Response to letter regarding article, "Impact of pretreatment with clopidogrel on initial patency and outcome in patients treated with primary percutaneous coronary intervention for ST-segment elevation myocardial infarction: A systematic review"


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Response to Letter Regarding Article, “Impact of Pretreatment With Clopidogrel on Initial Patency and Outcome in Patients Treated With Primary Percutaneous Coronary Intervention for ST-Segment Elevation Myocardial Infarction: A Systematic Review

We thank Dr Ryding et al for their comments on our systematic review that investigated the impact of pretreatment with clopidogrel on initial coronary patency (Thrombolysis in Myocardial Infarction trial 2/3 flow) before primary percutaneous coronary intervention (PCI) for ST-elevation myocardial infarction.1

No published randomized trials on this subject exist, so we investigated the impact of clopidogrel pretreatment by comparing treatment groups in studies in which patients received pretreatment with clopidogrel with those in which patients did not. To eliminate as much potential biases from the beginning, we used rigorous inclusion and exclusion criteria with regard to study quality, patient selection, and detailed information on the use of premedication. As a result, except for clopidogrel, all patients were similarly pretreated with aspirin and heparin before undergoing initial angiography. Studies or subgroups were excluded when they reported optional pretreatment with clopidogrel, pretreatment with glycoprotein IIb/IIIa inhibitors, or fibrinolysis. Therefore, pretreatment with glycoprotein IIb/IIIa inhibitors cannot be a confounder on our primary end point, initial patency. In addition, we carried out secondary analyses to account for baseline differences between the treatment groups and to investigate the robustness of our findings. In these analyses (in which we adjusted for symptom duration and year of publication, for example), clopidogrel pretreatment remained consistently associated with higher rates of initial patency and improved clinical outcome.

However, as correctly observed by Dr Ryding et al and also mentioned in the Study Limitations section,1 we cannot rule out that the inclusion of studies with different trial designs, PCI strategies, and pharmacological therapies during and after PCI have induced heterogeneity in our (secondary) end points.

With regard to symptom onset to PCI time interval, we feel that Dr Ryding et al misinterpreted our data by summing up both the means and medians of the included studies to 1 weighted mean. This approach is incorrect because the variable shows no normal distribution. For example, the difference in symptom onset to PCI time interval observed by Dr Ryding et al directly disappears when we use the mean (4.1 hour) instead of the median (3.1 hour) symptom onset to PCI time interval for the Thrombus Aspiration during Percutaneous coronary intervention Study (TAPAS) trial.1

In conclusion, we believe that the results of our systematic review, together with previously published data on pretreatment with clopidogrel, support the administration of a loading dose of clopidogrel in patients as early as possible after electrocardiographic confirmation of ST-elevation myocardial infarction.

Disclosures

None.

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Reference


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