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Total (**732**/800)

Title (13/30)

The role of PCI in stable angina in light of the ORBITA trial

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Context (117/80-120)

More than 500,000 percutaneous coronary intervention (PCI) procedures are performed worldwide each year for stable coronary artery disease (CAD). In addition to medical therapy, physiologically-targeted PCI reduces urgent revascularization in this group [1] but, unlike in acute coronary syndromes, evidence supporting a reduction in myocardial infarction and mortality is lacking [2], especially in those with low ischaemic burden [3]. Consequently, in stable CAD, PCI is used predominantly for symptomatic relief. It is therefore remarkable that, 40 years after Andreas Grüntzig's first PCI, we only now have results of the first double-blind, placebo-controlled trial of PCI in stable angina; the ORBITA (Objective Randomised Blinded Investigation with optimal medical Therapy of Angioplasty in stable angina) trial [4].

Methods (149/100-150)

Patients with stable angina and single-vessel disease underwent symptomatic and clinical assessment before and after a six-week phase of intensive anti-anginal therapeutic optimisation. Prior to randomisation, patients underwent cardiopulmonary exercise testing (CPET) and dobutamine stress echocardiography (DSE). Two hundred patients were randomised 1:1, to PCI or a sham PCI. Randomised patients underwent repeat invasive angiography with intra-coronary physiological (pressure-wire) assessment. The study was fully blinded. Operators were unaware of the physiological findings. Patients, were sedated and wore headphones during the procedure were unaware of whether they had undergone PCI or not. All patients were treated as though they had undergone PCI. After six weeks, patients underwent repeat clinical assessment including CPET and DSE by blinded researchers. The study was powered to detect the primary end point which

was a between-group difference in incremental exercise time of ≥30 seconds. Analysis was on an intention-to-treat basis.

Findings (92/75-100)

105 patients were randomised to PCI and 95 to placebo. Baseline characteristics were similar; 98% had Canadian Cardiovascular Society class II or III angina and >90% had normal left ventricular function. At follow up, there was no statistically significant between-group difference in exercise time increase, time to 1mm ST depression, peak oxygen uptake, or angina symptoms scores. Exercise time increased by 28.4 s in the PCI group and 11.8 s in the placebo group (between-group comparison P=NS). The DSE peak stress wall motion score index improved more with PCI than placebo (<0.0001).

Commentary (302/250-300)

ORBITA was a commendable study in many respects. The investigators had the courage and motivation to perform an elegant randomised-controlled trial of a therapy widely accepted to be effective, despite funding challenges [5]. The study design was exemplary, especially in terms of the intensive, guideline-directed optimisation of medical therapy and the blinding of researchers and patients throughout the trial. The inclusion of sham PCI was innovative and the incorporation of multiple objective endpoints rigorous. However, some aspects of its conduct were unlike real-world practice. During the initial therapeutic optimisation phase, patients had up to three consultations with a consultant cardiologist per week and direct access at any time. In fact, therapeutic optimisation was so effective that 11% of included patients were free from angina at randomisation and would not therefore have qualified for PCI in most healthcare systems. Nearly one third of randomised patients had no physiological evidence of ischaemia (negative pressure-wire assessment) which, according to guidelines, should not be intervened upon and should be treated medically. Baseline exercise times were notably high, more so in the PCI group. Prospective power calculations were appropriate, but the exercise time results suggest (retrospectively) the sample size may have been too small to definitively detect the primary outcome. Few patients underwent ST depression analysis. The authors themselves highlight that drug intolerance or patient choice may still favour PCI over pharmacotherapy. Furthermore, ORBITA only included patients with stable, single-vessel disease and results should not be extrapolated to more advanced CAD. Finally, with six weeks follow up, this symptoms-focussed study was too short to assess longer term effects such as myocardial infarction and mortality.

Implications for practice (72/50)

ORBITA highlights the importance of ensuring patients actually receive optimal medical therapy in stable, single vessel disease, the need for improved and rigorous coronary physiological assessment, and a refreshing approach to study design. Interventional cardiologists are likely to defer changing practice significantly until the results of the much larger ISCHEMIA trial (NCT01471522) are known, a study of >5000 patients with stable CAD which is assessing long term prognostic benefit.

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