Reviewer’s report

Title: The Favorable Kinetics and Balance of Nebivolol-Stimulated Nitric Oxide and Peroxynitrite Release in Human Endothelial Cells

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Reviewer: chieko mineo

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In the manuscript entitled “The Favorable Kinetics and Balance of Nebivolol-Stimulated Nitric Oxide and Peroxynitrite Release in Human Endothelial Cells”, Mason et al. reported that Nebivolol stimulates NO and ONOO- production from cultured human umbilical vein endothelial cells (HUVEC) at a slower rate than other agonists for #3 receptor or P2Y receptor. Combining an amperometric biosensor to measure NO/ONOO- and a pharmacological approach, the authors demonstrated that Nebivolol stimulates NO/ONOO- through dual pathway (ATP efflux and interaction with #3 receptor). They conclude that the slower kinetics exerted by Nebivolol contributes to its cardioprotective effects through prevention of eNOS uncoupling.

The experiments were well-designed, the results were clearly presented, and the interpretations were appropriate. The conclusions were supported by the data.

The limitation of the work is the use of only one source of endothelial cells: HUVEC. The endothelial cells from more relevant vascular beds are available commercially, and the confirmatory experiments using these cells would have strengthened the conclusion.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests.