

# Moving forward from statistical to clinical considerations regarding complete revascularization

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**This commentary refers to 'Conclusions of complete revascularization meta-analysis are challenged by state-of-the-art methods' by A. Jobs et al., 2020;41:2223–2224.**

First of all, we would like to thank Jobs et al. for their constructive comment.<sup>1</sup> The benefit in terms of cardiovascular death related to complete revascularization in patients with ST-segment elevation myocardial infarction (STEMI) and multivessel disease (MVD) certainly deserves a deeper debate. Jobs et al. advocated the use of the Hartung–Knapp adjustment for random effect meta-analysis. Although this method may be of interest, some concerns are still present. As an example, its use has been largely accepted in meta-analysis of small studies,<sup>2</sup> usually resulting in wide confidence interval. Sincerely, we are not sure that this consideration can be applied to our meta-analysis considering the overall number of studies ( $n = 6$ ) and patients ( $n = 6528$ ). Jobs et al. also questioned the use of the random effect, as compared to the fixed one. Starting from the observation that the application of fixed effect does not change our findings, it should be noted that the Cochrane book suggests its selection in case of lack of heterogeneity.<sup>3</sup> It should be noted that the follow-up length, the sample size, the intervention (e.g. determination of the severity of the coronary artery disease) strongly differ between studies.<sup>4</sup> This may explain why a random model should be preferred. Regarding the weight of smaller randomized clinical trials (RCTs), this was widely discussed in the manuscript.<sup>4</sup> We have underlined in sensitivity analysis with the 'leave-one-out approach' that data about cardiovascular death were not confirmed after the removal of small studies.<sup>4</sup>

Therefore, in the specific subset of our meta-analysis, we do not believe that are present enough data to select a different statistical approach. We applied the best available method for study-level meta-analysis in agreement with previous worthy studies. Our data should be re-considered only in presence of individual patient-level meta-analysis or additional RCTs. Available RCTs on this topic are consistent and in the same direction. Complete revascularization reduces revascularizations and reinfarctions in relatively young STEMI patients with MVD at low anatomical complexity. This is associated, in the mid- and long-term follow-up, with a reduction of car-

diovascular death. As showed in the Figure of Jobs et al., independently from the applied test, hazard ratio is consistently in favour of complete revascularization (around 0.60). The real challenge for the scientific community is if this data can be translated to sicker and older patients seen in daily practice.<sup>5</sup> For example, the benefit of immediate multivessel revascularization has not been confirmed in the more complex subset of patients with myocardial infarction and cardiogenic shock.<sup>6</sup> In addition, we have several RCTs on STEMI patients with MVD, but few evidences regarding the optimal management of patients with MVD admitted for Type 1 no ST-segment elevation myocardial infarction (NSTEMI). The real gap in knowledge is to understand if complete revascularization reduces cardiovascular death in high-risk populations or NSTEMI patients. The management of myocardial infarction patients would benefit from the clarification of this unmet clinical need and the results of ongoing RCTs are eagerly awaited (NCT03772743, NCT03135275, and NCT03621501).

**Conflict of interest:** none declared.

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