Saphenous Vein Coronary Artery Bypass in Patients with “Preinfarction Angina”

By D. Craig Miller, M.D., David S. Cannom, M.D., Thomas J. Fogarty, M.D., John S. Schroeder, M.D., Pat O. Daily, M.D., and Donald C. Harrison, M.D.

SUMMARY
Among the first 400 patients undergoing saphenous vein coronary artery bypass at Stanford Medical Center, 67 (18%) met criteria for “preinfarction angina.” Angina was alleviated and possible myocardial infarction was prevented utilizing these surgical techniques. The overall operative mortality rate in the preinfarction angina patients was 10.4%, which contrasted strikingly with a 1.5% operative mortality for elective coronary artery bypass at Stanford. Of the seven operative deaths resulted from myocardial infarction, two of which were related to technical factors. Operative mortality appeared to be related to degree of preoperative congestive heart failure and hypotension, pump time, sex, and number of atherosclerosis risk factors present. Fifty-two of the 60 patients leaving the hospital (87%) received good symptomatic benefit from surgery, including no late infarction, over a 6.8 month mean follow-up period. The late death rate was 3.3%, and the late infarction rate was 10% during the follow-up period. Angina can be alleviated and impending myocardial infarction may be prevented with aggressive surgical intervention.

Additional Indexing Words:
Coronary disease Myocardial infarction Coronary angiography
Angina pectoris

Since 1967, aortocoronary saphenous vein bypass has been utilized widely for the surgical treatment of patients suffering from ischemic heart disease.1-3 The predominant surgical indication for this procedure has been angina pectoris; however, saphenous vein bypass has also been employed with varying degrees of success in patients with “preinfarction angina,” acute myocardial infarction, postinfarction angina, congestive heart failure, ventricular tachyarrhythmias, and those in cardiogenic shock.6-21

Although the syndrome of preinfarction angina has different definitions in various medical centers, we have established standardized criteria and have applied them in patients referred for diagnosis and treatment of atherosclerotic coronary arterial disease during the past 27 months.

Among the first 400 patients to receive bypass grafts at Stanford Medical Center, 18% (67 patients) had preinfarction angina, as defined below, and underwent operation on an emergency basis to treat refractory angina and to attempt to prevent myocardial infarction with its ominous complications. The results in these 67 patients are described in this report.

Methods and Materials

Definitions
The symptomatology of ischemic heart disease encompasses a spectrum of clinical syndromes. Clearly, there is a transitional stage which represents a precarious state of imbalance between myocardial oxygen supply and metabolic demand. However, in many cases, it is difficult to differentiate clinically between myocardial ischemia and actual cell necrosis. Even sophisticated histochemical and electron microscopic techniques reveal an intermediate zone.22-27 This transitional state is thought to correlate with the older clinical term, acute coronary insufficiency, but is also known as unstable angina, preinfarction angina, intermediate syndrome, impending myocardial infarction, and status anginosus. Whether this clinical syndrome corresponds with Edwards’ histologic “twilight zone”28 is indeed problematic. It is possible to categorize distinctly by the following four criteria a
subpopulation of this general group. Although others avoid the specific designation “preinfarction angina” without knowledge of the future, we have chosen to use it to emphasize the serious nature of the illness:

1. These patients have severe, unrelenting anginal pain, which occurs at rest without known precipitating factors, lasts longer than 15 minutes, is refractory to nitroglycerin, and usually requires narcotics for relief.

2. Electrocardiographic ST-T changes of myocardial ischemia are usually present without Q-wave patterns of infarction. The changes are usually transient and occur during pain.

3. In addition, serum CPK, SCOT, and LDH are characteristically not elevated to levels diagnostic of myocardial infarction.

4. Selective coronary angiography demonstrates 70% or greater narrowing of one or more of the three major coronary arteries. While this criterion does not distinguish patients with “preinfarction” from other patients with coronary artery disease, it is absolutely required for the patients with clinical states outlined above.

This classification of “preinfarction angina” is a modification of Favaloro’s type I acute coronary insufficiency, and represents a group of patients who are at risk for acute myocardial infarction and its intrinsic mortality and morbidity.$^1$ It should be emphasized that this subgroup of patients with preinfarction angina may represent a more severe degree of occlusive coronary artery disease. The above definition specifically excludes those patients with a crescendo exertional anginal pattern, who were operated upon at an earlier, and possibly less critical, stage of their disease.

**Series Profile**

Between October, 1968 and January, 1973, a group of 57 patients met our criteria for preinfarction angina. Eight of these patients were found to constitute a different subpopulation (vide infra); therefore, they were analyzed as a discrete subgroup in this study. Six of these eight had postinfarction angina and were in danger of extending their infarctions; the other two patients presented with fulminant, intractable congestive heart failure compounding their preinfarction angina.

Fifty-two men and 15 women were operated upon; the average age was 51 and ranged from 35 to 71 years (table 1). The average length of known heart disease preoperatively was 4.6 years. Twenty-three (34%) of the 67 patients had had heart disease for less than 1 year, and their preinfarction angina represented angina de novo in most cases. For the entire series of patients, the average number of previous myocardial infarctions was 1.1; 31 had not experienced any and 20 had had one. The mean length of time between the most recent myocardial infarction and operation for those who had had a previous infarction was 25.4 months. Sixty-one patients met generally accepted criteria for two or more of the clinically recognized atherosclerosis risk factors—(1) elevated cholesterol of greater than 280 mg/%; (2) hypertension, with diastolic pressure at least 100 mm Hg; (3) family history of early coronary disease; (4) diabetes mellitus, with abnormal 2-hour postprandial blood sugars; (5) obesity of more than 15% over ideal weight; and heavy smoking—with an average of 2.9 risk factors per patient.

Forty-nine patients had no symptoms of congestive heart failure, and their left ventricular end-diastolic pressures were less than 12 mmHg; 16 had clinical symptoms of moderate heart failure preoperatively, but LVEDP of less than 20 mmHg, and two were in fulminant congestive heart failure, with LVEDP greater than 30 mmHg. Seven patients required vasopressors to support their blood pressure preoperatively. Only four patients had normal resting and treadmill exercise preoperative electrocardiograms, while nine had a normal resting electrocardiogram with a positive treadmill EKG. Forty-two

<table>
<thead>
<tr>
<th>Table 1</th>
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<tr>
<td><strong>Patient Series Profile in Detail</strong></td>
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<td>Group:</td>
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<td>Age (yr):</td>
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<td></td>
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<td>Duration of heart disease (yr):</td>
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<td>No. of MI:</td>
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<td>CHF (mm Hg):</td>
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<tr>
<td>Angiographic coronary disease (no. vessels):</td>
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<td>Bypass grafts placed (no.):</td>
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<td>Angiographic left ventricular status:</td>
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</table>

Abbreviations: M = male; F = female; CHF = congestive heart failure.
patients had new ST-T changes of ischemia with or without the characteristic changes of old infarction. An additional twelve patients, in addition to new ischemic changes, had more severe changes, including varying degrees of A-V block and ventricular arrhythmias.

All 67 patients had preoperative selective coronary arteriography and left ventricular angiography. The angiograms of all patients revealed 70% or greater occlusion of one or more major coronary arteries; in 10 patients, there was involvement of only one vessel, two vessels in 31 patients, and in 26, all three vessels were involved. The functional status of the left ventricle by angiography was considered to be normal in 41 patients. However, various degrees of ventricular asynergy were noted in the other 26 patients; five evidenced isolated asynchrony, 16 additionally demonstrated asynergy or akinesia, and five showed definite dyskinesia, which was interpreted to represent a ventricular aneurysm. Moreover, moderate mitral insufficiency was documented by left ventricular angiography in four patients.

The previously designated subgroup of eight postinfarction patients was judged on the basis of 16 preoperative parameters to represent a distinct subpopulation (P < 0.01 by both Student’s t test and the nonparametric Mann-Whitney U-test). All of the six postinfarction angina patient were experiencing severe angina and/or were being treated intensively for ventricular arrhythmias and intractable pain. One of the patients in fulminating congestive failure was considered by some observers to be a transplant candidate; the other patient with severe heart failure had had a left ventricular aneurysm resected 4 years previously.

**Operative Technic**

The operative technic utilized in this series was essentially the same for all patients. A Bentley bubble oxygenator was primed with whole blood diluted with lactated Ringer's solution, and a Pemco roller pump was employed. Moderate hypothermia (32.0°-33.0°C) was utilized in nearly all patients, as well as electric fibrillation of the heart. In general, an effort was made not to cross-clamp the aorta for extended periods of time. This was accomplished by isolating the appropriate coronary artery between encircling Silastic tapes. Normally, the periods of cross-clamping were limited to less than 20 min, and therefore no local hypothermia was used. In the majority of patients left ventricular venting was performed. The suturing technic was the same in all patients: all anastomoses were carried out with continuous 6-0 Ethiflex or 6-0 Tevdek. An aortic button was always excised at the proximal anastomotic site. Gas endarterectomy or dissection endarterectomy utilizing small probes and/or a small (no. 2 French) Fogarty arterial embolectomy catheter was performed.

The mean pump time was 108 min per patient, and ranged from 32 to 300 min. Excluding one agonal case where the patient could not be weaned off cardiopulmonary bypass, the average was 57 min per graft.

Twenty-one patients received only one saphenous vein graft, 39 received two, five received three, and two patients had quadruple bypass procedures. Seventeen distal right coronary artery endarterectomies were performed in conjunction with grafts, and an additional five patients had total right gas endarterectomy without having a graft performed. Two patients had left ventricular aneurysms resected in addition to their vein grafts.

**Results**

The mean postoperative follow-up period has been 6.8 months and ranged from 1 to 17 months. Follow-up was obtained on all patients.

There were five hospital deaths in the 59 patients operated upon for uncomplicated preinfarction angina, which represents an 8.5% operative mortality rate (tables 2 and 3). This contrasts sharply with our elective coronary artery bypass mortality rate of 1.5% in more than 500 patients. There were seven deaths in the total group of 67 patients, which gave an overall operative mortality rate of 10.4%. Of the two deaths in the complicated preinfarction subgroup, one was the patient who was considered a transplant candidate, and the other was a postinfarction angina patient. Mortality was not related to age, number of grafts, years of heart disease, number of prior myocardial infarctions, proximity of last myocardial infarction, valve dysfunction, severity of ECG changes, number of vessels angiographically diseased, nor left ventricular asynergy. There was, however, a significant statistical relation (P < 0.05) to degree of congestive heart failure, degree of shock, pump time, sex, and number of atherosclerosis risk factors.

Six of the seven operative deaths were due to intraoperative, or immediately postoperative massive myocardial infarctions; two of these were considered to be due to technical factors related to coronary artery endarterectomy.

Gas endarterectomy had been performed in four of the six patients who died of infarctions (table 2). One additional patient sustained cardiac arrest during induction of anesthesia. Of those infarctions not related to endarterectomy or other technical factors, all were associated with acutely thrombosed grafts at postmortem. The seventh death was caused by an intravascular consumption coagulopathy associated with massive hemolysis which developed intraoperatively.

Significant operative morbidity was observed and treated in eight patients (12%); there were two cases which necessitated repeat thoracotomy for control of hemorrhage, four cases of pulmonary

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*Medidyne Corporation, Sun Prairie, Wisconsin.
embolism, and one case each of pulmonary edema and pneumonia.

Fifty-two of the 60 patients (87%) who left the hospital have exhibited significant symptomatic improvement in their anginal pattern over their basal preoperative status; 47 of these 60 patients (78.3%) have enjoyed excellent benefit from operative intervention defined by complete and long-lived abolition of angina, resolution of any signs of congestive heart failure, and return to full-time employment. No patient was observed to have more severe angina postoperatively than preoperatively. There have been only two late deaths (table 4), one which occurred suddenly 3 months after operation in a 53-year-old man, who had had good symptomatic benefit from surgery. No autopsy was performed, and myocardial infarction with ventricular fibrillation was the presumptive cause of death. The second death occurred in one of the patients with fulminant failure who had experienced no operative benefit.

There has been a total of nine diagnosed postoperative myocardial infarctions; three were associated with hospital deaths and have been described above, and a fourth is the presumptive case in one of the late deaths (table 5). Six have occurred more than 30 days postoperatively, giving a late infarction rate of 10%. Of these six, five occurred within 6 months, and the sixth at 16 months. As outlined above, only one presumed infarction was fatal; the other five have been uncomplicated.

Nineteen patients have now been restudied angiographically after operation; 11 had early (usually 1 week) studies, 13 had late (average 8.8 months) studies, and five patients have had both early and late studies. Only one graft of the 18 studied early was occluded. Ten of the 17 initially open grafts have subsequently been restudied for a second time; all of these 10 grafts were documented again to be widely patent.

Twenty-four grafts were studied late; six were closed, which yields a late patency rate of 75% at an average of 8.8 months after operation. This figure is less than that documented in our larger series of elective bypass grafts, where 82% have been patent (Alderman EL: Personal communication). Only one patient studied late demonstrated occlusion of the total number of grafts placed, two in this patient's case. However, a concurrently performed distal right endarterectomy remained widely open, and this patient is currently only minimally symptomatic and has not sustained an infarction.

### Table 2

**Causes of Operative Deaths**

<table>
<thead>
<tr>
<th>Group</th>
<th>Pt</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>Grafts (no.)</th>
<th>Endarterectomy</th>
<th>Cause of death</th>
<th>Graft status at postmortem</th>
</tr>
</thead>
<tbody>
<tr>
<td>PIA</td>
<td>HK</td>
<td>45</td>
<td>M</td>
<td>2</td>
<td>R</td>
<td>Postop MI with V Fib</td>
<td>Both closed</td>
</tr>
<tr>
<td>PIA</td>
<td>PM</td>
<td>49</td>
<td>F</td>
<td>1</td>
<td>R</td>
<td>Technical intraop MI</td>
<td>Patent</td>
</tr>
<tr>
<td>PIA</td>
<td>AL</td>
<td>51</td>
<td>M</td>
<td>4</td>
<td>—</td>
<td>DIC intraop</td>
<td>All 4 patent</td>
</tr>
<tr>
<td>PIA</td>
<td>BF</td>
<td>49</td>
<td>F</td>
<td>2</td>
<td>—</td>
<td>Postop MI with V Fib</td>
<td>No autopsy</td>
</tr>
<tr>
<td>PIA</td>
<td>SL</td>
<td>45</td>
<td>F</td>
<td>2</td>
<td>R</td>
<td>Anesthetic induction MI</td>
<td>Both closed</td>
</tr>
<tr>
<td>Postinfarction angina</td>
<td>JC</td>
<td>53</td>
<td>M</td>
<td>2</td>
<td>R</td>
<td>Technical-intraop MI</td>
<td>No autopsy</td>
</tr>
<tr>
<td>Severe failure + PIA</td>
<td>FS</td>
<td>61</td>
<td>M</td>
<td>1</td>
<td>—</td>
<td>Postop MI with V Fib</td>
<td>Closed</td>
</tr>
</tbody>
</table>

Abbreviations: V Fib = ventricular fibrillation; DIC = disseminated intravascular coagulation; PIA = preinfarction angina; R = right; intraop = intraoperatively.

### Table 3

**Early Operative Death Rates and Late Death Rates by Clinical Group**

<table>
<thead>
<tr>
<th>Group</th>
<th>Pt (no.)</th>
<th>Operative deaths (no.)</th>
<th>Operative mortality rate (%)</th>
<th>Pt surviving &gt;30 days (no.)</th>
<th>Late deaths (no.)</th>
<th>Late mortality rate (%)</th>
<th>Mean time of death postop (mo.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PIA</td>
<td>59</td>
<td>5</td>
<td>8.5</td>
<td>54</td>
<td>1</td>
<td>1.9</td>
<td>4</td>
</tr>
<tr>
<td>Postinfarction angina</td>
<td>6</td>
<td>1</td>
<td>16.7</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Severe failure + PIA</td>
<td>2</td>
<td>1</td>
<td>50.0</td>
<td>1</td>
<td>1</td>
<td>100.0</td>
<td>8</td>
</tr>
<tr>
<td>Total</td>
<td>67</td>
<td>7</td>
<td>10.4</td>
<td>60</td>
<td>2</td>
<td>3.3</td>
<td>6</td>
</tr>
</tbody>
</table>

Abbreviations: PIA = preinfarction angina.

*Circulation, Volume XLVII, February 1973*
Table 4

Causes of Late Deaths

<table>
<thead>
<tr>
<th>Group</th>
<th>Pt</th>
<th>Age (yr)</th>
<th>sex</th>
<th>Gifts (no.)</th>
<th>Endarterectomy</th>
<th>Clinical symptomatic benefit</th>
<th>Postop (mo.)</th>
<th>Cause of death</th>
<th>Graft status at postmortem</th>
</tr>
</thead>
<tbody>
<tr>
<td>PIA</td>
<td>HB</td>
<td>52</td>
<td>M</td>
<td>2</td>
<td>No</td>
<td>Good</td>
<td>4</td>
<td>Sudden-presumed MI</td>
<td>No autopsy</td>
</tr>
<tr>
<td>Failure + PIA</td>
<td>JW</td>
<td>50</td>
<td>M</td>
<td>1</td>
<td>No</td>
<td>None</td>
<td>8</td>
<td>CHF, pulmonary edema</td>
<td>Closed*</td>
</tr>
</tbody>
</table>

Abbreviation: PIA = preinfarction angina.

*Graft documented by angiography to be closed 1 month postop.

Of the total 42 individual grafts reinjected, seven were closed (four LADs and three in combination with RCA endarterectomy). Only two patients have been restudied after late infarctions; two of the three grafts which had been placed were patent, but diffuse progression of the coronary artery disease was evidenced in both cases.

Discussion

A large number of clinical reports dealing with coronary artery bypass for preinfarction angina have recently been published.1-17 Most series have been too small to enable one to reach any firm conclusions. Until current well-constructed, double-blind prospective studies are completed, the true natural history of the preinfarction syndrome will remain unknown. We believe that this series represents a homogeneous subpopulation of patients with coronary artery disease which can be validly termed “preinfarction angina.”

In various reports, it has been shown that men with stable angina pectoris are exposed to a yearly mortality of between 5 and 9%, and that more than one out of four can be expected to suffer a myocardial infarct within 5 years.30-32 The age of the patients, the severity of the disease, and other health factors, account for the various infarction and death rates. The prognosis for those with an unstable angina picture is known to be worse.33, 34 In some studies, between 22 and 50% of these patients progress within 3 months to infarction, with an associated mortality of 30%.35, 36 Anticoagulation in these patients still exposes them to an infarction rate of between 11 and 33%.37-39 The recent observations of DeSanctis and colleagues, which are the most optimistic for these patients with unstable angina, show a mortality rate of 14%40 during the first follow-up year.

Those acute myocardial infarction patients who are rapidly admitted to a modern Coronary Care Unit are still subject to a mortality rate of approximately 20% within 30 days. For those who survive their acute infarction, long-term disability is still present in 10-15%.

In view of our experience, we believe that early study and aggressive emergency surgical intervention is feasible for patients with preinfarction angina. The therapeutic goal is the relief of angina pectoris, as well as the prevention of infarction and preservation of the functional integrity of the left ventricle. It is interesting to note that, despite our aggressive approach to preinfarction angina at Stanford, seven preinfarction patients here have died of massive infarction before surgical intervention could be carried out.

In this series of 59 patients with uncomplicated preinfarction angina, the operative mortality was 8.5%, and in the overall group of 67 was 10.4%. This contrasts with rates of 0-19% reported in other large series.6-11 The wide variation in operative mortality reported for patients with this syndrome relates in part to the type of patients submitted for surgery. Clearly, the results show that in those patients with single-vessel disease and no prior myocardial infarction or congestive heart failure, there is a much smaller surgical risk than in those with three-vessel disease and one or more prior myocardial infarctions. In order to obtain a clear prognosis for saphenous vein bypass surgery, large groups of patients who can easily be divided into the various subcategories must be accumulated and analyzed. While the mortality from coronary arteriography is generally low, this must also be added to surgical mortality for an overall assessment of the procedure. In addition, we have shown that coronary angiography in these critical patients is relatively safe, and that their precarious status contributes little or no added risk to the usual published figures of between 0.1 and 1.0%.7, 8, 15, 17, 41

Published reports have stated that emergency revascularization “in the properly selected patient,” carries no additional operative risk over that of elective bypass.8 Our total experience and that of Effler’s group7 are at variance with this point.
Elective bypass at Stanford has carried a risk of 1.5% mortality, whereas that for preinfarction angina was 10.4%. This differential between operative mortality is highly significant ($P = 0.014$ by Fisher's exact test).

The six patients with early postinfarction angina do not constitute a large enough group to support broad conclusions, since others have demonstrated a higher mortality in this group. One of these patients died of a technically related intraoperative myocardial infarction. The five surviving patients have experienced excellent benefit from surgery, and none have sustained early or late postoperative infarction nor developed any congestive heart failure. Further surgical trials directed toward early intervention, with the postulate that border tissue to the infarction which is potentially viable can be salvaged, appear indicated in a controlled protocol.

Our experience would support the contemporary view that revascularization is fruitless in those patients with severe chronic congestive heart failure who possess insufficient myocardial reserve. However, a sensitive, specific and objective discriminant function which would preoperatively identify such patients is only now being formalized by us and others.

Although long-term and statistically valid actuarial data regarding the effects of coronary revascularization for preinfarction angina, and the results of randomized, controlled studies, will not be available for several years, we suggest these tentative conclusions based on our 27-month experience:

1. A distinct subset of unstable angina patients exists which can be identified clinically, and validly termed "preinfarction."

2. Emergency coronary angiography and saphenous vein coronary bypass are feasible in this group with an acceptable morbidity and mortality.

3. Emergency bypass clearly alleviates angina in a majority of patients and may prevent acute myocardial infarction.

4. Although endarterectomy transforms inoperable cases into operable ones, it produces significant added risk in terms of acute myocardial infarction.

**Acknowledgment**

We wish to acknowledge the excellent support by, and accessibility of, the Stanford Medical Center Computation Facility (ACME), whose computers and services were utilized for data acquisition and biostatistical analysis.
Additional thanks are due the medical and surgical house staff at Stanford University Hospital for the excellent care they gave to these patients.

References


Circulation, Volume XLVII, February 1975
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Circulation. 1973;47:234-241
doi: 10.1161/01.CIR.47.2.234

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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