



# Stable angina – taking time

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“Time is the great physician”  
Disraeli [1804–1881]

Stable angina that is chronic is, by definition, chronic and stable. This may seem obvious, but stability may often be overlooked by interventional cardiologists whose mind-sets are catheter-based rather than clinically based in the broadest context of the term. The real question is whether we can improve a patient's quality of life with the minimum risk. We recognize certain prognostically important anatomical subsets, such as left main-stem disease or triple-vessel disease with reduced left ventricular function, which benefit from surgical intervention but, to date, percutaneous coronary intervention (PCI) has not been shown to improve or reduce life expectancy. It follows that, once a patient at high prognostic risk has been identified (usually by exercise testing and subsequent angiography), we have time to optimize the management of those at lower risk. Time taken to address lifestyle issues and utilize drug therapy to its evidence-based best is time well spent.

The Clinical Outcomes Utilising Revascularisation and Aggressive Drug Evaluation (COURAGE) randomized trial addressed the question of whether, in patients with stable coronary artery disease, PCI as the *initial* management, followed by aggressive risk reduction, lifestyle advice, and drug treatment was superior to optimal medical treatment alone in reducing cardiovascular events over a median of 4.6 years of follow-up [1]. PCI as the initial strategy did not reduce the risk of death, myocardial infarction, or other major cardiovascular events when combined with optimal medical treatment. Optimal medical therapy was impressive in both groups with more than 70% taking an angiotensin-converting enzyme inhibitor or angiotensin II antagonist, 90% a statin, 95% aspirin and 85% a  $\beta$ -blocker.

The Medicine, Angioplasty or Surgery Study (MASS II) compared coronary artery bypass grafting

(CABG) with PCI and medical treatment in patients with stable multivessel disease over a 5-year period [2]. All three treatments were associated with similar low rates of death, and medical treatment was similar to PCI with regard to the long-term incidence of events and the need for revascularization.

Medical treatment has made a substantial impact on cardiac events in both the acute and chronic coronary settings, with the evidence base for, in particular, high-dose statin therapy being particularly strong [3]. In stable patients, the coronary atheroma is usually obstructive to flow and symptomatic, with plaque that, in turn, is usually stable (thick fibrous cap, lipid-poor, smooth muscle cells present), giving us time to optimize medical treatment. In the acute situation, a lipid-rich plaque that is usually non obstructive ruptures through its thin fibrous cap, often in the presence of evidence of inflammation – giving us little time to take action [4]. Both pathologies may coexist, and we know, from the Pravastatin or Atorvastatin Evaluation and Infection Treatment (PROVE-IT) trial in patients with acute coronary syndrome, that an aggressive lipid-decreasing approach with atorvastatin complemented intervention when used in addition to good evidence-based standard medical treatment, with a significant benefit occurring by 30 days (probably as a result of anti-inflammatory actions) and continuing beyond 2 years (plaque stability) [5]. Of importance is the need to continue medical treatment as optimally as possible into the long term [6].

In stable angina, the key is the stability of the clinical situation, and therefore the *time* to optimize overall treatment – not forgetting medical treatment continues after PCI or CABG. Given the evidence for a symptom-driven strategy, additional symptom-relieving treatment has a potentially important part to play.

Trimetazidine acts metabolically and is a very effective agent when used in addition to conventional hemodynamic therapy in stable angina, so its role is

likely to increase as part of the evolving paradigm [7]. In view of the findings of the COURAGE and MASS II trials, trimetazidine should be considered in patients whose condition is stable and who are receiving medical treatment if their symptoms are troublesome, and before angiography that is undertaken with a view to PCI or CABG. Medical treatment using trimetazidine in addition to conventional hemodynamic anti-anginal agents can be further optimized, which is good news for patients with stable coronary artery disease.

In this issue of *Heart and Metabolism*, we look at stable angina from all aspects, trying to find a balanced approach to both symptoms and prognosis. Whilst I am not obsessed with time, it is time that we have on our side, allowing us to optimize care with minimum risk, so we need to make the most of it.

“The physician’s best remedy is “Tincture of Time!””  
Shick [1872–1967] ■

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