
Stable angina: treatment selection

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Abstract

In the management of stable angina, there is time to optimize medical treatment while using stress testing to stratify long-term risk. Percutaneous coronary intervention does not decrease mortality or risk of myocardial infarction when compared with rigorously applied optimal medical treatment and should not be considered as part of a secondary prevention strategy. Whereas all patients should receive long-term medical therapy combined with advice on lifestyle, carefully selected patients will benefit from percutaneous coronary intervention and coronary surgery in addition. As in many areas of medicine, a balanced multidisciplinary approach based on evidence will offer the right treatment to the right patient at the right time.

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Introduction

In the UK each year, 320 000 people consult a physician because of angina. In both sexes, the prevalence increases with age. Between the ages of 45 and 54 years, 2–5% of the population have angina; this increases to 10–20% in those aged 65–74 years, and in those older than 75 years the prevalence is 1 in 3. In Europe, approximately 20 000 to 40 000 per 1 million of the population (both sexes) have angina, and the lives of 50% are significantly limited as a consequence [1]. As the population ages, although the death rates from coronary artery disease (CAD) are declining, the overall burden will not decrease, giving rise to increasing management challenges [2].

Treatment objectives

The aims of treatment can be summarized as:

- To reduce or abolish symptoms, resulting in an improvement in the quality of life.
- To improve prognosis by preventing myocardial infarction and death – quantity of life.

It may seem logical to aim for both objectives, but it needs to be remembered that, unfortunately, prolonging life does not always imply improved quality of life, and a shorter life of good quality may be preferable to many. That is to say, we are dealing with individuals, not statistics, although statistics and guidelines are fundamental to the advice we give [3].

Treatment strategies

There are three treatment modalities: medical treatment (which includes lifestyle issues), percutaneous coronary intervention (PCI), and coronary artery bypass grafting (CABG). Often depicted as competitors, they are in fact complementary, and the challenge is to select the right treatment at the right time for the right individual (male or female).

Surgery remains the treatment of choice for those with severe coronary artery disease, in particular severe stenosis of the left main stem coronary artery and when there is triple-vessel disease with reduced left ventricular function [4]. Recent studies have reinforced the PCI guidelines so that, in the context

of stable angina, PCI is primarily an option when medical treatment fails to relieve symptoms and restrictions to a satisfactory degree [5].

COURAGE study

The Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) study evaluated patients with stable angina who had objective evidence of myocardial ischemia and significant CAD [6]. After more than 35 000 patients had been screened, only 6.4% (2287) fulfilled the entry criteria: stenosis of at least 70% in at least one proximal coronary artery and evidence of ischemia on the resting electrocardiogram or after stress testing, or a lesion of more than 80% and symptomatic angina. In the former category, 25% were asymptomatic at entry. Enrolled patients (85% men, 86% white) were allocated randomly to receive PCI plus optimal medical therapy ($n=1149$) or optimal medical therapy alone ($n=1138$). The primary outcome was the composite of death from any cause and non fatal myocardial infarction during a mean follow-up of 4.6 years.

One of the remarkable features of COURAGE was the adherence to strictly defined optimal medical therapy for both arms of the study. Lifestyle issues were addressed, including diet, exercise, and smoking cessation, and there was an intensive approach to decreasing low-density lipoprotein cholesterol and triglyceride concentrations and blood pressure. Compliance with guideline-driven medical therapy was impressive, with 95% taking aspirin, 93% a statin, 85% a β -blocker with additional medication with amlodipine or isosorbide mononitrate alone or in combination. Lisinopril or losartan were prescribed if the left ventricular ejection fraction was $<40\%$. In the PCI group, drug-eluting stents were approved only towards the end of the study, so that only 2.7% of patients received them. Although this has been a focus of criticism, a recent analysis comparing bare-metal with drug-eluting stents in patients with stable angina revealed no difference in recurrent myocardial infarction or mortality [7]. Whether drug-eluting stents might have reduced the rates of revascularization – and therefore subsequent angina – is debated, but these are not the primary endpoints.

The study found that an initial strategy of PCI in patients with stable CAD did not reduce the cumulative rates of myocardial infarction and death (19.0% compared with 18.5%) or all-cause death (7.6% compared with 8.3%) when compared with optimal medical treatment alone. In addition, it was not cost effective [8]. PCI decreased the rate of anginal attacks initially, but by 5 years there was no difference. Crossovers did occur, and in the first year 16%

of the medical group underwent interventions; this increased to 33% by the end of the study. However, 21% of the PCI group needed re-intervention in the first year.

In the COURAGE study, PCI did not emerge as a significant contributor to secondary prevention when the established evidence base included lifestyle modification, lipid-decreasing treatment (statins), aspirin, β -blockade, and angiotensin-converting enzyme inhibitors. COURAGE participants all underwent an initial coronary angiogram, which is not routine practice, but we can deduce from this study that we have time to evaluate risk while initiating optimal medical therapy [9]. This will lead to a symptom-driven (failed medical therapy) or high-risk-driven (abnormal stress testing) approach to invasive evaluation (*Figure 1*) [10]. As multidetector computed tomography becomes more readily accessible, with reduced X-ray exposure, it may be expected to form an important part of the risk evaluation, complementing or replacing current stress-testing procedures.

Preceding studies

The Atorvastatin Versus Revascularization Treatment (AVERT) trial looked at the impact of intensive lipid decreasing (atorvastatin 80 mg) or PCI (no stents) in 341 patients [11]. In the medication group, 95% adhered to high-dose statin, but only 73% of those in the PCI group received statin therapy during the study (compare with COURAGE). In the medical group at the end of the 18-month study, there was a 38% reduction in ischemic events when compared with PCI (21% in the PCI group and 13% in the medical group).

The Second Randomized Intervention Treatment of Angina (RITA-2) study enrolled 1018 patients, with a 7-year follow-up [12,13]. The use of stents was introduced as the study progressed from its initiation in 1992, and PCI was compared with medical treatment. There was an initial symptomatic benefit in the PCI group, but this had disappeared by 7 years, and in the first 2 years the PCI group had experienced more adverse events (6.3% compared with 3.3%; $P=0.02$). The primary endpoint at 5 and 7 years – of death or myocardial infarction – was not different between the groups.

In the Medicine, Angioplasty or Surgery Study (MASS-II), CABG, PCI, and medical therapy were compared in 611 patients [14]. At 5 years there was no significant difference in overall mortality, although the secondary endpoint of angina was less frequent in the intervention group. However, medical therapy was suboptimal compared with that in the COURAGE study.

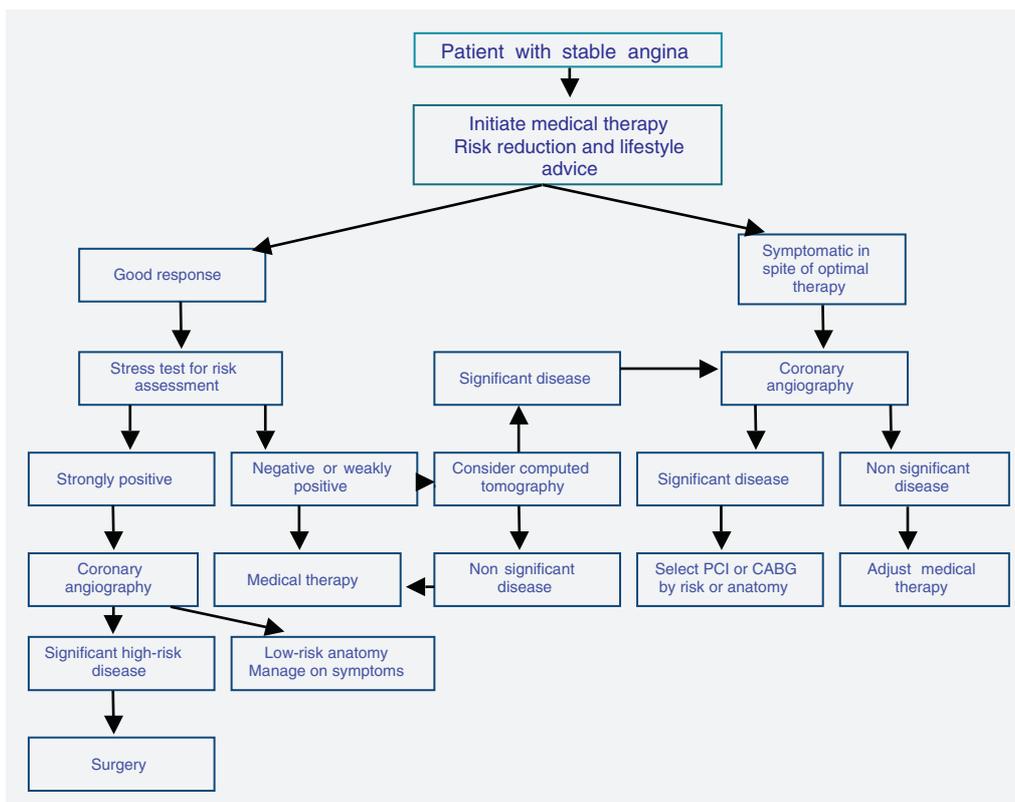


Figure 1. Investigative approach to the clinical evaluation of the patient with angina pectoris. Nuclear imaging and stress echocardiography complement this algorithm in selected cases. (From Jackson [10], with permission.)

Summary

In stable CAD, PCI has not been shown to decrease mortality or myocardial infarction when compared with optimal medical therapy rigorously applied. An initial conservative medical approach to relieve symptoms and reduce risk factors allows time for the prognostic risk to be assessed. Optimal medical treatment combined with lifestyle advice should be initiated in all patients with stable angina. It will not be the answer for everyone, but it will continue to be essential for those who need PCI or CABG in addition. ■

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