

Dear editors:

Thank you for your letter and for the reviewers' comments concerning our manuscript entitled " Clinical relevance of atrial septum aneurysm and patent foramen ovale with migraine: Findings from a single-center case-controlled study " (ID: 41016). Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have studied comments carefully and have made correction which we hope meet with approval. Revised portion are marked in red in the paper. The main corrections in the paper and the responds to the reviewer's comments are as flowing:

Reviewer #1 (Reviewer's code: 03652653):

1. Comment 1: Abstract, the results: the sentence starting with "After PFO closure..." is misleading since there were no differences in score between groups before or after procedure. This should be correctly stated in results and conclusion

Response: We completely agree with this valuable suggestion by the reviewer.. We have modified the manuscript accordingly in red in the results section.

2. Comment 2: Introduction, last sentence: "strength of association" was not tested in the present study. Thus, a different wording such as simply "the association of..." might be more appropriate.

Response: We are very sorry for our incorrect writing and thank you for your suggestion on this mistake of our manuscript. We have modified the manuscript accordingly.

3. Comment 3: Page number would be helpful

Response: We have already marked the page number at the bottom of the page in order.

4. Comment 4: The discussion appears a bit too long and should be more focused. It would be also important to state that presence/absence of an atrial septum aneurysm was associated with differences in baseline characteristics but not with differences in severity of migraine as demonstrated by the similar score results.

Response: Thank you for your suggestion, we have modified the manuscript accordingly in red in the research conclusions section.

Reviewer #2 (Reviewer's code: 03702209):

1. Comment 1: TITLE: replace atrial septum aneurysm with atrial septal aneurysm for uniformity of terminology; **2:** Page 2 line 10 replace with the condition with “on the condition”; **3:** Page 4 line 8 delete one of the ins; **4:** Page 5 line 2 at risk instead of a risk; **5:** Page 5 line 8 leave a gap between 450 and patients; **6:** Page 6 delete the phrase “all patients received antibiotics....”); **7:** Page 6 line 18 replace surgeon by interventional cardiologist; **8:** Page 7 line 5 delete the

phrase single-dose antibiotics...was administered intravenously to prevent infective endocarditis and...; 9: Page 7 line 18 delete with; 10: Page 7 line 19 add ...made by phone calls; 11: Page 9 line 7 replace include in by included; 12: Page 10 line 11 replace normal by normal; 14. Page 12 replace migraine by migraine

Response: Thank you for your detailed advice on a number of linguistic errors or spelling mistakes. We have modified the manuscript accordingly in red.

2. Comment 13: Page 11 first paragraph: in addition...is the proposed mechanism a speculation of the authors or is an appropriate reference to explain the findings necessary

Response: The paragraph "In addition, the presence of an ASA can change the direction of blood flow, allowing the blood flow of the inferior vena cava into the PFO and promoting a RLS, thus resulting in cerebral ischemic events", is not our reasoning or assumptions.

This paragraph is quoted from an article in the 1994 Stroke magazine ([Hanna JP, Sun JP, Furlan AJ, Stewart WJ, Sila CA, Tan M. Patent foramen ovale and brain infarct. Echocardiographic predictors, recurrence, and prevention. Stroke 1994; 25: 782-786 \[PMID: 8160221 DOI: 10.1161/01.STR.25.4.782\]](#)), which we have already cited it in the references. Accordingly, the subsequent references code has also changed.

Reviewer #3 (Reviewer's code: 03639986):

1. Comment 1: The title should be Patent foramen ovale combined with atrial septal aneurysm is associated with migraine: a single-center study

Response: Thank you for your kindly suggestion. We have already changed the title to "Clinical relevance of atrial septal aneurysm and patent foramen ovale with migraine".

2. Comment 2: Grammatical errors need to be corrected.

Response: Like your suggestion, Reviewer 2 also offers a lot of grammatical advice, and we've done our best to correct the most of it. In addition, because our native language is not English, in order to make the article more fluid and meet the English requirements, we also polished this article by AJE.

We tried our best to improve the manuscript and made some changes in the manuscript. These changes will not influence the content and framework of the paper. And here we did not list the changes but marked in red in revised paper. We appreciate for Editors/Reviewers' warm work earnestly, and hope that the correction will meet with approval. Once again, thank you very much for your comments and suggestions.

Thank you and best regards.

Yours sincerely,

Lu He