# PCI or CABG in coronary artery disease?

Published Online
March 20, 2009
DOI:10.1016/S0140-6736(09)60574-2

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In *The Lancet* today, Mark Hlatky and colleagues[1] report a pooled analysis of individual data from almost 8000 patients enrolled in ten randomised trials of percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG) over the past two decades. They conclude that, while at a median 6 years' follow-up there was no overall difference in survival, there was a significant survival advantage with CABG in patients with diabetes (hazard ratio 0·70, 95% CI 0·56–0·87) and in those aged 65 years or older (0·82, 0·70–0·97). Furthermore, the combined endpoint of death or repeat revascularisation was reduced with CABG (10%) compared with PCI (25%; 0·41, 0·37–0·45). Being probably the most definitive and authoritative analyses of the previous randomised trials, these conclusions are important and raise three important questions: are the findings robust; are they consistent with previous reports; and are they generalisable to most patients undergoing PCI or CABG? The last question is particularly relevant to the recent publication of the 1-year interim-analysis of the landmark SYNTAX trial.[2]

First, however, it is necessary to consider two potentially important limitations of the new analyses. Most importantly, the randomised trials only enrolled around 5–10% of the eligible population, most of whom had single-vessel or double-vessel disease and normal left ventricular function,[3] a group in whom it was already well established that there was no prognostic benefit with CABG.[4] By largely excluding patients with a known survival benefit from CABG (left-main or triple-vessel coronary artery disease, or both, and especially with impaired ventricular function[4]), the trials ignored the prognostic benefit of surgery in more complex coronary artery disease. Nevertheless, inappropriate generalisation of trial results from highly selected populations to most patients with multivessel disease has been ubiquitous in the literature and has, at least partly, justified the explosive growth in PCI in developed countries. Similarly, reports from several large registries of a consistent survival benefit of CABG over PCI in risk-matched patients with more complex coronary artery disease are often ignored.[5–10] In fact, the severity of coronary artery disease in today's analyses is more similar to that recently reported in the COURAGE trial which showed no prognostic benefit of PCI over optimum medical therapy,[11] which implies that many of these trial patients could now be managed with medical therapy rather than any intervention.

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A second obvious limitation is that neither the PCI nor the CABG in these trials would be considered optimum by contemporary standards. PCI patients did not receive drug-eluting stents and only 83% of CABG patients received an internal mammary artery, the most important prognostic factor for long-term survival after CABG and a benefit which persists long into the second decade of follow up.[12,13] Furthermore, although use of bilateral internal mammary arteries can offer even greater prognostic benefit,[14] best evidence shows that, although drug-eluting stents reduce the incidence of restenosis compared with bare-metal stents, they do not improve survival or reduce the incidence of myocardial infarction.[15,16] These observations are consistent with the hypothesis that, whilst bypass grafts to the mid-coronary vessel both treat the culprit lesion and also offer prophylaxis against new proximal disease, stents in the proximal coronary artery cannot protect against new disease.

With these caveats and for the first question above about robustness, Hlatky and colleagues, who are an eminent group of clinical and scientific academics in cardiovascular medicine (although without a surgeon among the 24 authors), argue persuasively that, by

contrast with previous meta-analyses, pooling data from individual patients provides more precise estimates of the effect of CABG and PCI on survival both in the total population and in subgroups.

For the second question about consistency, outcomes in today's study are broadly consistent with previous reports of a minor[17] or no[18] survival advantage of CABG over PCI, but with a far higher need for repeat intervention with PCI. Today's novel findings are of significantly better survival with CABG in older patients (≥65 years) and in patients with diabetes. Although the mechanism(s) of improved survival in these groups is not known, intuitively such mechanisms are most likely to reflect more advanced coronary disease, particularly so in diabetic patients. The survival benefit in patients with diabetes persisted even when the results of the BARI trial were excluded, but is consistent both with registry data[19,20] and the recent BARI report that the survival benefit for CABG persists at 10 years.[21] On the other hand, Hlatky and colleagues' observation that there was no significant effect of the extent of coronary artery disease on the relative effectiveness of PCI and CABG on survival is counterintuitive and at odds not only with the findings in older patients and those with diabetes in the new analyses but also with previous meta-analyses,[4] registry data,[5–10] and the SYNTAX trial.[2]

The third and most important question is how generalisable are these results to the population of patients with more severe coronary artery disease who require intervention? Despite the reservations above, new important evidence can be found in the interim analyses of SYNTAX in 1800 patients with left-main and/or three-vessel coronary artery disease who were randomised to PCI or CABG.[2] The unique strength of SYNTAX was not only as an "all-comer" trial of patients with the most complex coronary artery disease but also the maintenance of a parallel registry of patients excluded from randomisation (1077 in the CABG group whose disease was too complex for PCI, and 198 in the PCI group considered to be at excessively high surgical risk). At 1 year (with final analyses at 5 years), 12% of patients who had CABG and 18% of those who had PCI reached the primary composite endpoint of death, myocardial infarction, stroke, or repeat revascularisation. Although the difference was largely driven by repeat revascularisation but with no significant difference in mortality, PCI failed to reach the pretrial-specified criteria for non-inferiority, with the authors concluding that "CABG remains the standard of care for patients with three-vessel or left main coronary artery disease" (and by contrast with Hlatky and colleagues' study, there was a greater benefit with CABG in more severe disease). However, the 1-year result might greatly underestimate the survival benefit of CABG, which registry data has consistently shown to accrue with time compared with PCI and usually reaches statistical difference at 2–3 years.[5–10] Furthermore, although all patients who had PCI received drug-eluting stents, fewer than 30% of those who had CABG benefited from the potential prognostic benefit of bilateral internal mammary artery grafts.[14] Finally, it is uncertain whether the higher incidence of stroke at 1 year with CABG (2·2% *vs* 0·6%) was largely procedural or a consequence of substantially inferior secondary prevention (including dual antiplatelet, statin, antihypertensive, and angiotensin-converting-enzyme inhibitor) than in the PCI group.

So what can we conclude from the new study, especially in light of COURAGE and SYNTAX? For less severe coronary disease (mainly one-vessel or two-vessel disease and normal left ventricular function), there is little prognostic benefit from any intervention over optimum medical therapy. In such patients who do require intervention, perhaps for symptomatic reasons, there is no obvious survival advantage for either PCI or CABG (at least in patients who are not diabetic), but there is a significantly higher risk of repeat revascularisation with PCI. In patients with more severe coronary artery disease, and especially those with diabetes, CABG is superior in terms of survival and freedom from reintervention. However, SYNTAX also underlined that PCI is a good option—at least over the shorter term—in patients who are ineligible for or who refuse CABG, and also the importance of rigorous secondary prevention in patients who have CABG. Finally, in view of the prognostic benefit of surgery, a multidisciplinary team approach should be the standard of care when recommending interventions in more complex coronary artery disease, to ensure transparency, real patients' choice, and genuine informed consent in the decision-making process. For elective patients, this approach will necessitate separation of angiography from the intervention to allow appropriate time to make a truly informed decision.

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I declare that I have no conflict of interest.

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# Lipid lowering for primary prevention

Three large trials of rosuvastatin to prevent cardiovascular events have been completed.[1–3] Two of these, CORONA and GISSI-HF,[1,2] assessed 10 mg rosuvastatin daily. Substantial reductions in LDL cholesterol, a small increase in HDL cholesterol, and appreciable reductions in high-sensitivity C-reactive protein (hs-CRP) were reported. CORONA enrolled patients with ischaemic heart disease, whereas GISSI-HF included patients with ischaemic (40%), dilated (35%), and hypertensive (18%) causes of heart failure. Because such patients are probably at risk for future ischaemic vascular events, lowering of LDL cholesterol would be expected to reduce cardiovascular death, myocardial infarction, and stroke. Yet in neither trial was there a clear reduction in ischaemic vascular events or cardiovascular mortality (table).

By contrast, in the JUPITER trial,[3] 17 802 apparently healthy people, with LDL cholesterol less than 3·4 mmol/L and CRP concentrations above 2·0 mg/L, received rosuvastatin 20 mg daily. LDL cholesterol decreased by 50% and CRP by 37%. Over 1·9 years, there were substantial and significant reductions in ischaemic vascular events as well as total mortality, which were larger and more rapid than those in previous trials of rosuvastatin or other statins.[4]

How can we explain the apparently contradictory results of JUPITER compared with CORONA and GISSI-HF? In all three trials, CRP was raised, and substantial reductions in both LDL cholesterol and CRP occurred. The duration of the first two trials was much longer than that of JUPITER, and because the benefits of lipid lowering are enhanced by longer