Title: Effects of inosine on reperfusion injury after cardiopulmonary bypass

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Author's response to reviews: see over
Dear Mr Vipin Zamvar,

with reference to Your decision letter on our manuscript (MS: 5509817313567818, titled: “Effects of inosine on reperfusion injury after cardiopulmonary bypass”), we would like to thank You and the Reviewers for the critical and constructive review, and for offering us an evaluation of a revised manuscript. We understand that all reviewers and the Editor-in-Chief found our work potentially interesting. We also understand that a number of issues were raised, and additional work was required for a responsible revision. We are confident that these issues can be resolved by a careful revision. Thus, we have prepared a thoroughly and carefully revised version of the manuscript, which include additional, revised data, as well as alterations, as suggested by the reviewers.

Hereinafter please find our point-by-point response to the concerns of the reviewers, enclosed we send You the new, revised version of our manuscript for new evaluation and publication in the Journal of Cardiothoracic Surgery.

Hereby I declare that the manuscript, or part of it, neither has been published nor is currently under consideration for publication by any other journal.

All of the co-authors have read the manuscript and approved its submission to the Journal of Cardiothoracic Surgery.

We would be very glad to get Your kind support in publishing our manuscript.

Yours sincerely:

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Response to the Reviewers

We would like to thank the Editor-in-Chief and the two reviewers for the careful evaluation of our manuscript titled “Effects of inosine on reperfusion injury after cardiopulmonary bypass”. We understand that all reviewers and the Editor-in-Chief found our work potentially interesting. We also understand that a minor revision is necessary. Thus, we have prepared a revised version of the manuscript, which include additional, revised data, as well as alterations, as suggested by the reviewers.

Reviewer 1
We would like to express our thanks to Reviewer 1 (C. Szabo) for the careful evaluation of the manuscript and the helpful and constructive suggestions.

Minor point:

1.) “The only part of the manuscript that needs improvement is the Discussion section. How, then, is inosine exerting its beneficial effects? While PARP inhibition may be one of the possibilities, others may also be plausible. For instance, as discussed in Hasko et al, TIPS 25: 152, and references therein, anti-inflammatory effects of insulin have been reported. Is it possible that inosine may work, in part, as an anti-inflammatory agent. It has also been reported (most recently by Modis et al, Br J Pharmacol, 158: 1565, and previous references therein, that under hypoxia and ischemia, inosine may be converted back to ATP and may serve as a source of energy generation and survival. These possibilities and articles, as well as several other relevant ones, should be mentioned in a revised manuscript.”

We agree with Reviewer 1 (C. Szabo) comment, the Discussion section needs to be improved. We added new information and beneficial effects of the inosine into the Discussion part of our manuscript (see page 10, line 5-7 and page 11 line 23-25, page 12 line 1-5).

Reviewer 2

Minor comments:

Comments:

Introduction and background:
Myocardial protection is an all time favourite of cardiac research. Inosine may be a new player by exerting inotropic, vasodilatory and anti-inflammatory effects.

MM:

Correct model, proper planning and analysis

Results: As expected, favourable results in contractility and endothelial function

Discussion: provides all necessary information

Congratulations to your work!

We gratefully thank you your review on our article. We would like to thank you your support to publish our article in Journal of Cardiothoracic Surgery.