Indications for coronary artery surgery

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The objectives of aortocoronary bypass surgery (ACBS) are to relieve angina and, for some patients, to prolong survival. Success or failure with the first objective tends to be quite obvious, but with the second it is possible to identify only immediate failure.

In this article I propose to confine the discussion of the indications for surgical treatment to those in patients with chronic coronary heart disease, manifest by 'stable' angina or survival after a myocardial infarction.

Relief of angina

The immediate and dramatic relief of angina, which can be anticipated for the majority of operated patients, forms the basis of the principal indication for surgery: unacceptable angina in a patient with operable coronary disease, for whom the alternative approach of angioplasty is not feasible.

The term 'unacceptable angina' leaves considerable scope for clinical judgement, and whilst the severity of symptoms in relation to the patient's lifestyle is obviously one crucial factor, the final decision to operate must be influenced by the entire clinical setting and, in particular, the arteriographic anatomy. It is important to avoid surgical treatment too early in the natural history of the disease, for second operations are more difficult and hazardous than primary procedures: for example, early surgery would be appropriate for a patient with a long history of refractory angina with multiple vessel coronary disease, whereas in a patient with stable angina of equal severity but short duration (less than three to six months), and significant disease confined to one major vessel, it may be wise to defer the decision because there is every prospect that the angina will improve, or even disappear, spontaneously. Moreover, the decision to operate is inextricably linked with the assessment of the likely effect on the individual patient's prognosis.

It is important to emphasise the limitations of the operation. At the end of the first post-operative year about three-quarters of patients can be expected to be symptom-free (with nearly all the others greatly improved), but there is a tendency for angina to recur, particularly after the lapse of five years, and by ten years almost two thirds of surviving patients will have experienced a recurrence, though this is likely to be severe in only about one third [1]. Whilst the long-term results may improve with increasing use of the internal mammary artery rather than vein as the bypass conduit whenever possible, patients referred for ACBS must understand its essentially palliative nature.

Effect on prognosis

Perceptions of the logical consequences of a procedure which improves myocardial blood flow, and the results of several non-randomised comparisons of medical and surgical treatment raised the expectation that ACBS would be accompanied by an improved prospect of survival over that which could be anticipated with conservative management.

Three well planned and conducted randomised trials of medical and surgical treatment have been carried out. Although their results appear to be contradictory [2,3], they are more remarkable for their consistencies than for their disparities. Collectively, they provide a sound basis for recognition of the type of patient for whom improved survival can be anticipated from surgical treatment, and for whom, therefore, an operation should be considered even in the absence of 'unacceptable' angina.

All three trials were conducted in several cooperating centres, and the results were analysed primarily on the 'intention to treat' principle; in other words, the outcome was compared according to the initial random assignment, rather than on the basis of whether the patients actually underwent operation, were treated medically, or died before surgery could be carried out. The numbers of patients to be included in the trials were determined in advance and based on an assessment of the expected mortality with medical treatment and the extent of any improvement from surgery which would, if discovered, be clinically useful. These calculations were based on projections for the entire study populations, but provision was made in all three trials for the separate analysis of specified subgroups. Except for this basic similarity of design, the trials were very different, most importantly in respect of the criteria which were used to select patients for participation.

Veterans Administration Coronary Artery Bypass Surgery Study

The first trial, which was carried out in 13 Veterans Administration Hospitals, was designed to discover whether, for men under the age of 65 with stable disabling angina who had operable coronary disease, surgical treatment could improve the prognosis over that of medical treatment. Patients were not eligible for randomisation if they had had a myocardial infarction within the previous

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six months, if the diastolic blood pressure was over 100 mmHg despite antihypertensive therapy or if they had unstable angina or uncontrolled heart failure.

Between 1972 and 1974, 686 patients were randomised: 354 to medical treatment, and 332 to surgery. The survival curves diverged slightly in favour of the surgical group, and though at five years a 5 per cent advantage over the medical patients could have arisen by chance, at seven years the 77 per cent survival in the surgical patients was significantly better than the 70 per cent survival of the medical group. At 11 years, however, cumulative survival was virtually identical at 58 per cent and 57 per cent respectively [4]. Survival in certain predetermined subgroups was analysed to test the a priori hypothesis that patients at highest risk of death with conservative management would be those whose survival could be influenced most favourably by surgery.

The first subgroup to be considered comprised 91 patients with more than 50 per cent narrowing of the left main coronary artery [5]. The suspicion from earlier studies [6] that this condition is accompanied by a very poor prognosis with conservative management was confirmed. There was a rapid and progressive separation of the survival curves of the two groups, such that by 42 months the cumulative mortality among the surgical patients was less than 50 per cent of that amongst those in the medical group.

Even within this left main coronary disease subgroup there was considerable variation in prognosis: benefit from surgery was confined to those at especially high risk, in particular, patients with stenoses greater than 75 per cent, with abnormal left ventricular function, or possessing at least two of three clinical indices of risk (ST segment depression on the resting electrocardiogram, a history of hypertension, or a history of myocardial infarction). However, the number of patients in these subgroups is too small for conclusive analysis.

When the patients with left main coronary artery disease were excluded, overall survival in the medical and surgical groups was virtually identical. This similarity of outcome appears to be a reflection of an improved prognosis from surgery in patients at high risk, with no effect, or possibly even an adverse influence of surgery, on low risk patients. High risk was defined on the basis of angiography by the presence of disease in all three main divisions of the coronary circulation, combined with significant impairment of left ventricular function (ejection fraction less than 50 per cent, or more than 25 per cent of the left ventricular circumference showing a wall motion abnormality). All the remaining patients were considered to be at low risk. In the low risk group the medical and surgical survival curves were parallel, with a small, statistically insignificant, advantage with medical therapy; at 11 years cumulative survivals were 68 per cent in the medical and 61 per cent in the surgical patients. In the angiographic high risk patients, survival in the surgical group was 50 per cent better than in the medical group at five and seven years, after which the mortality in the surgical patients accelerated, though even at 11 years a statistically significant advantage from ACBS persisted with cumulative survivals of 50 per cent in the surgical and 38 per cent in the medical patients. Similarly, when the patients were stratified into terciles of risk on the basis of previously validated clinical criteria, randomisation to surgery was accompanied by improved survival over randomisation to medical treatment in the high risk tercile, but not in the mid or low risk terciles (risk was stratified according to the severity of angina, and on the presence or absence of a history of hypertension, myocardial infarction, and ST segment depression on the resting electrocardiogram). Not surprisingly, there was considerable concordance between the two methods of risk assessment.

In the Veterans Administration Cooperative Study (VA), therefore, surgical treatment resulted in a worthwhile improvement in the survival of patients with severe angina who had a severe stenosis of the left main coronary artery, or some other indication, either clinical or angiographic, of high risk.

Shortcomings in the quality of surgical treatment when judged by present standards limit the extent to which the findings of the VA study can be extrapolated to current practice. The operative mortality of 5.8 per cent and the perioperative 'Q wave' infarction rate of 9.9 per cent compare poorly with corresponding figures of 1-3.5 and about 6 per cent which are now achieved in experienced surgical units, and were documented in the later trials carried out by the European and Coronary Artery Surgery Study Group (CASS) groups. An average of two grafts per patient were implanted in the VA study compared with almost three grafts per patient in the subsequent trials, and this is almost certainly a reflection of incomplete revascularisation of the VA patients. Finally, graft patency among patients who were reinvestigated was only 70 per cent at one year and 67 per cent at five years, whereas patency rates of about 85 and 80 per cent at these times are now generally achieved. CASS registry data indicate clearly that perioperative infarction compromises the long-term survival of operated patients, and there is evidence that the completeness of revascularisation is another major factor which determines prognosis [7,8]. However, whilst these considerations suggest that the outlook with surgical treatment might be very much better in the late 1980s than in the mid-1970s, it should also be acknowledged that medical treatment has improved during the same period. Only about half of the medically treated patients in the VA study received a beta-blocker, and calcium antagonists were unavailable at that time.

Interpretation of the VA study is further complicated by the relatively high mortality in both groups of patients. This is probably a reflection of a more advanced stage of coronary heart disease present by the time of angiography and surgery than would be found in a contemporary series of patients, for whom the indications for angiography and operation have become more liberal than in the early 1970s, though a change in natural history, either spontaneous or as a result of medical treatment, cannot be discounted.

**European Coronary Surgery Study Group trial**

The second trial, which started recruitment in 1973, was
carried out by the European Coronary Surgery Study Group.

The protocol took account of the effectiveness of surgery in relieving angina (such that it was considered to be unacceptably high in the randomised patients with disabling symptoms), the good medium-term prognosis for patients with single-vessel coronary disease, and the preliminary data on survival of patients with left main disease in the VA study. It was also accepted that in many patients with initially mild angina for whom medical treatment would be an acceptable option, symptoms would progress and necessitate surgery during the proposed five-year period of the study.

The trial was therefore designed to determine whether a policy of early surgical treatment would improve survival for patients whose angina could be controlled medically, by comparing the mortality associated with this approach with that from a policy of medical therapy, but with surgery available for those whose symptoms deteriorated during follow-up.

Men up to the age of 65 with stable angina for at least three months were considered for randomisation. The severity of angina was defined somewhat loosely as ‘mild or moderate’. Angiographic criteria for entry were two- or three-vessel disease (greater than 50 per cent obstruction); left main disease was optional, and left ventricular function had to be essentially normal, with an ejection fraction of at least 50 per cent.

Seven-hundred-and-sixty-eight patients were randomised: 395 to surgical, and 373 to medical treatment.

At five years, 30 (7.6%) patients in the surgical group had died, compared with 61 (16.3%) of the medical group [9]. This 53 per cent difference in overall mortality (95% confidence limits 30% and 71%) was highly significant both statistically and, more importantly, clinically. As in the VA study, the results were analysed separately for several predetermined subgroups, and it was found that surgical treatment was accompanied by a 66 per cent better survival than medical treatment in patients with three-vessel disease, 60 per cent in patients with two- or three-vessel disease of which a component was obstruction in the proximal segment of the anterior descending coronary artery, and 60 per cent in patients who developed more than 1.5 mm ST segment depression during a bicycle ergometer test. No significant survival advantage from surgery was observed in patients with two-vessel disease who did not have obstruction in the proximal third of the anterior descending artery, or in those with lesser degrees of ST segment depression on exercise testing. Mortality was 56 per cent lower in patients with left main vessel disease randomised to surgery than in those randomised to medical treatment, but this difference was not statistically significant, probably on account of the small number of randomised patients. Early surgical treatment appeared to be of greatest prognostic value for older patients, those with evidence of previous infarction on their resting electrocardiogram, and for patients with peripheral arterial disease, all of whom had a high mortality with medical treatment, but younger patients, those with normal electrocardiograms, and those without peripheral arterial disease also benefited.

The European study showed, therefore, that surgical treatment prolonged the survival of patients with normal or nearly normal left ventricular function who had mild or moderate angina, three-vessel coronary disease or two-vessel disease accompanied by obstruction in the proximal segment of the anterior descending artery, particularly if these findings were accompanied by other indications of high risk. On the other hand, patients with normal ventricular function who had a normal resting electrocardiogram, and less than 1.5 mm ST segment depression during exercise testing, did not experience substantially improved survival from a policy of early surgery.

Coronary Artery Surgery Study

The third trial was the randomised part of the Coronary Artery Surgery Study [10].

The conduct of this trial implies that, like the European study, it was designed to compare a policy of early surgical treatment with one of initial medical therapy, followed by surgery for those in whom it was required for worsening angina, on the mortality of patients who had either very mild angina, or were asymptomatic after a myocardial infarction. Unlike the European trial, mild angina was defined strictly as Canadian Cardiovascular Society Class I or II.

Patients of either sex up to the age of 65 with greater than 70 per cent narrowing of one, two, or three coronary arteries were considered for entry, including those with up to 70 per cent narrowing of the left main stem. Another difference from the European study was that left ventricular function could be normal or modestly depressed. The patients were subdivided into those with mild angina and normal left ventricular function (ejection fraction greater than 50 per cent)—group A, those with mild angina and moderately depressed left ventricular function (ejection fraction 35-49%)—group B, and those who were asymptomatic after a myocardial infarction—group C.

A total of 16,626 patients were screened at 11 participating sites, and of these 28.3 per cent were excluded because of normal coronary arteries or minimal disease, 4.9 per cent because there were no operable vessels, 36.5 per cent because of class III or IV angina, and 1.5 per cent because of severe stenosis of the left main coronary artery. Some patients, of course, had more than one of these reasons for exclusion. Thus, for over 70 per cent of the patients who underwent coronary arteriography in the participating centres during the study period, the decision on medical or surgical treatment was uncontroversial. A further 16.1 per cent of patients were excluded for a variety of reasons including previous coronary bypass grafting, severe heart failure or age greater than 65, leaving only 12.7 per cent of the patients who were screened eligible for participation in the trial. In the event, only 4.7 per cent (780 patients) were randomised.

At five years, 29 of the 390 (7.4%) patients randomised to surgical treatment had died, compared with 36 of 390 (9.2%) assigned to medical treatment. This 30 per cent difference in mortality (95% confidence limits 61% re-
duction in mortality and 13% increase in mortality) could have arisen by chance.

By far the most important aspect of this result is the low mortality in the medically treated patients: the annual risk of death was 1.6 per cent per year, compared with 3.3 per cent per year in the medical group of the European study. In other words, the entry criteria for the CASS trial inadvertently defined a group of patients with an excellent prognosis, and in consequence the trial was not powerful enough to detect or exclude a large benefit from surgical treatment.

Analysis of the results of the pre-randomisation subgroups provides little extra information when considered in isolation, but in the context of the preceding trials is interesting. The survival of 514 patients in group A, those with mild angina who had well preserved left ventricular function, was virtually identical at 95 and 96 per cent in the medical and surgical groups respectively. Survival in the group C patients who were asymptomatic after a myocardial infarction was less favourable but, once again, similar in both the medical and surgical patients at 89 per cent. Of group B, however, which consisted of 106 patients with mild angina who had moderately impaired left ventricular function, 85 per cent survived in the medical group, compared with 96 per cent in the surgical group. The wide 95 per cent confidence limits of this difference cross the no difference line, possibly because of the small number of patients, but if real, the observed survival advantage would represent a very worthwhile surgical achievement; in effect surgical treatment appeared to counter, more or less completely, the adverse influence on survival of having moderately impaired left ventricular function. A subsequent analysis when the patients had been followed for up to seven years showed that for all patients with impaired left ventricular function (which included all patients in group B and some of those in group C) cumulative survival for those assigned to surgery was 86 per cent compared with 70 per cent for those assigned to medical treatment [11]. Further analysis of this small number of patients suggests that, as in the VA study, the significant advantage conferred by early surgical treatment was restricted to those with abnormal left ventricular function combined with disease in all three main coronary trunks.

Conclusions from the randomised trials

Whilst it would be absurd to deny certain discrepancies and the dangers of multiple subgroup analyses, the consistency within and between the three trials, which were carried out in groups of patients with widely differing prognoses during a period of rapidly evolving surgical technique, is inescapable. Collectively, they showed that for patients with reasonable left ventricular function but in whom a poor prognosis could be anticipated for other reasons, the outlook was improved by ACBS, whereas for those in whom the prognosis was favourable, surgical treatment improved symptoms, but had little, if any, influence on survival.

The principal discrepancy is that in the European trial the prognosis with medical treatment for patients with three-vessel coronary disease (all of whom had essentially normal left ventricular function) was rather poor, whereas for patients randomised in the CASS, apparently comparable coronary anatomy was accompanied by a low mortality. Data from the CASS registry [12] confirm that, in general, three-vessel disease is indeed an adverse prognostic factor (18% four-year mortality with medical treatment for patients with normal left ventricular function), and the most reasonable, though not wholly satisfactory, explanation for the difference between the two trials is that the European patients had a worse prognosis than the CASS patients in association with their more severe angina. A high mortality among patients with three-vessel disease was also observed in the VA study, in which 25 per cent of those in the medical group died within five years, though the 19 per cent five-year mortality in the surgical patients was not significantly superior; it seems probable that the failure to demonstrate a conclusive advantage from ACBS in these patients is related to the widely acknowledged limitations of surgical treatment during the period of the VA study.

Recommendations for clinical practice

How, then, can we recognise the high risk patient who is likely to have an improved prospect of survival from surgical treatment? The angiographic finding of ‘significant’ narrowing (certainly more than 75 per cent, and perhaps more than 50 per cent) of the left main coronary artery is widely accepted as an adverse prognostic sign in a patient with angina, particularly if associated with disease in the right coronary artery (or a dominant left coronary circulation), or with impaired left ventricular contraction. Multiple vessel coronary disease may be relatively benign in the medium term if left ventricular function is normal and the patient has mild angina. The exercise electrocardiogram is of great value in these circumstances, with a strongly ‘positive’ result at a low workload indicating high risk, while a well preserved exercise capacity, even if accompanied by pronounced ST segment depression, is reassuring even in the presence of extensive disease [13-15]. The response to exercise of the left ventricular ejection fraction (measured by radionuclide ventriculography) appears to discriminate reliably between a good or poor prognosis among patients with three-vessel disease [16]. Moderately impaired left ventricular function is highly predictive of a poor prognosis with medical treatment, and if accompanied by angina and multiple vessel disease there is good evidence that surgical treatment will improve survival. None of the trials randomised the patients at highest risk—those with severely impaired left ventricular function—and although there is some evidence from CASS registry data [17] of a beneficial influence of surgery in these circumstances, the risk of operation is increased, and surgery should be considered only for patients in whom angina, rather than breathlessness, is the dominant symptom.

Conclusions

Patients with angina which interferes with their everyday
working or social activities should be referred for coronary arteriography and, if the findings are appropriate, for surgical treatment. Many, but not all, of these patients will have high risk coronary disease, and the operation may well prolong their lives.

Patients with mild angina should be referred for angiography if the resting electrocardiogram is markedly abnormal, if there is evidence from clinical assessment, echocardiography or radionuclide ventriculography of significant left ventricular dysfunction, or if they are unable to exercise beyond the first two stages of the standard Bruce Protocol or equivalent, particularly if the test is accompanied by marked ST segment depression (2 mm or more), or by deteriorating left ventricular function on the radionuclide ventriculogram. If, in these circumstances, angiography shows important obstruction of the left main coronary artery, of all three coronary arteries, or of two vessels including the proximal segment of the anterior descending artery, surgical treatment should be considered with the expectation that it will improve the prognosis. From the limited data available, it seems reasonable to undertake coronary angiography on asymptomatic survivors of a myocardial infarction if the exercise test is markedly abnormal, for surgical treatment could be justified if the angiogram should show three-vessel or left main coronary disease, provided that left ventricular function is not severely impaired.

Patients without symptoms or with very mild angina who have a favourable exercise test can be expected to have a good prognosis during the succeeding five years, and prophylactic surgical treatment is inappropriate. Such patients should be kept under review and reassessed if their angina progresses or the exercise test deteriorates.

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When the College was in Pall Mall a strange portrait of Thomas Linacre hung over the fireplace in the Censors’ Room. Strange in that it was painted in 1810 by the College’s Bedell, William Miller. He was paid 20 guineas for his work which was copied from a supposed portrait of Linacre at Windsor. The fate of that picture was recorded 20 years ago by Dr Charles Newman. ‘... there hung Miller’s portrait of Linacre, as Founder of the College, until the early 1930s, when Dr Sidney Phillips, the Treasurer, discovered that Linacre, for about the last 20 years of his life, had been in Holy Orders. Dr Phillips was a relic of the anti-clerical feeling of many 19th century intellectuals, especially in France, and was so horrified by his discovery that he at once banished the picture to the cellars, and substituted the portrait of Henry VIII ... on the grounds that Linacre was not the Founder of the College: Henry VIII was, and he scored out the contrary statement in his official copy of Munk’s Roll. ... Sidney Phillips was a kindly old man, and a considerable financier: he more than quadrupled the College’s investment income during his reign, by playing bridge with friends from the City and moving the College’s money from one gilt-edged stock to another. He was of great age, and one of the terrors of lecturing to the College in the old lecture theatre was that he sat at the end of the row of College Officers, next to the fire, and always fell asleep and toppled towards it. A nursery fire-guard was put up to save him, but it was an agonising thing for the un instructed to watch him gradually nearing his doom. His ‘office’ was the North side of the table in the Censors’ Room: Sir Raymond Crawfurd, the Registrar, sat on the South side, near the corner, because from that spot he could see nothing, in the room or in Trafalgar Square, which was less than a hundred years old. Except Sidney Phillips, and he was so near that it didn’t really matter.’

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