Coronary stenting for stable coronary ischaemia: ain't misbehaving, just misunderstood

In the management of coronary artery disease, trepidation associated with the risk of future myocardial infarction weighs heavily on the minds of patients and physicians alike, given the well recognised and often publicly highlighted association with premature cardiovascular mortality. In the context of high risk acute coronary syndromes, the practice of early invasive coronary angiography with percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) is a Level IA (Grading of Recommendations Assessment, Development and Evaluation [GRADE]: Strong) indication for the reduction of recurrent myocardial infarction and cardiovascular mortality.[1]

However, PCI in the management of stable coronary artery disease has not demonstrated the same degree of benefit with additional insights gained from trial patients with the most severe degrees of myocardial ischaemia. Although the Surgical Treatment for Ischemic Heart Failure (STICH) trial from over a decade ago demonstrated moderate reductions in mortality associated with CABG for patients with reduced left ventricular function and coronary disease, more recent evidence of PCI for multivessel disease has not affected cardiovascular mortality or recurrent myocardial infarction.[2-4] In the Revascularization for Ischemic Ventricular Dysfunction (REVIVED-BCIS2) PCI study of 700 patients with left ventricular dysfunction (ejection fraction < 35%) and extensive coronary artery disease with demonstrable myocardial viability, a PCI strategy did not reduce all-cause mortality or heart failure admissions (PCI strategy, 37.2% *v* 38.0%; hazard ratio, 0.99; 95% CI, 0.78–1.27; $P = 0.96$).[4] These results are consistent with recent insight from the International Study of Comparative Health Effectiveness with Medical and Invasive Approaches (ISCHEMIA) study, a trial that did not demonstrate a reduction in all-cause mortality, myocardial infarction, unstable angina, hospitalisation, or cardiac arrest with routine revascularisation in patients with stable ischaemia or angina.[3] From this study, an analysis exploring the factors associated with mortality found no association with the extent of myocardial ischaemia on stress testing (largely nuclear perfusion imaging). An association with non-fatal myocardial infarction was no longer evident after adjustment for coronary disease burden. In contrast, the burden of coronary artery disease (ie, extent of coronary plaque) was strongly associated with future cardiovascular death or myocardial infarction.[5] Although these findings may be considered counterintuitive, they are entirely consistent with the previous subanalysis of the STICH trial. The STICH investigators found that the mortality benefit associated with CABG was not dependent on the degree of ischaemic viable myocardium; that is, there was benefit among patients with little to no ischaemia as there was among those with extensive ischaemia.[6] Such insights call into question the practice of functional ischaemia testing beyond the purpose of diagnosing symptoms (with functional–anatomic correlation), such as for the assessment of viability or silent ischaemia.

These recent data are congruous with many clinical trials over several decades which have demonstrated no evidence that PCI provides reductions in cardiovascular mortality or myocardial infarction among patients with stable coronary ischaemia. Outside the clinical presentation of an acute coronary syndrome or left main coronary artery disease, coronary stenting provides a relatively targeted and localised therapy that is effective in reducing angina symptoms, though evidence of its superiority over pharmacological therapies is not established.[7,8] Nevertheless, in patients with stable angina symptoms, resistant to pharmacotherapies or for patients unable to take these medications, PCI remains an attractive option for symptom relief. One may wonder about the long term mortality and recurrent myocardial infarction benefit of CABG seen in the STICH trial. This observation is likely explained by the fact that coronary grafting subtends a greater proportion of diseased coronary vessel, preventing myocardial infarction from plaque rupture upstream to the bypass graft, as opposed to the limited degree of plaque stabilisation offered by lesion-specific coronary stenting.

Thankfully, decades of cardiovascular research have delivered us a substantial number of strategies that do reduce the incidence of future myocardial infarction and, therefore, cardiovascular death. These include diet and exercise modification, cessation of smoking, aspirin and antiplatelet therapy, and low-density lipoprotein (LDL) and triglyceride reduction.[9] Importantly, the therapeutic options for LDL reduction continue to expand, offering the ability to target low levels of LDL in a greater proportion of high residual risk patients with stable coronary artery disease. Of course, these strategies target coronary plaque stability and atherosclerosis burden rather than coronary ischaemia specifically.

Choosing therapies well, with the patient's preference, requires an understanding of the temporal risk profile of coronary artery disease. It has long been demonstrated that the risk of mortality and recurrent myocardial infarction is highest immediately following an acute coronary event and that this risk diminishes over subsequent days to weeks.[10] This provides the rationale for culprit lesion revascularisation in the treatment of acute coronary syndromes. Beyond this time, the ongoing risk of mortality and myocardial infarction is determined by coronary artery disease burden, and not residual ischaemia. Understanding that established revascularisation practices will persist

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for clinical scenarios not well studied within the recent randomised trials, coronary stenting for ischaemia and angina is one therapeutic option for the management of symptom burden, but we need not attribute benefits beyond this to coronary stenting. For the prevention of premature cardiovascular death, the effective management of plaque burden should remain at the forefront of the clinician's and patient's minds, requiring us all to think beyond the coronary lesion alone.

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