EDITORIAL

"Preinfarctional" Angina

A Need for an Objective Definition and for a Controlled Clinical Trial of its Management

SAPHENOUS vein aorta-coronary grafting has recently become available for the treatment of angina pectoris and is being applied in the management of "preinfarctional" angina in an increasing number of institutions. In this discussion we shall address ourselves to two issues: one, the question of whether preinfarctional angina (better called unstable angina) can be recognized and defined by objective criteria, and, two, the need for a controlled clinical trial of saphenous vein grafting in the management of angina pectoris.

Can one predict when angina pectoris portends imminent myocardial infarction or sudden death? When one plans to interrupt the natural history of an illness by application of a new variety of therapy which may be both effective and hazardous, one must insist upon a knowledge of the natural history of that illness. The risks and benefits of treatment may then be weighed against the results of careful observation for deterioration or complications.

For example, information concerning the natural history of patients with patent ductus arteriosus was incomplete when Gross developed a method of surgical closure of the ductus in 1939. Fortunately, the mortality rate of this surgical procedure is sufficiently low that closure can be advised in almost every patient, despite our inadequate knowledge. On the other hand, the immediate course of the asymptomatic or slightly limited patient with mitral stenosis is sufficiently benign, and the risk of open cardiac surgery for mitral commissurotomy or mitral valve replacement sufficiently great, that delay of the surgical procedure and continued observation are justified until the patient develops progressive restriction under medical management.

In the case of preinfarctional angina, the physician is faced with several difficulties. First, the syndrome is usually defined by clinical criteria which are in part subjective. Second, both its immediate and remote natural history are not known. Third, the risks of diagnostic and surgical interventions in patients in this somewhat precarious state of unstable imbalance between myocardial oxygen need and supply are uncertain.
Until recently, the merit of "myocardial revascularization" procedures was sufficiently dubious that the physician was not faced with a difficult decision in regard to the management of patients with unstable angina. Recent observations of inadequate blood flows through internal mammary arteries implanted into the myocardium for the treatment of coronary artery disease and the lack of correlation between patency of the implant and the clinical results have confirmed the deficiencies of this procedure.

However, the development of the saphenous vein aorta-coronary graft offers promise of significant increase in distal coronary flow in many patients with proximal occlusive disease of major coronary arteries. A number of institutions have hastened to apply this procedure to patients diagnosed as having preinfarctional angina even though the risks of coronary arteriography and coronary bypass grafts in these patients are unknown, information concerning the course of these patients under medical management is fragmentary, and the long-term fate of these grafts is yet to be determined. The purpose of this article is to make a plea for the following: (1) a better definition of this syndrome to include a study of the natural history of the disease; and (2) a controlled clinical trial to establish the hazards of coronary arteriography and the risks and benefits of coronary bypass surgery in this disease.

An adequate scientific investigation requires objective criteria to define the problem to be studied. The term "preinfarctional angina" is an unfortunate one since many, and possibly most, patients with unstable angina pectoris of recent onset neither develop myocardial infarction nor die unexpectedly of a cardiac arrhythmia. The term "preinfarctional angina" is also unfortunate because its prognostic implications may lead cardiologists and surgeons to precipitate and, at times, ill-advised action. There are other terms which might be used for this disease: unstable angina, acute coronary insufficiency, threatened infarction, status anginosus, or the intermediate coronary syndrome. The patients in question are those who have a sudden onset of one or more anginal attacks a day from a previous background of good health or who have had a dramatic change in the symptomatic pattern of previously recognized coronary disease. The usual variety of anginal pain or discomfort lasts between 30 sec and 30 min, and is related to effort; in patients with unstable angina, the attacks, in addition to being more frequent, are also often of longer duration and may occur at rest without an apparent precipitating event.

The foregoing description is the first criterion for the diagnosis of unstable angina. During the attack of pain, such patients may demonstrate paroxysmal hypertension and sinus tachycardia and/or ischemic S-T-segment depression on electrocardiogram. By definition, the electrocardiogram between attacks shows no evidence of recent infarction, and such serum enzymes as the glutamic oxaloacetic transaminase or the creatine phosphokinase show no diagnostic alterations. For scientific study, however, it is desirable to define the syndrome further by requiring that selective coronary artery arteriography demonstrate 50% or greater narrowing of one or more of the major coronary arteries. Then the syndrome will be objectively defined.

Given the foregoing definition, one might then proceed with plans to study the disease. Such plans should include observation of a series of such patients under medical management in cardiac monitoring units to determine the natural history of the illness. One purpose of such a study would be to determine whether the mortality rate of the disease is great enough to warrant a controlled trial of surgical treatment. The mortality risk of coronary arteriography is estimated to lie between 0.1 and 1%. The operative mortality rate of saphenous bypass grafting may average 10% in experienced hands and ranges from 3% in patients with one-vessel disease to approximately 21% in those with three-vessel disease. It is quite possible that most patients with unstable angina treated without a surgical procedure have a better chance of survival.
A second purpose of such a study would be to identify, if possible, subsets of patients who might be predicted to have a higher risk. These groups might well include patients with previous infarction, those with arrhythmias, or those with more widespread and more severe arterial obstructive disease demonstrated by selective arteriography. It is hoped that methods for recognizing such patients by less invasive methods might be developed as a by-product of such a study. For example, intravenous injection of cesium isotopes\(^1\) might be used to give information concerning myocardial uptake at the capillary level. Another goal of such a study would be to define the long-term outlook for morbidity and mortality in such patients by observation for 5 to 10 years.

If as a result of the study proposed here one could identify a group of patients with unstable angina in whom the mortality rate is high enough to justify the risk of the saphenous vein graft, then a prospective controlled clinical trial might be undertaken. Patients whose illness is defined as unstable angina by the objective criteria stated earlier, and whose risk for infarction or death is sufficiently great, might then be assigned at random to surgical treatment or no surgical treatment. It is clear that historical controls or controls composed of patients who refuse surgical treatment are not acceptable.\(^12\) Medical management should be the same in both groups. The series should be large enough to randomize other coronary and surgical risk factors, e.g., previous myocardial infarction, left ventricular dysfunction, extent of obstructive coronary disease, diabetes mellitus, systemic hypertension, smoking, age, and sex. The end points of such a study might be: (1) pain relief; (2) prevention of infarction; (3) left ventricular function at rest; (4) mortality rate; (5) exercise tolerance studied by stress electrocardiography after recovery; and (6) longevity.

The saphenous vein bypass graft for coronary disease is becoming an extremely common operation in many hospitals.\(^1, 2, 7, 13, 14, 15\)

In some clinics dozens of such operations are done each week.\(^16\) If someone does not now perform adequately controlled clinical trials of this procedure, in 10 years many lives perhaps will have been needlessly sacrificed and information may still be lacking for an objective decision about the place of this procedure in the management of either acute or chronic coronary artery disease.

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