both the anterior descending and circumflex branches of the left coronary artery. It is not unusual for severe disease of the left main coronary artery to extend into its bifurcation and the proximal portions of the anterior descending and circumflex branches. Frequently, the anterior diagonal branch of the anterior descending coronary artery is large and suitable to accept a bypass graft. Furthermore, with multiple bypass grafts to the left coronary artery, closure of one graft does not place the entire left coronary tree in its preoperative state of jeopardy from the left main coronary stenosis. In this series, 71% of patients had multiple grafts to the left coronary system. The higher percentage of patients receiving multiple grafts to the branches of the left coronary artery in 1971 than in 1970 reflects a more aggressive surgical attempt at complete revascularization rather than a difference in the extent and severity of the coronary artery disease.

Direct anastomosis of the left internal mammary artery to the left coronary artery has been introduced as another means of direct coronary artery bypass. Early work has suggested that long-term patency may be greater than with saphenous vein bypass grafts. In this series, left internal mammary to left anterior descending coronary artery anastomosis was performed in only three instances. Since January 1972, however, this method of direct coronary bypass has been employed more frequently. The surgical preparation of the internal mammary artery for coronary bypass may be time consuming. In patients with left main coronary artery stenosis, especially those who are unstable with anesthesia induction, the more expedient saphenous vein bypass procedure may be more desirable.

Patients who have diffuse coronary artery disease involving the distal branches are less likely to benefit from coronary bypass surgery. The technical difficulties in performing anastomoses into small, diffusely diseased arteries and the poor run-off in such vessels adversely influences long-term graft patency. A previous study from our institution by Walker et al. has shown that blood flow in the grafts, measured at surgery, was a valuable means of predicting long-term graft patency. It is important to carefully evaluate the distal vessels on preoperative selective coronary arteriograms. In the present study, involving patients with severe left main coronary stenosis, it was not necessary to reject any patients because of diffuse distal coronary disease. In each patient in this study at least one suitable graft to a major branch of the left coronary artery could be carried out.

The overall patency of 83% for the 75 grafts in 31 patients studied postoperatively compares favorably with other studies of graft patency. Moreover, the 91% graft patency in 34 grafts to the left anterior descending coronary artery or its diagonal branch is most encouraging. Nine patients who had surgery in 1970 had a "Y" graft to the anterior descending and circumflex coronary arteries with a single aortic ostium. Both limbs of the "Y" graft were found to be widely patent in four of five patients who had postoperative angiography. Walker et al. have found that long-term patency results with subsidiary branches of the "Y" graft were less promising than with other aorto-coronary vein grafts. Subsequent to these studies, which were performed at our institution, the "Y" graft has been abandoned except in an occasional patient with severe arteriosclerosis of the thoracic aorta in whom multiple aortic anastomoses might be a technical problem.

Patients with critical left main coronary artery stenosis are in jeopardy of suffering massive anterolateral myocardial infarctions, which may result in either death or severe left ventricular dysfunction with congestive heart failure. One patient in this series underwent emergency surgery in the early stages of an acute myocardial infarction. He had an excellent clinical result from bypass of the anterior
descending and diagonal branches of the left coronary artery. On the other hand, there have been six additional patients, not included in this series, who suffered and survived massive antero-lateral infarctions secondary to severe left main coronary stenosis. Post-infarction catheterization studies demonstrated left main coronary occlusion and left ventricular aneurysm with gross left ventricular decompensation. Attempted surgery, consisting of left coronary bypass and aneurysm resection in these six patients, resulted in the deaths of five patients, an 83% operative mortality. As the result of this experience, we seldom recommend surgery for patients with left main coronary occlusion and left ventricular aneurysm.

Patients with left main coronary artery stenosis may have severe myocardial scarring in the absence of a discrete left ventricular aneurysm. Angiographic evidence of diffuse myocardial scarring (Class IV ventriculogram) was associated with an increase in operative mortality. In general, patients with severe left main coronary artery stenosis, adequate distal vessels, and associated diffuse myocardial scarring with left ventricular dysfunction are recommended for coronary bypass surgery if they are disabled with angina pectoris. On the other hand, surgery is usually not recommended in such patients if the left ventricular dysfunction is of such a magnitude that overt left ventricular failure rather than angina pectoris prevails clinically.

Abnormal left ventricular hemodynamics with exercise have been well documented in patients with coronary artery disease and angina pectoris. Earlier studies by Manley et al. have shown that patients with functioning bypass grafts could exercise to greater levels than preoperatively without angina pectoris or its associated deterioration of left ventricular function. The six patients in this series who exercised preoperatively with supine bicycle ergometry developed typical symptoms of angina pectoris at a light work load associated with gross deterioration in left ventricular hemodynamics. Preoperatively, exercise resulted in a fall in stroke work index and a marked increase in left ventricular end diastolic pressure. After successful bypass surgery, supine bicycle exercise was performed without angina, with a normal increase in stroke work index, and with less of a rise in left ventricular end diastolic pressure. Five of the six patients could exercise to three times the preoperative work load without symptoms and with improvement in the above parameters of left ventricular performance.

A large population of patients with left main coronary stenosis followed on medical therapy is not available. Three of nine unoperated patients reported by Lavine et al. died within one month of coronary arteriography. In another group of 10 patients with 50% or greater left main coronary stenosis, who did not have surgery, there was a 50% mortality with an average follow-up of 25 months. From these small series and the clinical impression of most investigators, the long-term outlook for patients with severe left main coronary stenosis on medical treatment alone is not good. On the other hand, there have been 27 surgical survivors, combined from two previous studies, followed from five to 18 months with no late deaths. In our series, 50 patients survived coronary bypass surgery and 48 patients (96%) are alive from 12 to 36 months postoperatively with an average follow-up interval of 24.5 months. Furthermore, all but three of the survivors are improved clinically and 76% are asymptomatic from a cardiac standpoint. To date, these long-term survival statistics would appear to indicate a favorable result from surgery in this severely symptomatic and unstable population of patients with coronary artery disease.

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