arbitrary as correctly stated by Moreno et al., in their current letter, came from previous suggestions and analyses done by experts (as we stated in our methods section) and it was a predefined form of subgroup analysis to assess whether the main result was also maintained in the subgroups, or there were different trends, as previously explained. Indeed, we also performed other subgroup analyses, but they were all burdened by significant heterogeneity. Moreover, the references 4 and 5 used by Moreno et al. in their current letter refer to two studies performed in coronary vessels with a large range of vessel size and not only small ones, thus the cut-off of 35% after angioplasty as residual stenosis indicating suboptimal result may not correctly apply to small vessels. Finally, in our opinion, the intention-to-treat analysis (including cross-over from balloon angioplasty to stent, considered in each trial as bail-out and not provisional) was the best approach as we did not want to simply compare stenting with balloon, but we would like to understand why there were different results in trials with similar design and whether the possible benefit of routine stenting was real or could be balanced by a strategy of provisional stenting.

The real value of a meta-analysis relies on the correct selection of data and also on the right statistical methods used. The best approach to reconcile Moreno's and our work would be an individual patient data approach as we did not want to simply compare stenting with balloon, but we would like to understand why there were different results in trials with similar design and whether the possible benefit of routine stenting was real or could be balanced by a strategy of provisional stenting.

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Pierfrancesco Agostoni
Interventional Cardiology Unit
S. Raffaele Hospital
"Vita e Salute" University
University of Milan
Via Olgettina
60 20132 Milan, Italy
Tel.: +39-349-4303888
Fax: +39-(0)45-914727
E-mail address: agostonipf@genie.it

Giuseppe G.L. Biondi-Zoccai
Interventional Cardiology Unit
S. Raffaele Hospital
"Vita e Salute" University
University of Milan

Gabriele L. Gasparini
Department of Biomedical and Surgical Sciences
Section of Cardiology
University of Verona
Verona, Italy

Maurizio Anselmi
Department of Biomedical and Surgical Sciences
Section of Cardiology
University of Verona
Verona, Italy

Giorgio Morando
Department of Biomedical and Surgical Sciences
Section of Cardiology
University of Verona
Verona, Italy

Marco Turri
Department of Biomedical and Surgical Sciences
Section of Cardiology
University of Verona
Verona, Italy

Antonio Abbate
Department of Medicine
Virginia Commonwealth University
Medical College of Virginia Campus
Richmond
VA, USA

Eugene P. McFadden
Thoraxcenter
Erasmus MC
Rotterdam,
The Netherlands

Corrado Vassanelli
Department of Biomedical and Surgical Sciences
Section of Cardiology
University of Verona
Verona, Italy

Piero Zardini
Department of Biomedical and Surgical Sciences
Section of Cardiology
University of Verona
Verona, Italy

Antonio Colombo
Interventional Cardiology Unit
S. Raffaele Hospital
"Vita e Salute" University
University of Milan

Patrick W. Serruys
Thoraxcenter
Erasmus MC
Rotterdam,
The Netherlands

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Facilitation of primary PCI with ReoPro

With great interest, we read the paper by Győngyi et al. who describe the results of the ReoPro-BRIDGING trial. However, we feel that the study results should be interpreted with caution. The primary endpoint is the corrected TIMI frame count (CTFC) of the infarct related vessel (IRV) at initial angiography. However, the limitation of CTFC is that it can only be measured in patients with TIMI 2 flow or more, as the dye will not reach the distal landmark in patients with TIMI 0 or 1 flow. At initial angiography, 50-70% of patients will have TIMI 0 or 1 flow of the IRV, despite the pre-treatment with aspirin, heparin, and a glycoprotein 2b/3a blocker. Therefore, in the sample-size calculation, one should correct for the 50-70% of patients in whom the primary endpoint cannot be assessed.

We also have concern about the assumption that CTFC would be a median of 16.1 frames higher in the intervention group when compared with the control group, on the basis of the difference in CTFC in patients treated with thrombolytic therapy and in healthy controls. First of all, the median CTFC values in either the abciximab or the control group were much higher than the values of patients after thrombolytic therapy (39.1) or healthy controls (23). Secondly, by using the comparison of lytic treated patients vs. healthy controls, one assumes that after pre-treatment with abciximab, 100% of IRV's have normal restoration of flow. This is highly optimistic and far from daily life experience.
In addition, no referral is made to other randomized controlled trials with the same design and 2b/3a blocker used, which did not show a difference in the initial TIMI flow. In these studies, the rate of initial TIMI 3 flow in the control or placebo arm was considerably higher than the 7% found in the ReoPro-BRIDGING study. If only one patient in the placebo arm would have been scored as TIMI 3 flow, instead of TIMI 2 flow, the difference would no longer be statistically significant (P = 0.11).

Therefore, the results of the study should be interpreted with caution, as the study is underpowered to detect a difference in the primary endpoint, especially due to the fact that the primary endpoint could be assessed in <50% of the study population.

References

Facilitation of primary PCI with ReoPro: reply

The corrected TIMI frame count (CTFC) method has been prospectively validated as providing independent risk stratification above and beyond the conventional TIMI flow grades. In myocardial infarction studies including patients with an occluded infarct-related artery, a frame count of 100, a value that is the 99th percentile of that for patent vessels, is imputed to an occluded vessel. As recommended by Gibson et al., a CTFC of 100 was scored for TIMI grades 0–1 flow of the infarct-related artery in the ReoPro-BRIDGING study, similar to that seen in other studies, e.g. the SPEED, TIMI 4, 10A, 10B, and 14 trials. A sample-size calculation for only those patients having TIMI flow grade 2 or 3 in a STEMI study with primary percutaneous coronary intervention (pPCI), where a majority of the patients had occluded infarct-related artery at the time of the qualifying angiography, would have resulted in a serious bias.

The upstream therapy with abciximab prior to pPCI does not replace the thrombolytic therapy and pPCI; of course, the pPCI CTFC was higher in our study than thrombolysis studies. However, as we pointed out, no data concerning the CTFC values before and after abciximab treatment exist. Therefore, we used already published findings and our own data on the normal values and standard deviations, with the CTFC value as accepted difference between an infarct-related artery treated with thrombolysis and normal arteries. Thereby, we did not assume that abciximab therapy would result in 100% flow restoration.

Comparisons of randomized studies with a similar design have revealed similar initial TIMI flow 3 grades in the respective control groups, i.e. 2% in the study of Zorman et al., 7.9% in ERAMI trial, and 7% in ReoPro-BRIDGING study. The combined TIMI flow 2+3 (not given separately) was 48% in REOMOBILE and 33% in ReoPro-BRIDGING studies.

The TIMI flow scoring is limited by a relatively high interobserver variability and its categorical nature, as we pointed out in our study. If we recalculate the difference between the groups with regard to TIMI flow 3, also using the combined TIMI flow 2+3, as in other studies, the difference between the groups in ReoPro-BRIDGING study remains statistically significant, similar to that seen in the meta-analysis of Montalescot et al., but different from the On-TIME study, where the TIMI 3 flow was not different, whereas the combined TIMI 2+3 flow was different between the groups.

We are aware that our study was underpowered with regard to the clinical endpoint of the study, and that clinical conclusion based on surrogate parameters should be interpreted with caution. We are, however, sure that the primary endpoints of our study were assessed correctly, as cited earlier.

References