

Please find below our responses in blue to the comments by the reviewers.

Reviewer #1:

Scientific Quality: Grade A (Excellent)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: the problem of vascular complications after TAVR is an important one this meta analysis , mainly using retrospective data, is important as it shows clearly the advantage of the radial approach for the secondary access

Dear reviewer, thank you for your comments. We agree that vascular complications are important in this study. We reported the odds ratio for vascular complications in the All Primary Access (APA) group, but we did not perform a subgroup analysis to report the odds ratio for vascular complication in the Trans-Femoral Primary Access (TFPA) group because only 3 out of 5 studies had reported their findings on this specific outcome in this subgroup. We had decided early on to run analyses only if at least 4 studies reported on an outcome to improve confidence in our results. We are happy to run the analysis on the 3 studies alone, however this may undermine the strength of this statistic. Please advise.

Reviewer #2:

Scientific Quality: Grade D (Fair)

Language Quality: Grade A (Priority publishing)

Conclusion: Major revision

Specific Comments to Authors: Dear author has cited 4 kinds of vascular complications like stroke ,bleeding ,vascular complications and all cause mortality and the author has stated that transradial access as a secondary access is safer .However ,the author has significantly failed to establish how the transradial access has influenced the so significantly .I feel there are many other variables which have influenced the outcome has been ignored by the author like for one examples :EURO score ,the anatomy of the primary access sites and other comorbidities .Please define and specify the bleeding and vascular complications and provide objective details

Dear reviewer, thank you for your comments. Please find the individual comments addressed below.

1) **How has the TR access influenced the outcomes significantly?** We address this question in the third paragraph of the "Discussion" section. However, we realize that our explanation may not stand out as well as it could, hence we have slightly altered the prose to address your question more clearly and conspicuously. We hope our revised response satisfies your question.

2) **What about other variables which could have influenced the outcome:** In the second paragraph under "Study Characteristics", we mention that risk-adjustment was reported in 3 out of 5 studies. For example, one of the studies (Fernandez-Lopez) adjusted for EuroScore, BMI, NYHA functional class etc. Unfortunately not all studies reported on their adjustment strategies. The lack of uniform risk-adjusted data is certainly a limitation to our study, which we have highlighted in our limitation section.

3) Define and specify bleeding and vascular complications and provide objective details.

The definitions of bleeding and vascular complications are according to the VARC-2 criteria in 4 out of 5 studies and according to VARC criteria in 1 out of 5 studies, as mentioned under the study characteristics and in Tables 1. We felt that elaborating the definitions of the VARC and VARC-2 criteria is beyond the scope of this article.

Reviewer #3:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: Thank you for opportunity for reviewing this paper "Transradial versus transfemoral secondary access outcomes in TAVI - A systematic review and meta-analysis". This article is interesting, but some issues should be explained more.

Dear reviewer, thank you for your comments. Please find our responses to your individual comments in blue below.

1. Who are the independent investigators? The first author (SLR) and a second investigator (FD) who is credited in the "Acknowledgement" section conducted the literature search.

2. It will be better to show kappa for the selection and data extraction. Please show the data of kappa of agreement during the systematic searches. How disagreements were solved during the systematic search among two independent reviewers? Given that there are not very many studies published on this topic, the decision to include or exclude studies was relatively simple. There was uniform agreement between both investigators on what studies to include or exclude. In this scenario, the kappa correlation would be 1. We have now added a clause reporting this in the manuscript.

3. Please add previous systematic reviews and what are their limitations and what was your rationale of doing this meta-analysis in the introduction section. We did find one meta-analysis by Jhand et al. previously published on the same topic, we repeated the analysis with 5 studies instead of 6 like they did, as we did not agree with their inclusion of one of the studies. We have now added this clause in the introduction section.

4. In addition to the Newcastle Ottawa Scale, which is a validated tool and was an acceptable choice. However, to enhance the reproducibility and comparability of this review to future reviews of a similar topic (possibly an update of this review) I also recommend including a risk of bias assessment using ROBINS-I, since it is the newest and most robust method of assessing risk of bias in systematic reviews/meta-analyses. Thank you for this recommendation. We will incorporate the ROBINS-I tool as recommended.

5. What are your primary and secondary outcomes? The 4 main outcomes highlighted in this study are all primary outcomes. No secondary outcomes were looked into.

6. The GRADE tool is suggested. Thank you for your suggestion. We will certainly keep in mind to use it in future projects.

7. Discussion should include what your review updates the previous evidence. If the above suggestions are incorporated and the paper is thoroughly edited, it will be a strong contribution to the literature. We have added a clause to fortify this in our discussion section.

5 EDITORIAL OFFICE'S COMMENTS

Authors must revise the manuscript according to the Editorial Office's comments and suggestions, which are listed below:

(1) *Science editor:*

1 Scientific quality: The manuscript describes a meta-analysis of the TF versus TR secondary access TAVI outcomes. The topic is within the scope of the WJC.

(1) Classification: Grade A, Grade C and Grade D;

(2) Summary of the Peer-Review Report: The problem of vascular complications after TAVR is an important one this meta-analysis, mainly using retrospective data, is important as it shows clearly the advantage of the radial approach for the secondary access. Discussion should include what your review updates the previous evidence. The questions raised by the reviewers should be answered; and

(3) Format: There are 2 tables and 4 figures. A total of 13 references are cited, including 8 references published in the last 3 years. There are no self-citations.

2 Language evaluation: Classification: Grade A, Grade A and Grade B.

3 Academic norms and rules: The authors provided the Biostatistics Review Certificate and PRISMA 2009 Checklist. The authors need to provide the signed Conflict-of-Interest Disclosure Form and Copyright License Agreement. No academic misconduct was found in the CrossCheck detection and Bing search.

4 Supplementary comments: This is an unsolicited manuscript. The topic has not previously been published in the WJC. The corresponding author has not published articles in the BPG.

5 Issues raised:

(1) I found no "Author contribution" section. Please provide the author contributions; This has been added.

(2) I found the authors did not provide the original figures. 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; Please find a power point file attached with the figures used in this study.

(3) I found the authors did not add the PMID and DOI 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. The references have been formatted to meet your specifications.

(4) I found the authors did not write the "article highlight" section. Please write the "article highlights" section at the end of the main text. We have added an article highlight section as requested.

6 Re-Review: Required.

7 Recommendation: Conditionally accepted.

(2) *Editorial office director:* I have checked the comments written by the science editor.

(3) *Company editor-in-chief:* I have reviewed the Peer-Review Report and the full text of the manuscript, all of which have met the basic publishing requirements, and the manuscript is conditionally accepted with major revisions. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report and the Criteria for Manuscript Revision by Authors. Before final acceptance, authors need to correct the issues raised by the editor to meet the publishing requirements. Re-Review: Required by reviewer 03722832.