Percutaneous coronary intervention outcomes in patients with stable obstructive coronary artery disease and myocardial ischemia: a collaborative meta-analysis of contemporary randomized clinical trials

CRD summary
The review concluded that for patients with stable coronary artery disease and objectively documented myocardial ischaemia, percutaneous coronary intervention with medical therapy was not associated with a reduction in death, nonfatal myocardial infarction, unplanned revascularisation or angina compared with medical therapy alone. The authors’ conclusions reflect the evidence presented and seem reliable for the primary outcome of interest.

Authors' objectives
To compare the effectiveness of percutaneous coronary intervention and medical therapy with medical therapy alone in patients with stable coronary artery disease.

Searching
PubMed and Cochrane Library databases were searched from 1970 to November 2012 for articles in any language. Search terms were reported. Bibliographies of retrieved articles and previous reviews were searched.

Study selection
Eligible were randomised controlled trials (RCTs) that compared percutaneous coronary interventions and medical therapy against medical therapy alone. Eligible patients had stable coronary artery disease. Included studies had to have stent implantation in at least 50% of percutaneous coronary intervention procedures and statin medications in at least 50% of patients in both percutaneous coronary intervention and medical therapy arms. Trials had to report the outcomes of death and nonfatal myocardial infarction. Myocardial ischaemia or abnormal fractional flow reserve had to be documented in some or all patients prior to randomisation. Trials of stable patients following a completed myocardial infarction were excluded.

Medical therapy included aspirin, beta-blockers, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers and statins. All studies allowed crossover from medical therapy to percutaneous coronary intervention for intolerable symptoms. Two studies used drug-eluting stents in 37% and 95% of patients. Stress testing varied between studies. From 62% to 100% of the participants were men. From 22% to 100% of participants had diabetes and from 25% to 40% had a prior myocardial infarction. Mean ejection fractions ranged from 57% to 69%. The extent of coronary artery disease ranged from single-vessel to three-vessel disease. Stents were implanted in 66% to 100% of patients. Outcomes assessed included death from any cause, nonfatal myocardial infarction (variably defined), unplanned revascularisation (percutaneous coronary intervention or coronary artery bypass graft) and angina. Studies were conducted in Brazil, North America and Europe.

The authors did not state how many reviewers selected studies for inclusion.

Assessment of study quality
Study quality was assessed using Jadad criteria of randomisation, blinding and withdrawals. It appeared that two reviewers independently assessed study quality.

Data extraction
Two reviewers independently extracted outcome data for all patients who had documented either myocardial ischaemia on stress testing or an abnormal fractional flow reserve. In the case of no events recorded, a nominal amount of 0.5 cases was added to the results for both groups. Intention-to-treat data were used to calculate odds ratios and 95% confidence intervals. Data were extracted at the longest follow-up period for each outcome up to a maximum of five years. Primary study authors were contacted for missing data (including unpublished data and data on subsets of patients with ischaemia at the time of randomisation in studies where not all were required to have ischaemia on stress testing).
Methods of synthesis
Pooled odds ratios and 95% confidence intervals were calculated using the inverse variance method with a random-effects model. Statistical heterogeneity was assessed using the Q and I² tests. Subgroup analyses were prespecified and performed based on the requirement of ischaemia for trial entry versus no requirement for ischaemia at trial entry and for trials that enrolled patients prior to 2000 versus enrolment after 2000. Sensitivity analyses were conducted for each outcome, removing individual trials one at a time. Publication bias was assessed using a funnel plot and the Egger test.

Results of the review
Five RCTs were included in the review (4,064 participants with ischaemia at randomisation, range 101 to 1,938). All trials reported random assignment and reported withdrawal descriptions. No trials reported blinding. Follow-up ranged from 231 days to five years.

There were no significant differences between treatment with percutaneous coronary interventions with medical therapy or medical therapy alone for patients with stable coronary artery disease and objectively documented myocardial ischaemia for death (OR 0.90, 95% CI 0.71 to 1.16), nonfatal myocardial infarction (OR 1.24, 95% CI 0.99 to 1.56), unplanned revascularisation (OR 0.64, 95% CI 0.35 to 1.17) and recurrent or persistent angina (OR 0.91, 95% CI 0.57 to 1.44). There was evidence of heterogeneity for the analyses of unplanned revascularisation (I²=90%) and angina (I²=72%). Results of subgroup analyses did not significantly alter the results.

Removal of one trial resulted in a statistically significant reduction in the number of unplanned revascularisations in favour of the percutaneous coronary intervention group compared to medical therapy (OR 0.49, 0.26 to 0.91). The remaining sensitivity analyses did not significantly change the overall results. There was no evidence of publication bias.

Authors’ conclusions
In patients with stable coronary artery disease and objectively documented myocardial ischaemia, percutaneous coronary intervention with medical therapy was not associated with a reduction in death, nonfatal myocardial infarction, unplanned revascularisation or angina compared with medical therapy alone.

CRD commentary
The review question and inclusion criteria were clearly defined. Some relevant sources were searched. No language restrictions were applied and this reduced potential for missed studies. There was no evidence for publication bias but this test is not deemed accurate for fewer than 10 studies. Some areas of the review process were conducted independently which reduced potential for reviewer error and bias. Study quality was assessed and the results reported for individual studies.

The methods of analysis appeared appropriate. There was substantial statistical heterogeneity for the outcomes of revascularisation and angina which were not explored. Among other limitations, the authors noted that trials enrolled only patients with coronary artery disease considered appropriate for revascularisation with percutaneous coronary intervention so these results may not be generalisable to other modes of revascularisation.

The authors’ conclusions reflect the evidence presented and seem reliable in terms of the primary outcomes of interest. Results for outcomes where high statistical heterogeneity was detected may be less reliable.

Implications of the review for practice and research
Practice: The authors stated that the evidence underscored existing clinical practice guidelines that recommended an initial approach of contemporary medical therapy for patients with stable coronary artery disease and ischaemia rather than proceeding directly to ischaemia-guided percutaneous coronary intervention.

Research: The authors did not state any implications for research but they identified an ongoing trial.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.