PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Risk factors for contrast-induced acute kidney injury (CI-AKI): Protocol for systematic review and meta-analysis
AUTHORS	Liu, Yong; Liang, Xingcheng; Xin, Shaojun; Liu, Jin; Sun, Guo-li; Chen, Shi-qun; cen, xiaolin; dai, xiaohua; He, Yibo; Song, Feier; Liang, Yan; Hu, Yu-Ying; Zhou, Yingling; chen, zhujun; Tan, Ning; Chen, Ji-yan

VERSION 1 - REVIEW

REVIEWER	Dr Gemma E Currie University of Glasgow UK
REVIEW RETURNED	20-Mar-2019

GENERAL COMMENTS	I read with interest the protocol paper by Liu et al who are conducting a meta-analysis of factors influencing risk of contrast-induced nephropathy. The key question is clear and the methodology in general seems sound. A few factors need to be revised/clarified however. 1) The justification for repeating a meta-analysis that was last conducted in 2017 needs to be clearer. The authors state they will also investigate "novel" risk factors but make no further comment on what these may be or cite any literature linking alternative risk factors to contrast-induced nephropathy. How many new studies have been published since the previous meta-analysis was conducted? 2) The list of keywords seems rather limited for such a wide-ranging question and may result in important papers being omitted. 3) The authors should speculate how identification of risk factors would alter patient management - would high risk patients be offered specific therapies/pre-hydration etc? 4) There are some areas of the manuscript where the language used is incorrect and difficult to understand. For example, selection of studies section, page 8 lines 6-7 "The same queue of the population will be treated as the same study and then excluded". Some redrafting with attention to clarity of the text would be of benefit.

REVIEWER	Francesco Paolo Schena University of Bari, Italy
REVIEW RETURNED	25-Mar-2019

GENERAL COMMENTS	The authors of this study describe the protocol for a systematic review and meta-analysis on the potential risk factors for the development of a contrast-induced nephropathy. The protocol needs language revision by English writer -p4 line11 we will perform -p5 line8 delete clearly identify line11 delete also systematic line21 Allen et al (5) and Silve et al (6) -p6 line1 but there has been no systematic assessment of the absolute...... line3 we will conduct line14 it will be not appropriate line17 will be conducted -p7 line3 we will choose..... on the English publications line17 will be CIN line20 has been defined -p8 line2 titles line3 abstracts line3 delete the two authors line5 YL line14 two authors (who?) -p9 line16 Question mark

REVIEWER	Wisit Cheungpasitporn University of Mississippi Medical Center
REVIEW RETURNED	17-Apr-2019

GENERAL COMMENTS	Search terms in Ovid Medline and Embase are different. Please attach search terms that were used in each database as supplement for Data source and search strategies in the manuscript. Please provide details search terms in supplementary documents. Please attach syntax used in each database as supplementary. Recommend the authors apply the ROBINS-I (Risk of Bias in Nonrandomized studies of Interventions) tool in addition to NOS. The authors already planned to apply 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 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.
	The term "Contrast-induced nephropathy (CIN)" has been updated to "Contrast-induced acute kidney injury (CI-AKI)"
	Some revision of the English language is needed. There are some parts of the paper where it is quite difficult to make sense of some sentences English edit will help to improve the quality of the manuscript. To mention as a few as below:
	"induclidng" is misspelled.
	"evaluatation" is misspelled.
	"predict models" is not correct. It is "prediction models"
	"to identity" is not correct.
	"In addtion modifiable" is not correct.
	"intellectual" is not correct.

VERSION 1 – AUTHOR RESPONSE

Response to reviewer 1

1. The justification for repeating a meta-analysis that was last conducted in 2017 needs to be clearer. The authors state they will also investigate "novel" risk factors but make no further comment on what these may be or cite any literature linking alternative risk factors to contrast-induced nephropathy. How many new studies have been published since the previous meta-analysis was conducted?

Response: Thank you for your good comments. Actually, there were not any previous meta-analysis about all the risk factors for CIN. The meta-analysis in 2017 aimed to evaluate risk models for CI-AKI, not risk factors. To improve the clinical significance as your suggestions, we have added "This will be the first, and largest systematic review about the risk factors associated with CI-AKI. " in Introduction section in the revised manuscript. (Paragraph 1, Page 4)

2.The list of keywords seems rather limited for such a wide-ranging question and may result in important papers being omitted.

Response: Thank you for your sincere comments. Our search strategies are comprehensive and detailed and the list of keywords in this article is just a simplified description. We have add "acute renal insufficiency; risk factor; risk Assessment; multivariate analysis; multivariable logistic regression; models." in Initial keywords section in the revised manuscript. The literature searches yielded over 17557 studies in this meta-analysis. In order to keep this secret, we plan to show the search strategies in achievements in scientific research. (Paragraph 2, Page 5)

3.The authors should speculate how identification of risk factors would alter patient management - would high risk patients be offered specific therapies/pre-hydration etc?

Response: Thank you for your sincere comment. To improve the clinical significance as your suggestions, we have added "The use of a risk prediction tool for CI-AKI could have several benefits. They may help identify the patients at high risk for the disorder, who might benefit from per-procedural

strategies that protect the kidneys."in Introduction section in the revised manuscript. (Paragraph 1, Page 4)

4.There are some areas of the manuscript where the language used is incorrect and difficult to understand. For example, selection of studies section, page 8 lines 6-7 "The same queue of the population will be treated as the same study and then excluded". Some redrafting with attention to clarity of the text would be of benefit.

Response: Thank you for your sincere comments. We have redrafted the article by a native speaker. Selection of studies section, "The same queue of the population will be treated as the same study and then excluded" has change into "To avoid overlapping patient data in duplicate publications, registry analyses were cross-checked with institutional studies and compared with other registry studies, and the larger or more complete publication will be included." (Paragraph 2, Page 10)

Response to reviewer 2

The protocol needs language revision by English writer

-p4 line11 we will perform

-p5 line8 delete clearly identify

line11 delete also systematic

line21 Allen et al (5) and Silve et al (6)

-p6 line1 but there has been no systematic assessment of the absolute......

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-p7 line3 we will choose..... on the English publications

    line17 will be CIN

line20 has been defined

-p8 line2 titles

line3 abstracts

line3 delete the two authors

line5 YL

line14 two authors (who?)

-p9 line16 Question mark

Response: Thank you for your sincere and detailed comments. The manuscript has been redrafted by a professional press. We have highlighted the changes to our manuscript within the document by using coloured text.

Response to reviewer 3

1.Search terms in Ovid Medline and Embase are different. Please attach search terms that were used in each database as supplement for Data source and search strategies in the manuscript. Please provide details search terms in supplementary documents. Please attach syntax used in each database as supplementary.

Response: Thank you for your sincere comment. In order to get all articles about contrast induced nephropathy, we have used different search strageties in different database. The whole search terms are attached in a supplementary file.

2.Recommend the authors apply the ROBINS-I (Risk of Bias in Nonrandomized studies of Interventions) tool in addition to NOS. The authors already planned to apply 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 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.

Response: Thank you for your sincere suggestions. We have read the article about ROBINS-I and find it a more appropriate evaluation tool, especially in future high-quality meta-analysis. But

compared with NOS, ROBINS-I is more complex and time-consuming. We will apply both ROBINS-I (Risk of Bias in Nonrandomized studies of Interventions) tool and NOS. We have add " In additions, we will use the ROBINS-I (Risk of Bias in Nonrandomized studies of Interventions) tool to enhance the reproducibility and comparability of this review to future reviews of a similar topic." (Paragraph x, Page x) in Quality assessment section in the revised manuscript.

In addtion, we have added arcticle about ROBINS-I as a reference (Paragraph 1, Page 10)

8. Sterne Ac,Hernán M A,Reeves B C, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions.BMJ, 2016, 355: i4919. (Paragraph 2, Page 10)

3.The term "Contrast-induced nephropathy (CIN)" has been updated to "Contrast-induced acute kidney injury (CI-AKI)"

Response: Thank you for your sincere comments. We have changed "Contrast-induced nephropathy (CIN)" into "Contrast-induced acute kidney injury (CI-AKI)" in the revised manuscript.

VERSION 2 – REVIEW

REVIEWER	Schena Francesco Paolo University of Bari Italy
REVIEW RETURNED	26-Jun-2019

GENERAL COMMENTS	The paper is suitable for publication

REVIEWER	Wisit Cheungpasitporn University of Mississippi Medical Center, USA
REVIEW RETURNED	06-Jun-2019

GENERAL COMMENTS	The authors have addressed all of my concerns adequately. I am now confident to recommend this protocol for publication

VERSION 2 – AUTHOR RESPONSE

Response to reviewer 3

The authors have addressed all of my concerns adequately. I am now confident to recommend this protocol for publication.

Thank you for your approval!

Response to reviewer 2

The paper is suitable for publication.

Thank you for your approval!