



April 21st, 2016

Scientific editor: Shui Qiu

Re: Manuscript NO 25700 entitled "Association of blood transfusion with acute kidney injury after transcatheter aortic valve replacement: A systematic review and meta-analysis"

Dear Prof. Qiu,

Thank you for the thoughtful input and review of our manuscript. The reviewer's input is extremely helpful. We believe as a result of this review, our study would have more value for your readers. We revised the manuscript based on the reviewer's suggestions. We have attached our point by point response.

Thank you for your time and consideration. We look forward to hearing from you.

With many thanks for your attention, we remain

Sincerely yours,

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Response to Science Editor, Editorial Office

Comment 1:

Please offer the audio core tip, the requirement are as follows:

In order to attract readers to read your full-text article, we request that the first author make an audio file describing your final core tip. This audio file will be published online, along with your article. Please submit audio files according to the following specifications:

Acceptable file formats: .mp3

Maximum file size: 10 MB

To achieve the best quality, when saving audio files as an mp3, use a setting of 256 kbps or higher for stereo or 128 kbps or higher for mono. Sampling rate should be either 44.1 kHz or 48 kHz. Bit rate should be either 16 or 24 bit. To avoid audible clipping noise, please make sure that audio levels do not exceed 0 dBFS.

Response: We thank you for reviewing our manuscript. We have now provided the audio core tip as your suggestion.

Comment 2:

Please reformat all the reference numbers like this. Please check throughout. Thank you! The Authors should put the number of the references in Arabic numerals according to the citation order in the text. Put reference numbers in square brackets in superscript at the end of citation content or after the cited author's name. For citation content which is part of the narration, the coding number and square brackets should be typeset normally. For example, "Crohn's disease (CD) is associated with increased intestinal permeability^[1,2]."

The reference number is in front of the full stop, check all the text!

Response: We agreed and revised our reference throughout the manuscript as the instructions.

Comment 3:

Please provide "Comments"

Background

Research frontiers

Innovations and breakthroughs

Applications

Terminology

Peer-review

Please write the comments. Writing requirement see the file named "Format of Original Articles"

Response: We agreed and have provided Comments as the following in the manuscript.

"Background

Transcatheter aortic valve replacement (TAVR) is an exciting new approach to the treatment of high-risk or inoperable patients with severe aortic stenosis. Despite advances in TAVR procedures, acute kidney injury (AKI) is one of the most frequent complications of TAVR, associated with significant morbidity and mortality following the procedures.

Research frontiers

The association of AKI with RBC transfusion after TAVR is conflicting in the findings of previous literature. It is thus necessary to assess the impact of periprocedural RBC transfusion on the risk of AKI after TAVR.

Innovations and breakthroughs

In this study, we verified a significant association between peri-procedural RBC transfusion and AKI after a TAVR with an overall 1.95-fold increased risk of AKI compared to those who did not receive transfusion.

Applications

The data in this study highlights the importance of vigilance when considering transfusions and should impact the clinical management of the high-risk group of patients undergoing TAVR.

Terminology

AKI, acute kidney injury; CHF, Congestive Heart Failure; CKD, chronic kidney disease; COPD, Chronic Obstructive Pulmonary Disease; DM, diabetes mellitus; eGFR, estimated GFR; HTN, Hypertension; LVEF, left ventricular ejection fraction; MI, Myocardial Infarction; PHTN, Pulmonary Hypertension; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; PVD, Peripheral Vascular Disease; RIFLE, Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease; SCr, serum creatinine; STS, Society of Thoracic Surgeons; TA, Transapical Approach; TAVR, transcatheter aortic valve replacement; VARC, Valve Academic Research Consortium; VC, Vascular Complication.

Peer-review

This is a reasonable first meta-analysis of association of blood transfusion with acute kidney injury after transcatheter aortic valve replacement. The results have potential clinical applications.”

Comment 4:

Please add PubMed citation numbers and DOI citation to the reference list and list all authors. Please provide PubMed citation numbers for the reference list, e.g. PMID and DOI, which can be found at <http://www.ncbi.nlm.nih.gov/sites/entrez?db=pubmed> and <http://www.crossref.org/SimpleTextQuery/>, respectively. The numbers will be used in the E-version of this journal. Thanks very much for your co-operation.

Such as: 1 Nayak S, Rath S, Kar BR. Mucous membrane graft for cicatricial ectropion in lamellar ichthyosis: an approach revisited. Ophthal Plast Reconstr Surg 2011: e155-e156 [PMID: 21346670 DOI: 10.1097/IOP.0b013e3182082f4e]

Response: We agreed and revised references according to your suggestion.

Response to Reviewer#1

Reviewer's code: 03546531

Reviewer's country: 0

Science editor: Shui Qiu

Date sent for review: 2016-03-22 15:20

Date reviewed: 2016-03-23 20:19

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input checked="" type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

Response: We thank you for reviewing our manuscript. We really appreciated your input and found your suggestions very helpful. We revised the manuscript based on your suggestions.

COMMENTS TO AUTHORS

1) Is there any difference in AKI post TAVR with regards to the approach (trans femoral vs trans apical vs trans aortic?) 2) Since at least part of AKI could be explained from aortic thrombus embolization to the renal arteries are there any differences with regards to valve size and AKI?

Response: Thank you for raising very important point since different TAVR approaches especially transapical approach and valve size may result in different AKI risk. We look into the data as the reviewer's suggestion. However, the data on the TAVR approach and valve size in included studies are limited. We agree this is important point. Thus, we

added this point in the discussion as our limitation. The following text in **bold** has been added to the discussion.

“Although the included studies in our meta-analysis were all of moderate to high quality, there are some limitations of this study that bear mentioning. First, there were statistical heterogeneities among the enrolled studies. The potential sources of these heterogeneities include the variations in the diagnostic methodology of AKI after TAVR and the differences in confounder adjustment methods. Second, the data on severe AKI requiring RRT after TAVR is lacking. Further studies are certainly warranted to further delineate the impact of transfusions after TAVR with specific regard to the severity of AKI. **Third, the data on valve size and approaches for TAVR procedure were limited. These factors might have affected the risk of AKI following TAVR.** Lastly, this is a meta-analysis of observational studies with the inherent limitation that a causal relationship cannot be inferred.”

Response to Reviewer#2

Reviewer's code: 00503334

Reviewer's country: United States

Science editor: Shui Qiu

Date sent for review: 2016-03-22 15:20

Date reviewed: 2016-03-29 02:29

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

COMMENTS TO AUTHORS

n/a

Response: We thank you for reviewing our manuscript.