Editorial

Revascularization strategies for multi-vessel coronary artery disease in patients undergoing primary percutaneous coronary intervention: is the evidence COMPLETE?

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Despite advancements in primary percutaneous coronary interventions, the question of whether to revascularize a non-infarct related artery (non-IRA), during an acute ST-elevation myocardial infarction (STEMI), has remained a conundrum. To address this dilemma, numerous observational studies were performed between 2001 and 2014. These data suggested that revascularization of non-IRA may be associated with worse outcomes. On the basis of these observational studies, previous guidelines recommended against revascularization of non-IRA (Class III) (1). Subsequently, moderate sized randomized clinical trials (RCT) have disputed these concerns; the guidelines were updated by ACC/AHA to a class IIb (2) recommendation, while European Society of Cardiology changed it to a class IIa recommendation (3). However, a knowledge gap remains as these RCTs were moderately sized and were powered for the composite of major adverse cardiac events (MACE) and not hard outcomes such as mortality and myocardial infarction. Subsequent meta-analyses of these RCTs showed that there were no difference in hard outcomes of all-cause mortality and myocardial infarction (MI). Reduction in MACE was mainly due to reduction in urgent revascularization when compared to infarct related artery only vascularization (4,5).

In this context, the most recent RCT published, the COMPLETE (6) trial, aids in addressing this knowledge gap. With 4,041 patients enrolled, COMPLETE is the largest RCT to date, that was powered to evaluate the composite of cardiovascular mortality or MI. The COMPLETE trial randomized patients with STEMI and multi-vessel disease to revascularization of IRA-only versus complete revascularization of non-IRA, performed as a staged procedure (performed 1 to 45 days after the index procedure). At a median follow-up of 3 years, complete revascularization reduced risk of the composite of cardiovascular mortality or new MI [hazards ratio (HR) =0.74, 95% confidence interval (CI): 0.60–0.91, P=0.004), driven by a reduction in MI (HR =0.68, 95% CI: 0.12–0.26). This primary outcome of cardiovascular mortality and MI occurred in 7.8% of the complete revascularization arm versus 10.5% in the culprit only arm. Additionally, there was a reduction in the secondary outcome of cardiovascular death, MI, and ischemia-driven revascularization (HR =0.51, 95% CI: 0.43–0.61, P<0.001). Performing the procedure before or after discharge did not affect the benefit observed (7).

With the recently published results of the COMPLETE trial and other RCTs, there is now stronger evidence supporting complete revascularization, as this approach has proven to reduce cardiovascular mortality or MI. One can adapt complete revascularization as a default strategy for patients with STEMI and multi-vessel coronary artery disease. Nonetheless, it is important to note that relatively stable patients are usually enrolled in clinical trials as compared to often sicker patients seen in daily clinical practice. This observation was highlighted by the low SYNTAX score for non-IRA patients in the COMPLETE trial. For high complexity patients, a patient-individual approach may be more suited. Of note, the COMPLETE

trial showed that the reduction in the composite of cardiovascular mortality or MI was driven by a reduction of MI. A recently published meta-analysis of 6 RCTs (8), with 6,528 patients, showed that complete revascularization may reduce cardiovascular mortality; however, a trial sequential analysis performed refuted the results and suggested larger trials with at least 11,000 patients are required to answer this question, which is unlikely to be conducted. Additionally, it remains unknown whether a complete revascularization approach would be more cost-effective.

Albeit the above-mentioned studies guide towards recommending complete revascularization of non-IRA in patients with STEMI without cardiogenic shock, this is not the case for those who have cardiogenic shock and STEMI. The CULPRIT-SHOCK (9) trial showed a significantly lower rate of new renal replacement therapy or composite endpoint of death within 30 days in the IRA only revascularization arm as compared to the complete revascularization arm (relative risk =0.83, 95% CI: 0.71–0.96). This trend towards lower mortality in IRA only group was observed until 12 months (10). Thus, the updated 2017 European Society of Cardiology STEMI guidelines (11) recommend revascularization of IRA only in patients with STEMI and cardiogenic shock. Of note, the risk of mortality was similar between the two groups beyond 30 days. Moreover, there was nearly 20% patient crossover from IRA only revascularization to complete revascularization, which may have resulted in an overestimation of benefit with IRA only percutaneous coronary intervention.

In summary, the COMPLETE trial taught us that the findings of observational studies should be challenged with well-designed RCTs, and confirmed that a complete revascularization approach improves the outcomes in patients with multi-vessel disease undergoing primary percutaneous coronary intervention.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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