

EDITORIAL COMMENT

Complete Revascularization in Left Main Disease

Is it Important?*

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The concept of complete revascularization (CR) as a method to improve the outcomes of patients with chronic coronary disease has gained increased consideration in recent years. In particular, CR is being explored as a potential solution to the lack of benefit seen in randomized controlled trials of coronary revascularization compared with medical management alone, as well as the inferior results of percutaneous coronary intervention (PCI) compared with coronary artery bypass graft (CABG) surgery.^{1,2} Coincidentally, CR is increasingly being facilitated by improved drug-eluting stents, new drug-coated balloons, and safer, more efficacious techniques for the treatment of chronic total occlusions, with success approaching 90%.³ In a meta-analysis of 35 studies including 89,883 patients, CR was achieved in approximately 50% of patients with multivessel disease and was associated with lower long-term mortality (risk ratio [RR]: 0.71; $P < 0.001$), myocardial infarction (RR: 0.78; $P = 0.001$) and repeat revascularization (RR: 0.74; $P < 0.001$) and was more common after CABG than PCI (75% vs 44%, respectively; $P < 0.001$).^{4,5} The totality of the evidence has been compelling enough for the 2018 European Society of Cardiology guidelines on myocardial revascularization to

recommend the consideration of achieving CR when choosing revascularization strategies.⁶

The newest group of patients facing a choice of revascularization strategies are those with left main coronary artery (LMCA) disease. For these patients, revascularization with either CABG or PCI confers a survival benefit,⁷⁻¹⁰ and recently, both options were supported by the American College of Cardiology/American Heart Association revascularization guidelines.¹¹ Because these patients often have concomitant multivessel disease, differences between CABG and PCI in achieving CR vs incomplete revascularization (IR) might have prognostic implications. However, to date, CR vs IR in patients with LMCA disease has not been well studied.

In this issue of *JACC: Asia*, Kim et al¹² describe a prespecified analysis of the PRECOMBAT (Premier of Randomized Comparison of Bypass Surgery Versus Angioplasty Using Sirolimus-Eluting Stent in Patients With Left Main Coronary Artery Disease) trial evaluating the impact of CR vs IR on long-term (10-year) outcomes in 600 patients who were randomly assigned to PCI or CABG for revascularization of LMCA disease. Coronary disease was defined anatomically, on the basis of the presence of $\geq 50\%$ stenosis in arteries with diameter ≥ 2.5 mm. On the basis of this definition, almost 75% of these patients had disease in ≥ 2 vessels in addition to LMCA disease. The rate of CR was high and similar in both the PCI (68.3%) and CABG (70.3%) groups, likely because of the inclusion criterion stating that the disease had to be “comparably treatable” by both methods. At 10-year follow-up, there were no statistically significant differences in major adverse cardiac and cerebrovascular events (MACCE) (all-cause death, stroke, myocardial infarction, and ischemia-driven target vessel revascularization) between the CABG and PCI groups. However, although the difference in 10-year MACCE between patients achieving CR, whether by

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PCI or CABG, was similar (28.3% vs 25.7%, respectively; adjusted HR: 1.19; 95% CI: 0.91-1.73), the patients achieving IR by PCI had a substantially more MACCE compared with those achieving IR by CABG (33.2% vs 22.2%, respectively; adjusted HR: 1.64; 95% CI: 0.92-2.92). This difference was driven primarily by increased ischemia-driven target vessel revascularization (15.1% vs 6.4%, respectively; HR: 2.71; 95% CI: 0.97-7.62; log-rank $P = 0.024$ comparing all 4 groups). This trend toward worse outcome in patients treated with PCI achieving IR is notable because similar statistically significant findings were seen in the higher powered SYNTAXES (Synergy Between PCI With Taxus and Cardiac Surgery: SYNTAX Extended Survival) trial of patients with 3-vessel or LMCA disease, with increased all-cause mortality in the PCI patients achieving IR (33.5%) compared with the PCI patients achieving CR (22.2%) and the CABG patients (achieving CR, 23.8%; achieving IR, 24.3%; $P < 0.001$ across all groups).¹³

Some of the limitations of this study are shared by the many prior studies of CR vs IR. The decision to perform CR or IR was not randomized, and the treatment of lesions likely depended on coronary anatomy, technical considerations, patient comorbidities, and operator skill set, all potential confounders that could influence outcomes. For example, in the present study, IR patients had greater baseline angiographic disease burdens than CR patients as measured by “extent of disease” and SYNTAX score. The CR substudy of ISCHEMIA (International Study of Comparative Health Effectiveness With Medical and Invasive Approaches) showed that adjustment for such observed potential confounders decreased the difference in outcomes between CR and IR.¹⁴ Other limitations include 1) the different CR determination techniques used for the PCI patients (angiograms) and the CABG patients

(surgeons operative reports); and 2) the lack of blinding to revascularization outcomes in the PCI patients, all of whom had postprocedural angiograms, which could potentially trigger the “occulostenotic reflex,” whereas the CABG patients did not. Limitations unique to the present study include the use of first-generation sirolimus-eluting stents, which have been shown to be inferior to contemporary stents,¹⁵ and the relatively low statistical power. Finally, like the other studies of CR, there was no evaluation of its effect on health status (symptoms, function, quality of life), which is important outcome because it is the only outcome proven to improve with revascularization in chronic coronary disease. A CR substudy of ISCHEMIA showed that CR was associated with better health status than IR.¹⁶

In conclusion, although Kim et al’s¹² study of PRECOMBAT and CR helps inform the consideration of CR vs IR (and CABG vs PCI) for LMCA disease, the larger body of observational evidence suggests that CR may be valuable for improving patient outcomes and health status when it is achievable without incurring risks outside the norm. This leaves intact the current advocated principle of considering the achievement of CR as one of several factors when choosing a revascularization strategy. Ultimately, randomized controlled trials of CR vs IR must be undertaken to understand the absolute risks, benefits, and cost of CR vs IR.

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