Coronary artery bypass surgery—an assessment

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Introduction

The surgical treatment of coronary artery disease has a long, chequered and, until recently, undistinguished history. It has gone through a number of stages; surgical sympathectomy was suggested towards the end of the last century and was reported as a successful treatment for angina pectoris in 1916; abrasion of the epicardium and of the pericardium was introduced in the 1930s; the application of a variety of pedicles or organs (omentum or spleen) to the surface of the heart was introduced in the early 1940s; occlusion of the coronary sinus was carried out later in the same decade; anastomosis between the aorta and the coronary sinus or arterial perfusion of the coronary venous circulation were introduced in the late 1950s; ligation of the internal mammary artery and then implantation of this vessel into the ventricle were utilized in the early 1960s. All of these procedures were initially announced with enthusiasm which then rapidly waned.

Accompanying the development of these operations there has been an increasing appreciation of the natural history of coronary artery disease. In addition, there have been important advances in the medical treatment of angina pectoris, particularly β -adrenergic blockade, and there is now widespread recognition of the important placebo effects of a variety of treatments of a disease in which one of the principal clinical manifestations, i.e. angina pectoris, is largely subjective.

With the development of aorto-coronary artery bypass surgery we have a procedure of qualitatively greater importance than those hitherto available. This operation (1) immediately delivers substantial quantities of blood to previously ischaemic myocardium; (2) can be accomplished by a skilled, experienced surgical team with a relatively low mortality; (3) results in the relief of angina pectoris in most patients. The procedure is being rapidly extended from patients with incapacitating angina pectoris, in whom it was first applied, to those with acute myocardial infarction, unstable angina pectoris, cardiogenic shock and, in some instances, even to patients with minimal symptoms but anatomically favourable lesions.

Clearly then, coronary bypass surgery represents a

form of therapy that can, under appropriate circumstances, favourably alter the clinical expression of arteriosclerotic coronary artery disease. Accompanying this widespread optimism, however, is a growing uneasiness that by simple common consent, rather than by rational analysis of data, we may be adopting for general use a form of treatment that has yet to prove itself. Some fear that even though the long-term effectiveness of direct revascularization has not yet been demonstrated, we may be propelled into a position in which it will be considered poor medical practice to withhold this form of therapy from almost any patient with coronary artery disease and in which the physician who does not recommend coronary arteriography in almost every person who might have coronary sclerosis may be subject to severe criticism.

Unresolved issues

Many questions must be answered. First and foremost, how do the survival rates compare in closely matched groups of patients with and without the operation? How does operation affect the incidence of myocardial infarction, congestive heart failure, arrhythmias, angina and other symptoms? How do the clinical effects of revascularization compare with vigorous dietary and anti-lipidaemic treatment, particularly in patients with relatively mild disease? If the natural history of coronary artery disease is favourably altered, then what are the implications for patients with relatively few symptoms but with seriously disturbed coronary anatomy which may be suitable for surgical treatment? This question leads inevitably to an even broader question—how are patients to be selected for coronary arteriography? What are the long-term patency rates of the grafts? What are the long-term changes in the interposed venous segment? Does the presence of hypertriglyceridaemia or other forms of hyperlipidaemia increase the risk of graft closure? What is the rate of development of arteriosclerotic disease in the coronary vessels distal to the anastomosis when they are exposed to systemic pressure and are no longer 'protected' by a more proximal stenosis? What is the mechanism of the disturbingly high incidence of the occlusion of the

native vessel proximal to the insertion of the graft? Does it represent a natural progression of coronary artery disease? What are the relative advantages and disadvantages of using the internal mammary artery as opposed to the saphenous vein? What are the possibilities of using synthetic materials? What are the effects of bypass surgery on the contractile activity of previously ischaemic myocardium? What is the mechanism of pain reduction? How often is it due to increased perfusion? To what extent is there an alteration of sensory nerve function after the diseased vessels have been manipulated surgically? What role does the placebo effect play?

The problem of evaluating this operation is, of course, compounded by the fact that the answers to these and other questions must be sought among many different groups of patients. The effects of the operation will have to be analysed in patients by sex, age, arterial pressure, number of previous infarcts, extent of myocardial dysfunction, by the presence of risk factors such as diabetes, hyperlipidaemia, hypertension, etc. Obviously, this will be a difficult task, but one that is essential; one hopes it will be carried out sooner rather than later.

Effects of operation on mortality

While ignorance in this field is great, some important information has been accumulated in the last few years. First of all, there is agreement that the survival following surgical treatment is constantly improving, at least in those centres performing a large number of operations from which the results are reported. Thus, Cannom *et al.* (1974) reviewed the results of the first 400 consecutive patients having saphenous vein coronary artery graft surgery at Stanford University Hospital; the operative mortality was 6.5%; those in whom the operation was carried out electively had a mortality of 0.8% and, despite the operative mortality, the operated patients showed a 3-year survival of 88.5%. Hutchinson *et al.* (1974) reported an extremely low operative mortality rate of 0.8% and of operatively induced infarctions (1.9%) in a group of thirty-six consecutive patients. Tector and McNabb (1974) reported a 1-year series of 196 consecutive patients who underwent coronary artery bypass surgery without a hospital death, while Bennett *et al.* (1974) reported a progressive reduction in the annual operative mortality from 4.1% in 1967 to 0.95% in 1973. Spencer *et al.* (1974) have reported an operative mortality of less than 3%, an overall graft patency rate of 71% and an intra-operative infarction rate of 10%. Life-table analysis of their series showed a 5-year survival of 77% and a 5-year cardiac survival of 81%; a comparable population group without coronary disease would be expected to have 92% survival. Cohn, Boydon and Collins (1975) have reported in their experience at the Peter

Bent Brigham Hospital in 330 patients operated largely for disabling angina. The operative mortality was 1.2% and the long-term mortality over a 4-year period was 4%. The results of their life-table analysis suggested that in patients with 2- and 3-vessel coronary artery disease who received complete revascularization there was a significant prolongation of life when compared to a large series of medically treated patients studied by coronary arteriography at the Cleveland Clinic before the widespread use of bypass surgery. A number of retrospective studies have defined the annual mortality rate in medically treated patients as 2% for 1-, 7% for 2- and 11% for 3-vessel coronary disease (Reeves *et al.*, 1974).

Dawson *et al.* (1974) have reported that the mortality rate following coronary artery bypass surgery was higher in patients who had previously suffered a myocardial infarction, particularly in those in whom it occurred within 2 months of operation. It has been observed repeatedly that the mortality rate is high and the clinical improvement limited in patients who underwent myocardial revascularization primarily because of symptoms of left ventricular dysfunction (Editorial, 1976). The inability to demonstrate ventriculographic or haemodynamic augmentation of overall ventricular function after bypass operation is not surprising when it is recognized that improvement could not be expected to occur either in patients in whom ventricular function before operation is normal nor in patients whose ventricular function is impaired by previous infarction and scar or aneurysm formation.

A limited number of studies have provided a comparison between the surgical and non-surgical treatment of coronary artery disease in suitably matched patients. In one of these, a prospective randomized study, Mathur and Guinn (1975) found at follow-up that 6% of the operated patients and 10% of the medically treated group had died, a difference which was not significant. Also, anginal symptoms improved in both the surgically and medically treated groups, but a large fraction of the former became asymptomatic. Treadmill tests also revealed increased exercise tolerance in the patients who had had surgery. Thus, whatever the mechanism that was responsible, the quality of life had certainly been improved in the operated patients. Aranow and Stemmer (1974) compared two small groups of patients, one treated medically and the other surgically, concurrently and in the same institution. In the surgically treated patients both the mortality and the incidence of myocardial infarction were slightly higher and the abolition of angina more frequent than in the medically treated group. Although this is a small series, it may actually be more representative of the results obtained at institutions which do not have large numbers of patients. It is well to recall

that many patients with coronary artery disease are being operated on in hospitals which do not publish their surgical results, and the results of Aranow and Stemmer (1974) may therefore be more relevant to patients operated on in such institutions than those reported from the larger centres.

In obstructive disease of the left main coronary artery, operative treatment has clearly resulted in improved survival rates in comparison to non-operative treatment. For example, Talano *et al.* (1975) studied 145 patients with left main coronary artery disease; at 1-year follow-up, 82% of operated patients were alive, compared to 61% of medically treated, operable patients. On the other hand, there is general agreement that survival is not improved by operation in patients with single vessel coronary artery disease, with the possible exception of those with obstructive lesions involving the left anterior descending coronary artery proximal to the origin of the first septal branch.

The considerable disagreement concerning the indications for, and/or results of, bypass surgery is attributable to a number of factors: (1) although it is acknowledged that different groups of patients with coronary artery disease exist, the morbidity and mortality of patients in each group have not been defined. Therefore, it is difficult to estimate the natural history of patients not treated by operation, and attempts to define a beneficial effect of operation are thereby compromised; (2) most life-table analyses of patients with ischaemic heart disease utilize patients in whom the diagnosis was proved by coronary arteriography. As a rule, it is only symptomatic patients who are subjected to arteriography. Thus, the use of life-table analyses to document the history of untreated coronary disease may represent a biased approach since untreated, asymptomatic or mildly symptomatic patients with comparable findings on coronary arteriography are excluded; (3) the indications for surgical treatment and the effectiveness of operation vary among institutions and surgeons, thus causing inter-institutional comparisons to be of limited value. It is not known whether the operation can forestall infarction or other complications of coronary artery disease (Lesch, Ross and Braunwald, 1977).

The largest group of potential candidates for operation consists of patients with 2- or 3-vessel disease and some disorder of left ventricular function, in the majority of whom the only certain effect of operation is the relief of symptoms. However, recent data from centres reporting on 3- to 7-year follow-up of surgically treated patients using the life-table analysis technique, suggest, but do not prove, that bypass graft surgery favourably affects the natural history of coronary artery disease when patients with similar degrees of angiographically proved disease

who have been treated medically are used as controls (Cohn *et al.*, 1975).

While a large, prospective, randomized trial is appropriate to settle the issue of the effect of the procedure on survival, it must be recognized that in view of the progressively decreasing mortality rate commented on above (approximately 1–3% in many centres) and the small overall late mortality rate (approximately 2% per year) such a trial between medically and surgically treated patients will take many years before definitive conclusions can be reached. Although it is possible that such a study may show that surgical treatment does not improve survival in all but the patient with left main coronary artery disease, with the excellent results of surgical treatment now being reported from the leading centres, it seems extremely unlikely that better survival can occur in a series of comparable patients treated medically. When this consideration is coupled with the marked reduction of angina pectoris resulting from the procedure in the large majority of patients, a persuasive case can be made for operating on patients with multi-vessel coronary artery disease with more than trivial angina.

Mechanism of angina relief

A number of studies have shown quite clearly that coronary artery bypass grafts can improve myocardial perfusion. For example, myocardial blood flow has been measured at the operating table by determining the myocardial clearance of ¹³³xenon injected into the distal bypass graft, recording its wash-out, while measuring the flow through the graft with a flowmeter; the mass of myocardium perfused by the graft could then be calculated. Such studies suggest that the myocardial mass perfused by the graft averages approximately 110 g (Kreulen *et al.*, 1974).

It is now clear that the reduction or elimination of angina pectoris can, in most instances, be attributed to the increased blood flow to the ischaemic myocardium but, as Ross (1975) has pointed out, this is not an adequate explanation in all patients. For example, relief of symptoms in the presence of occluded grafts could be due to infarction of the ischaemic or angina-producing segment of the myocardium. Segmental wall motion and ventricular function have frequently been shown to deteriorate in patients with occluded grafts. The occurrence of this phenomenon in patients without graft occlusion must be assumed to be due to intra-operative myocardial infarction. Thus, improvement of angina pectoris after aorto-coronary artery bypass operations is not solely related to the patency of the grafts but it may, in some instances, be associated with impaired left ventricular contractile function secondary to

infarction. Estimates of the frequency of peri-operative infarction range from 1% to 15%.

The well known placebo effect of operation is another possible mechanism for symptomatic improvement, but relief due to this mechanism would not be expected to be long lasting. The fact that symptomatic relief is attributable to increased blood flow and that placebo effect cannot be entirely responsible for the relief of pain is supported by the occasional fortuitous arteriographic demonstration that pain abruptly recurs when a graft becomes occluded. The application of precordial imaging following intravenous injection of radioactive potassium (^{43}K) or thallium (^{201}Th) with the patient at rest and during exercise provides a useful, non-invasive approach to the assessment of regional perfusion and to distinguishing ischaemic muscle from that which has been infarcted and is fibrotic (Zaret, 1976). When abnormal images are demonstrated in the face of diminished angina, it is clear that the latter results not from increased blood flow but rather from the intra- or post-operative infarction which might have occurred.

Flow through vein grafts measured at the time of operation correlate well with their subsequent patency. Flows of less than 40 ml/min are associated with significantly higher occlusive rates than are higher flow rates. This is probably related to the size of the distal vessels and the severity of atherosclerotic disease present in them. There are three possible explanations for the observed high incidence of new total occlusions and new disease in the artery proximal to the saphenous vein graft: (1) they may represent a natural progression of coronary atherosclerosis, but this possibility is unlikely because of the relative rarity of the development of new lesions in the patients' ungrafted vessels over the same period of time; (2) the new lesions may be related to surgical manipulation of the severely diseased coronary artery; (3) they may be due to a reduction in flow to a segment of the bypassed artery, because with a severe proximal obstruction the graft will perfuse the portion of the proximal artery which lies between it and the obstruction in a retrograde manner. This reduces the pressure gradient across the proximal stenosis and the resultant stasis may lead to a thrombus which then may propagate both proximally and distally.

The occlusions of venous grafts may be related to medial and/or intimal proliferation; the former may result from the destruction of the vasa vasorum, while the latter appears to be secondary to the intraluminal pressure and/or oxygen saturation, both of which are abnormally elevated for a venous channel. Frick, Harjola and Valle (1975) showed that 75% of the grafts that eventually become occluded were already closed a few weeks after operation. Occluded

grafts tend to be accompanied by the persistence of collaterals, which usually disappear or diminish in patients with patent grafts. It is interesting that Allard *et al.* (1974) found, in a study in which graft patency was evaluated 2 weeks, 1 year and 3 years after operation, that patients with hypertriglyceridaemia had a higher risk of occlusion or stenosis of vein grafts than did those with normal lipid levels. A partial solution to the problem posed by the closure of venous grafts may be provided by use of the internal mammary artery. Kay *et al.* (1974) compared internal mammary artery and saphenous vein grafts 12–36 months post-operatively; the internal mammary arteries were patent in 98.5% of cases and the saphenous vein bypasses in 84.3%.

Unstable angina pectoris

The question of the efficacy of saphenous vein bypass grafting in unstable angina persists. Bonchek *et al.* (1974) reported on fifty-five patients with unstable angina; there were three operative and one late death, six early and three late infarctions, and a 93% survival rate in the 3 years post-operatively. On the basis of these results, it was concluded that emergency saphenous vein bypass grafting is effective therapy for unstable angina. Wisoff *et al.* (1974) operated on seventy-seven patients with unstable angina. The hospital mortality was 1.3% and the graft patency was 95% in the restudied patients. These results also led these authors to suggest that in patients with unstable angina, coronary revascularization should be carried out immediately following coronary arteriography. Favourable early and long-term benefits of emergency myocardial revascularization have also been described by Bolooki *et al.* (1974) in patients with the so-called intermediate coronary syndrome, unresponsive to medical management.

Conti (1976) recently reviewed the literature dealing with the surgical treatment of unstable angina. Of 743 published cases treated surgically, there was an 8.4% hospital mortality and an 8.7% incidence of myocardial infarction. In contrast, of 506 patients with unstable angina treated medically, there was a 5% hospital mortality and a 4% incidence of myocardial infarction. These groups were not randomized or studied prospectively. However, the preliminary results of a co-operative, prospective, formal, randomized trial of medical and surgical therapy of patients with unstable angina pectoris have also recently become available (Conti, 1976). Of eighty patients randomized to medical therapy there were two in-hospital deaths and seven myocardial infarctions, with three late deaths and five late infarcts. Of seventy patients randomized to surgery there were three early deaths and fifteen early infarctions with three late deaths and five late

infarcts. Thus, the incidence of myocardial infarction has been greater with surgical than with medical treatment, although the mortality rate is similar in both groups. Angina persisted in a larger fraction of the medically (forty-two of seventy-five, i.e. 56%) than the surgically treated patients (eight of sixty-four, i.e. 13%).

In addition to angina, treatment of refractory arrhythmias should be considered a possible indication for myocardial revascularization, but the total experience is still rather limited. For example, Alexander, Makar and Ellis (1974) reported a patient with increasingly severe angina pectoris with recurrent episodes of ventricular fibrillation refractory to medical therapy: after emergency operation no further episodes of ventricular fibrillation occurred. Ikram *et al.* (1974) also described a patient who had suffered a previous myocardial infarction and who had multiple attacks of ventricular tachycardia refractory to pharmacological and electrical therapy who was improved by coronary bypass surgery.

Conclusions

On the basis of personal experience, and published data, the situation can be summarized as follows: the objectives of surgical treatment include the relief of symptoms and improvement of exercise tolerance; improvement of ventricular function; prevention of myocardial infarction and improvement of life expectancy. The ability of the procedure to relieve pain is clear; the relief of angina occurs in the majority of patients with unstable as well as chronic angina. Available data have not shown that the procedure is capable of improving ventricular function. Also, there appears to be no firm evidence to recommend surgical treatment of patients with coronary artery disease simply to prevent acute myocardial infarction. The evidence that life is prolonged by operation is questionable, except in patients with stenosis of the left main coronary artery.

In view of these considerations, the role of this operation in the treatment of ischaemic heart disease cannot be defined precisely at this time and it is, therefore, possible to list indications only in terms of current practice (Lesch *et al.*, 1977). Three factors are usually considered in arriving at a decision to advise coronary bypass operations: (1) the symptomatic status and age of the patients; (2) the coronary anatomy as demonstrated by coronary arteriography; (3) the ventricular function as determined by left ventricular angiography and haemodynamics. Most patients advised to undergo operation are symptomatic, although the severity of the symptoms in surgical candidates varies widely among institutions. The ideal candidate has severe (80% or greater) obstructive lesions in the proximal portions of at least two of the three major coronary

arteries. Patients with severe lesions in the left main coronary artery are at high risk and should have operative therapy regardless of the presence of symptoms if there are no strong contra-indications. The best results are obtained in patients with normal ventricular function or at most a single area of impaired myocardial contractility.

Major controversy persists as to the indications for operation in the asymptomatic or mildly symptomatic patient with obstructive coronary artery disease. If the suggestions purporting to demonstrate a beneficial effect of the operation on the natural history of the disease can be confirmed, the indications will obviously be less stringent than if relief of symptoms is the only goal of the procedure. Patients who have definite symptomatology but in whom significant relief with medical therapy is obtained, present a most difficult problem. We generally treat older patients, e.g. those over 70 years, medically, unless the symptoms are truly disabling, whereas we require less disability before advising operation in a younger individual.

An important additional factor frequently not discussed relates to the technical skills of the surgical and diagnostic teams and the quality of care in the early post-operative period. Obviously, the greater the expertise and the better the results in any given institution the more aggressive can the approach be in borderline patients.

Coronary artery surgery is very much in the public and even in the political eye at this time. The media have been in large measure responsible for this state of affairs in the U.S.A. Patients, their families, as well as general practitioners and internists, apply increasing pressures on cardiologists to carry out coronary arteriography and on cardiac surgeons to perform corrective procedures. The financial implications of this operation are profound. It is estimated that during 1976 there will be approximately 60,000 coronary artery bypass operations performed in the U.S.A.; at an estimated cost of \$15,000 each, the total annual cost of this treatment approaches one billion dollars! If we accept the principle that the total resources for health care are fixed, the enormous funds which are now being devoted to coronary artery surgery reduce by an equal amount the support available for other aspects of medical care. For all of these reasons we have the very serious responsibility to examine the subject of the efficacy of this procedure very carefully indeed and to carry out this examination not only now, but on a continuing basis.

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