Author’s response to reviews

Title: Fluid upstream shear stress of rabbit aortic stenosis inhibits neointimal hyperplasia by promoting endothelization after balloon injury

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Author’s response to reviews:

Dear Editor:

We thank the reviewers for the valuable comments on our manuscript entitled “Fluid upstream shear stress of rabbit aortic stenosis inhibits neointimal hyperplasia by promoting endothelization after balloon injury

Running title: Shear stress weakens neointimal hyperplasia ”.

We revised the manuscript accordingly (marked red) and below are our point-to-point responses to Reviewers.

Thanks for consideration.

Gaoxing Zhang and co-authors
Responses to Reviewer comment:

1. It has come to our attention that throughout the manuscript there is significant text overlap with other publications. While we understand that you may wish to express some of the same ideas contained in these publications, please be aware that we cannot condone the use of text from previously published work. We would therefore be grateful if you could provide a justification for the overlap in text between your manuscript and other sources. Please be informed that we cannot proceed with handling your manuscript before this issue is resolved, and the sections of text in question have been reformulated. The report has been attached to further help your revisions.

Please note that the software used to detect overlaps is imperfect and highlights two or more consecutive matching words, therefore, please just focus on those whole sentences/paragraphs highlighted. If this study uses methodology from a previously published work, please provide a summarizing statement in the methodology together with a citation to the original paper.

Response: Done. We carefully revised all related texts overlap with other publications, especially in background part and discussion part. Texts about methodology were added with appropriated reference.

2. Please clarify where the animals were sourced from and if permissions were required for their use in this study.

Response: Done. Please see the Methods section, line 20, page 5: 40 New Zealand white rabbits were purchased from cavenstech company (Changzhou, China, permission code for experimental animals: SCXK2016-0010).

3. Please add a “Conclusions” section after the “Discussion” section. This should state clearly the main conclusions of the research article and give a clear explanation of their importance and relevance.

Response: Done. Please see the Conclusion section, line 13, page 15: Appropriate low unidirectional SS is beneficial for the inhibition of intimal hyperplasia after balloon angioplasty, and it is a potential management target of in-stent stenosis.

4. Please amend the Consent to publish statement, this refers to patient consent, not authors. As this is not applicable in this study, please write "Not applicable".
Response: Consent to publish statement was amended. Please see the Consent to publish section, line 7, page 16: Not applicable.

5. Please represent authors' names using their full initials, not their full name, in the Authors’ Contributions section. If there are any duplicated initials, please differentiate them to make it clear that the initials refer to separate authors.

Response: Done. All authors are represent with their full initials. Please see Authors' Contributions section, line 12, page 16:

JX Liu: Study concepts, Study design

YC Peng: Study concepts, Study design

JX Lai: Literature research, Clinical studies, Experimental studies

WD Gao: Data acquisition, Data analysis, Statistical analysis

AJ Song: Data acquisition, Data analysis, Statistical analysis

GX Zhang: Clinical studies, Experimental studies, Guarantor of integrity of the entire study

All authors have read and understand manuscript; all authors approved the content of the study in manuscript to be published.

6. Please include a statement in the Authors' contributions section to the effect that all authors have read and approved the manuscript, and ensure that this is the case.

Response: Done. We wrote a statement of approval from all authors, and are ensure that this is the case. Please see Authors' Contributions section, line 12, page 16:

JX Liu: Study concepts, Study design

YC Peng: Study concepts, Study design

JX Lai: Literature research, Clinical studies, Experimental studies

WD Gao: Data acquisition, Data analysis, Statistical analysis

AJ Song: Data acquisition, Data analysis, Statistical analysis

GX Zhang: Clinical studies, Experimental studies, Guarantor of integrity of the entire study
All authors have read and understand manuscript; all authors approved the content of the study in manuscript to be published.

7. The Availability of data and materials section refers to the raw data used in your study and presenting tables and figures is not sufficient to state that all data is contained within the manuscript and additional files. Please only use this statement if you have indeed provided all raw data on which your study is based. We strongly encourage all authors to share their raw data, either by providing it in a supplementary file or depositing it in a public repository and providing the details on how to access it in this section. If you do not wish to share your data, please clearly state this in this section along with a justification. Data availability statements can take one of the following forms (or a combination of more than one if required for multiple datasets)

Response: Availability of data and materials section was amended as one of recommend forms. Please see Availability of data and materials section, line 9, page 16, The datasets used and/or analysed during the current study available from the corresponding author on reasonable request

8. Please provide figure legends for Figures 9 and 10 in the Figure Legends section.

Response: There are 9 figures in our manuscript, and we added figure legends for Figures 8 and

9. Please see figure legend part, line 5, page 22: Fig.8 Effects of vascular stenosis and balloon injury on re-endothelialization in the downstream of the constricted abdominal aorta in each group(200×). Immunohistochemical staining for CD31 was performed and the ratio of re-endothelialization was evaluated. Typical observations of endothelial cells stained by anti-CD31 antibodies in the upper panel and the re-endothelialization ratio quantified in the lower panel. **P<0.05 significantly different from the groupⅢD; **P<0.05 significantly different from the groupⅣD.D=downstream.

Fig. 9 Schematics of the proposed mechanisms for disturbed blood flow in both upstream and downstream

9. At this stage, please upload your manuscript as a single, final, clean version that does not contain any tracked changes, comments, highlights, strikethroughs or text in different colours. All relevant tables/figures/additional files should also be clean versions. Figures (and additional files) should remain uploaded as separate files.

Response: We revised our manuscript as a single, final, clean version.