Oct. 26, 2021

Dr. Lian-Sheng Ma Editorial Office Director, Company Editor-in-Chief, Editorial Office World Journal of Clinical Cases

Dear Dr. Lian-Sheng Ma

Thank you for your revision letter of "World Journal of Clinical Cases Manuscript NO: 71301 – Notification on manuscript revision", in which you encouraged us to revise our manuscript entitled "Atrial fibrillation burden and the risk of stroke: systematic review and dose-response meta-analyses".

Please find attached the revised version with highlighted changes of our manuscript and our response, point by point, to the reviewers' comments.

We would like to thank the editors and the reviewers for their comments and recommendations that have greatly improved the quality of this paper. We hope our responses are satisfactory.

> Sincerely, Lina Wang

1.Responds to reviewer's comments:

Reviewer 1

Comment 1: An interesting review for a common problem with an increasing prevalence. However, as long as there was a liner dose-response between increasing AF burden and risk of future stroke, how the decision was made that the 5 minutes limit can be considered a threshold?

Response: Thanks! As most original studies concerned, AF burden more than 5 minutes was a common risk factor associated with the future progression in clinical practice, and it was still in controversial that AF burden would increase the risk of future stoke. Italian AT 500 Registry study showed patients with the AF episodes more than 5 min had no significant risk of stroke (*J Am Coll Cardiol* 2005; **46**: 1913-1920). However, ASSERT Clinical Trials study reported episodes lasting more than 5 minutes were associated with an increased risk of ischemic stroke or systemic embolism (*N Engl J Med* 2012; **366**: 120-129). And also, some other clinical researches were considered the 5 minutes limit as the AF burden threshold for the stroke risks. So in this systematic review, we conducted a systematic review and meta-analysis on the AF burden with 5 minutes limit threshold and stroke risks.

Reviewer 2

Comment 1: There are some scientifically/ grammatically errors in the paper. Please control the text in that manner.

Response: Thanks for your correction. We have asked for the native English speaker Mr. Satyajit Kundu to polish and revise the M.S. and expressed our thanks in the text.

Comment 2: The "abstract" should be modified and written more scientifically. The "aim" part should be modified. Also, please mention atrial fibrillation (AF) in "aim". **Response:** Thanks for suggestion. We have already modified the abstract.

Comment 3: The paper needs proper punctuation and should be written scientifically. **Response:** Thanks for your correction. We have invited the native English speaker Mr. Satyajit Kundu to polish and revise the M.S. and expressed our thanks in the text.

Comment 4: The keywords should be modified (Keywords: Atrial fibrillation, Stroke, Dose-response, Meta-analysis).

Response: Thanks for your correction. We have modified the keywords as you suggested.

Comment 5: The figures shown are not at high resolution. Also the figures 1, 2, 3, 5, and 6 are unclear and are not acceptable.

Response: Thanks! We had uploaded the original figure documents separately, which were edited in the PowerPoint file as the reviewer suggested.

Reviewer 3

Comment 1: The authors performed an excellent PRISMA review and MA to determine whether atrial fibrillation burden > 5min was associated with the increased stroke risk and explore a dose response effect of AF burden on the risk of stroke. The authors found that atrial fibrillation burden > 5min is associated with the increased risk of clinical atrial fibrillation (adjusted RR=4.18, 95%CI: 2.26-7.74), but was not associated with the increased risk of all-cause mortality (adjusted RR=1.55, 95%CI:0.87-2.75). In my opinion, the work has a remarkable value in cardiology. **Response:** Thanks for your constructive comments.

2 LANGUAGE POLISHING REQUIREMENTS FOR REVISED MANUSCRIPTS SUBMITTED BY AUTHORS WHO ARE NON-NATIVE SPEAKERS OF ENGLISH

Response: Thanks for your correction. We have invited the native English speaker Mr. Satyajit Kundu to polish and revise the M.S. and expressed our thanks in the text.

3 ABBREVIATIONS

Response: We have corrected our abbreviations according to the basic rules you suggested.

4 EDITORIAL OFFICE'S COMMENTS

(1) Science editor:

Comment 1: The "Author Contributions" section is missing. Please provide the author contributions

Response: We have provided the author contributions on the first page of M.S. (Page 1).

Comment 2: The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor;

Response: We have provided original pictures in "original figure"file. And also, we edited the final version of figures in PowerPoint. Please find the figures in the files.

Comment 3: PMID and DOI numbers are missing in the reference list. Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references. Please revise throughout;

Response: Thanks! We have revised the references throughout according to the "Format for References Guidelines".

Comment 4: The "Article Highlights" section is missing. Please add the "Article Highlights" section at the end of the main text.

Response: Thanks! We have added the "Article Highlights" section at the end of the main text (Page 17).

Comment 5: It is unacceptable to have more than 3 references from the same journal. To resolve this issue and move forward in the peer-review/publication process, the authors must revise the

reference list accordingly.

Response: Thanks! We have revised the reference list accordingly.

2)(1, 2) Company editor-in-chief:

Comment 1: Before final acceptance, uniform presentation should be used for figures showing the same or similar contents; for example, "Figure 1Pathological changes of atrophic gastritis after treatment. A: ...; B: ...; C: ...; D: ...; E: ...; G: ...". Please provide decomposable Figures (in which all components are movable and editable), organize them into a single PowerPoint file. Please authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content.

Response: Thanks! We have modified and uploaded our figures and tables as you requested. Please find the attachments of the revision.