

Stable angina the not so phantom menace

“A bit of angina, nothing to worry about.” Is it possible to fulfil this assumption?

Dr Caroline Daly

Introduction

Coronary artery disease has been the plague of industrialised nations since the latter half of the twentieth century. Stable angina is the most prevalent manifestation of this menacing disease, which affects millions world-wide. The cost to society is enormous, in terms of premature mortality and reduced quality of life, in addition to the significant economic burden caused by inflationary medical costs and loss of employment. Angina not only impairs quality of life, which may be improved either by medication or revascularisation, but it also identifies a population of which a proportion are at increased risk of future cardiovascular events and mortality. Although the overall annual mortality is not high at 1-3%, there is a proportion of patients at substantially higher risk, and it is in this high-risk group, if they can be accurately identified, that there is considerable room to improve prognosis. Left ventricular function, the coronary anatomy and inducible ischaemia are strong predictors of outcome. However, conventional (and some non-conventional) risk factors may also assist in assessing the risk of future events and mortality.

In most cases, subjects presenting with anginal symptoms have an initial clinical assessment and a form of provocative or functional assessment. This will either take the form of exercise electrocardiography, stress echocardiography or myocardial perfusion scan which allows stratification into high and low risk groups and influences referral for further invasive investigation by cardiac catheterisation. Factors which influence prognosis include, on history, age, sex, the course and frequency of anginal pain, the severity of heart failure symptoms and prior history of MI, cerebrovascular or peripheral vascular disease. On examination, factors include the presence of a ventricular gallop or carotid bruit, and on baseline investigations, Q waves or ST changes on the ECG and heart size on chest radiograph. An initial assessment of risk based on these features has been shown to be at least as accurate, and possibly superior (trend rather than statistically significant difference) to exercise ECG in isolation for the prediction of 3-year survival in patients referred for non-invasive testing for suspected coronary disease. Clinical assessment, including history, examination, resting electrocardiography, and chest radiography remains a powerful tool, even in this

technologically advanced age, providing incremental information with regard to prognosis, even in patients in whom the coronary anatomy is known.

Smoking, hypercholesterolaemia, hypertension and diabetes, are associated with an adverse outcome in coronary disease. Of the conventional risk factors, diabetes mellitus carries the greatest prognostic weight in risk stratification of patients with coronary disease. In patients with type II diabetes, the risk of recurrent coronary events is approximately six times that of non-diabetics. A large proportion of this excess risk is associated with the high prevalence of other risk factors including hypertension, obesity, and dyslipidaemia in the diabetic population. However, when corrected for the presence of other conventional risk factors in multivariate analysis, diabetes remains a strong predictor of adverse cardiac outcome. In patients with known coronary disease, diabetes is associated with a RR of mortality 1.4-1.9, even after adjustment for coronary anatomy. In multivariate analysis of non-invasive strategies, including clinical assessment, exercise ECG and thallium scanning, in 8,411 patients, the presence of diabetes and hypertension remained predictive of cardiac death when the non-invasive tests were included in the analysis. The adverse impact of diabetes and hypertension on prognosis was also borne out in the subgroup analysis of the APSIS trial. Triglycerides, homocysteine, C-reactive protein (CRP) and fibrinogen have also been shown to contribute prognostic information in subjects with angina or known coronary disease.

Functional capacity

Exercise electrocardiography is a widely accepted, well validated and relatively inexpensive method of assessing prognosis in coronary artery disease. The presence of ST depression is a powerful indicator of the presence of coronary disease, but in predicting prognosis is superseded by other measures. Exercise capacity, time to ST depression, angina with ST depression or chronotropic incompetence perform better than simple presence or magnitude of ST depression when predicting survival or event-free survival. In patients with more than 2 mm of ST depression, exercise time <6min, 6-9mins and >9 mins may be used to dis-

criminate between high, intermediate and low risk groups with two-year survival, respectively.

The power of exercise capacity to discriminate between high and low risk groups is greatest in the case of extensive coronary disease. In the CASS study, for example, in patients with three vessel disease, the ability to achieve stage V or greater on the Bruce protocol was associated with almost 100% four-year survival, while those who could only achieve stage I or II had a 53% four-year survival.

Imaging techniques

Stress echocardiography and myocardial perfusion are alternative methods of determining the presence of inducible ischaemia. They also provide information useful to prognosis regarding previous myocardial injury or infarction. Echocardiography may be performed using exercise or pharmacological stress. Semi-quantitative assessment of wall motion abnormalities is obtained by using a scoring system to describe wall motion in each of 16 ventricular segments. The presence of new wall motion abnormalities, the number of new defects or extent of ischaemia and the extent of regional wall motion abnormality at rest, particularly infarcted territory, have been shown to influence prognosis. Stress echo contributes additional prognostic information independently of clinical, exercise and catheterisation data, and in some studies is superior to exercise ECG and coronary angiography in attributing risk.

The prognostic value of myocardial perfusion scanning

in patients with suspected coronary disease and with angiographically proven coronary disease has been comprehensively reviewed, and numerous studies have established the value of planar thallium myocardial perfusion scanning in predicting prognosis in coronary disease. High-risk findings include multiple reversible defects, large reversible defects, increased uptake in the lungs or transient left ventricular dilatation post exercise.

However, some studies have identified the presence of a fixed perfusion defect as the single scintigraphic variable most predictive of cardiovascular events. It has also been demonstrated that thallium SPECT scanning provides additive prognostic information to clinical and exercise variables in the evaluation of stable suspected angina, with cardiovascular mortality of 0.1% per year in patients with normal SPECT scans compared to 1.5% per year with abnormal SPECT imaging.

C a r d i a c catheterisation contributes significantly to prognostic assessment by documenting left ventricular function, and the extent and location of coronary disease. These are two of the most powerful predictors



of prognosis in angina. Ejection fraction and the number of diseased vessels were highlighted as the most potent predictors of survival in the medically treated cohort of the CASS study. In this study, four-year survival of medically-treated patients with one, two and three vessel disease was 92%, 84% and 68%, respectively. Stratification by ejection fraction yielded an even starker contrast, with four-year survival of 92%, 83% and 58% corresponding to ejection fractions of >50%, 35-49%, and <35%, respectively.

These results are similar to those from medically treated patients in other cardiac surgery studies, including the Veterans Administration Coronary Artery study and the European Coronary Artery Surgery study. The use of a prognostic index (such as that proposed by Mark et al., modified in Table 1) allows knowledge of the coronary anatomy to be readily translated into an estimated probability of 5-year survival.

How to improve prognosis

The treatment of angina must be guided by two objectives: improving prognosis and abolishing, or at least controlling, symptoms. Medical therapy is more than merely a means to achieve symptomatic relief, but also provides an adjunct to surgical or percutaneous intervention aimed at reducing the progression of disease, and the rate of acute events. Risk factor modification, including the cessation of smoking, is an important part of medical treatment. Smoking cessation reduces the risk of cardiovascular events, and should be

strongly advocated in any patient with coronary disease. Lipid-lowering measures, antihypertensive drugs and glycaemic control in diabetics may be expected to slow the rate of disease progression, and particularly in the case of lipid lowering, have been shown to reduce the rate of acute events and mortality.

The benefits of cholesterol lowering, particularly LDL cholesterol reduction, are well established. In a meta-analysis of the randomised controlled trials of statins, active treatment conferred an ~30% reduction in risk of coronary disease mortality in the secondary prevention trials (4S, CARE, LIPID). The benefits of statin therapy are evident not just in patients with elevated cholesterol levels, but across a broad range of cholesterol values.

In terms of anti-thrombotic therapy, the prognostic benefit of aspirin in angina is undisputed. There has been on average a 33% reduction in risk of adverse cardiovascular events in over 3000 stable angina patients treated with aspirin in a meta-analysis of antiplatelet studies. There is ongoing research into the potential of ACE inhibitors to reduce mortality in the coronary disease population. This is in addition to their proven benefit in those at high risk of atherosclerotic complications in the HOPE study.

Anti-anginal medication is effective in reducing symptoms (symptoms are controlled in 40-50% of patients on treatment), but other than in the post-infarction population, in whom beta blockade confers definite prognostic benefit, convincing evidence of reduced mortality on current anti-anginal medication is lacking. Prognostic benefit

of treatment in the stable angina population is difficult to prove, because of the ethical considerations of a placebo-controlled study and the numbers required to show statistical benefit in a population with an overall annual mortality of less than 2%.

Revascularisation

Knowledge of left ventricular function and the coronary anatomy allows not only the discrimination of patient groups at high risk of cardiovascular death and MI, but also identifies those patients who benefit prognostically from revascularisation. There is evidence of improved prognosis with surgical revascularisation in selected groups of patients, particularly those with left main stem stenosis and three vessel disease with reduced left ventricular function.

Data from the Duke database suggests that patients with single vessel disease involving proximal LAD disease have a better 5-year survival with PTCA than with medical therapy. However, a randomised, controlled trial is necessary to confirm this suggestion before clinical practice may be so guided. For the present, evidence exists to support the use of PTCA for symptomatic relief in patients with single vessel disease, but there is no definite evidence of prognostic benefit. In patients with multi-vessel disease, without left main stem disease, or other prognostically compelling angiographic findings, PTCA has been shown to be a safe alternative to surgical revascularisation for symptom control. However, it has not been proven to improve prognosis and has been associated with more revascularisation procedures during the ensuing years.

Conclusion

An awareness of the impact of specific anti-anginal drug therapy, surgery and angioplasty on prognosis in the population with angina as a whole and on specific groups is essential when formulating an individual patient management plan tailored to improve event-free and overall survival. Risk factor modification, statins and aspirin are of proven benefit in improving outcome in all patients with coronary disease, while surgical revascularisation is of prognostic benefit in selected patients groups only. Angioplasty,



although an effective means of controlling symptoms, has not been convincingly shown to improve prognosis in stable patients. The emergence of ACE inhibitors and other drugs aimed at reducing ischaemia and halting or reversing the advance of atherosclerosis proffer hope for the future, but much remains to be done to improve the management of stable angina.

Dr Caroline Daly, MRCPI, is a research fellow at the Royal Brompton Hospital, London.

Table 1. Coronary artery disease prognostic index (medical treatment).

Extent of CAD	5-year mortality rate (%)
1 vessel disease 75%	7
1 vessel disease >95%	9
2 vessel disease	12
2 vessel disease, both >95%	14
1 vessel disease, >95% proximal LAD	17
2 vessel disease, >95% proximal LAD	21
3 vessel disease	21
3 vessel disease, >95% in at least 1	27
3 vessel disease, >95% proximal LAD	41