

A balanced approach to the management of patients with stable coronary disease: medicine, stents, surgery

The care of patients with coronary artery disease needs perspective and balance.

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The issue of the optimal management of patients with chronic stable coronary disease remains unsettled. There are strongly held views, and much emotive language is used in discussion. Not all opinions are entirely objective and practitioners' self-interest is all too often a powerful driver of the discussion. Patients have touching faith in the newest technology and firmly believe that some interventions provide significant prolongation of life.

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We would like to offer some perspective and questions to ask ourselves when caring for patients with chronic stable angina. Importantly, we believe that there is no single answer applicable to all, but a need exists to develop a lifelong strategy for each individual patient. The aims of the strategy are simply to relieve symptoms and improve prognosis if feasible. There is almost always time to think, discuss the management options with the patient and plan a long-term treatment strategy.

It is important to emphasise that we are discussing the management of chronic stable angina, which is the first manifestation in about 40% of patients. These are patients with infrequent or controlled angina, a positive exercise test or those who are asymptomatic following remote myocardial infarction. We firmly believe that it is time for some maturity to be introduced into the discussion and that we should go beyond debates on the merits of medical therapy versus percutaneous intervention (PCI) versus coronary bypass surgery (CABG) to a judicious and prudent application of all therapeutic modalities in the best interests of all of our patients.

Prognosis

What is the prognosis in chronic stable angina? It is essential that we understand this when selecting treatment strategies. Several large studies indicate that the annual incidence of death is about

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1.5% and the annual incidence of myocardial infarction about 1.4%.¹ It is immediately obvious that revascularisation interventions that have a higher mortality or risk of myocardial infarction will be very unlikely to be able to significantly influence prognosis in a condition with this sort of low annual mortality and event rate. Coronary stenting has no influence on prognosis in stable angina and coronary surgery a small but significant positive impact. In contrast, there is excellent evidence from very large studies that simple medical strategies, the prescription of aspirin, statins, angiotensin-converting enzyme inhibitors (ACE inhibitors), and lifestyle interventions such as quitting smoking, increasing physical activity and dietary change have a major impact on prognosis. All too often the important benefit of these interventions is forgotten and patients consider that after stent placement or coronary bypass surgery they no longer need chronic medication and they can ignore lifestyle modification.

What constitutes optimal medical therapy?

Patients should be reminded that medical therapy is a lifelong commitment and compliance should be stressed and checked at every visit.

Aspirin 150 mg daily should be prescribed to all patients unless contraindicated. Clopidogrel 75 mg daily should be prescribed if aspirin allergy is present. Combination therapy is not more effective than either alone and increases major bleeding.²

Beta-blockers are effective for symptomatic relief of chronic stable angina. Calcium-channel blockers (long-acting dihydropyridines) are equally effective and may be the preferred choice of drug when quality of life and exercise capacity is the main need. Beta-blockers are the preferred choice in patients with previous myocardial

infarction, heart failure and decreased LV function, as there is an added prognostic benefit over symptom control. Combination therapy, particularly the addition of long-acting nitrates, gives added efficacy.

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Lifestyle modification and aggressive treatment of risk factors cannot be overemphasised. Strict blood pressure control is essential (aim for BP <140/90 mmHg according to the SA Hypertension Guidelines).³ Statins should be prescribed for all (aim for LDL cholesterol <1.8 mmol/l for very high risk or 1.0 - 1.5 mmol/l reduction in LDL over 5 years).⁴ Diabetic control should be targeted to an HBA_{1c} of 7%. Patients should be encouraged to stop smoking, follow a Mediterranean diet and partake in moderate degrees of exercise 30 min/day 5 days per week.

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ACE inhibitors or angiotensin-receptor blockers should be considered in all patients with underlying vascular disease. The benefit of these drugs is greatest in higher-risk patients (those with diabetes, heart failure, depressed LV function, nephropathy).⁵ Although ACE inhibitors remain the first choice, angiotensin-receptor blockers have been shown to be equally effective. Combination therapy does not provide additional benefit.⁶

The therapies and targets as used in the COURAGE trial (Table 1) serve as an example of what we should be doing.⁷

A revascularisation procedure should be considered when severe angina interferes with lifestyle despite optimal medical therapy. All revascularisation procedures, both PCI and CABG, offer superior symptomatic

Table 1. Therapies and targets (used in COURAGE)

Therapies

- Aspirin or clopidogrel, if aspirin-intolerant
- Long-acting metoprolol, amlodipine, and isosorbide mononitrate (alone or in combination)
- Lisinopril or losartan
- Statin

Targets

- Cholesterol <2.20 mmol/l
- BP control <130/85 mmHg
- HBA_{1c} <7%

relief to that afforded by medical therapy alone. The issue as we see it, is do they offer an improved prognosis in stable angina when symptoms are mild or infrequent?

A revascularisation procedure should be considered when severe angina interferes with lifestyle despite optimal medical therapy.

Percutaneous intervention versus medical therapy

Is PCI superior to conventional medical therapy? The benefit of medical therapy as opposed to PCI has been well tested. In a meta-analysis of several trials there was no benefit in terms of prognosis, i.e. reduction of death or acute myocardial infarction.⁷ The most recent such trial, the COURAGE study, confirmed those findings and confirmed that an initial conservative strategy of optimal medical therapy combined with lifestyle modification was safe and decisions on revascularisation could be deferred.⁸ Compliance with medical therapy in the COURAGE trial was >90% and must be ensured to obtain similar results in 'real-world' practice. Most informative was a quality-of-life analysis. Most of us have considered that angina was a condition that continued, unchanged forever. The quality-of-life analysis of COURAGE has changed our perspective on that.⁹ Patients treated by PCI had better improvement in angina and quality of life early on, but by 3 years the differences between the groups had disappeared and nearly 60% of patients treated medically were free of angina. This was not different from those treated by PCI initially and other more general quality-

of-life indicators were reported to follow a similar pattern. A cost-effectiveness analysis concluded: 'The cost for 1 patient to have clinically significant improvement in angina for between 6 and 36 months exceeds \$100 000.' That is a huge cost to pay for short-lived symptomatic benefit that is not coupled to any prognostic benefit.

Coronary bypass surgery versus medical therapy

This was well tested in a series of small but important studies in the eighties, the results of which have informed cardiology practice over the last few decades.¹⁰ In brief, CABG offers improved prognosis to some patients with coronary disease. The magnitude of benefit is not enormous but it is real and is greatest in patients at highest risk by virtue of extent of coronary disease, left ventricular dysfunction or severity of symptoms of ischaemia. Of course, those trials are old and can be criticised in today's practice. Most of the patients were men, statins and ACE inhibitors were not used, anti-platelet agents and beta-blockers were not widely used. But they are all we have and they show, after the initial mortality cost of the procedure, that at about 18 months the survival curves deviate and offer surgically treated patients a small but distinct advantage over medically treated patients for about a decade. The actual benefits in terms of duration of life gained are surprisingly small and one may question the relevance for any individual patient. No such benefit has ever been demonstrated for PCI compared with medical therapy.

Coronary bypass surgery versus percutaneous intervention

There have been quite good trials evaluating these two strategies head to head. The greatest problem in analysis is that in all trials both arms were (presumably) well treated medically and higher risk patients known to have a small prognostic benefit over

medical therapy were generally excluded. The results of multiple analyses show no mortality benefit for PCI over CABG and a consistent finding from both trials and very large registries is that patients initially treated by PCI have a greater need for repeat revascularisation procedures during follow-up.¹¹⁻¹⁴

The perception that PCI carries a lower procedural risk than CABG is not supported by the available published information. The short-term risks are very similar if patients are matched for degree of illness.¹⁵

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A commonly heard argument is that PCI carries a lower risk of neurological damage than CABG. Unfortunately, that is not supported by the randomised studies where the neurological complications over a prolonged period of follow-up are identical and this is consistent with the need for repeat re-intervention in those undergoing PCI. Each intervention carries a defined risk of neurological harm.¹⁶

Does prior PCI increase the risk of subsequent CABG?

It is often argued that PCI can be used as a temporising measure until CABG becomes necessary. This would be an acceptable argument provided that PCI carried a lower risk than CABG, which is not always the case, and if it did not increase the risk of CABG performed at a later date. There is some disturbing information that prior PCI may in fact increase the hospital mortality at the time of later CABG.¹⁵ Multiple explanations can be advanced for this, but none are entirely satisfactory.

Have drug-eluting stents changed things?

Unfortunately they have not. Drug-eluting stents have reduced but not abolished the need for re-intervention after initial PCI, but to obtain this optimum benefit patients need to remain on dual anti-platelet therapy for a considerable (optimal duration unclear)

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period of time. Firstly, such therapy is expensive and is often discontinued prematurely because patients themselves face competing economic imperatives or the administrators of hospitals and medical aid funds consider that their resources are best spent elsewhere. Secondly, such therapy does increase the risk of bleeding and may need to be discontinued prior to elective or emergency surgery. Discontinuation carries the risk of stent thrombosis and myocardial infarction, which may be fatal. The ability to continue long-term dual anti-platelet therapy needs to be carefully considered in each individual patient with stable angina before a drug-eluting stent is placed at the time of PCI. A drug-eluting stent placed in the coronary artery of a patient who cannot or will not adhere to appropriate therapy can change a stable lesion, causing minimal symptoms with little prognostic implication, into a life-threatening one. Drug-eluting stents are often used by cardiologists in complex anatomical subsets (bifurcation lesions, chronic total occlusions) to reduce incidence of in-stent restenosis. It is important to remember that these indications were excluded from the original trials and that such 'off-label' use of drug-eluting stents carries a higher incidence of early and late stent thrombosis.¹⁷

Does all this matter?

For the individual patient it may matter a great deal. Coronary disease is incurable and usually requires lifelong treatment. The preservation of patients' financial resources to ensure that they are able to afford long-term medical interventions of proven value (statins, blood pressure control, ACE inhibitors) is essential. Placement of stents should only be one part of a detailed and carefully planned strategy and should be reserved, in patients with chronic stable coronary disease, for those whose symptoms, despite optimal treatment, interfere with a reasonable lifestyle.

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In a nutshell

- The issue of the optimal management of patients with chronic stable coronary disease remains unsettled.
- There is no single answer applicable to all, but a need exists to develop a lifelong strategy for each individual patient.
- The aims of the strategy are simply to relieve symptoms and improve prognosis if feasible.
- Chronic stable angina is the first manifestation of coronary disease in about 40% of patients.
- These are patients with infrequent or controlled angina, a positive exercise test or those who are asymptomatic following remote myocardial infarction.
- The prognosis in chronic stable angina: the annual incidence of death is about 1.5% and the annual incidence of myocardial infarction about 1.4%.
- Revascularisation procedures with a higher risk of mortality or myocardial infarction will be unlikely to influence prognosis.
- Simple medical strategies, the prescription of aspirin, statins, angiotensin-converting enzyme inhibitors, and lifestyle interventions such as quitting smoking, increasing physical activity and dietary change have a major impact on prognosis.
- A revascularisation procedure should be considered when severe angina interferes with lifestyle despite optimal medical therapy.
- All revascularisation procedures, both PCI and CABG, offer superior symptomatic relief to that afforded by medical therapy alone.
- However, the prognostic value of revascularisation in chronic stable angina is less clear.
- Patients treated by PCI have better improvement in angina and quality of life early on, but by 3 years the differences between the groups have disappeared and nearly 60% of patients treated medically are free of angina.
- Drug-eluting stents have reduced but not abolished the need for re-intervention after initial PCI, but to obtain this optimum benefit patients need to remain on dual anti-platelet therapy for a considerable and unclear period of time.

Single Suture

Climbing doctors experience lowest blood oxygen levels ever recorded

Blood oxygen in doctors climbing Everest fell to the lowest levels ever recorded in a healthy person, which may mean that some people in intensive care could tolerate lower oxygen levels than previously thought.

The study was published in the *New England Journal of Medicine* and was based on 4 doctors who took samples of their own blood at 8 400 m above sea level, 448 m below the summit of Everest. The 4 had spent weeks acclimatising to the altitude.

The average blood oxygen level was 3.28 kPa, with the lowest at 2.55 kPa. These levels are sometimes seen in people who are dying after cardiac arrest, but the doctors were able to walk, talk, take the blood gas and think clearly with these levels.

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