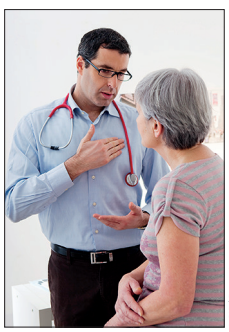
Last nail in the coffin for PCI in stable angina?



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Interventional cardiology began in Switzerland in 1977, when Andreas Gruentzig performed the first successful percutaneous transluminal coronary angioplasty (PTCA) on a 38-year-old man with angina and a focal proximal stenosis of the left anterior descending coronary artery. Despite numerous subsequent randomised trials and meta-analyses of these trials, which have shown no reduction in death or myocardial infarction,[1] the use of percutaneous coronary intervention (PCI) has grown exponentially. Some of this growth was driven by data from clinical trials suggesting that PCI was more effective in relieving angina than medical therapy alone. For example, in 1992, the results of the Angioplasty Compared to Medicine (ACME) study,[2] showed that at 6 months, 61 (64%) of 96 patients in the PTCA group were free of angina compared with 47 (46%) of the 102 medically treated patients (p=0·01). The patients in the PTCA group also had a greater improvement in duration of exercise (2·1 min) than the medically treated patients (0·5 min; p<0·0001). More recently, Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE)[3] and other studies using contemporary versions of optimal medical therapy have also found a short-term reduction in angina in the PCI group compared with the medical therapy group. In COURAGE, 30 days after randomisation, 21% of patients with angina who underwent PCI were angina-free compared with 10% of patients treated with optimal medical therapy, but that improvement was no longer present at 3 years.

On the basis of these and other data, the American College of Cardiology (ACC)/American Heart Association (AHA) and the European Society of Cardiology have made a class IA recommendation for PCI to improve symptoms only in patients with unacceptable angina despite guideline-directed medical therapy.[4,5] However, in actual use, PCI has always been provided to many more patients than are indicated by this recommendation; only half of all PCI procedures for stable coronary artery disease are appropriate according to ACC's criteria.[6] Despite the findings in COURAGE showing the importance of optimal medical therapy for all patients with coronary artery disease, an analysis of data from the US National Cardiovascular Data Registry showed that less than half of patients undergoing PCI were receiving optimal medical therapy, with no increase following the publication of COURAGE.[7] More importantly, despite the known placebo power of invasive procedures, until now, there had not been a blinded clinical trial of PCI in its entire 40 year history.[8]

In a landmark new study in *The Lancet*, the investigators of the Objective Randomised Blinded Investigation with optimal medical Therapy of Angioplasty in stable angina (ORBITA) group[9] have filled this important gap. We commend them for challenging the existing dogma around a procedure that has become routine, ingrained, and profitable. The results of ORBITA show (once again) why regulatory agencies, the medical profession, and the public must demand high-quality studies before the approval and adoption of new therapies. These ORBITA data put PCI in the category of other abandoned therapies for cardiovascular disease, including percutaneous transmyocardial laser revascularisation[10] and catheter-based radiofrequency renal artery sympathetic denervation[11]—procedures for which the initial apparent benefit was later shown in sham-controlled blinded studies to actually be due to the placebo effect.

The ORBITA investigators are to be applauded for the rigour of their trial. They enrolled 230 patients with angina or equivalent symptoms, ischaemia, and at least one severe coronary stenosis in a single vessel. Upon enrolment, all patients underwent 6 weeks of medical optimisation with initiation and up titration of antianginal therapy. After medical optimisation, 200 patients, of whom 195 (98%) had class II or III angina, were randomly assigned to PCI with a drug-eluting stent or a sham procedure. After the procedure, both patients and their care providers were blinded to treatment assignment, and the blinding index supported the validity of this blinding. At follow-up, 6 weeks after randomisation, patients in both groups were receiving a mean of 2·9 medications. The primary outcome was change in exercise time on a treadmill. Secondary endpoints were change in peak oxygen uptake, change in exercise time to 1 mm ST-segment depression, angina severity, physical limitation, angina stability and angina frequency,

Duke treadmill score, and change in dobutamine stress echocardiographic (DSE) wall motion score index. By the end of the study, ORBITA was clearly a negative trial, with no difference in either the primary or secondary endpoints between groups, except for a statistically significant, but clinically insignificant, improvement in DSE wall motion score index in patients who underwent PCI. The short duration of the study actually favoured PCI, as any haemodynamic benefit from PCI occurs early and the benefits of medical therapy continue to accrue over years. We look forward to future reports from the ORBITA investigators.

The implications of ORBITA are profound and far-reaching. First and foremost, the results of ORBITA show unequivocally that there are no benefits for PCI compared with medical therapy for stable angina, even when angina is refractory to medical therapy. Based on these data, all cardiology guidelines should be revised to downgrade the recommendation for PCI in patients with angina despite use of medical therapy. ORBITA highlights the importance of including sham controls and double blinding in a trial to avoid being fooled by illusory improvements due to the powerful placebo effect of procedures such as PCI. Although sham-control procedures are associated with some adverse outcomes, those complications are dwarfed in magnitude by the rate of adverse events in the approximately 500 000 patients who undergo PCI for symptomatic relief of stable angina in the USA and Europe each year. These adverse events include death (0·65%), myocardial infarction (15%), renal injury (13%), stroke (0·2%), and vascular complications (2–6%).[12] Health-care providers should focus their attention on treating patients with stable coronary artery disease with optimal medical therapy, which is very effective, and on improving the lifestyle choices that represent a large proportion of modifiable cardiovascular risk, including heart-healthy diets, regular physical activity, and abstention from smoking.

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A SENIOR moment? Bare-metal stents in elderly patients

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The WHO International Day of Older Persons[1] was on Oct 1, 2017, and saw the release of guidelines on integrated care and equality of care for older people. Now, 40 years since the first percutaneous coronary intervention (PCI),[2] we still do not know the optimal revascularisation strategy in elderly patients. Interventionalists face two important questions when considering PCI in elderly patients. First, should drug-eluting stents (DES) be mandated in elderly patients since they tend to have greater numbers of complex coronary lesions with calcification, tortuosity, and bifurcations than do younger patients[3] and DES have been shown to be better than bare-metal stents