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Does a hybrid approach to multivessel revascularisation really make sense?

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In the current issue, Wrigley and colleagues ask whether a hybrid approach, using a combination of coronary artery bypass grafting (CABG) and percutaneous coronary intervention (PCI) using stents, might be the best method of revascularisation in multivessel coronary artery disease (CAD), at least in selected patients[1]. Their basic premise, that a combination of internal mammary artery grafting (IMA) to the left anterior descending (LAD), with its proven survival benefit at up to two decades of follow-up[2,3], combined with newer-generation stents to other coronary territories rather than vein grafts, is an important question that is increasingly debated.

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The article, by an experienced interventional cardiology and cardiac surgery team, is well written, comprehensive, clear and concise. However, their hypothesis makes two suppositions that are fundamentally flawed and, ultimately, undermine the basic premise.

The main rationale for a hybrid approach using PCI is the progressive deterioration of vein grafts over time so that by ten years only around 50% are patent and, of these, half are severely diseased[4]. On the other hand, there is abundant angiographic evidence of the superior patency of bilateral IMA (BIMA) grafts with a recent study showing patency rates of 90% at 20 years[5], a scenario that is highly unlikely ever to be seen with vein grafts, even accepting that statin therapy may slow the process of vein graft intimal hyperplasia[6]. This superior patency of BIMA grafts appears to translate into a survival benefit. In 2001, our group published a systematic review including a meta-analysis of 15,962 patients receiving either single IMA (SIMA) or BIMA grafting and matched for age, gender, ventricular function and diabetes[7]. At a median of four years of follow-up, the BIMA group had a significant reduction in mortality (hazard ratio 0.81, 95% CI: 0.70-0.94) compared to the SIMA group with no study showing significantly harmful effect of BIMA grafts.

The cardiac surgery community should be legitimately criticised for the very low rates of use of BIMA grafting, being only around 5% of patients in the USA and fewer than 10% in Europe. In an effort to acquire more data on this issue, the Arterial Revascularisation Trial (ART) randomised 3,102 patients in 28 centres in seven countries to SIMA or BIMA grafting[8]. The one-year outcomes show the excellence of contemporary CABG with mortality rates for both SIMA and BIMA of around 2% and the incidence of stroke, myocardial infarction and repeat revascularisation all under 2%. While this does not prove long-term superiority of BIMA over SIMA grafts, it does show that BIMA grafting can be performed at least as safely as SIMA grafting with regard to conventional major adverse cardiac and cerebrovascular events (MACCE) outcomes. Furthermore, the use of BIMA grafts added 23 minutes to what was essentially a three-hour operation and prolonged the duration of ventilation by 90 minutes on an average duration of ventilation of 14 hours.

The most important caveat to the use of BIMA is the risk of sternal wound dehiscence. The ART trial demonstrated the excellent healing of the sternum in more than 99% of patients with a SIMA graft and 98% with BIMA grafts. Nevertheless, sternal dehiscence, a major complication of surgery, occurred in 1.9% of the BIMA group versus 0.6% of the SIMA group in the ART trial. However, 24% of all patients in ART had diabetes and it is noteworthy that in the BIMA group requiring sternal reconstruction 50% had diabetes. Therefore, with a more selective use of patient inclusion (i.e., excluding diabetic patients who also have obesity or poor lung function) and a modified harvesting technique (skeletonisation rather than pedicled) then the rates of sternal wound problems would almost certainly be reduced.

A second weakness of the hybrid premise is a failure to understand not only the differences in clinical outcomes of contemporary

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trials and registries of CABG and PCI, but also the likely pathophysiological mechanism that predominantly underpins these differences. The authors state that "despite randomised studies comparing CABG and DES in multivessel disease the optimal revascularisation strategy is far from clear and there are limitations with the SYNTAX trial that make it fall short of being the definitive study". While the latter part of this statement is a generic comment that can be applied to every randomised trial, the initial part of the statement is directly at odds with the totality of the best available evidence. Indeed, it is striking that many of those cardiologists who greeted the one-year outcomes of SYNTAX with great enthusiasm now disparage the same trial when observing the five-year outcomes. The five-year results of SYNTAX are very convincing: CABG in comparison to PCI significantly reduced overall MACCE (27% vs. 37%; p<0.001), cardiac death (5.3% vs. 9.0%; p=0.003), myocardial infarction (3.8% vs. 9.7%; p<0.001) and repeat revascularisation (14% vs. 26%; p<0.001) but not overall death (11.4% vs. 13.9%; p=0.10) or stroke (3.7% vs. 2.4%; p=0.09)[9]. Accepting that, as the primary endpoint (MACCE at one year) of non-inferiority for PCI vs. CABG was not reached, and that subsequent analyses are therefore only observational and "hypothesis generating", the relative efficacy of CABG and PCI appears dependent on the complexity of anatomical CAD. Overall, patients with lower and intermediate severity CAD had similar survival between PCI and CABG while in the group with severe CAD CABG resulted in significantly lower mortality (11.4% vs. 19.2%; p=0.005), myocardial infarction (3.9% vs. 10.1%; p=0.004) and repeat revascularisation (12% vs. 31%; p<0.001). The benefits of CABG on MACCE also appeared greater in patients with isolated three-vessel disease (24% vs. 38%: p<0.001) than with left main disease (31% vs. 37%: p=0.12). Finally, the true benefit of CABG may actually still be underestimated as at five years there is continuing divergence of MACCE rates in favour of CABG, in all categories of anatomical severity of CAD. As the results of the SYNTAX trial are entirely in accordance with the findings of ten propensity matched registries of patients undergoing PCI or CABG in routine clinical practice over the last decade, including one with over 190,000 patients[10], we can be reassured that the SYNTAX findings are real.

The authors also make the ubiquitous and "ever shifting goalposts" cardiology argument that clinical outcomes will be better with the next generation of stents (with the implication that all existing evidence, which is not supportive, is therefore obsolete and can be ignored). While newer-generation stents may indeed reduce the need for repeat target vessel revascularisation (at least in the early to intermediate period), crucially it does not apply to the most important clinical benefits that are seen with CABG. Each newer generation of stent has, repeatedly, been shown not to reduce mortality or myocardial infarction in comparison to previous generation stents[11]; the failure to understand why illustrates a lack of comprehension of the fundamental difference in effects achieved by the two interventions. Bypass grafts to the mid-coronary vessel not only make the complexity of proximal disease irrelevant but also offer prophylaxis against development of further proximal disease. In contrast, stents of whatever generation, while effectively treating less complex proximal lesions, can quickly have their benefits nullified by the development of further disease proximal to, within, or immediately distal to the stent. It is these differing pathophysiological effects that explain the consistently lower incidence of subsequent myocardial infarction, repeat revascularisation and – most crucially – mortality observed with CABG.

So is there a need for a trial of hybrid revascularisation in routine clinical practice? In patients with three-vessel disease this could only be justified in patients with lower tercile SYNTAX scores because of the survival benefit with CABG in intermediate and high-risk tercile patients. In low tercile patients the only obvious difference in the SYNTAX trial between PCI and CABG was a lower need for repeat revascularisation with surgery. The same applies for left main in the lower and intermediate tercile groups (as is the case for the current EXCEL trial) where PCI performed, at the very least, as well as, if not better than CABG.

So is there a role for hybrid revascularisation already present and obvious in clinical practice without randomised trials? In my "anecdotal" experience there most certainly is. The classic situation is an octogenarian with a tight calcified distal left main lesion, with or without additional proximal disease in the left coronary artery system, and further moderate disease in the right coronary artery (where the only graft that will reliably survive residual competitive flow is a vein graft). In this scenario BIMA grafting, performed off-pump, with subsequent stenting of the right coronary artery is the ideal technique, not least because when CABG is done off-pump, using BIMA grafts, it permits a aortic no-touch technique reducing the potentially single worst outcome for any patient undergoing cardiac surgery, i.e., a stroke.

However, if hybrid revascularisation effectively denies most patients the opportunity to receive BIMA grafting for the sake of a smaller (though not necessarily less painful) incision, its rationale is severely weakened. To use an English aphorism "penny wise, pound foolish". Surgeons promoting hybrid revascularisation would provide a far better service to the majority of their patients if they routinely offered BIMA grafting rather than being preoccupied with which incision to approach the heart.

Conflict of interest statement

The author has no conflicts of interest to declare.

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