FEATURED CORRESPONDENCE

Multivessel revascularisation in ST-elevation myocardial infarction: too early to change the guidelines

To the Editor: With great interest we have read the article by Politi *et al*[1] on revascularisation of patients with ST-elevation myocardial infarction and multivessel disease. The authors are to be complimented on the largest randomised trial on this subject, with the longest follow-up.

However, we question whether this study is the 'justification for complete revascularisation at the time of primary angioplasty', as the paper is labelled by the accompanying editorial. Apart from the considerable imbalance in patient numbers, which remains unexplained, there are several other major concerns.

First, there is no mention of routine non-invasive testing for ischaemia after discharge in the culprit-only revascularisation (COR) group, as is currently advocated by the guidelines.[2] It is thus not clear if the additional percutaneous coronary intervention procedures in the COR group were unexpected events or a result of planned non-invasive testing. All these events were considered major adverse cardiac events in the COR group, while planned revascularisations in the staged revascularisation (SR) group were not.

Second, testing for ischaemia is relevant because 40% of non-culprit lesions do not produce ischaemia, as we demonstrated in a recent randomised trial of fractional flow reserve-guided early (7.5 days) additional revascularisation compared with COR.[3] Also, we found that after 6 months death and myocardial infarction had occurred only in the early treatment group. This underlines that early additional treatment is probably not without risk, while benefit is not to be expected in a considerable number of patients.

Third, the importance of complete revascularisation is emphasised in the discussion, but it is not clear in how many patients of the complete revascularisation or SR group this was actually achieved. As more complex lesions are to be expected in a population with multivessel disease, in which for instance approximately 30% of the patients have a chronic total occlusion, this is a relevant question. It has been suggested that the presence of a chronic total occlusion is the only independent factor that determines the additional risk in patients with multivessel disease.[4]

For now, it seems that staged percutaneous coronary intervention of non-culprit lesions guided by ischaemia testing is still the most reasonable treatment strategy for patients with multivessel disease and ST-elevation myocardial infarction. We agree with the authors that more research is clearly needed to define the optimal treatment in these patients.

Jan-Henk Dambrink, Arnoud van 't Hof

Isala Klinieken, Department of Cardiology, Zwolle, The Netherlands

Correspondence to Dr Jan-Henk E Dambrink, Isala Klinieken, Groot Wezenland 20, 8011 JW Zwolle, The Netherlands; j.h.e.dambrink@isala.nl

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The Authors' reply: We thank Drs Dambrink and Van 't Hof[1] for their interest in our publication.[2] This study showed that in the setting of primary angioplasty, patients with multivessel coronary disease treated with complete revascularisation during the index or staged procedure have a reduced rate of long-term major adverse coronary events. In the accompanying editorial,[3] Drs Malik and Gerber appoint this study as the 'justification for complete revascularisation at the time of primary angioplasty'. Indeed, this is the largest randomised trial supporting the results of recent non-randomised or smaller studies that described more benefits with an aggressive rather than a conservative approach in patients with ST-elevation myocardial infarction (STEMI) and diffuse coronary disease.[4 5]

We are pleased to have the opportunity to clarify some issues that, due to word count restrictions, might not have been sufficiently detailed.

As stated in our paper, except the planned procedures in the staged revascularisation (SR) group, all additional percutaneous coronary interventions (PCI) were unexpected procedures driven by recurrent symptoms, re-infarction or evidence of significant ischaemia on provocative testing. Nevertheless, exercise testing was not routinely planned, but it was performed only in the case of dubious symptoms at the clinical examination. By study protocol, patients were all discharged on maximal anti-ischaemic therapy and followed by clinical periodical visits. Of note, current guidelines[6] do not advocate, rather simply judge 'appropriate', outpatient exercise testing (bicycle or treadmill) or stress imaging (using scintigraphy, echocardiography, or MRI) within 4–6 weeks of STEMI. Furthermore, the guidelines underscore that the 'relative advantages or disadvantages of these stress tests in a post-STEMI population are not well established'.

The authors quote their recent randomised trial[7] showing that 6 month death and myocardial infarction occurred only in patients with additional (fractional flow reserve-guided) treatment of non-culprit lesions. This result led them to conclude that the conservative strategy of treating the infarct related artery (IRA) only could avoid the complications arising from repeat procedures, but the majority of infarctions in the invasive group (6/11) occurred before fractional flow reserve and then are not a consequence of new PCI. In our population SR and complete revascularisation (CR) strategies were safer than culprit-only revascularisation, which showed a higher mortality, even if not significantly different. We explained this possible protective effect of complete PCI by an effect of stilling other potentially unstable plaques. Indeed, the inflammatory reaction arising during acute coronary syndromes and responsible for plaque instability is not limited to the culprit lesion, but involves the entire coronary tree.[8]

Both the SR and CR group received a complete revascularisation but at different times: in the CR group at the time of primary angioplasty, whereas in the SR group during the planned procedure (ie, after a mean of 57 days). We agree that chronic total occlusion (CTO) represents an independent additional risk factor in patients with multivessel disease. We examined our population and no patients had CTO, probably because subjects with concurrent STEMI and CTO often develop haemodynamic instability or shock, which were exclusion criteria of the study.

Our study shows that patients with STEMI and 70–99% diameter stenosis of non-culprit coronary arteries have a high-risk profile such that a conservative strategy may be unsafe, thus complete early or subacute revascularisation should be considered.

Finally, we agree with the authors that it may be too early to change the guidelines; however, our study represents the first stone for building new evidence for the treatment of STEMI in the setting of multivessel disease and encourages further research before changing the recommendations in this field.

Luigi Politi, Giuseppe Massimo Sangiorgi, Maria Grazia Modena

Cardiology Department, Policlinico Hospital, University of Modena and Reggio Emilia, Modena, Italy

Correspondence to Dr L Politi, Cardiology Department, Policlinico Hospital, via del Pozzo 71, 41100 Modena, Italy; luigi.politi@unimore.it

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Long-term dual antiplatelet therapy after percutaneous coronary intervention

To the Editor: The statistics of propensity adjustment which Harjai *et al*[1] have used with some modifications is a recognised tool to increase the value of non-experimental data.[2 3] However, these authors have used propensity statistics less efficiently than other studies in this area.[2 3] In fact, propensity statistics have only been introduced by Harjai *et al* in their multivariate regression analysis, but no 1:1 propensity matching has been made to identify two patient subgroups of identical size (derived from the cohorts who continued or discontinued the treatment, respectively) or to compare outcomes between these two matched pair subgroups.

No specific rules have yet been devised to determine the size of the cohorts to be included in propensity analyses. Nonetheless, since propensity studies have less quality of evidence than randomised studies, one can reasonably assume that the number of patients included in propensity studies should not be smaller than the number of patients one would include in a randomised study aimed at the same question.

In patients receiving percutaneous coronary intervention, the opportunity to continue clopidogrel at 6 or 12 months is presently a matter of debate. Using non-inferiority power calculations (power=0.80, α=0.05, event frequency around 10%, clinically meaningful RR reduction set at 20%), a total of at least 2500 patients (1250 per arm) would be needed to adequately power a randomised study. Event frequencies of <10% would give even larger sample sizes.

Two propensity analyses have recently addressed this issue.[1 4] The study by Harjai *et al*[1] analysed 835 patients treated with bare metal stents and 1024 treated with drug-eluting stents, while Shin *et al*[4] examined fewer patients (N=844) treated with drug eluting stents (with the advantage that a matched-pair analysis was tried). Both studies suggest that prolonging clopidogrel beyond 6 or 12 months confers no benefit. Although these findings have been interpreted in this way, it has not been observed that these studies were largely underpowered to adequately address this therapeutic problem. Hence, a large-scale randomised study is still needed in this area. Alternatively, a propensity score investigation could be useful provided that at least 3000 patients are included in the matched pair analysis.

Andrea Messori, Valeria Fadda, Sabrina Trippoli

Laboratory of Pharmacoeconomics, SIFO, Prato, Italy

Correspondence to Andrea Messori, Laboratory of Pharmacoeconomics, SIFO, via Guimaraes 7, 59100 Prato, Italy; labsifofe@gmail.com

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The Authors' reply: There are two different approaches to using the propensity score in statistical analyses. The first method, propensity score-adjusted multivariate analysis, involves the use of the propensity score as a covariate in the multivariable analysis. This is the method we used in our study. The second method, called propensity matching, entails the inclusion of only those subjects with similar propensity scores. Propensity matching limits the total number of patients that can be included in the analysis. We therefore chose to use propensity-adjusted multivariate analysis.[1]

We agree with Andrea Messori *et al*[2] that our study may not be adequately powered to evaluate small differences in outcomes between patient groups, and that large-scale randomised clinical studies are the best way to define the optimal duration of dual antiplatelet therapy.

Kishore J Harjai,[1] Judith Boura[2]

[1]Guthrie Clinic, Sayre, Pennsylvania, USA; [2]William Beaumont Hospital, Royal Oak, Michigan, USA

Correspondence to Kishore J Harjai, Director, Cardiac Catheterization Laboratories, Guthrie Health System, One Guthrie Square, Sayre, PA 18840, USA; harjai_kishore@guthrie.org

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Notes