CORONARY ARTERY DISEASE is a life-threatening illness with an unpredictable clinical course. The intensity and quality of pain and the incidence of sudden and unexpected death creates fear in both the patient and those, including the physician, responsible for the care. The astute physician realizes that allaying the fear of the patient and his family is as important as the relief of pain. In planning therapy, however, the physician must separate his own fears and uncertainties from those of the patient and the patient’s family.

It is comforting to know that a patient presenting with evidence of an evolving myocardial infarction can, as discussed in the preceding article, be taken to the operating room within 6.5 hours of the onset of pain and expect an operative mortality of only 1.3% and a late mortality of only 2.8%. Furthermore, for reasons which are not clear, the operation may, at least for a while, relieve the pain in 80–90% of the patients.

Many physicians realize that such an activist or aggressive approach to clinical management is often more satisfying to the patient and his family than a passive or more conservative one. When serious complications or even death occur, the activist can say, “We did everything that could have been done.” Rarely, if ever, is he asked, “Was too much done?”

The moment that surgery is considered, decision-making and responsibility become shared. In a litigious society such as ours, sharing of responsibility, to many, is very desirable and comforting.

But the physician who practices both the art and the science of medicine must answer not only the question, “Can you,” but also the question, “Should you?” Therefore, careful evaluation of the preceding manuscript by Phillips et al., describing the use of coronary artery revascularization in the treatment of an evolving myocardial infarction, is appropriate.

For surgery to have a significant role, the operation must be shown to limit and/or reduce infarct size and decrease the overall early morbidity and mortality compared with nonoperative management; it must also be shown, after several years of careful follow-up, to be more effective in postponing premature death and preventing the late complications of coronary artery disease than nonoperative therapy in similar patients.

As indicated by Phillips and his colleagues, there is experimental evidence to suggest that revascularization within 3–4 hours of coronary occlusion may prevent myocardial necrosis and improve the functional state of the left ventricle, both acutely and chronically. However, there is also substantial evidence that reperfusion of ischemic muscle after temporary vascular occlusion (usually 4–6 hours) may cause a hemorrhagic infarct, lead to further deterioration of already compromised function, and contribute to an increase in mortality.

Many of the changes that occur in the myocardium during ischemia have been studied and their progression, as a result of the prolongation and intensification of ischemia, have been described, but the “point of no return,” when the ischemia-induced injury results in irreversible damage, has not been defined. Thus, the inclusion of coronary artery revascularization in the therapy of an evolving myocardial infarction in man must be considered to be pioneering research.

In undertaking revascularization of patients with evolving myocardial infarctions, Phillips and his colleagues concluded that the results of studies done in animals with normal coronary circulation cannot be extrapolated to patients with chronic atherosclerotic changes. They believe that collaterals would have developed in patients, and as a result, ischemia would be better tolerated than in animals with previously normal coronary circulation. Therefore, they operated on patients as late as 25 hours after the onset of symptoms (range 3.5–25 hours; average 6.5 hours). Although this conclusion may be proven correct, it is still, in our judgment, little more than speculation based on scant objective data. Operating on patients with evolving myocardial infarctions tends to ignore the value of understanding by experimental means the sequence of the development of ischemia, and precludes the opportunity of appreciating in a controlled manner how favorable and unfavorable changes might be introduced into the process. Justification of these criticisms will have to rest on whether the course of coronary artery disease in patients with an evolving myocardial infarction was favorably altered by the surgery.

Patients who present to an emergency room with an evolving myocardial infarction can usually be classified into a low-risk or “uncomplicated” group and a high-risk or “complicated” group. Moss et al. reported that the 4-month post-hospital cardiac mortality was 4% for the low-risk group and 14% for the
high-risk group. McNeer et al.\textsuperscript{13} reported that by the fifth hospital day, patients could be separated into a "complicated" group of patients who had a subsequent hospital mortality of 14\% and an incidence of serious complications of 51\%, compared with an "uncomplicated" group of patients who had no incidence of mortality and serious complications. The mortality 6 months after discharge for the two groups was 6\% and 8\%, respectively. Silverman and associates\textsuperscript{14} separated a group of patients classified as Killip class I and II into two subgroups with widely different short-term mortalities. This division was based on thallium-201 myocardial perfusion scans performed within 12 hours after admission to the coronary care unit. Of a small subgroup of 12 patients, eight were dead within 7 months, compared with none of the 29 low-risk patients.

In considering a new therapy, it is not enough to demonstrate that "you can;" the essential question is "should you?" Both the early and late mortality of consecutive patients admitted to the coronary care unit with an evolving myocardial infarction vary greatly. Thus, a study to evaluate the role of revascularization must be designed carefully.\textsuperscript{15} The patients who constitute the experimental population must be defined by precise diagnostic criteria. But prediction of the prognosis cannot be made immediately at the time of presentation; it requires hours. Care should be taken not to introduce a bias into the study population by selecting only low-risk patients.\textsuperscript{16} Finally, the results of the therapy in the carefully defined population must be compared with the results in similar patients treated by more conventional means with similar proficiency.\textsuperscript{2, 15, 17, 18}

How were the patients selected for surgery by Phillips and his associates\textsuperscript{1} and how precisely were they characterized? Can the results of this study be compared with similar patients treated without surgery? The patients were referred "soon after the onset of symptoms to the involved physicians." Such a practice is not likely to contribute to selection of a representative nonbiased sample of patients with evolving acute myocardial infarction. The patients had "clinical, electrocardiographic and enzymatic findings documenting an evolving myocardial infarction." They had no "significant chronic illness." Such exclusions might be expected to favor the selection of low-risk patients. Despite these criticisms the authors separated from the total study population a small subgroup that "required vasoactive medications to maintain hemodynamic stability;" this subgroup might be expected to have consisted of predominantly high-risk patients.

Based on their data, the selection criteria used by Phillips et al.\textsuperscript{1} were limited and lacked the precision required for describing a population of patients that can be compared to a similar but nonoperated population. The size and/or the tempo of the progression of the infarction at the time of surgery was defined only by routine ECGs, CPK determinations and a radiographic sign. Sixty-five patients had electrocardiographic evidence of an acute anterior wall infarction and 10 an acute posterior wall myocardial infarction. Fifty-nine patients, who might be considered "uncomplicated," had an average CPK of 504 IU/l; this value for 14 "complicated" patients was 802 IU/l. Two patients were in cardiogenic shock and had CPK values greater than 2000 IU/l.

The percent of the enzyme value that reflected a rise in the myocardial fraction is unknown; it is unknown when in the course of the evolution of the myocardial infarction the sample was taken. This relatively low value could reflect a successful limitation by the revascularization procedure of a further rise of the enzyme and indicate a successful salvage of ischemic myocardium that is potentially destined to die. It could also represent a small, already completed infarction in a patient who will do well.\textsuperscript{19, 20} Patients with "heavy trabeculation on the ventriculogram" were excluded by Phillips et al.\textsuperscript{1} Such a criteria has limited usefulness in classifying patients because it is not a commonly appreciated finding and its recognition is highly subjective.

What do we know about the results of the therapy as carried out by Phillips et al.\textsuperscript{21} Only one patient (1.3\%) died during the immediate hospitalization; but the procedure did not appear to prevent the development of electrocardiographic evidence of myocardial damage. Only five patients had normal ECGs at the time of hospital discharge; 39 had evidence of residual transmural myocardial infarctions; 22 had subendocardial infarctions and eight had nonspecific changes.

Forty patients were restudied by cardiac catheterization an average of 2 weeks after surgery. It is not surprising that there was an improvement in the hemodynamic findings at the time of the second study compared with measurements at the time of the initial study that was carried out when the patient had an evolving myocardial infarction. It is encouraging that only one graft was demonstrated to be occluded at that time.

But what is known about the long-term benefits of this surgical effort? The patients were followed from "1–38 months;" two patients died suddenly 3 and 5 months postoperatively. Both of these patients were preoperatively "hypotensive." No other pertinent information is supplied regarding the long-term function of the myocardium, or the patency of the grafts, or the progression of the disease in the native circulation, or the success of the procedure in postponing premature death.

Phillips and his associates\textsuperscript{1} have clearly demonstrated that you can operate on patients with an evolving myocardial infarction; but in their preliminary report they have not demonstrated that you should. They concluded that a "clinical trial of emergency revascularization in a highly select group of patients with evolving myocardial infarction is warranted."

New treatment modalities currently used in many centers to manage patients with acute myocardial infarctions are evolving so rapidly that comparison of the effectiveness of surgery with historical controls has
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little meaning. Such a trial as recommended by Phillips et al.1 must therefore be carefully controlled; ideally, the study should be randomized.2,18,19 Some claim that randomization is difficult, if not impossible, to carry out, and may be unethical.20-22 We strongly disagree with this. A randomized study may be difficult, but it is neither impossible nor unethical.2, 17, 18, 20 Despite the low operative mortality in the study by Phillips et al., it is unknown whether revascularization will be of long-term benefit to the patient with an evolving myocardial infarction, either complicated or uncomplicated. How can randomization in such a situation be considered unethical? Halsest described radical mastectomy as the best treatment for cancer of the breast in 1894.28 Based on his recommendations and those of others the procedure was performed on countless women for 83 years. But over the years its efficacy in prolonging life was seriously challenged, and it has finally been demonstrated by a prospective multicenter randomized trial not to increase longevity.27

If a carefully controlled study is to be carried out to evaluate the role of emergency revascularization in a patient with an evolving myocardial infarction, reliance alone on CPK, as was done by Phillips et al.,1 as a marker for the size of an evolving myocardial infarction within the first 2 hours after the onset of pain is inadequate. The enzyme does not begin to rise predictably until 3-4 hours after the onset of chest pain. Other techniques for determining infarct size are being investigated in animal laboratories and in patients. These include precordial ST-segment mapping,28 regional ejection fractions by radionuclide,29 two-dimensional echocardiography,30, 31 thallium-201 uptake scans,32 and others. The number of approaches that have been and are being evaluated to define infarct size emphasizes the dilemma that will limit the usefulness of studies such as that of Phillips et al.1 There is no ready, generally acceptable and available technique to define the size and progression of an evolving myocardial infarction; definition of the “point of no return” of an ischemic cell remains elusive.

Thus, one cannot, based on short-term studies as reported by Phillips et al.,1 be confident that the patient with an evolving myocardial infarction will benefit from emergency revascularization. There are too many unanswered questions about the long-term patency of grafts, the long-term effects on myocardial function after graft closure, the progression of the disease in the native circulation after revascularization and the success of revascularization in preventing subsequent myocardial infarctions, arrhythmias, congestive heart failure and premature death.2, 20, 34 In fact, the patient with an evolving myocardial infarction may be harmed by the late complications of surgery.

Long-term results must remain the criteria for evaluating the efficacy of emergency revascularization of patients with evolving myocardial infarctions. Until these results are available, one may do a disservice to large numbers of patients with evolving myocardial infarctions by operating at that stage of the natural history of the disease.

References


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Long-term Serial Angiographic Studies After Coronary Artery Bypass Surgery

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SUMMARY Twenty-six patients underwent repeat coronary angiography 5–8 years after saphenous vein coronary artery bypass surgery (SVCABG). These patients were selected from the first cohort of 117 patients who had SVCABG because they had obtained essentially complete relief of angina, and because all grafts were patent at initial angiography 11.2 months (mean) after surgery. Of the 39 grafts (1.5 grafts per patient) patent at 1 year, 34 (87.2%) were patent at reexamination 76 months (mean) (range 65–103 months) after SVCABG. Graft occlusion could not be predicted by the early angiographic appearance of the graft itself or its proximal or distal anastomosis. In some cases, narrowing or irregularity consistent with intimal hyperplasia appeared to progress, while in others it developed at late follow-up. Progressive narrowing occurred in 96% (22 of 23 grafted vessels) of the native coronary arteries proximal to the graft anastomosis. Progression to a stenosis >75% or total occlusion was seen distal to the graft anastomosis in eight of 39 grafts (20%). Of 103 non-bypassed major vessels, 56% showed some progression of disease and half of these progressed to significant stenoses (>75% luminal narrowing). There were no apparent predictors to indicate whether progression in nongrafted coronary arteries would occur preferentially in a previously stenotic or nonstenotic vessel, although 80% of vessels with initial stenoses >75% progressed to total occlusion.

THERE HAS BEEN widespread acceptance of saphenous vein coronary artery bypass graft surgery (SVCABG) since it was introduced in 1968.1 Coronary bypass surgery has been of definite value in the symptomatic relief of angina pectoris,2,3 and the results of extended clinical trials, although limited, are encouraging.4,5 The long-term fate of saphenous vein grafts and the native coronary circulation after SVCABG is controversial because of the inexorable tendency of obstructive coronary artery disease to progress.

Patient Selection

Our study group was derived from the first 117 consecutive patients who underwent coronary bypass surgery at Stanford University Medical Center between 1968–1971 (fig. 1). Of the 106 1-year survivors (a mortality rate of 9% at that time), 72 patients (68%) consented to angiography 1–14 months postoperatively (mean 11.5 months). At the initial clinical and angiographic follow-up, 52 patients were virtually asymptomatic (New York Heart Association functional class I or II), while 20 were symptomatic. Details of this study have been previously reported.6

In an attempt to eliminate the bias due to technical
Emergency coronary artery revascularization of patients with acute myocardial infarction: you can ... but should you?
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