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EDITORIAL

# Do we need to be fully complete in multivessel acute myocardial infarction?

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In 2012, the European Society of Cardiology (ESC) Guidelines for the management of acute ST-segment elevation myocardial infarction (STEMI) stated that primary percutaneous coronary intervention (PCI) should be limited to the culprit vessel with the exception of cardiogenic shock (Class IIa, Level of Evidence B recommendation) and, in case of multivessel disease with non-culprit lesions suitable for revascularisation stress testing, or imaging for ischaemia or viability is indicated (Class I, Level of Evidence A recommendation).

In the past 10 years, these recommendations have shifted almost in the opposite direction. It started with the PRAMI study, the first randomised controlled trial (RCT) that challenged the concept that primary PCI should be limited to the culprit vessel only and disregarded the need for additional ischaemia testing for non-culprit lesions[1]. PRAMI randomised patients between culprit-only treatment and angiography-guided complete revascularisation by PCI (preventive PCI) and showed that a preventive PCI strategy significantly reduced the composite endpoint of cardiac death, recurrent non-fatal myocardial infarction and refractory angina. Even without the "soft" endpoint of refractory angina, the study was positive for the composite of the two "hard" endpoints of cardiac death and myocardial infarction. The PRAMI trial was followed by the smaller CvLPRIT trial, showing a similar benefit in the composite of major adverse cardiac events (MACE; all deaths, non-fatal myocardial infarction, ischaemia-driven revascularisation and heart failure) with an angiography-guided complete revascularisation strategy[2]. Simultaneously to PRAMI and CvLPRIT, two other RCTs were conducted with a slightly different approach. Both the DANAMI-3-PRIMULTI and COMPARE-ACUTE trials also challenged the concept of infarct-only treatment but incorporated fractional flow reserve (FFR) testing of non-culprit lesions in the subacute or acute setting of the complete revascularisation arm[3,4]. Again, both RCTs showed an early significant benefit in MACE of a complete revascularisation (FFR-guided) against a culprit-only strategy. This benefit remained intact and became even more significant at 27- and 36-month follow-up, respectively, for the DANAMI-3-PRIMULTI and COMPARE-ACUTE trials. The final verdict on the culprit-only strategy came from the mother of all multivessel STEMI trials, the COMPLETE trial[5]. This large RCT (4,041 patients) provided, for the first time, evidence on individual hard endpoints (cardiovascular death or new myocardial infarction) indicating that an early complete revascularisation strategy is significantly better compared to a culprit-only strategy.

If you think that this was the end of the discussion, then you are mistaken. Although the recent FIRE trial[6] also confirmed that (physiology-guided) complete revascularisation was significantly better on hard endpoints compared to the conservative culprit-only strategy in elderly acute myocardial infarction patients, the recent FULL REVASC results have shaken up the discussion again[7]. FULL REVASC was a large-scale (1,542 patients) RCT comparing an FFR-guided complete revascularisation strategy to a culprit-only strategy in a mix of STEMI and non-STEMI (NSTEMI) patients. It showed no benefit in the composite of all-cause death, myocardial infarction or unplanned revascularisation. The FULL REVASC trial has some issues. After 3 years, only 38% of the intended 4,052 patients were enrolled, and trial enrolment was stopped prematurely because of feasibility and ethical reasons after the COMPLETE trial publication. Even after changing the primary endpoint and extending the follow-up from 1 to 4.8 years, the study power remained below 80%. In addition, the trial

did not exclusively enrol STEMI patients, but also high-risk NSTEMI patients. This is different compared to the previously mentioned trials (except from FIRE) which exclusively enrolled STEMI patients, in whom the culprit lesion is much easier to identify and often has a different aetiology compared to NSTEMI lesions. Nevertheless, the FULL REVASC trial raises questions about the validity of an FFR-guided complete revascularisation strategy in acute myocardial infarction patients with multivessel disease as it did not show any signal of reducing hard endpoints such as death and myocardial infarction.

What should be done in case of inconsistent or insufficient evidence from different studies? Meta-analysis is one of the answers.

In this issue of EuroIntervention, Laudani et al report a very comprehensive and contemporary meta-analysis of the 14 major RCTs in the field of multivessel disease and acute myocardial infarction, in which they adopted the frequentist five-node analysis which combines both the timing and guidance of non-culprit lesion revascularisation[8]. Considering the multiple treatment strategies and the mixed results across studies investigating similar approaches, this paper holds significant clinical relevance. It helps to distil the optimal treatment strategy in this frequently occurring clinical scenario. By including all recent non-shock trials, and performing multiple sensitivity analyses, this network analysis paper is a thorough piece of work.

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Laudani and colleagues found that complete revascularisation, whether angiography- or physiology-guided, reduces recurrent myocardial infarction compared with culprit-only revascularisation strategy. This benefit was most prominent in an immediate complete revascularisation strategy. In our eyes, the latter remains a topic of discussion. By study design it is impossible to accurately detect periprocedural myocardial infarction in an immediate revascularisation strategy, and part of the benefit is caused by periprocedural myocardial infarctions in a staged complete revascularisation strategy. In any case, good clinical judgement remains the best advice on when to perform complete revascularisation in STEMI patients.

Is this the end of the discussion? No. Many questions remain, like what is the role of physiology compared to intravascular imaging or angiography guidance, and do we obtain the same strategy results in multivessel NSTEMI patients? In the absence of patient-level meta-analyses (unlike the network meta-analyses by Laudani et al), in order to better determine which patients or lesions might benefit from which strategy, we must eagerly await the results of the ongoing COMPLETE-2 trial – wire-based physiology- versus angiography-guided complete revascularisation (ClinicalTrials.gov: NCT05701358), FRAME-AMI2 – IVUS- versus FFR-guided complete revascularisation (NCT05812963), and COMPARE STEMI ONE – OCT- versus angiography-guided complete revascularisation (NCT05491200).

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## Conflict of interest statement

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