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IN PERSPECTIVE
Acute Coronary Syndromes

BIOVASC trial in perspective: complete revascularization strategies in patients presenting with acute coronary syndromes and multi-vessel coronary disease

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Evidence before the study

In patients hospitalized with acute myocardial infarction, multi-vessel coronary artery disease (MVD) is common (50–60%) and is associated with an increased risk of post-discharge mortality and recurrent myocardial infarction.[1,2] Multiple randomized controlled trials (PRAMI, DANAMI-3-PRIMULTI, CvLPRIT, Compare-Acute, and COMPLETE) have demonstrated that complete revascularization (CR) is superior to culprit-only recalculation in patients presenting with stent thrombosis (ST)-segment elevation myocardial infarction (STEMI).[3–6] The largest study (COMPLETE trial) randomized $n = 4041$ patients presenting with STEMI and MVD to culprit-only or separate staged CR procedure with 45 days of randomization.[7] It found that CR reduced death or myocardial infarction [hazard ratio (HR) 0.74; 95% confidence interval (CI) 0.60–0.91]. As of today, the optimal timing of CR in this population remains unclear with studies have protocolized immediate, in-hospital staged, or post-discharged staged CR.[3,4,7]

Contribution to the literature

Data considering the optimal timing in CR of the non-culprit lesion(s) are scarce or conflicting.

Aim of the study

The goal of the Percutaneous Complete Revascularization Strategies Using Sirolimus-Eluting Biodegradable Polymer-Coated Stents in Patients Prenting with Acute Coronary Syndrome and Multivessel Disease (BIOVASC) trial was to evaluate the optimal timing for a CR strategy in patients with acute coronary syndromes (ACS) and MVD.

Study design

The BIOVASC trial was a prospective, investigator-initiated, multicenter, open label, randomized non-inferiority trial that randomized patients to either (i) immediate complete revascularization (ICR) at the time of the index-PCI or (ii) staged complete revascularization (SCR) with PCI of the non-infarct related lesions within 6 weeks of the index procedure.[8] Coronary physiological assessment was used at the discretion of the operator.

The primary end point was a composite of all-cause mortality, non-fatal myocardial infarction, unplanned ischaemia-driven revascularization, and cerebrovascular events (MACCE) through 1-year post-index procedure.

The study planned to enrol 1525 patients at 30 sites in Belgium, Italy, Netherlands, and Spain. It had an 80% power with a non-inferiority α of 0.5 assuming an event rate of 10.5% in the immediate CR and 11% in the staged arm.

Study patients

The study *included* patients 18–85 years with ST-segment elevation and non-ST-segment elevation ACS with MVD with identifiable culprit lesion and aimable for PCI using the Orsiro platform (Biotronik AG, Bűlach, Switzerland) stent platform.

The significant coronary disease was defined as a 70% stenosis in a vessel ≥ 2.5 mm by visual estimation or positive coronary physiological testing. Selected *exclusion criteria* included cardiogenic shock, PCI within 30 days, presence of a chronic total occlusion, and previous coronary artery bypass grafting.

Principle findings

The study enrolled 1525 patients (764 in the ICR-arm and 761 in the SCR-arm) at 29 sites. The mean patient age was 65 years, 22% female, 21% with diabetes, and 40% presented with a STEMI.[9]

The 1-year primary outcome

The 1-year primary MACCE outcome occurred in 7.6% of the ICR-arm and 9.4% in the SCR-arm (HR 0.78, 95% CI 0.55–1.11, $P = 0.001$ for non-inferiority; $P = 0.166$ for superiority).

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1-year secondary outcome(s)

- Cardiovascular mortality or myocardial infarction (2.9 vs. 5.2%, HR 1.56, 95% CI 0.68–3.61, $P = 0.30$)
- Non-fatal myocardial infarction (1.9 vs. 4.5%, HR 0.41, 95% CI 0.22–0.76, $P = 0.0045$)
- Unplanned ischaemia-driven revascularization (4.2 vs. 6.7%, HR 0.61, 95% CI 0.39–0.95, $P = 0.030$)
- Target vessel revascularization [3.5 vs. 6.1%, HR 0.56 (0.34 to 0.90, $P = 0.061$)]

All were lower in the ICR-arm. The differences in myocardial infarction were mainly driven by differences in Type I myocardial infarction.

No differences were observed between the ICR-arm and the SCR-arm, respectively for the following secondary endpoints:

- Net adverse clinical events [composite of major bleeding Bleeding Academic Research Consortium (BARC 3 and 5), All-cause mortality, myocardial infarction (MI), and stroke [6.0 vs. 7.2%, HR 0.82 (0.55–1.22), $P = 0.32$],
- Major bleeding (BARC 3 or 5) [1.6 vs. 0.9%, HR 1·73 (0.68–4.39, $P = 0.25$)]
- Probable or definite stent thrombosis [0.8 vs. 0.9%, HR 0.86 (0.29–2.55, $P = 0.78$)]

Other salient features

Invasive coronary imaging (5.9 vs. 14.6%) and coronary physiology testing (15.4 vs. 23.3%) were more commonly performed in the SCR-arm.

No information on acute kidney injury, renal failure, or quality-of-life was reported.

In a post-hoc analysis of clinical outcomes that excluded procedure-related (type 4a) myocardial infarctions the primary MACCE outcome (7.5 vs. 8.7%, $P = 004$) and myocardial infarction (1.7 vs. 3.3%, $P = 0.051$) were lower in the ICR vs. the SCR-arm.

In a secondary landmark analysis for up to 30-days, MACCE, myocardial infarction, and unplanned target vessel revascularization remained lower in the immediate CR arm (HR 0.38, 95% CI 0.22–0.66, $p_{superiority} = 0.0007$).

In perspective

The BIOVASC trial showed that among patients with ACS and MVD undergoing primary PCI, ICR was non-inferior to SCR within 6-weeks of the index event at reducing MACCE (all-cause mortality, non-fatal myocardial infarction, any unplanned ischaemia-driven revascularization) at 1-year post-index procedure. CR was beneficial if performed either during or within 6 weeks after the index hospitalization. The BIOVASC study results are aligned with those of the COMPLETE timing sub-study where treatment of non-culprit lesions during the index hospitalization or after discharge but within 45 days had similar beneficial effects on both co-primary end points.[10] This is highly reassuring; however, some issues remain.

Although superiority for the primary endpoint was not met, an ICR was superior at 30 days from the index procedure. At 1 year after the index procedure, fewer myocardial infarctions occurred with the ICR strategy compared to the SCR strategy. Taken together, ascertainment bias, while adjudicating MI in patients early after the index event when cardiac troponins have not returned to normal, may be suspected. In addition, invasive coronary imaging and functional coronary assessment were only performed in a minority of patients. This may be perceived as a limitation to the trial and raises the question if all interventions, in both arms of the trial, were clinically justified.

Regardless, and in conclusion, one may concur with the authors that an ICR strategy might be particularly effective in patients with only two-vessel disease and reasonably simple lesions, with a high likelihood of procedural success without excessive use of radiation, contrast dye, or other resources. Future fine tuning of this treatment strategy to substantiate a role for intracoronary physiology assessment and intracoronary imaging may be warranted.

Author contributions

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