Perioperative Myocardial Infarction: Late Clinical Course After Coronary Artery Bypass Surgery

RICHARD J. GRAY, M.D., JACK M. MATLOFF, M.D., CAROLYN M. CONKLIN, R.N., WILLIAM GANZ, M.D., YZHAR CHARUZI, M.D., RALPH WOLFSTEIN, M.D., AND H.J.C. SWAN, M.D., PH.D.

SUMMARY The effects of perioperative myocardial infarction (MI) on long-term survival and symptomatic status after coronary bypass surgery was assessed by a 64.9-month follow-up of the survivors (225) of all isolated coronary bypass surgery (227) performed at our institution from November 1975 to July 1976. Patients were separated into three groups: group 1 (111 patients) showed no postoperative ECG changes; group 2 (31 patients) showed appearance and persistence of new or enlarged Q waves with localized ST elevation; and group 3 (83 patients) showed less specific ECG changes. Group 2 had greater technetium pyrophosphate scan positivity (eight of 19 vs one of 35, \( p < 0.0005 \)) and higher peak MB-CK activity (83 ± 20 vs 20 ± 3 IU/L (mean ± SEM) \( p < 0.01 \)) than group 1. Using the ECG criteria of group 2, the incidence of perioperative MI was 13.7% (31 of 227 patients).

Groups 1 and 2, compared according to age, prior infarction, number of diseased vessels, left main stenosis, coronary collaterals, left ventricular ejection fraction and number of grafts inserted, were not significantly different. However, both ischemic (aortic cross-clamp) time and total pump time were greater in group 2 than in group 1 (65 ± 3 vs 51 ± 2 minutes and 166 ± 7 vs 132 ± 3 minutes, respectively, \( p < 0.05 \)).

There were no perioperative (30-day) deaths in group 1, whereas group 2 had a perioperative mortality rate of 3.2% (one of 31). The 5-year survival rates of group 1 (94.3%), group 2 (96.8%) and group 3 (91.1%) were not significantly different. Late perioperative status regarding relief of angina, dyspnea, level of physical activity, and use of cardiac medications were not different between the groups. In all patients and in those age 55 years or younger, work status was not different.

Although perioperative MI may be associated with a higher operative mortality, late survival and cardiac status were not affected by it in 5 years of follow-up.

THE GOALS of therapy for coronary atherosclerosis include relief of angina pectoris, modification of the incidence of myocardial infarction, protection against sudden death and increased longevity. Considerable debate has centered on the relative merits of medical and surgical therapy in achieving these goals. The occurrence of perioperative myocardial infarction has been cited as a significant limitation to surgical therapy.

This attitude has largely been influenced by the long-term result of naturally occurring myocardial infarction, which is associated with serious morbidity and mortality, especially in subsets of patients with ventricular ectopy.\(^1\)\(^-\)\(^3\) Further, variable reports of the incidence and significance (mortality) of perioperative myocardial infarction in regard to early and intermediate implications have added to the confusion over this issue. Some of these differences have been an expression of the variable criteria used to make the diagnosis. Recent reports have focused on the relative diagnostic merits of electrocardiography, quantitative MB-CK release and technetium pyrophosphate scintigraphy.\(^4\)\(^-\)\(^7\)

To test the hypothesis that perioperative myocardial infarction may adversely affect the outcome of coronary artery bypass surgery, we performed a long-term follow-up study. Electrocardiographic, enzymatic and scintigraphic criteria were used to diagnose perioperative myocardial infarction.

Patients and Methods

From November 1975 to July 1976, 227 patients (197 male and 30 female) had isolated coronary artery bypass graft surgery and form the basis for this study. The mean age of this group was 57 years. Based on preoperative historical and ECG findings, 104 (46%) had evidence of previous (more than 2 weeks earlier) myocardial infarction. Coronary arteriography revealed significant coronary disease (50% or greater diameter reduction) in 2.4 vessels per patient; 24 patients (11%) had left main stenosis. The mean Friessinger coronary score (maximum score of 15 points represents total occlusion of all three major vessels) was 11 for our patients.\(^8\) The mean ejection fraction calculated from the right anterior oblique ventriculogram was 62%.

Anesthesia was induced and maintained using i.v. morphine sulfate and diazepam. Supplementation with a mixture of nitrous oxide (50%) and oxygen (50%) was occasionally used. Nitroprusside by i.v. infusion and small doses of i.v. propranolol (0.5–2.0 mg) were used to blunt the hypertension and tachycardia occasionally seen with endotracheal intubation and sternotomy.

The surgical technique at that time included cardiopulmonary bypass with a bubble oxygenator, hemodilution and intermittent aortic cross-clamping, with mild-to-moderate systemic hypothermia. The coldest
temperature reached varied from 28° to 32°C. No chemical cardioplegia was used. All distal anastomoses were done using aortic cross-clamping on cardiopulmonary bypass; proximal anastomoses were done with a side-gripping forceps. A mean of 3.1 grafts per patient was inserted. The mean cardiopulmonary bypass and total ischemic times were 139 and 57 minutes, respectively. Two patients died because they could not be weaned from cardiopulmonary bypass.

Three independent observers unfamiliar with the patient's clinical status compared postoperative ECGs (for 10.6 ± 3.8 days, mean ± sd) and assigned them to one of three categories based upon ECG criteria to be described below. Differences in interpretation were resolved by consensus. Each ECG was evaluated based upon specific features thought to represent myocardial infarction. Twenty-eight of 31 abnormalities (90%) first appeared within 24 hours of surgery; but those appearing at any time during the postoperative hospitalization were included. Group 1 consisted of 111 patients who had unchanged postoperative ECGs and were considered to have no evidence of perioperative myocardial infarction. Group 2 consisted of 31 patients who had persistent, pathologic, new or enlarged Q waves with localized ST elevation (≥ 1 mm). Group 3 consisted of patients with persistent pathologic Q waves but without ST elevation (22 patients), patients with only transient Q-wave development or enlargement without ST elevation (17 patients), and patients with isolated nonspecific ST- and T-wave changes or localized diminished R wave height (44 patients). Because our intention was to compare patients who had more traditional ECG signs of perioperative myocardial infarction with those whose ECGs were normal, we expected that certain patients with equivocal criteria or some with subendocardial infarction would be assigned to group 3.

Six patients had postoperative left bundle branch block. In three in whom it was present before surgery, it was associated with no further ECG changes or enzyme abnormalities; these patients were assigned to group 1. Three patients had new left bundle branch block. In two it was transient (< 24 hours) and allowed traditional ECG evaluation; one of these two patients was assigned to group 2 and the other to group 3. The remaining patient developed asymptomatic left bundle branch block 5 days postoperatively, but before that he had been assigned to group 3.

Serial MB-CK data obtained 0, 8, 16, 24 and 48 hours after surgery was available in 183 patients. Some data were missing because of an oversight in obtaining properly timed samples or misplacement of laboratory results. A mean peak value within 16 hours is reported for each ECG group (mean ± SEM). To demonstrate which of the ECG groups may be different from group 1 and thus represent perioperative myocardial infarction, statistical comparison of peak 16-hour postoperative MB-CK was performed using the Kruskall-Wallis analysis of variance9 (table 1). Patients in group 2 had the highest MB-CK values, which were statistically different from group 1 (p < 0.05), but not from group 3 (p < 0.09).

Postoperative technetium pyrophosphate scintigraphy was performed in 97 patients using multiple-view images obtained 1–2 hours after the injection of 15 mCi of technetium-99m pyrophosphate. We obtained as many pyrophosphate scintigrams as possible; but this study was initiated when such studies were not available on a portable basis. Consequently, scans were not obtained unless the patient was stable enough to leave the intensive care area for the required time. This often necessitated waiting beyond the optimal time for imaging. The results were considered positive when uptake was interpreted as discrete and of 2 + or greater intensity. The incidence of scan positivity in group 1 was compared with that in each of the other ECG groups. This comparison, done with a Fisher exact test,10 was used to determine which patients deviate from the normal group, further establishing a group with unequivocal perioperative myocardial infarction (table 2). Group 2 had the highest incidence, statistically different from group 1 (p < 0.0005), but not from group 3 (p = 0.281).

The ECG criteria in group 2 (persistent, pathologic, new or enlarged Q waves with localized ST elevation) are similar to those used by others.11 Based on these criteria and strengthened by the correlation with MB-CK and technetium pyrophosphate scan data, we considered only those 31 patients in group 2 to have sustained a definite perioperative myocardial infarction. All such patients had either a positive scan or peak MB-CK of > 40 IU/l in addition to the described ECG criteria. In our clinical experience and in that of others,5 a peak MB-CK of 40 IU/l or greater correlates well with other indicators of perioperative myocardial infarction. In this report, these patients will be contrasted repeatedly to those in groups 1 and 3 to highlight any differences between the group with the definite perioperative myocardial infarction, the normal group and all patients with less certain electrocardiographic findings (group 3).

<table>
<thead>
<tr>
<th>Group</th>
<th>Incidence of positivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1/35 (3%)</td>
</tr>
<tr>
<td>2</td>
<td>8/19 (42%)*</td>
</tr>
<tr>
<td>3</td>
<td>7/30 (23%)†</td>
</tr>
</tbody>
</table>

*p < 0.0005 vs group 1.
†p = 0.281 vs group 1.
Long-term follow-up was completed on all 225 survivors of surgery and was obtained through telephone interview of the patient. Data on postoperative treadmill or angiographic studies were not available.

Results

There were two operative deaths (0.9%) in the entire cohort. Since these patients had no postoperative ECGs, they could not be classified into a group, and the remainder of the study involved the 225 surgical survivors.

The contribution of age, presence of previous myocardial infarction, number of diseased coronary vessels, Friesinger coronary score, left main disease, coronary collateral formation, preoperative ejection fraction, number of grafts inserted, and the number of postoperative hospital days are shown in Table 3. Comparing between groups 1, 2 and 3 show that none of these variables had any significant relationship to perioperative myocardial infarction. Total cardiopulmonary bypass time and total ischemic time (aortic cross-clamp time), however, were significantly longer in group 2 than group 1, 166 ± 7 vs 132 ± 3 minutes and 65 ± 3 vs 51 ± 2 minutes (p < 0.05).

The 30-day mortality rate for the total group was four of 227 (1.8%), including the two surgical deaths. One patient in group 2 (3.2%) died 5 days postoperatively due to cardiac arrest from which he could not be resuscitated. One patient in group 3 (1.2%) died 10 days postoperatively from severe neurologic sequelae of sudden massive postoperative hemorrhage. Of the 31 patients in group 2, the infarction was anterior (including anteroseptal) in 12 (39%), inferior in 15 (48%) and posterior in four (13%). In six (19%), the perioperative myocardial infarction represented an extension in the same site as a previous myocardial infarction (enlargement of Q waves).

The long-term follow-up extended to 64.9 months (average 59.5 ± 0.2 months). There have been 12 late deaths (six in group 1, none in group 2, and six in group 3). The causes of late death include sudden cardiac death in six (three in group 1 and three in group 3), congestive heart failure in two (one in group 1, one in group 3), cancer in two and hepatitis in two.

Figure 1 illustrates the probability of survival up to 65 months after coronary bypass surgery for group 1 (93.9%), group 2 (96.8%), and group 3 (91.1%). No significant differences between groups can be demonstrated after 5 years of follow-up. There have been no late deaths in the group with perioperative myocardial infarction. The annualized mortality rate of the 225 operative survivors is 1.3%.

Symptomatic outcome is shown in Table 4. Since coronary bypass surgery is expected to alleviate angina (and not traditionally done for relief of dyspnea), patients who continue postoperatively to have angina (unchanged, symptomatic) were included with those whose angina worsened after surgery, whereas those who continue to have dyspnea (unchanged, asymptomatic) are included with those who had no dyspnea before or after surgery (unchanged, asymptomatic). The incidence of angina or dyspnea (and current level of physical activity) is not different between groups 1, 2 and 3.

In groups 1, 2 and 3, respectively, 17%, 23% and 14% of the patients were using nitrates, 31%, 13% and

Table 3. Factors Analyzed for Contribution to Perioperative Myocardial Infarction

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n = 111)</th>
<th>Group 2 (n = 31)</th>
<th>Group 3 (n = 83)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>57</td>
<td>55</td>
<td>57</td>
</tr>
<tr>
<td>Male</td>
<td>89</td>
<td>29</td>
<td>76</td>
</tr>
<tr>
<td>Female</td>
<td>22</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>48%</td>
<td>45%</td>
<td>45%</td>
</tr>
<tr>
<td>No. of diseased vessels</td>
<td>2.3</td>
<td>2.5</td>
<td>2.5</td>
</tr>
<tr>
<td>Friesinger score</td>
<td>10</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>Left main disease</td>
<td>9%</td>
<td>16%</td>
<td>10%</td>
</tr>
<tr>
<td>Coronary collaterals</td>
<td>41%</td>
<td>42%</td>
<td>36%</td>
</tr>
<tr>
<td>Ejection fraction</td>
<td>61%</td>
<td>64%</td>
<td>62%</td>
</tr>
<tr>
<td>No. of grafts/patient</td>
<td>3.1</td>
<td>3.3</td>
<td>3.1</td>
</tr>
<tr>
<td>Days in hospital</td>
<td>12</td>
<td>12</td>
<td>13</td>
</tr>
<tr>
<td>Pump time (minutes)</td>
<td>132 ± 3 *</td>
<td>166 ± 7</td>
<td>138 ± 4.2</td>
</tr>
<tr>
<td>Ischemic time (minutes)</td>
<td>51 ± 2 *</td>
<td>65 ± 3</td>
<td>58 ± 2.2</td>
</tr>
</tbody>
</table>

*p < 0.05 vs group 1.

Table 4. Symptomatic Outcome

<table>
<thead>
<tr>
<th>Current symptoms</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angina pectoris</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Improved</td>
<td>73%</td>
<td>60%</td>
<td>67%</td>
</tr>
<tr>
<td>Unchanged (asymptomatic)</td>
<td>22%</td>
<td>23%</td>
<td>20%</td>
</tr>
<tr>
<td>Worse</td>
<td>5%</td>
<td>17%</td>
<td>13%</td>
</tr>
<tr>
<td>Dyspnea</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Improved</td>
<td>53%</td>
<td>57%</td>
<td>59%</td>
</tr>
<tr>
<td>Unchanged (symptomatic and asymptomatic)</td>
<td>38%</td>
<td>37%</td>
<td>36%</td>
</tr>
<tr>
<td>Worse</td>
<td>9%</td>
<td>7%</td>
<td>5%</td>
</tr>
</tbody>
</table>

*Figures illustrate the probability of survival up to 65 months after coronary bypass surgery for group 1 (93.9%), group 2 (96.8%), and group 3 (91.1%). No significant differences between groups can be demonstrated after 5 years of follow-up. There have been no late deaths in the group with perioperative myocardial infarction. The annualized mortality rate of the 225 operative survivors is 1.3%.*
26% β blockers, 16%, 13% and 17% antiarrhythmic medication, 24%, 23% and 29% diuretics, and 23%, 13% and 13% digoxin. The proportions are not significantly different between the groups.

The employment status of our patients is shown in Table 5. Patients were considered improved if they were working only after surgery; unchanged if they returned to their preoperative work (or were unemployed both before and after surgery); and worsened if working before surgery but currently unemployed. Sixty percent of the patients are employed. No significant differences were found between the proportion of patients in any group in any of these categories. Since patients approaching retirement age might be expected to ask for early retirement after surgery, not necessarily for health reasons, all persons age 55 years or younger (at the time of surgery) were analyzed separately. Again, no significant differences were found between groups in this age category.

Discussion

Because patients were recruited during a relatively short period (9 months) and all consecutive coronary bypass patients were included in the study, major changes in patient selection, surgical technique and postoperative management during the study were minimized. This was apparent from analysis of the clinical variables.

Although the diagnostic criteria for perioperative myocardial infarction may never be uniform, there is agreement that electrocardiography, cardiac-specific enzyme determination and scintigraphy are all useful.

The analysis of this patient cohort began with application of several descriptive ECG criteria to try to define a “normal” postoperative group and a definite infarction group. Then, the enzymatic and scintigraphic characteristics of each group were contrasted statistically. In this manner, group 2 patients were isolated as statistically different from group 1. Since localized ST elevation was required in addition to persistent Q-wave development, we undoubtedly excluded from our perioperative myocardial infarction cohort some patients likely to have been included in other studies.4-6, 12, 13 Group 3 was created for those who had ECG evidence of acute ischemic injury diagnosed by ST- or T-wave abnormalities without Q-wave appearance or enlargement. Some of these patients may have had myocardial necrosis, presumably subendocardial. The separation of this intermediate group was designed to allow another group of patients with singularly diagnostic ECG, enzyme and scintigraphic criteria (group 2) to be contrasted with a selected group of patients with no such abnormalities (group 1).

Specifically, group 3 may well contain patients whose ECG or MB-CR response indicates a small-to-moderate perioperative myocardial infarction, such as with subendocardial necrosis. If these patients were included in group 2, our incidence of perioperative myocardial infarction would increase, but because patients in group 3 may well have smaller amounts of myocardial damage, they would not be representative of patients with signs of clear-cut transmural perioperative myocardial infarction. The need for a separate, intermediate classification of such patients has been recognized.6 Three patients in group 1 had MB-CR > 40 IU/L, but none had positive ECG or scintigraphic findings; similarly, none of the patients in group 3 with abnormal MB-CR had positive scintigraphic results, making it unlikely that any patients in this group have extensive myocardial damage.

In our patients, perioperative transmural myocardial infarction as defined by new or enlarged Q waves with localized ST elevation, carried no additional risk of mortality or morbidity during long-term follow-up, in contrast to naturally occurring myocardial infarction. The electrocardiographic changes in our patients are identical to those of nonsurgical infarction, except that Q waves often mark the appearance of infarction from the beginning with the usual later resolution of ST and T changes. Our long-term survival results are similar to those in other studies with a somewhat shorter period of follow-up.4, 11, 14 The rate of freedom from angina at 64.9 months (95% group 1, 83% group 2, and 87% group 3) is the same with or without a perioperative myocardial infarction. The proportion of our patients who worked after surgery was high and unrelated to the presence or absence of perioperative myocardial infarction even in patients younger than 55 years. These findings are similar to those reported by Fennell and co-workers.6

Although the surgical (30-day) mortality in our perioperative myocardial infarction patients (3.2%) is above that for the entire cohort (1.8%), these figures compare favorably to those reported by others.6, 12 While the operative mortality may be higher, no other factors distinguish the remainder of the postoperative and long-term course with perioperative myocardial infarction, suggesting that the amount of involved myocardium may be quite limited. Support for this assertion is speculative, but several factors should be considered. First, the intraoperative occurrence of most of these events suggests that perioperative myocardial infarction is due not to bypass graft failure.15, 13

### Table 5. Employment Status*

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n = 105)</th>
<th>Group 2 (n = 30)</th>
<th>Group 3 (n = 76)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All ages</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total currently employed</td>
<td>64%</td>
<td>63%</td>
<td>53%</td>
</tr>
<tr>
<td>Improved</td>
<td>12%</td>
<td>10%</td>
<td>12%</td>
</tr>
<tr>
<td>Unchanged</td>
<td>65%</td>
<td>77%</td>
<td>53%</td>
</tr>
<tr>
<td>Worse</td>
<td>23%</td>
<td>13%</td>
<td>35%</td>
</tr>
<tr>
<td>≤ 55 years</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total currently employed</td>
<td>71%</td>
<td>100%</td>
<td>67%</td>
</tr>
<tr>
<td>Improved</td>
<td>4%</td>
<td>0%</td>
<td>8%</td>
</tr>
<tr>
<td>Unchanged</td>
<td>74%</td>
<td>100%</td>
<td>63%</td>
</tr>
<tr>
<td>Worse</td>
<td>22%</td>
<td>0%</td>
<td>29%</td>
</tr>
</tbody>
</table>

*Improved = now working full- or part-time, not employed preoperatively; unchanged = no postoperative change in employment status; worse = employed preoperatively, not employed now.
but to other factors, such as inadequate myocardial preservation in the presence of a low threshold for segmental myocardial ischemia. In this manner, the area affected by the perioperative myocardial infarction participates in any benefits of early reperfusion. Also, residual cardiac and systemic hypothermia may last for several hours after cardiopulmonary bypass and confer some measure of protection to any areas of reversibly damaged myocardium.

An important consideration is that of estimating the actual amount of injured or necrotic myocardium. Although such estimates have been made, further insight into certain of the apparently benign features of perioperative myocardial infarction will come when the areas of injury are quantified in large groups of such patients. One may then be able to establish, for instance, that perioperative myocardial infarction is commonly associated with a small area of necrosis and that other factors tend to exaggerate the resulting level of MB-CK enzyme activity. Such factors might include the presence of good local myocardial perfusion capable of washing out all released MB-CK or other physical and chemical factors that may act to enhance the enzyme activity of CK. Hypocalcemia, hypermagnesemia, hyperglycemia, hemodilution, hypothermia, respiratory alkalosis, anemia and diminished urea levels, all of which are seen during or after cardiopulmonary bypass, should be studied to determine if they affect the chemical activity of MB-CK. Other factors that may decrease the clearance of MB-CK, such as morphine sulfate and pentobarbital, must also be considered.

During surgery, we have found progressively elevated MB-CK levels, beginning from the time of aortic cross-clamping, in patients with and without perioperative infarction. Preceding this release is a uniform finding of myocardial ischemia as evidenced by myocardial lactate release.

Rucker et al. studied release of MB-CK after coronary bypass. They found that for the group mean (normal vs abnormal), the peak MB-CK release occurs immediately after surgery with or without perioperative myocardial infarction. As expected, continued slow release persisted for as long as 36 hours with perioperative myocardial infarction. Thus, MB-CK occurs early such that the peak level is seen within the 16-hour period of our routine sampling.

While the amount of myocardium affected by perioperative myocardial infarction may be small, as a rule, a large infarction can have very serious effects. Presumably, many of the patients with adequate cardiac function preoperatively who die in surgery due to cardiac pump failure have severe myocardial necrosis.

We believe that efforts should continue to evaluate old and develop new methods of myocardial preservation and safer methods of anesthesia. We believe that the widespread use of hypothermic cardioplegia will result in a lower incidence of myocardial damage during myocardial revascularization. Using contemporary myocardial preservation techniques, the incidence of perioperative myocardial infarction may be as low as 6%.

Acknowledgment

The authors gratefully acknowledge the assistance of JoAnn Praise, Elaine Marcus, Helen Schamroth and Lance LaForteza.

References

Perioperative myocardial infarction: late clinical course after coronary artery bypass surgery.

R J Gray, J M Matloff, C M Conklin, W Ganz, Y Charuzi, R Wolfstein and H J Swan

_Circulation_. 1982;66:1185-1189
doi: 10.1161/01.CIR.66.6.1185

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1982 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/66/6/1185.citation

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Circulation_ is online at:
http://circ.ahajournals.org/subscriptions/