Author's response to reviews

Title: Meta-analysis of randomized controlled trials on the efficacy and safety of intracoronary administration of tirofiban for no-reflow phenomenon

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Version: 4 Date: 22 August 2013

Author's response to reviews: see over
Author's covering letter for initial submission

Title: Meta-analysis of randomized controlled trials on the efficacy and safety of intracoronary administration of tirofiban for no-reflow phenomenon

Authors:

Version: 1 Date: 20 August 2013

Comments: see over
Dear Editor,

Thank you very much for your email of August 5, 2013. According to the reviewers’ and editorial comments, we have revised the entire manuscript entitled: Meta-analysis of randomized controlled trials on the efficacy and safety of intracoronary administration of tirofiban for no-reflow phenomenon (MS: 1335507369941231). We acknowledge your suggestions and the two reviewers’ comments very much. Overall, the comments have been fair, encouraging and constructive, which are very valuable in improving the paper’s quality. We hope that the revised manuscript is acceptable for publication. If you have any question about this paper, please don’t hesitate to let us know.

Our detailed responses to the comments are as follow.

Response to reviewer 1 (Massimo Mancone):

Reviewer's report:
The study is methodologically well designed and well written. Moreover, The major limitations of the paper is the definition of no-reflow (NR). In fact, the authors define the NR as reduction of TIMI flow. Normally no-reflow is defined by a reduction of myocardial blush grade. In fact, NR occurs also in patient with a normal epicardial coronary artery flow (TIMI 3). Numerous authors (M. Gibson; G Stones; etc) demonstrated that a “brisk” epicardial flow (TIMI3) could be associated to a reduced
microvascular coronary perfusion (MBG 0-1) causing a NR. Moreover, Stones et al observed that patients, with same TIMI 3 but different MBG, present different incidence of MACE. The authors should discuss this major limitations in the discussion section. In particular focusing the attention on the correct definition of angiographic NR.

**The authors’ answer:** For the definition of NR in our paper, we referenced the Piana’s published in Circulation, 1994. With the development of technology and research, TIMI is not the golden standard for NR any longer. Several authors (Stone; van’t Hof; etc) had suggested that MBG was an important supplement of TIMI. We admit that MBG is superior to TIMI when assessing the reperfusion in high risk patients. And MBG should be prompted as an important supplement of TIMI during angiography. When designing the enrolled criteria and the search strategies, we had tried to use MBG. But unfortunately, there is only one eligible study providing the data of MBG in the comparison of trofiban versus verapamil. Therefore, when evaluating the efficacy of the treatment, we used TIMI to complete the analysis.

Above is our response to your comment. And we had added this part to the “Study limitation” section in the revised manuscript. We hope that you would satisfy our response. Thank you very much for the excellent and professional comment of our manuscript.
Response to reviewer 2 (Aniket Puri):

We are grateful for your careful reading of our manuscript and the valuable suggestions. And we have carefully considered the comments and revised the manuscript accordingly. Our responses to the comments are listed as follow:

Comments:

1) what was the dose of tirofiban used? it needs to be clarified as it is my understanding that at a higher concentration Tirofiban works better (ADVANCE trial), however at that concentration the volume used is very large at it is a challenge to infuse so much in the coronary directly.

The authors’ answer: The ADVANCE trial is a meaningful study which propose high-dose bolus tirofiban (25µg/kg) could significantly reduce the incidence of ischemic/thrombotic complications during high-risk PCI. In our study, the detailed IC administration of tirofiban has been presented in the modified Table 1 (Study design of the included randomized controlled trials). Nearly all the eligible studies administrated tirofiban with the dosage of 10µg/kg. We could just analyze the efficacy and safety of tirofiban with that dosage. We also hope to find out the optimal dosage of tirofiban for NR, that would be a great help in the clinical practice. But the aim of our study was mainly focus on the comparison of tirofiban versus conventional drugs. The effect of different dosages of tirofiban for the treatment was not involved.

2) most of the figure/tables don't have legends?
The authors’ answer: we have added the legends of figures/table accordingly.

3) minor grammatical errors throughout the text eg. page 4 line 2. "only enrolled the patients occurred NRP during PCI". kindly read text once again for grammatical errors.

The authors’ answer: the sentence has been changed to “the patients with NR during PCI were enrolled” and we have also corrected some other expression errors.

4) Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

The authors’ answer: we have carefully rechecked our data and modified the table so that they could explain more accurately and clearly.

Editorial comments:

1) Competing interests - Please include a 'Competing interests' section between the Conclusions and Authors' contributions.

The authors’ Answer: The 'Competing interests' section has been added to the revised manuscript accordingly.

2) Authors' contributions - Please include an 'Authors' contributions' section before the Acknowledgements and Reference list.

The authors’ Answer: The 'Authors' contributions' section has been added to the revised manuscript accordingly.
Once again, we would like to thank the editors and the two reviewers (Massimo Mancone and Aniket Puri) for their helpful suggestions.

Sincerely yours,

Meng-Hua Chen

2013.8.20