Fractional flow reserve to guide percutaneous coronary intervention in people with stable coronary artery disease

An international multicentre randomised controlled trial reported that people with stable coronary artery disease who had significant stenosis according to fractional flow reserve values had better outcomes with percutaneous coronary intervention plus medical therapy than with medical therapy alone.

Overview: Coronary artery disease is caused by narrowing (stenosis) of the arteries that supply the heart muscle (NICE 2003). Stable coronary artery disease typically manifests as stable angina, which is characterised by chest pain occurring at predictable levels of exertion, emotion, or another stressor.

One possible treatment for coronary artery disease is percutaneous coronary intervention (PCI). In PCI, a small balloon is inflated in the affected artery to widen it (angioplasty), and a metal mesh tube called a stent may be put in place to hold the artery open (NHS Choices 2013). Whether PCI is beneficial in people with stable coronary artery disease is controversial, with some evidence suggesting that PCI is no better than medical therapy in these individuals (Pursnani et al. 2012).

Fractional flow reserve (FFR) is a physiological parameter that can be used to determine the extent to which stenosis narrows a coronary artery (NICE 2014). The FFR within the affected vessel is measured with a coronary pressure wire during angiography or PCI. An FFR value of 0.80 or less indicates that the stenosis has caused a drop in maximal blood flow of 20% or more and has the potential to cause myocardial ischaemia (that is, the stenosis is functionally significant).

PCI does not appear to be beneficial in people who have non-significant stenosis on the basis of FFR values (Pijls et al. 2007), but may improve outcomes in people with functionally significant stenosis (De Bruyne et al. 2012).

Current advice: The NICE guidance on management of stable angina recommends PCI for people with stable angina and suitable coronary anatomy whose symptoms are not satisfactorily controlled with optimal medical treatment and in whom coronary artery bypass graft surgery is not appropriate.
NICE has technology appraisal guidance on [coronary artery stents](#) for people with either stable or unstable angina or with acute myocardial infarction, and on [drug-eluting stents for the treatment of coronary artery disease](#).

The NICE pathway on [acute coronary syndromes](#) brings together all related NICE guidance and associated products on the conditions in a set of interactive topic-based diagrams.

**New evidence:** De Bruyne et al. (2014) did an open-label randomised controlled trial of PCI plus medical therapy versus medical therapy alone in people with stable coronary artery disease and functionally significant stenoses, as determined by FFR (the [Fractional Flow Reserve versus Angiography for Multivessel Evaluation 2 (FAME 2) trial](#)).

People with stable coronary artery disease who were suitable for PCI were recruited from 28 sites in Europe and North America. People who had at least 1 stenosis in a major coronary artery with an FFR of 0.80 or less were randomly assigned to PCI plus medical therapy or to medical therapy alone.

People in the PCI group received second-generation drug-eluting stents in all stenoses that had an FFR of 0.80 or less. All participants received daily aspirin, a beta-blocker (alone or in combination with a calcium-channel blocker, a long-acting nitrate or both), an angiotensin-converting-enzyme inhibitor or angiotensin-receptor blocker, and atorvastatin alone or in combination with ezetimibe (not licenced for coronary artery disease in the UK).

Between May 2010 and January 2012, 1220 people were enrolled to the study. A total of 888 had at least 1 stenosis with an FFR of 0.80 or less and were randomly assigned to undergo PCI plus medical therapy (n=447) or to receive medical therapy alone (n=441). The primary end point was a composite of death from any cause, non-fatal myocardial infarction, or urgent revascularisation within 2 years.

At 2 years, significantly fewer people in the PCI group than in the medical therapy group experienced at least 1 primary outcome event (8.1% versus 19.5%; hazard ratio=0.39, 95% confidence interval [CI] 0.26 to 0.57, p<0.001). The difference between the groups was largely because fewer people needed urgent revascularisation in the PCI group compared with the medical therapy group (4.0% versus 16.3%; hazard ratio=0.23, 95% CI 0.14 to 0.38, p<0.001). The groups did not differ significantly in their rates of death or myocardial infarction.

The authors concluded that PCI plus medical therapy is more effective than medical therapy alone in people with stable coronary artery disease who FFR has identified as having functional ischaemia. Limitations of this study include that recruitment was stopped early because of a highly significant between-group difference in the primary outcome. In addition, the participants had stenoses in large coronary arteries with a mean FFR of 0.64, indicating profound and extensive ischaemia. The findings may not therefore be generalisable to people with lesser stenosis.

**Commentary by Dr Darlington Obi Okonko, Consultant Cardiologist, King's College Hospital NHS Foundation Trust, London:**

“Current US and European cardiac society guidelines support the use of FFR measurements to guide revascularisation decisions in people with stable coronary artery disease. This approach is particularly important when the degree of stenosis is intermediate, when evidence of ischaemia is lacking, and when symptoms or stenosis severity on angiography are not in line with previous ischaemia testing. PCI confers risks to treated people, costs time and money, and does not improve survival compared with optimal medical therapy, so objective metrics such as FFR are welcomed as means of preventing unnecessary procedures.

“[To this end,](#) the FAME investigators have conducted 2 trials assessing the impact of FFR-guided PCI on outcomes. In the current report of FAME-2 by De Bruyne et al. (2014), use of FFR to guide PCI reduced the primary composite end point by 77% relative to medical therapy, with the results driven by reductions in urgent revascularisation.
“Although these results might improve the current uptake of FFR in the UK, enthusiasm should be tempered by a methodological flaw in the trial. FAME-2 was an open-label study, and the lack of appropriate blinding, preferably with a sham intervention group, minimises its clinical value. “Given that they were aware of their study arm allocation, people in the medical therapy alone arm of FAME-2 might have been more anxious and therefore more likely to present with angina, triggering urgent revascularisation. Additionally, doctors might have been more likely to diagnose unstable angina in people who they knew had significant coronary stenoses. “Urgent revascularisation and, to a lesser extent, myocardial infarction are ‘soft’ end points that are suboptimal for testing a procedure that can add risk, time and cost to routine catheter lab work. Sham-controlled FFR trials are needed to fully justify widespread use of this exciting measure.”

**Study sponsorship:** St Jude Medical.

**About this article:** This article appeared in the August 2015 issue of the *Eyes on Evidence* newsletter. This free monthly newsletter from NICE Evidence Services outlines interesting new evidence and what it means for current practice. The articles do not constitute formal NICE guidance. The commentaries included are the opinions of contributors and do not necessarily reflect the views of NICE.

To receive the Eyes on Evidence newsletter, please complete the [online registration form](#).