Incomplete revascularization: appropriate and inappropriate

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In the current issue of the Journal, Head et al. [1] report the incidence and predictors of incomplete revascularization (IR) after percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) surgery in the SYNTAX trial and, crucially, the clinical ramifications. Their main conclusion, that IR is associated with adverse events after PCI but not after CABG, carries very important clinical implications for these competing interventions and immediately raises two questions. Is their conclusion justifiable by the data presented and is it consistent with what is already known on this topic?

But first some necessary background. The SYNTAX trial is unquestionably the most important trial ever conducted of PCI and CABG. In contrast to all such previous trials that enrolled highly selected patient populations, not typical of those encountered in every day clinical practice [2], the SYNTAX investigators attempted a real-world ‘all comer’ trial [3]. Even so it is important to appreciate that almost one-third of all patients had coronary artery disease of such severity that they were considered ineligible for PCI and underwent CABG and consequently were enrolled in a registry.

The 3-year outcomes of the SYNTAX trial were recently published in this journal [4] and demonstrated a significantly higher incidence of MACCE in the PCI than in the CABG patients. Most importantly, in patients with three-vessel disease, there was an almost 5% survival advantage for patients undergoing CABG rather than PCI (and no difference in the incidence of cerebrovascular accident) whereas for left main stem disease there was no survival difference between the two treatment strategies but a higher incidence of stroke with CABG. In a ‘hypothesis generating’ subgroup analyses of the left main stem cohort group, PCI had a lower mortality in patients with lower and intermediate SYNTAX scores (<33) whereas CABG had a survival benefit in those with SYNTAX scores >33. The latter findings are in contrast with those of the only other large trial of PCI and CABG in patients with left main stem disease (the PRECOMBAT trial from Korea), which included patients with left main disease of comparable severity to those in the SYNTAX trial with scores <33 and showed no increase in mortality or stroke with CABG [5]. These discrepant observations should hopefully be resolved by the EXCEL trial which is currently randomizing 2600 patients with left main stem stenosis and SYNTAX scores <33 to PCI or CABG.

The existing literature on IR is confused by varying definitions of IR and further complicated by often creating a ‘post hoc’ definition of IR after the intervention. A major strength therefore of the current study is that the authors pre-defined IR (failure to revascularize any vessel >1.5 mm with at least a 50% stenosis) for both PCI and CABG. Consequently, the apparently relatively high rates of IR in the current study at 43% for PCI and 37% for CABG are at least in part explained by this robust definition of IR. Furthermore, as the incidence of IR is also known to be higher in patients with more complex coronary artery disease, this will also be reflected in the SYNTAX trial which enrolled patients with much more complex disease than those in previous trials of PCI and CABG.

Intuitively, it is easier to achieve complete revascularization (CR) with three localized proximal lesions in otherwise normal coronary vessels than in patients with multiple, complex and diffuse lesions in small coronary vessels. Accordingly, in the current study, the number of lesions and total occlusions were predictors of IR for PCI as were the number of lesions and diffuse disease or small vessels for IR in CABG patients.

Probably, the most important finding in the study is that IR resulted in a higher MACCE rate in PCI patients (34% for IR versus 24% for CR) but not in CABG patients (22 versus 20%). Disconcertingly, the composite safety endpoint was higher with IR in the PCI group (16.8% for IR versus 12.2% for CR; P = 0.05) but not the CABG group. Most worryingly, IR in the PCI group did result in an increased mortality (10.2 versus 7.4%; P = 0.13) and although not reaching conventional statistical significance is clinically important if confirmed in a larger cohort of patients. Finally, IR resulted in a higher rate of repeat revascularization in the PCI patients (24 versus 16%; P = 0.001) but not for CABG patients (12.8 versus 9.4%; P = 0.11).

These findings are consistent with existing literature. There is a strong body of evidence that IR with PCI results in adverse long-term outcomes in terms of MACCE including increased mortality [6]. Park’s group also recently reported that in 1400 patients with drug-eluting stents and 514 CABG patients angiographic IR was observed in 59% of PCI and 33% of CABG patients [7]. While overall at 5 years CR patients had a similar composite end point of death, MI stroke and repeat revascularization as IR patients, crucially however in the 18% of patients with multi-vessel IR there was a greater risk of death, MI stroke and repeat revascularization (30.3 versus 22.1%; P = 0.079).

Similarly, earlier studies of CABG from the 1980s also demonstrated adverse outcomes with IR, but this effect seems to be less apparent with much more widespread use of the internal mammary artery (IMA) grafting to the left anterior descending (LAD) coronary artery. Indeed, Mohr et al. [8] reported in a cohort of 8806 CABG patients with multi-vessel disease that in
~10% with IR of the circumflex or right coronary artery (but all with an IMA to the LAD), there was no detrimental effect on 1- or 3-year survival in comparison to those with CR. The authors also reported that IR was five times more common in patients with more complex disease and that despite receiving fewer grafts operating times were still longer implying the technically more challenging nature of these patients.

Why might there be a discrepancy between the potential adverse impact of IR between PCI and CABG patients? From a technical perspective, the most likely reason for IR during CABG is the operative finding of a small or diffusely diseased vessel that may therefore not subtend a particularly large or even viable area of myocardium. In contrast, the success of PCI is heavily dependent on the nature and complexity of the proximal lesion, including occluded vessels and if technically unsuccessful may therefore leave a relatively large distal vessel and a large area of myocardium non-revascularized. In contrast, leaving large distal vessels ungrafted is an unlikely scenario during CABG as the graft is to the mid-coronary vessel that is usually disease free. There is good evidence that it is the burden of ischaemia that is an important determinant of outcome and this is a more likely proposition where there is a large non-revascularized vessel subtending a large area of viable myocardium. In such a setting, bypass grafting is invariably successful whereas the complexity of the proximal lesion may preclude successful PCI. In other words, we need to distinguish between IR which is appropriate (AIR) and that which is inappropriate (IIR). While the former is unlikely to impact adversely on clinical outcomes, the latter certainly does and the fact that IIR is more likely with PCI than CABG, and particularly with increasing complexity of disease, almost certainly contributes to the survival advantage of CABG with increasing durations of follow-up.

While it also needs to be appreciated that patients with IR may already have a poorer long-term prognosis, because IR is a surrogate marker of a greater burden and complexity of coronary as well as other vascular disease, this effect should not operate differentially on the clinical outcomes between PCI and CABG. The 3-year outcomes of SYNTAX show that such patients (i.e. those with the intermediate and higher tercile SYNTAX scores) invariably do better with bypass grafting than with PCI and almost certainly as a consequence in more complete revascularization. This fact underlines the need to distinguish between IIR and AIR.

REFERENCES