Can improved quality of care reduce the costs of managing angina pectoris?

J. G. F. Cleland

From the CRI in Heart Failure, University of Glasgow, Glasgow, U.K.

Angina pectoris is a common symptom in patients over 50 years and is usually secondary to myocardial ischaemia resulting from coronary artery disease. The management of angina should be aimed at the maintenance or improvement of quality of life and delaying death. There are three strategies that may be adopted: medical, percutaneous transluminal coronary angioplasty and surgery. The majority of patients with angina can be controlled symptomatically most of the time by medical treatment alone. Any assessment of cost of treatment must take into account the cost of investigation, treatment, the morbidity associated with procedures or side effects of drugs, together with that of recurrent hospitalization, prolonged life and premature death. In addition, the duration of treatment has a major bearing on cost. Taking these factors into account, medical therapy is the least expensive short- and long-term treatment for angina pectoris. A medical approach to treatment also has considerable advantages over an interventional approach in terms of major morbidity. Only one of six surgical trials has demonstrated a survival benefit.

(Eur Heart J 1996; 17 (Suppl A): 29-40)

Key Words: Angina pectoris, PTCA, CABG, cost benefit.

Introduction

Angina pectoris is a common symptom in patients over the age of 50 years and is usually secondary to myocardial ischaemia due to atheromatous coronary artery disease (CAD). CAD is one of the leading causes of mortality in industrialized countries, both in the total population and in those under the age of 65 years[1-4]. As angina pectoris, by definition, is symptomatic, it is easier to identify than other manifestations of chronic CAD, such as 'silent' ischaemia or asymptomatic CAD.

The two components of the management of angina pectoris are to maintain or improve the quality of life and to delay death. Anginal symptoms constitute one component of quality of life for which there are essentially three management strategies: medical, percutaneous transluminal coronary angioplasty (PTCA) and surgery. Currently there is a widespread belief that surgery and PTCA offer additional survival benefits to several large subgroups of patients, though the size and significance of such benefits are disputed. However, the idea that by treating angina we will substantially reduce mortality from CAD may not be correct. Data from the Framingham study indicate that only about 25% of patients admitted with a myocardial infarction (MI) will have an obvious history of angina prior to the event[5-7]. Thus, 75% of patients having an infarct will be missed by a strategy that concentrates solely on the treatment of angina. Furthermore, there is no evidence from controlled interventional trials that surgery or PTCA reduce the incidence of MI at all.

Against this background we must judge the relative merits of different approaches to managing patients with angina pectoris. However, in order to judge the best approach it is first necessary to consider the size and nature of the problem.

Epidemiology of angina and coronary disease

The incidence and prevalence of angina have been determined in a number of community screening programmes with varying methodologies[1-4,6-10], of which the most rigorous was probably that of Ghandi et al.[4], which included screening of suspect cases using treadmill exercise tests. The incidence of angina appeared similar to that of previous reports in the U.K. and the U.S.A., though not in Israel[2], although methodological differences may account for this latter anomaly. The prevalence of angina appears roughly similar across largely Caucasian populations but may be higher in people from the Indian subcontinent[11]. The overall prevalence of angina in the population over 30 years of age is 24 000 per million (average of men and women) with about 800 per million new cases per year[4,10]. If we were to assume that the system only treated new cases and that intervention were required in...
all patients, approximately 200,000 procedures would need to be undertaken per year in the U.S.A. Since over 100,000 coronary artery bypass grafts (CABGs) are currently performed in the U.S.A. each year and a similar, or greater, number of PTCA's, it is logistically feasible to treat all patients by intervention at least once in their lifetime. But is it to their best advantage? The U.K. in general, and Scotland in particular, has been identified as having a high mortality rate from CAD. However, the quality control of death certification data is variable. In the context of a clinical trial the total mortality in a population would be assessed, rather than deaths attributable to one cause. If CAD is a major killer, then the incidence of CAD should cause variations in life expectancy between countries. However, the U.K. male population appears to live somewhat longer than men from most other industrialized nations, including Italy and France which are countries generally considered to have less CAD. Interestingly, the pattern is different for women, who also have much lower rates of premature CAD. National differences in mortality due to CAD may be due to over certification of this cause of death in the UK or under reporting in other countries.

**Natural history of angina**

The high prevalence of angina compared with incidence suggests that the prognosis of such patients is not generally poor. The prognosis of angina pectoris treated medically is probably improving. Some of the most recent studies suggest that, with the introduction of the widespread use of aspirin, the annual risk of MI or death are both less than 2% (Table 1) and with more aggressive medical management further improvements may be expected. Moreover, the procedural morbidity and mortality of PTCA or CABG (see below) are similar to, or exceed, the annual mortality of the medically treated condition and this must be taken into account when advising on treatment for symptoms.

Another important feature of angina is that, contrary to popular belief, it is not a condition in which symptoms progress inexorably. The severity of angina commonly fluctuates and 30–40% of patients will have spontaneous remission of angina for 2 or more years. This represents a significant problem when it comes to management. The patient is usually going to be referred to a cardiologist during an exacerbation of symptoms and it is likely that symptoms will tend to improve spontaneously. Therefore, it is difficult to know if the cardiologist should carry out interventions on the basis of symptoms at the time of referral or wait, and if so, for how long. This problem is compounded by the increased risk of infarction and death during the first few weeks after symptoms appear. When considering risk stratification it is also important to remember that many patients with angina will already have had an MI or have heart failure.

**Cost-effective management of angina**

**General considerations**

There is no justification for a treatment which is inexpensive if it is also ineffective. In order to judge whether a treatment is good value for money, it is first necessary to know if it is effective and then determine the magnitude of benefit. An effective treatment can be defined as one that maintains or improves quality of life and delays death. Only once the magnitude of benefit has been determined is it appropriate to consider cost. Quality of life is a complex issue and is easier to consider in parts, rather than as a whole. However, it is an act of sometimes mistaken faith that, by treating one aspect of the disease, patient quality of life will be

---

**Table 1 Medical prognosis of patients with angina**

<table>
<thead>
<tr>
<th>Study</th>
<th>Start year</th>
<th>Population</th>
<th>CABG (% per annum)</th>
<th>MI (% per annum)</th>
<th>Death (% per annum)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Framingham131, 1972</td>
<td>1958</td>
<td>119 men</td>
<td>?</td>
<td>3.1</td>
<td>2.0</td>
</tr>
<tr>
<td></td>
<td>14-year follow-up</td>
<td>108 women</td>
<td>2</td>
<td>1.9</td>
<td>0.9</td>
</tr>
<tr>
<td>Veterans14, 1992</td>
<td>1972–1974</td>
<td>354 men</td>
<td>2.4</td>
<td>2.3</td>
<td>3.7</td>
</tr>
<tr>
<td>18-year follow-up</td>
<td>1972–1974</td>
<td>373 men</td>
<td>3.0</td>
<td>2.2</td>
<td>2.4</td>
</tr>
<tr>
<td>ECSS15, 1985/88</td>
<td>1973–1976</td>
<td>780 (90% men)</td>
<td>3.8</td>
<td>2.2</td>
<td>2.1</td>
</tr>
<tr>
<td>12-year follow-up</td>
<td>1979</td>
<td>309 (90% men)</td>
<td>5.8</td>
<td>2.6</td>
<td>1.7</td>
</tr>
<tr>
<td>CASS17, 1984/90</td>
<td>1987</td>
<td>1099 no aspirin*</td>
<td>0.7</td>
<td>1.8</td>
<td>2.1</td>
</tr>
<tr>
<td>5-year follow-up</td>
<td>1987</td>
<td>1206 aspirin*</td>
<td>0.7</td>
<td>1.2</td>
<td>1.6</td>
</tr>
</tbody>
</table>

*about 50% were women.

CABG=coronary artery bypass graft; CASS=Coronary Artery Surgery Study; ECSS=European Cooperative Surgical Study; MI=myocardial infarction.

Eur Heart J, Vol. 17 (Supplement A), 1996
wholly changed. Treatment to improve quality of life should be directed not only at improving symptoms and increasing mobility, but also at minimizing patient anxiety and the side effects of treatment. The anxiety, pain and complications of PTCA and CABG need to be included as part of the potential morbidity related to angina, while prevention of MI and stroke are also major considerations.

There are few data on the direct measurement of quality of life in angina, although the appearance of CAD has a major adverse effect on patient well being[22]. Moreover, opinion is divided about how well relief of symptoms and improvements in exercise testing are reflected in estimates of quality of life.

The issue of mortality is also more complex than might appear at first sight, since everybody will eventually die and the longer you live the greater is the risk of significant morbidity. Indeed, a recent survey showed that the majority of subjects felt that sudden cardiac death was easily the preferred way to die[23]. Thus, a selective reduction in premature death, however that is defined, and reduction in deaths other than sudden might be ideal, but probably impossible to achieve.

Assigning cost to a particular management strategy is also far from simple. The cost of investigation, treatment, the morbidity of procedures or side effects of drugs, together with the cost of recurrent hospitalization, prolonged life and premature death must all be taken into account. In addition, the duration of treatment has a major bearing on cost. Furthermore, such costs must be considered from the viewpoint of the health service, the individual and society as a whole.

Which patient?

The majority of patients with angina can be controlled most of the time by medical treatment alone. PTCA and CABG could, theoretically, offer advantages, such as reduced risk of infarction or death, fewer symptoms and the freedom from the need for regular medical therapy. Of course, the risk of these procedures needs to be weighed against the risks associated with medical management of the disease. Similarly, the pain and anxiety associated with procedures needs to be balanced against continuing symptoms and the need for regular therapy.

For the patient with intractable angina, whether stable or not, medical treatment is obviously no longer satisfactory and assessment of the relative cost-benefit analysis in this situation compares only PTCA to CABG.

Medical management

Changes in lifestyle

Stopping smoking reduces the risk of re-infarction and death[24] and smoking may negate the anti-anginal benefits of nifedipine[25]. Regular exercise is, potentially, a very cost-effective treatment and, intuitively, may be considered to have the most positive effect on quality of life[26]. However, there is no evidence that exercise can reduce mortality in those with angina[27].

Dieting to reduce obesity is also likely to have a benefit on symptoms of angina. Reduction in dietary fat intake appears to retard the progression of angiographic coronary atherosclerosis[28] but, in post-MI patients, this strategy has not reduced mortality or re-infarction, although this may be achieved by other dietary interventions[27].

Treatment of risk factors

Treating risk factors may not only reduce major morbidity and mortality, but also slow, or even reverse, the tendency for angina to get worse. The most accurate ‘risk factor’ for the presence of coronary atheroma is identification of the atheroma itself. Furthermore, it is likely that patients with angina obtain much greater benefit from risk factor control than the general population. However, there are few data on the effects of risk factor control in such a population.

Studies in hypertensive patients over the age of 65 years have demonstrated that thiazide diuretics in particular are effective in reducing the rates of MI, heart failure and other manifestations of CAD[29–31] and their more widespread use should be encouraged. β-blockers have an obvious advantage since they reduce the complications of hypertension, are effective anti-anginal agents and reduce mortality in patients after MI[27]. In patients with well-preserved ventricular function, the calcium antagonists verapamil and diltiazem also improve prognosis after MI and are also effective anti-anginal treatments[27], although diltiazem is associated with an increase in heart failure in patients with impaired ventricular function[32,33]. The dihydropyridine calcium antagonist, amlodipine, is also an effective anti-anginal and anti-hypertensive. Furthermore, unlike other calcium antagonists, it can also be used in patients with compromised ventricular function. Results from the mortality study Prospective Randomised Amlodipine Survival Evaluation (PRAISE)[34] have demonstrated that amlodipine (as opposed to other calcium antagonists) does not worsen mortality or morbidity in patients with severe heart failure. In fact, in a subgroup of patients, whose heart failure was not due to ischaemia, amlodipine produced a favourable effect on survival. In those with ventricular dysfunction, angiotensin converting enzyme (ACE) inhibitors reduce the frequency of hospitalization for angina, recurrent MI and mortality[27].

Lipid-lowering agents have been highly successful in reducing the incidence of new onset angina and other coronary events in high-risk populations[35,36]. More recently the ‘statins’, a new class of lipid-lowering agent, have been introduced. The benefits in preliminary studies indicated a startling reduction in coronary
events, with marked benefit after only 6 months of treatment[37]. More recently the Scandinavian Simvastatin Survival Study (4S)[38] demonstrated a reduction in myocardial infarction, need for repeat coronary interventions and mortality with the use of simvastatin 40 mg. day$^{-1}$ in patients with a total cholesterol above 5.5 mmol. l$^{-1}$ despite dieting. Benefits were similar in patients with and without prior infarction[39].

Evidence that aggressive control of diabetes per se has an effect on coronary events is controversial. However, treatment of hypertension and hyperlipidemias in patients with diabetes probably has an even greater impact on vascular events than in other patients with angina.

Aspirin and warfarin

The benefits of aspirin in patients post-MI, at least when ventricular function is well preserved, are well publicized[27]. The Swedish Angina Pectoris Aspirin Trial (SAPAT)[20] and others[40] also noted a reduction in coronary vascular events in patients treated with aspirin and a β-blocker. The benefits of warfarin in this population may be even more striking[27,41].

Nitrates[27,42]

Sublingual nitrates are highly effective for the relief of angina and are very inexpensive. Short-acting nitrates may be used even more effectively by administering them before activity likely to provoke angina and, when used in this fashion, they will usually delay or prevent the appearance of symptoms. However, nitrates have not been shown to reduce major events such as MI, although mortality benefit was observed in patients with heart failure, many of whom had CAD, when used in combination with hydralazine[42].

When using long-acting nitrate preparations, the most important principle is to consider the possibility of nitrate tolerance, which can occur within days of initiating treatment. A nitrate-free interval of 6–8 h is required each day to prevent tolerance from occurring. The principal side effect of nitrates is headache. The low frequency of serious side effects make nitrates an attractive option, especially for elderly patients.

β-blockers[27,42]

β-blockers are also highly effective for the management of angina. Unlike nitrates, tolerance is not a problem and many of these agents may be given once daily and provide 24-h action.

Side effects of β-blockers are numerous but usually minor. β-blockers should not be used in asthmatics, in patients with resting limb ischaemia or uncontrolled heart failure. β-blockers have remarkably little effect on intermittent claudication in most patients.

Dihydropyridine calcium antagonists[27,42]

The recent Total Ischaemic Burden European Trial (TIBET) indicated that nifedipine was as effective as atenolol in controlling angina, although the agents were better in combination than when used singly[45]. This fact was confirmed in the recent Canadian Amlodipine/ Atenolol in Silent Ischemia Study (CASIS) combining amlodipine and atenolol[46].

The principal side effects associated with these drugs are flushing, headache, swollen ankles, hypertension and, especially in elderly patients, exacerbation of angina. The latter may reflect a fall in coronary perfusion and a reflex tachycardia. Newer, long-acting dihydropyridines, such as amlodipine, may give rise to fewer side effects due to their smoother pharmacodynamic profile.

There is no evidence that these agents reduce mortality in patients with angina or after MI when used alone. Indeed, there is a trend to excess mortality or infarction, both in patients with minor CAD receiving nifedipine[47] and after MI[27]. However, when used with a β-blocker there is some evidence, inconclusive as yet, that they exert an additional benefit in terms of reducing unstable angina and infarction[45,48]. Evidence that dihydropyridine antagonists can retard the progression of atheroma is weak and the studies purporting to show such an effect are notable for the increase in coronary events in the group receiving active treatment[44,47,49,50]. Nifedipine generally exacerbates symptoms of heart failure. In contrast, preliminary studies of amlodipine in heart failure suggest that this agent has a favourable effect on symptoms. Data from the mortality study, PRAISE, (as reported previously)[34] have recently been presented.

Diltiazem[27,42]

Diltiazem is an effective anti-anginal agent and has a favourable side-effect profile. The Asymptomatic Cardiac Ischemia Pilot (ACIP) trial[48] indicated that aggressive treatment regimens designed to suppress 'silent' as well as symptomatic ischaemia, incorporating a combination of atenolol and nifedipine or diltiazem and isosorbide dinitrate, could reduce the requirement for coronary interventions and were not associated with any increase in MI or mortality. However, because of the risk of bradycardia, heart block and their additive
negative inotropic effects, the combination of diltiazem and β-blockers should be used with caution. There is no evidence that diltiazem alone reduces mortality in patients with angina. After MI, among patients with well-preserved ventricular function, diltiazem probably does reduce the risk of re-infarction and death. This is balanced by a trend to an excess of heart failure and mortality in patients with substantial ventricular dysfunction[32].

Verapamil [27,42]

Verapamil is as effective as a β-blocker for controlling symptoms. Side effects of verapamil include constipation and an exacerbation of heart failure. Constipation often improves with time and may be less of a problem with slow-release preparations. Verapamil should be given to patients on a β-blocker only under the most expert supervision, due to the risks of inducing bradycardia, complete heart block or heart failure.

There is no evidence that verapamil reduces mortality in patients with angina. After MI, among patients with well-preserved ventricular function, verapamil reduces the risk of re-infarction and death. This is balanced by a trend to an excess of heart failure and mortality in patients with ventricular dysfunction[31]. There is some evidence that verapamil can retard the progress of atheroma[44].

Other agents

Theophylline, a coronary vasoconstrictor, has some benefit in angina[32]. Evidence that ACE inhibitors reduce or exacerbate myocardial ischaemia is controversial[55] and any therapeutic effect on ischaemia, as opposed to infarction, is probably clinically irrelevant. However, there is substantial, though not conclusive, evidence that long-term ACE inhibition can reduce episodes of unstable angina and MI[27].

A series of agents, including trimetazidine, that may improve ischaemic metabolism are being tested currently[54] and sinus node modulators are also in development. Amiodarone, currently used mainly as an anti-arrhythmic agent, is also a very effective anti-anginal agent. Transcutaneous spinal stimulation has been used for patients with intractable, inoperable angina[55].

Interventional management

PTCA

It is amazing that so much of the health budget is consumed by a procedure which is essentially untested! There is only one controlled trial of angioplasty compared with medical therapy for chronic stable angina[21]. This showed a marginal benefit in terms of relief of angina over 6 months of follow-up but a considerable excess of MI and need for CABG in the angioplasty group. Thus, a marginal improvement in symptoms was paid for not only in terms of cost, but also by the morbidity associated with both the procedure itself and with complications of the procedure. Comparisons between PTCA and CABG are no more promising[56]. PTCA is associated with a similar mortality and a higher re-infarction rate, need for repeat PTCA and need for further CABG.

Data from Medicare in the United States, probably the largest interventional database, indicated that the mortality within 30 days and 1 year of an angioplasty was 3.8% and 8.2%, respectively[57]. If the indication for angioplasty was restricted to angina then the figures were 1.9% and 6.0%, respectively. Although some centres may believe that their results are better, it is likely that this large database represents the true state of affairs. Furthermore, it seems doubtful whether patients are being properly informed by doctors of the risks and benefits of PTCA, otherwise patients would presumably be more reluctant to entrust themselves to the procedure[58].

Therefore, it is to be hoped that PTCA will be reserved for the management of intractable symptoms, either resulting from single-vessel disease or when the patient is inoperable. There is a continuing need for ethically approved research into the possible benefits of PTCA. The role of PTCA in unstable angina and as a primary procedure after MI remains to be properly defined, although there is some supportive evidence for its use in this situation[27]. However, the routine use of angioplasty after thrombolysis is to be deplored[27].

Surgery

Six trials[14-18,59-61] of CABG have been conducted, of which only one showed a significant benefit from surgery in terms of mortality. None of the trials suggested that surgery reduced the risk of MI. Moreover, there is no evidence that surgery in patients without symptoms improves prognosis[17,18].

It has been argued that the lack of difference between medical and surgical outcomes resulted from patients being crossed over from medical treatment to surgery if their symptoms were too severe. This argument is flawed on at least two counts: (1) the crossover rates to surgery were not large, being in the order of 3-4% per year; (2) the landmark studies with ACE inhibitors in heart failure were able to identify benefits despite crossover rates of up to 30%[27]; (2) good medical practice indicates that those patients with intractable symptoms should be treated surgically regardless of prognosis.

It is also said that surgical techniques have improved, which is undoubtedly true, and that this will have led to a lower operative mortality and better long-term results. However, medical treatment for angina has
also improved. Surprisingly, mortality within 30 days of CABG was 6.4% and within 1 year 11.8% (5.1% and 10.8%, respectively, if confined to angina as the indication) (US Medicare system — 1992 report); these figures are no better than for the older surgical trials. It is likely that surgery on higher-risk individuals accounts for much of the failure of surgical mortality to decline. In any case, the lack of a positive result for surgery because of inadequate study design hardly justifies the use of surgery and, therefore, a more convincing positive trial result is still required.

The duration of the benefits of surgery is also open to doubt. Surgical trials have indicated that after 5 years there is little difference in the severity of symptoms or the amount of medication required whether patients are randomized to surgery or not (Fig. 1). This probably reflects spontaneous improvements of symptoms in some medically managed patients.

**Figure 1** Severity of angina at baseline, 1 and 5 years by treatment assigned. Numbers at top of bars are numbers of patients with angina scores. (Reproduced with permission from Hultgren et al.162.)

**Figure 2** Total number of hospitalizations including those for coronary artery bypass graft surgery (CABG). Excluded are scheduled hospitalizations for coronary arteriography done on some patients at approximately 18 and 60 months after entry as part of the study protocol. (Reproduced with permission from the CASS Investigators163.)

Eur Heart J, Vol. 17 (Supplement A), 1996
and the benefits of (delayed) surgery in others. Overall the number of hospitalizations was greater in those randomized to surgery and the rate of hospitalization, even excluding initial surgery, was no different between groups (Fig. 2).

**Risk stratification**

The exercise test appears a reliable tool for predicting the risk of death and, possibly, the need for surgery in patients with angina. There is no evidence that coronary angiography is superior to exercise testing and clinical assessment in predicting prognosis. Myocardial scintigraphy and, more importantly, measurement of ventricular function may enhance the predictive accuracy of the exercise test. However, the test has been criticized because, although it accurately identifies mortality, it may fail to predict MI. Since surgery and PTCA have not been shown to modify the risk of MI, the inability of the exercise test to predict MI is irrelevant when judging the need for intervention. It can also be argued that the exercise test does not reliably predict those patients with left main coronary artery stenosis. However, the CASS registry indicated that 7.3% of patients undergoing angiography had a left main coronary stenosis >50% but that only 0.3% were asymptomatic. The prognosis of left main disease is not uniformly poor and it is likely that the exercise test does identify those patients with left main disease who require surgery. Similarly, it would appear that exercise testing can identify those patients with three-vessel disease who do or do not need surgery.

The major problem retarding progress in the management of CAD is the concept that it is the lesion >70% that is most likely to occlude. However, the data show that most coronary occlusions occur on minor atheromatous plaques, ignored by those planning surgery or PTCA. The poor prognosis associated with triple-vessel disease compared with that for patients with a lesser number of affected vessels is probably more closely related to the surface area of the coronary arteries involved with atheroma, rather than to the severity of the lesions.

There is no doubt that once an angiogram has been undertaken it is emotionally difficult not to intervene. The obvious solution is not to do the angiogram. A critically important study is now under- way in the U.K. which will compare the outcome in patients undergoing routine angiography for angina compared with those being assessed by treadmill exercise testing alone.

**The efficacy argument: conclusions**

Medical management of CAD is the strategy which offers the greatest efficacy for the vast majority of patients with angina because: (1) medical treatment is associated with the lowest morbidity, when the morbidity associated with interventional procedures is taken into account; (2) mortality associated with medical treatment is not appreciably higher than with interventions; (3) the potential benefits of angioplasty are generally unproven; (4) 'aggressive' medical treatment of angina pectoris has improved prognosis dramatically in the last 5 years.

Therefore, medical treatment for angina is the most effective treatment if symptoms are satisfactorily controlled. But is it the least expensive?

**The cost of treating angina**

Assessing the total costs of different strategies is fraught with hazard. Ultimately, a regime which successfully prolongs life is likely to be the most expensive as the patient, in living longer, is likely to exhibit greater morbidity, which is where the major costs of treatment lie. The simple analysis presented here assesses cost as that of drugs and procedures and benefits in terms of reduction in MI and death.

**Costs of surgery and angioplasty**

The costs of surgery and PTCA are shown in Table 2. Costs have been calculated in a number of recent studies comparing the two procedures. The cost of the procedure account for about a third of the total cost attributable to surgery. Intensive care unit costs, time in hospital and the need for revision of surgery account for the other two-thirds. Procedural costs account for more than 50% of the total attributable costs of PTCA, with the remainder being accounted for by hospitalization costs. The costs of emergency surgery as a result of a complication of PTCA and of a second CABG are considerably higher due to the greater morbidity and the longer hospital stay, particularly that part spent in intensive care. The cost of CABG in these circumstances may be four or more times greater.

<table>
<thead>
<tr>
<th></th>
<th>CABG</th>
<th>PTCA</th>
</tr>
</thead>
<tbody>
<tr>
<td>van den Brand et al. (71) 1990</td>
<td>Dfl</td>
<td>21,000</td>
</tr>
<tr>
<td></td>
<td>ECU</td>
<td>10,000</td>
</tr>
<tr>
<td>Cohen procedure (72) 1993</td>
<td>US$</td>
<td>5500</td>
</tr>
<tr>
<td></td>
<td>ECU</td>
<td>4500</td>
</tr>
<tr>
<td>Cohen total (72) 1993</td>
<td>US$</td>
<td>21,000</td>
</tr>
<tr>
<td></td>
<td>ECU</td>
<td>17,500</td>
</tr>
<tr>
<td>Hlatky (73) 1990</td>
<td>US$</td>
<td>17,500</td>
</tr>
<tr>
<td></td>
<td>ECU</td>
<td>14,500</td>
</tr>
</tbody>
</table>

ECU/£0.79=US$1.2=DM1.9=DFL2.1=Y122

(Continued from Financial Times, August 1994).

Eur Heart J, Vol. 17 (Supplement A), 1996
A number of assumptions have been made, tending to bias cost estimates against medical treatment: (1) that all the patients on medical treatment will be treated with a β-blocker, calcium antagonist, aspirin and sublingual nitrate. Lipid-lowering drugs are relatively expensive and are added in parentheses, since there are arguments that all three treatment strategies will tend to bias cost estimates against medical treatment: (2) that once a patient has had CABG or PTCA they never subsequently require medical treatment but that medically treated patients will require continued medical treatment even if crossing over to intervention. Both assumptions are obviously false. After PTCA, patients may be taking no less medical treatment than those treated medically by the end of the first year, while 5 years after CABG patients are taking a similar amount of medical treatment to those managed medically[21,62,63]: (3) that the number of outpatient visits will be similar in patients managed by medical and interventional means. However, it is likely that there will be an excess of visits in the interventional groups, in the short term, with a possible diminution in the medium term. In the long term, it is likely that medically and interventionally managed patients will require a similar number of visits; (4) that there is no difference in the level of investigations in the different groups. However, the interventional groups will all require coronary angiography, while only those patients in the medical group who require subsequent intervention will undergo such procedures. Thus, investigation should be less expensive in the medically treated group.

### Costs of medical treatment

The costs of medical treatment will vary widely depending on how much treatment is needed to control symptoms and how aggressively risk factors are controlled. It is obvious that the annual cost of even the most aggressive medical treatment is far lower than the procedural cost for interventions (Table 3).

### Comparative costs of medical treatment, PTCA and CABG

Four trials have been used as models to test the cost benefit of medical treatment, PTCA and CABG. It should be noted that these costs are not intended to be absolute but, rather, relative costs. As CABG has been shown not to affect subsequent need for hospitalization and as it is unlikely that PTCA or surgery reduce the overall number of clinic visits, these costs have been assumed to be the same regardless of strategy. Since it is appropriate to assess cost benefit over a single arbitrary span of time, it is necessary to study the consistency of benefit across a series of time frames. Costs have also been calculated as though all patients had survived, while real costs would be lower, since those that die are no longer treated. Although the costs of surgery in the medically assigned group have been taken into account, the costs of lipid-lowering therapy have not been added, which could have totalled up to 2-4 million ECU, had all 1000 patients been treated for 8 years.

A number of assumptions have been made, tending to bias cost estimates against medical treatment: (1) that all the patients on medical treatment will be treated with a β-blocker, calcium antagonist, aspirin and sublingual nitrate. Lipid-lowering drugs are relatively expensive and are added in parentheses, since there are arguments that all three treatment strategies will need an equal amount of risk factor control; (2) that once a patient has had CABG or PTCA they never subsequently require medical treatment but that medically treated patients will require continued medical treatment even if crossing over to intervention. Both assumptions are obviously false. After PTCA, patients may be taking no less medical treatment than those treated medically by the end of the first year, while 5 years after CABG patients are taking a similar amount of medical treatment to those managed medically[21,62,63]; (3) that the number of outpatient visits will be similar in patients managed by medical and interventional means. However, it is likely that there will be an excess of visits in the interventional groups, in the short term, with a possible diminution in the medium term. In the long term, it is likely that medically and interventionally managed patients will require a similar number of visits; (4) that there is no difference in the level of investigations in the different groups. However, the interventional groups will all require coronary angiography, while only those patients in the medical group who require subsequent intervention will undergo such procedures. Thus, investigation should be less expensive in the medically treated group.

### Trial data

A number of trials have assessed outcome in patients with angina for progressively longer periods post initiation of treatment. The ACIP trial[48] compared outcome at 3 months in patients treated medically to reduce symptoms only, those treated using an 'aggressive' medical regime to normalize the exercise test/eliminate ischaemia and a group treated by surgery or PTCA. The Angioplasty Compared to Medicine (ACME) trial[21] compared the effects of medical treatment and PTCA on outcome at 6 months in 200 patients with single-vessel disease, while the Randomised Intervention Treatment of Angina (RITA) trial[56] compared outcome at 2-5 years in 1011 patients randomized to surgery or angioplasty. The latest report of the European Cooperative Surgical Study (ECSS)[15,14] showed outcome at 12 years for patients randomized to medical treatment or surgery.

### Costs up to 3 months pre-treatment

The costs of CABG, PTCA and 'aggressive' medical treatment have been calculated on the basis of the ACIP study. No deaths had occurred in the interventional group or medical treatment group by this time. It has been assumed that the need for PTCA and CABG after the initial procedure was confined to those that had an initial PTCA and that half the CABG required in the first 3 months was a result of complications from PTCA and costs awarded accordingly.

Medical treatment was found to be by far the cheapest option and also entailed a lower risk of MI. Although the need for PTCA and CABG was higher in those randomized to medical therapy, this was still a small fraction of the total number of procedures to which the other groups were subjected. CABG cost about twice as much as PTCA (Table 4a).
The cost of managing angina pectoris

Costs up to 6 months

The costs of medical treatment over this period were less than 20% of those associated with PTCA. The one death that occurred in ACME was within the medical treatment group, but in a patient who insisted on having angioplasty. The patient died during the procedure but, as randomized, remains in the medical group. The need for repeat PTCA and CABG was higher in the interventional group, adding considerably to cost, and there were more infarcts in the PTCA group. Many of the PTCA patients still required medical treatment but this has not been added to the cost of PTCA shown in Table 4b.

Costs up to 2-5 years post-treatment

The additional costs 2-5 years after CABG were only slightly higher. Mortality after CABG was not significantly different from PTCA but there were more infarcts in the PTCA group. The costs of PTCA had

Table 4

<table>
<thead>
<tr>
<th>Costs (ECU)</th>
<th>CABG</th>
<th>PTCA</th>
<th>Medical</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>a Relative costs and benefits of treating 1000 patients for 3 months</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Procedure 10 million</td>
<td>4 million</td>
<td>0.1 million</td>
<td></td>
</tr>
<tr>
<td>3 months (ACIP) 10 million</td>
<td>5.3 million</td>
<td>0.5 million</td>
<td></td>
</tr>
<tr>
<td>Death 0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Morbidity MI</td>
<td>1-9%</td>
<td>1-0%</td>
<td></td>
</tr>
<tr>
<td>(Repeat) PTCA</td>
<td>0-9%</td>
<td>1-5%</td>
<td></td>
</tr>
<tr>
<td>(Repeat) CABG</td>
<td>2-4%</td>
<td>3-0%</td>
<td></td>
</tr>
<tr>
<td>Total procedures 1000</td>
<td>1033</td>
<td>45</td>
<td></td>
</tr>
<tr>
<td><strong>b Relative costs and benefits of treating 1000 patients for 6 months</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Procedure 10 million</td>
<td>4 million</td>
<td>0.1 million</td>
<td></td>
</tr>
<tr>
<td>6 months (ACME) 10 million</td>
<td>6.8 million</td>
<td>0.7 million</td>
<td></td>
</tr>
<tr>
<td>Death 2%*</td>
<td>0</td>
<td>1%</td>
<td></td>
</tr>
<tr>
<td>Morbidity MI</td>
<td>5%*</td>
<td>3%</td>
<td></td>
</tr>
<tr>
<td>(Repeat) PTCA</td>
<td>None*</td>
<td>15%</td>
<td></td>
</tr>
<tr>
<td>(Repeat) CABG</td>
<td>None*</td>
<td>7%</td>
<td></td>
</tr>
<tr>
<td>Total procedures 1000</td>
<td>1220</td>
<td>110</td>
<td></td>
</tr>
<tr>
<td><strong>c Relative costs and benefits of treating 1000 patients for 2-5 years</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Procedure 10 million</td>
<td>4 million</td>
<td>0.1 million</td>
<td></td>
</tr>
<tr>
<td>2-5 years (RITA) 10.8 million</td>
<td>8.4 million</td>
<td>0.1 million</td>
<td></td>
</tr>
<tr>
<td>Death 3-6%</td>
<td>3-2%</td>
<td>1%</td>
<td></td>
</tr>
<tr>
<td>Morbidity MI</td>
<td>4-0%</td>
<td>6-9%</td>
<td></td>
</tr>
<tr>
<td>PTCA</td>
<td>3-2%</td>
<td>18-2%</td>
<td></td>
</tr>
<tr>
<td>CABG</td>
<td>0-8%</td>
<td>18-8%</td>
<td></td>
</tr>
<tr>
<td>Total procedures 1040</td>
<td>1370</td>
<td>100*</td>
<td></td>
</tr>
<tr>
<td><strong>d Relative costs and benefits of treating 1000 patients for 8-12 years</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Procedure 10 million</td>
<td>4 million</td>
<td>0.1 million</td>
<td></td>
</tr>
<tr>
<td>8 years (ECSS) 16.0 million</td>
<td>6.7 million</td>
<td>0.1 million</td>
<td></td>
</tr>
<tr>
<td>Death 10-4%</td>
<td>6-7%</td>
<td>18-5%</td>
<td></td>
</tr>
<tr>
<td>Morbidity MI</td>
<td>14-0%</td>
<td>9-1%</td>
<td></td>
</tr>
<tr>
<td>(Repeat) CABG</td>
<td>7-2%**</td>
<td>26-8%</td>
<td></td>
</tr>
<tr>
<td>Total procedures 1072</td>
<td>268</td>
<td>110</td>
<td></td>
</tr>
<tr>
<td>12 years (ECSS) 19.2 million</td>
<td>10.6 million</td>
<td>0.1 million</td>
<td></td>
</tr>
<tr>
<td>Death 29-4%</td>
<td>33-3%</td>
<td>110</td>
<td></td>
</tr>
<tr>
<td>Morbidity MI</td>
<td>??</td>
<td>7%</td>
<td></td>
</tr>
<tr>
<td>CABG</td>
<td>11-0%</td>
<td>36%</td>
<td></td>
</tr>
<tr>
<td>Total procedures 1110</td>
<td>360</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Based on references[146-17]; ** assumes 0-9% per annum based on RITA[56] and 12-year ECSS data[55,56]; ACIP=Asymptomatic Cardiac Ischemia Pilot trial; ACME=Angioplasty Compared to Medicine trial; CABG=coronary artery bypass graft; ECSS=European Cooperative Surgical Study; MI=myocardial infarction; PTCA=percutaneous transluminal coronary angioplasty; RITA=Randomised Intervention Treatment of Angina trial.

Eur Heart J, Vol. 17 (Supplement A), 1996
risen considerably due to the need for further PTCA or CABG. The additional costs of medical treatment in these two groups have not been taken into account. PTCA remains somewhat cheaper than CABG but the additional morbidity due to repeated interventions and higher rates of infarction need to be remembered (Table 4c). Medical treatment was least expensive.

**Costs up to 8–12 years**

After a period of 8 years, the medical treatment strategy cost less than half that of surgical intervention. The cost of drug therapy in the increasing proportion of patients with recurrent angina in the CABG group was not taken into account and, therefore, the costs are actually an underestimate of the true costs associated with a surgical strategy. Moreover, medical costs have been calculated on the basis of patients requiring anti-thrombotic treatment and treatment with all three of the major classes of anti-anginal drugs simultaneously, representing an obvious overestimate of cost.

It was clear that CABG offered no advantage in terms of preventing MI. For every 1000 patients treated surgically, 81 lives would have been saved over 8 years at a cost over and above medical therapy of about 115 000 ECUs per life saved. This is expensive when compared with the cost of lives saved by other treatments. However, 919 patients would have been operated on without a significant benefit in terms of morbidity or mortality. Moreover, it is likely that prognosis with medical treatment has improved. Therefore, even given a relative benefit of surgery over medical treatment, it is likely that the absolute difference in benefit has shrunk, adding further to the relative excess cost of a first-line surgical approach (Table 4d).

**Conclusions**

Medical therapy, even allowing for routine use of lipid-lowering agents and two to three anti-anginal agents, is the least expensive short- and long-term treatment for angina pectoris. The advantage of a medical strategy of treatment is also considerable in terms of major morbidity. Risk stratification is a logical approach to deciding who should have surgery but, as outcome in high-risk subsets was not the primary, prospectively defined, goal of the surgical studies, considerable doubt remains as to who needs surgery. Further doubts as to the symptomatic benefits of interventions are raised because interventions cannot be conducted double blind, leading to patient and investigator bias on outcomes other than death. It is also not clear that coronary angiography, which probably generates many unnecessary interventional procedures, is needed to accurately predict those who will benefit from surgical intervention.

Many patients who require surgery experience delays or are unable to obtain the treatment they require. While some of the blame must lie with lack of provision for care, it is undoubtedly true that resources are being squandered on unnecessary procedures. Moreover, government agencies may believe that more, unreviewed, provision of resources for interventions may lead to a relative increase in the number of unnecessary procedures. A demonstrable effort to accurately select only those patients who will benefit from invasive investigation and intervention and proper discussion of the benefits and drawbacks to patients may be rewarded by a more sympathetic hearing from government. While it is important to maintain freedom of clinical judgement and practice, formal peer review would probably lead to more effective deployment of resources12.74. It is better that cardiologists put their own house in order rather than have it done for them.

**References**


[16] Varnauskas E. Survival, myocardial infarction, and employ-
The lipid research clinics coronary primary prevention trial


coronary artery disease of lipid-lowering diet, or diet plus cholestyra-


Mannheimer C, Augustinsson LE, Carlsson CA, Manhem K,


