Surgical Approach for Patients With Unstable Angina Pectoris: Role of the Response to Initial Medical Therapy and Intraaortic Balloon Pumping in Perioperative Complications After Aortocoronary Bypass Grafting

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The role of the response to initial medical therapy and intraaortic balloon pumping in perioperative complications was evaluated in 194 consecutive patients with unstable angina pectoris who underwent cardiac catheterization and coronary surgery from July 1975 through December 1977. Sixty-four patients (33 percent) responded to medical therapy within 48 hours after the initiation of full medical therapy in the coronary care unit and underwent elective cardiac catheterization and coronary surgery; 130 patients (67 percent) did not respond to medical therapy. Of these 130 patients, 75 (58 percent) received the preoperative assistance of an intraaortic balloon pump and underwent emergency cardiac catheterization and surgery. Fifty-five patients (42 percent) of the medical nonresponders were not treated with an intraaortic pump and underwent emergency cardiac catheterization and surgery. Chi square analysis revealed that the clinical characteristics of the patients in all three groups were similar.

The overall rate of operative mortality was 6.1 percent. Medical responders had no operative mortality, medical nonresponders with intraaortic balloon pumping had an operative mortality rate of 5.3 percent and medical nonresponders without balloon pumping a rate of 14.5 percent. The overall incidence rate of perioperative myocardial infarction was 13 percent; it was 6 percent in medical responders, 6.6 percent in nonresponders with intraaortic balloon pumping and 29 percent in nonresponders without intraaortic balloon pumping. Thus, this study suggests that perioperative complications can be minimized by initial aggressive medical therapy. If this therapy fails, intraaortic balloon counterpulsation can produce a reduction in perioperative complications similar to that produced by medical therapy.

Surgical treatment for patients with unstable angina pectoris continues to be enthusiastically recommended.[1–7] Several investigators[8–11] consider unstable angina an acute emergency requiring immediate cardiac catheterization and surgery for optimal therapeutic results. However, there are no convincing data to support this approach. It is possible that surgical intervention may be more effective and associated with a lower operative mortality rate and a lower incidence rate of perioperative myocardial infarction if it is preceded by a period of intense medical therapy.

This study was undertaken to evaluate (1) the effect of initial medical therapy and delayed semielective surgery on perioperative complications in patients with unstable angina pectoris, and (2) the effect of intraaortic balloon pumping and urgent coronary surgery on patients with unstable angina who fail to respond to medical therapy.

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Materials and Methods

Patients

Cardiac catheterization and coronary arterial bypass grafting were performed in 194 consecutive patients with unstable angina pectoris at Yale-New Haven Hospital from July 1975 through December 1977. These patients were included in the study only after the following criteria for the diagnosis of unstable angina pectoris were satisfied: (1) prolonged typical anginal pain (longer than 20 minutes in duration), (2) typical anginal pain occurring at rest, (3) pain not completely relieved by nitroglycerin, (4) unstable ST-T waves in the electrocardiogram, and (5) failure to document an acute myocardial infarction with serial electrocardiograms and serial enzyme determinations.

Patients responding to medical treatment: After admission to the coronary care unit, all 194 patients were treated medically. The medical management included absolute bed rest, sedation, reassurance and the relief of pain with the administration of narcotic drugs in addition to long- and short-acting nitrates, isosorbide dinitrate, 5 mg sublingually every 3 hours, nitroglycerin tablets sublingually, nitroglycerin ointment, 2 percent (1 to 2 inches [2.5 to 5 cm] every 4 hours) and large oral doses of propranolol.

Sixty-four patients (33 percent) responded to medical therapy within 48 hours after the initiation of full medical therapy in the coronary care unit. All of these patients were free of angina at rest but remained symptomatic with minimal effort. These 64 patients underwent elective cardiac catheterization an average of 12 days (range 6 to 18 days) after admission and elective operation within 2 weeks after cardiac catheterization.

Nonresponders to medical treatment: One hundred thirty patients (67 percent) did not respond to medical therapy and their condition continued to be unstable 48 hours after the initiation of full medical therapy. Of these 130 patients, 75 (58 percent) received intraaortic balloon assistance (Avco Intra-aortic Balloon, Hoffmann-La Roche Inc., Nutley, New Jersey) and underwent emergency cardiac catheterization an average of 2 days (range 1 to 4 days) after the insertion of an intraaortic balloon pump and emergency coronary surgery an average of 2 days (range 0 to 3 days) after cardiac catheterization. Fifty-five of the medical nonresponders (42 percent) did not receive an intraaortic balloon either because the device was not available (48 patients) or because technical difficulties interfered with its placement (7 patients). These 55 patients underwent emergency cardiac catheterization an average of 2.5 days (range 1 to 5 days) after admission and cardiac surgery an average of 2 days (range 0 to 5 days) after cardiac catheterization. Medical therapy was continued up to the day of surgery in medical responders as well as nonresponders. However, in some patients with intraaortic balloon assistance, the total daily dose of propranolol was reduced gradually, and in some patients administration of the drug was completely discontinued before surgery. No recurrence of symptoms was noted in any patient during the withdrawal of propranolol.

Cardiac Catheterization and Coronary Arteriography

These procedures were performed according to standard methods. The single plane right anterior oblique left ventriculogram was analyzed for ejection fraction, regional wall motion and the presence of mitral regurgitation. A coronary arterial lesion of greater than 70 percent luminal obstruction was considered significant. Coronary artery disease was classified as one, two or three vessel disease. Left main coronary artery disease was considered equivalent to two vessel disease.

Intraaortic Balloon Pump

When the intraaortic balloon pump was used, it was introduced through the common femoral artery with an end to side 10 mm Dacron® graft and advanced into the descending thoracic aorta. This procedure was performed under local anesthesia in the surgical intensive care unit. When difficulties were encountered or anticipated, a wire-guided central lumen catheter balloon[12] was introduced under direct fluoroscopy in the cardiac catheterization laboratory. Details of introduction of the balloon and its management have previously been reported.[13] All 75 patients with a preoperative intraaortic balloon used its assistance during the operative procedure up to the time when they were placed on cardiopulmonary bypass. In all 75 patients who received cardiac assistance with an intraaortic balloon pump preoperatively, the balloon was removed within 48 hours after operation.

Coronary Arterial Surgery

Coronary bypass grafts were performed using saphenous vein grafts for the right and left circumflex coronary arteries and, wherever possible, a left internal mammary artery graft was utilized for the left anterior descending coronary artery. A disposable blood oxygenator (Temptrol disposable blood oxygenator, model Q 100, Bentley Laboratories, Inc., Santa Ana, California; or Kolobow disposable membrane oxygenator, Sci-Med., Minneapolis, Minnesota) primed with lactated Ringer's solution was used with moderate hypothermia (28 to 30° C). The left ventricle was vented in all patients by a catheter passed through the right superior pulmonary vein or the ventricular apex into the left ventricular cavity. All blood aspirated into the extracorporeal circuit from the vent or the cardiac suction lines was filtered through a millipore filter before being returned to the oxygenator (Swank-Micro Emboli Filter, Pioneer Filter Co., Beaverton, Oregon). Whole blood was used only if perfusate hematocrit decreased to less than 25 percent. Blood potassium levels were monitored, and additional potassium was added to the oxygenator if the perfusate level decreased to less than 4.0 mEq/liter. When aortocoronary saphenous vein grafts were planned, all proximal anastomoses were constructed with a partially occluding aortic clamp before the institution of cardiopulmonary bypass whenever the patient's condition was stable. Dissection of the left internal mammary artery from the chest wall was accomplished without cardiopulmonary bypass. Distal anastomoses for saphenous vein and internal mammary grafts were performed with the aorta or recipient coronary artery cross-clamped and the heart fibrillating. Each distal anastomosis was probed near its completion to ensure that the anastomotic communication was wider than the grafted coronary artery and hence would not limit blood flow through the system.

Perioperative complications: Myocardial revascularization was considered "incomplete" if grafts were not placed in every diseased coronary branch. Operative mortality was classified as either in-hospital mortality or death up to 6 weeks postoperatively. Perioperative myocardial infarction was diagnosed if serial electrocardiograms revealed evidence of myocardial necrosis within 1 week postoperatively. Serial enzyme determinations were not used as evidence of myocardial infarction because creatinine phosphokinase isoenzyme data were not available in all patients and serum creatinine phosphokinase and glutamic oxaloacetic transaminase levels are elevated by musculoskeletal operative trauma.[14] All patients had a standard 12 lead electrocardiogram recorded

TABLE I

Clinical Characteristics of 194 Patients With Unstable Angina Pectoris

	Patients	
	no.	%
Sex		
Male	154	79
Female	40	21
Previous chronic stable angina	185	95
Remote myocardial infarction	124	64
Congestive heart failure	37	19
Hypertension	68	35
Cardiac enlargement	50	25
Abnormal LVEDP (>12 mm Hg)	89	46
Abnormal LV wall motion	120	62
Abnormal EF (<50%)	84	43
Diseased coronary vessels		
One	22	11
Two	58	30
Three	114	59
LMCD	35	18
Coronary grafts		
One	31	16
Two	84	43
Three or more	79	40
Complete revascularization	89	46

EF = ejection fraction; LMCD = left main coronary artery disease; LV = left ventricular; LVEDP = left ventricular end-diastolic pressure.

TABLE II

Clinical Characteristics of 194 Patients With Unstable Angina Pectoris Classified According to Clinical Groups

	Medical Responders (no.)	Medical Nonresponders With IABP (no.)	Medical Nonresponders Without IABP (no.)	Total (no.)
Sex				
Male	56	50	48	154
Female	17	10	13	40
Previous chronic stable angina	63	60	62	185
Remote myocardial infarction	40	45	39	124
Congestive heart failure	12	14	11	37
Hypertension	19	25	24	68
Cardiac enlargement	17	13	20	50
Abnormal LVEDP (>12 mm Hg)	27	31	31	89
Abnormal LV wall motion	40	37	43	120
Abnormal EF (<50%)	26	28	30	84
Diseased coronary vessels				
One	6	8	8	22
Two	20	18	20	58
Three	35	40	39	114
LMCD	8	14	13	35
Coronary grafts				
One	9	13	9	31
Two	30	25	29	84
Three or more	23	27	29	79
Complete revascularization	27	33	29	89

IABP = intraaortic balloon pumping; other abbreviations as in Table I.

within 24 hours before operation and serial tracings recorded after operation, with the first tracing obtained immediately on arrival in the surgical intensive care unit. The electrocardiographic diagnosis of acute myocardial infarction was based only on the appearance of new pathologic Q waves.[15] The appearance of new intraventricular conduction disorders, increased size of previously present Q waves and S-T segment or T wave changes without new abnormal Q waves were not considered diagnostic of myocardial infarction.

Statistical analysis: A contingency table chi square test was used to examine each of the study factors in relation to the outcome variable (operative mortality or perioperative myocardial infarction). From this analysis the factors associated with each dependent variable could be determined. A difference was considered statistically significant if the probability (P) value was less than 0.05.

Clinical Characteristics

The average age of the patients in this series was 57 years (range 35 to 78); 154 patients (79 percent) were male and 40 (21 percent) female. One hundred eighty-five patients (95 percent) had had chronic stable angina for at least 6 months before inclusion in this study; 124 (64 percent) had evidence of a remote myocardial infarction; 37 (19 percent) had symptoms and signs of congestive heart failure; 68 (35 percent) had hypertension, and 50 (25 percent) had cardiac enlargement on standard chest X-ray film (cardiothoracic ratio greater than 50 percent). The average daily dose of propranolol for the entire group of 194 patients was 380 ± 50 mg (mean ± standard error) after full medical therapy in the coronary care unit. The propranolol dose was rapidly increased until the angina was completely relieved, the patient's resting heart rate was 50 to 55 beats/min or there was clinical evidence that the heart failure could not be controlled with standard therapy.

Eighty-nine patients (46 percent) had abnormal left ventricular end-diastolic pressure (greater than 12 mm Hg); 120 (62 percent) had abnormal left ventricular wall motion in at least one left ventricular segment, and 84 (43 percent) had a depressed ejection fraction (less than 50 percent). Twenty-two patients (11 percent) had one vessel coronary artery disease, 58 (30 percent) two vessel disease, 114 (59 percent) three vessel disease and 35 (18 percent) left main coronary artery disease. The average number of diseased arteries was 2.5 ± 0.7. Thirty-one patients (16 percent) received a single coronary graft, 84 (43 percent) two grafts and 79 (40 percent) three or more grafts. The average number of coronary grafts performed in each patient was 2.4 ± 0.9 (mean ± standard deviation). However, only 89 patients (46 percent) received complete revascularization (Table I). There were no significant differences in clinical, hemodynamic, angiographic and operative factors among medical responders and nonresponders (Table II). However, the daily dose of propranolol was slightly lower in the medical responders (320 ± 40 mg, mean ± standard error) than in the nonresponders (400 ± 80 mg).

Results

Operative mortality: The overall rate of operative mortality for these 194 consecutive patients with unstable angina pectoris was 6.1 percent (12 of 194). There were no deaths among the patients who responded favorably to medical therapy, but the operative mortality rate in patients who did not respond to medical therapy was 9.5 percent (12 of 130); this difference was statistically significant (P <0.05). Medical nonresponders with intraaortic balloon pumping preoperatively had a significantly lower rate of operative mortality (5.3 percent, 4 of 75) than those without balloon pumping

TABLE III

Operative Mortality and Incidence of Perioperative Myocardial Infarction in 194 Patients With Unstable Angina

	no. of Cases	Deaths		Perioperative Myocardial Infarction	
		no.	%	no.	%
Medical responders	64	0	0	4	6
Medical nonresponders	130	12	9.2	21	16
With IABP	75	4	5.3	5	6.6
Without IABP	55	8	14.5	16	29
Overall	194	12	6.1	25	13

IABP = intraaortic balloon pumping.

(14.5 percent, 8 of 55) ($P < 0.05$). However, the operative mortality rate of medical nonresponders with preoperative balloon pumping was higher (5.3 percent, 4 of 75) than the rate of patients who responded to medical therapy (0 percent, 0 of 64), but the difference was not statistically significant (Table III).

Analysis of other probable preoperative or operative risk factors for operative mortality using contingency table chi square analysis revealed that operative mortality rate was not related to clinical, hemodynamic, angiographic or operative factors (age, sex, previous chronic stable angina, remote myocardial infarction, congestive heart failure, hypertension, cardiac enlargement, abnormal left ventricular end-diastolic pressure, abnormal left ventricular wall motion, abnormal left ventricular ejection fraction, number or degree of diseased coronary vessels, number of aortocoronary bypass grafts or completeness of revascularization) in the three groups of patients (medical responders and medical nonresponders with and without intraaortic balloon pumping).

Perioperative myocardial infarction: The overall incidence rate of perioperative myocardial infarction in all patients was 13 percent (25 of 194). The rate in patients who responded to medical therapy was 6 percent (4 of 64) and in nonresponders 16 percent (21 of 130) ($P < 0.05$). Nonresponders with preoperative intraaortic balloon pumping had a significantly lower incidence rate of perioperative myocardial infarction (6.6 percent, 5 of 75) than those without balloon pumping (29 percent, 16 of 55) ($P < 0.001$). The difference in incidence rate of perioperative myocardial infarction in medical responders (6 percent, 4 of 64) and nonresponders with intraaortic balloon pumping (6.6 percent, 5 of 75) was not significant (Table IV).

Analysis of probable risk factors for perioperative myocardial infarction showed that myocardial infarction was not related to any other variable present in each clinical group. The perioperative myocardial infarction was located in the anterior wall in 8 patients, the inferior wall in 14 patients and the anterolateral wall in 3 patients. Electrocardiographic signs of a perioperative myocardial infarction appeared within the first 24 hours postoperatively in 18 patients and within 72 hours postoperatively in all patients studied.

Discussion

Patients were included in this study only if they met rigid diagnostic requirements and if they underwent diagnostic cardiac catheterization and coronary arterial surgery during the same hospital admission. We estimate that the number of patients excluded from the study because they failed to meet our criteria was as large as the number of patients reported on. Our definition of the syndrome of unstable angina corresponds to the one discussed by Hultgren[10] and identified as "type II, or angina at rest, or acute coronary insufficiency." Because of our strict criteria for selection, our patients constitute a relatively homogeneous clinical group.

In this study, the patients were classified into two groups according to their response to medical therapy 48 hours after the initiation of full therapy in the coronary care unit. Thirty-three percent (64 of 194) of the patients with unstable angina responded promptly to medical therapy, but 75 percent (130 of 194) continued to have angina pectoris at rest despite full medical therapy. Previous reports[16–18] have indicated that the condition of some patients with unstable angina pectoris can be controlled effectively with medical therapy.

Operative mortality: The overall rate of operative mortality in this study of patients with unstable angina was 6.1 percent, which is comparable with the rate reported by our group[19] in a previous study as well as the rate reported from several medical centers.[1–6,20] There were no operative deaths among the patients who responded to medical therapy and then underwent elective cardiac catheterization and surgery. Our published retrospective study[19] including patients treated at our institution from January 1974 to July 1975 suggested that the response to medical therapy was one of the factors determining operative mortality. The present prospective study confirms this finding. However, it does not answer the critical question of whether surgery improves the rate of survival or prevents myocardial infarction.

The operative mortality rate in patients whose anginal symptoms were not controlled with medical therapy was 9.2 percent, a rate significantly higher than that of patients responding to medical therapy. However, those patients receiving preoperative intraaortic balloon assistance had a lower operative mortality rate (5.3 percent) than that of patients who did not receive balloon assistance (14.5 percent). An intraaortic balloon pump was inserted in patients who did not respond to medical therapy if an intraaortic balloon pump console was available and if the presence of severe peripheral vascular disease did not totally preclude passage of an intraaortic balloon catheter.

Analysis of the distribution of all probable preoperative and operative risk factors for operative mortality with a contingency table chi square test disclosed no significant differences among the three clinical groups (medical responders and medical nonresponders with and without intraaortic balloon pumping).

Perioperative myocardial infarction: The reported incidence[20,21] of perioperative myocardial in-

farction is sufficiently great to offset the overall results of coronary bypass grafting in patients with unstable angina. The overall incidence rate of perioperative myocardial infarction in this study was 13 percent, a rate similar to that reported from other large medical centers.[20]

Our medical responders had a perioperative myocardial infarction rate of 6 percent, which was significantly lower than the 16 percent rate in medical nonresponders. If medical nonresponders had intraaortic balloon pumping preoperatively, their perioperative myocardial infarction rate was not different from the rate of medical responders. The distribution of all probable risk factors for perioperative myocardial infarction among the three clinical groups was closely comparable according to contingency table chi square analysis. Therefore, we believe that perioperative myocardial infarction in patients with unstable angina undergoing coronary surgery may be significantly minimized with initial successful medical therapy followed by elective cardiac catheterization and surgery. If medical therapy fails, preoperative cardiac assistance with an intraaortic balloon pump may produce a decrease in the rate of perioperative myocardial infarction almost identical to the decrease produced with medical therapy.

Clinical implications: The preliminary results from the national randomized study for unstable angina pectoris[20] indicate that the rates of in-hospital mortality in the medical and surgical groups are almost equal (medical 6 percent and surgical 5 percent). The rate of early incidence of myocardial infarction is higher in the surgical group (because of a perioperative myocardial infarction rate of 17 percent), and the incidence rate of angina pectoris in the late follow-up period is higher in the medical group. Our study is not designed to determine whether medical or surgical therapy is superior for patients with unstable angina pectoris but rather to identify the best approach for patients with angina pectoris for whom surgical therapy is selected.

The following conclusions are the result of our experience in surgically treating a selected group of 194 patients with unstable angina pectoris from July 1975 through December 1977: (1) the condition of a large number of patients with unstable angina pectoris can be controlled with aggressive medical therapy; (2) patients who respond to medical therapy have a low rate of operative mortality and a low incidence rate of perioperative myocardial infarction; and (3) if medical therapy fails to control unstable angina pectoris, intraaortic balloon pumping minimizes the risks of coronary surgery (operative mortality[22] and perioperative infarction).

It is attractive to hypothesize that if the operative mortality rate and the rate of perioperative myocardial infarction are diminished, surgery is the most appropriate therapy for unstable angina pectoris. Although our results demonstrate that the combination of initial aggressive medical therapy and the preoperative insertion of an intraaortic balloon pump decreases the rate of both operative mortality and perioperative myocardial infarction, we cannot conclude from this study that surgical therapy is preferable to medical therapy in patients with unstable angina.

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