Author’s response to reviews

**Title:** CHA2DS2-VASC score as a preprocedural predictors of contrast-induced nephropathy among patients with chronic total occlusion undergoing percutaneous coronary intervention: a single center experience

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Editor Comments:

1) We note that there is textual overlap in the Methods, Results and Limitations with previously published works, in particular: Kurtul et al. (2017) The American Journal of Cardiology 119(6); Aguiar-Souto et al. (2010) International Journal of Cardiology 139(1); Cicek and Yildirim (2018) Kardiologia Polska 76(1).

Please re-phrase these sections in your own words to ensure no overlap.
Answer: I have re-phrase these sections in my own words, Thank you!

2) Please ensure that the abstract in the main manuscript is the same as the abstract on the submission system.
Sorry, maybe i have made a mistake, This manuscript should be according to the main manuscript if contradictions occur

3) Please include the heading “Declarations” at the start of this section.
Answer: corrected, Thank you!
4) Please represent authors' names using their full initials, not their full name, in the Authors’ Contributions section. If there are any duplicated initials, please differentiate them to make it clear that the initials refer to separate authors.
Answer: corrected, Thank you!

5) Please note that listed author contributions of Zhang, Chen and Yu does not automatically qualify them for authorship. Revising the manuscript is not sufficient to qualify for authorship. We ask that you ensure that author contributions are in line with the ICMJE guidelines (http://www.icmje.org/recommendations/browse/roles-and-responsibilities/defining-the-role-of-authors-and-contributors.html), and that all listed authors have performed all four points specified below.
An 'author' is generally considered to be someone who has made substantive intellectual contributions to a published study. According to the ICMJE guidelines, to qualify as an author one should have performed all 4 of the following points:

A. Made substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data;
B. Been involved in drafting the manuscript or revising it critically for important intellectual content;
C. Given final approval of the version to be published. Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content; and
D. Agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
Answer: corrected, Thank you!

6) I am afraid the quality of the English used throughout your manuscript does not currently meet our requirements. We recommend that you ask a native English speaking colleague to help you copyedit the paper. If this is not possible, you may need to use a professional language editing service. Use of an editing service is neither a requirement nor a guarantee of acceptance for publication.
Answer: I have used a professional language editing service to polish the language. Thank you!

Reviewer reports:

Alparslan Kurtul (Reviewer 1): This article can be accepted in this last form. Thank you for your corrections.
No correction is needed.

Reviewer 2 (Reviewer 2): PEER REVIEWER COMMENTS: To view the full report from the academic peer reviewer, please see the attached file.

REVIEWER COMMENTS FROM REPORT: The study needs significant improvements. The methods for estimation of predictors is unclear.
1. The objectives of the study are not driven by an biological hypothesis and appear to be data driven.
Answer: It seems that this study is driven by biological hypothesis, however, this is not true. CIN is an important complication after interventional procedures, especially in the setting of CTO lesions. The mechanism of CIN is still not fully understood today, however, accumulating evidences had suggested
CIN is closely related to heart failure, hypertension, age ≥75 years, diabetes and even female patients. As CHADS2-VASc score included quite a lot of risk factors of CIN. That is to say this study is driven by an biological hypothesis not just data driven.

2. It is not clear what the authors mean by prediction. Do they refer to independent predictor as lots of variables can predict lots of outcomes.
Answer: As CHADS2-VASc score included quite a lot of risk factors of CIN, we use it preprocedurally to predict CIN of CTO patients undergoing PCI. ROC curve analysis revealed that the area under the curve for predicting CIN was 0.742 (sensitivity 69.2%, specificity 78.0%, 95% CI 0.682 to 0.797, p<0.001) for the presence of CHA2DS2-VASC score ≥3. Moreover its predict value is comparable to Mehran risk score. Thank you!

3. The selection of a consecutive rather than random sample raises problems which are not discussed.
Answer: Consecutive cases of CTO undergoing PCI were enrolled, each patient had a CHADS2-VASc score. The patients were divided into three groups according to the CHA2DS2-VASC score: low risk group (1 point, n=64), intermediate risk group (2 points, n=135) and high risk group (≥3 points, n=40). And we divided into two group according to CIN or not. We use CHADS2-VASc score or CIN as a criteria of grouping. There is no random in this study. Thank you for your careful revision!

4. There is no clear description on what are the important outcomes of interest and what are the relevant gold standard. We learn about these the first time in the discussion section or figures.
Answer: In this study, we aimed to investigate the incidence of CIN in patients with CTO undergoing PCI. Then we tried to investigate the predictable value of CHA2DS2-VASC score in CIN. Meantime we tried to compare CHA2DS2-VASC score with Mehran risk score (this is the mostly used score to predict CIN. There is an inevitable hysteresis for the prediction of CIN, as contrast volume was acquired after the procedure.

5. The discussion does not include the latest references on preventing CIN and is very limited in acknowledging limitations.
Answer: This study focused on the predictable value of CHADS2-VASc score in CIN, so we didn’t discuss the prevention of CIN. Thank you for your kind and professional revision. We are sure you are a senior specialist in scientific research. We hope to gain your understanding and further help.

REQUESTED REVISIONS:
Please address issues 1-5 above before the manuscript can be reconsidered.

Samet Yilmaz (Reviewer 3):
1. How did you categorise low risk, intermediate risk and high risk patients according to CHADS-VASc score? CHADS-VASc score of 2-3 are at intermediate risk category in the manuscript. How did you determine it? Please add a reference.
Answer: To be honest, this is my own method of risk stratification. We retrieved the literature and found a similar method of risk stratification.
Cicek G, Yildirim E. CHA2DS2-VASc score predicts contrast induced nephropathy in patients with ST-segment elevation myocardial infarction who were undergoing primary percutaneous coronary intervention.[J]. Kardiologia Polska, 2017.

2. Risk of CIN according to CHADS-VASc score is equal to males and females? There is no female
patient in low risk category (CHADS-VASc score of 1), could these group have a same risk with female patients with CHADS-VASc score of 2?

Answer: The CHA2DS2–VASc score was calculated by giving one point for congestive heart failure (CHF), HT, (DM, age between 65-74, female gender and presence of a vascular disease, 2 points for age of ≥75 years, history of stroke or transient ischemic attack (TIA). Vascular disease was defined as presence of a previous MI, complex aortic valve, re-vascularization, peripheral artery disease (PAD)-related amputation or presence of angiographic evidence of PAD. Patients in this study all had angiographic evidence of coronary artery occlusion or a history of MI, so female patients were not included in CHADS-VASc score of 1. Female patients had a score of at least 2 (giving one point for MI and one point for female).

3. Total amount of used contrast is higher in patients with high risk category. This may be related to high CIN numbers in high CHADS-VASc risk category. Please explain this.

Answer: In high CHADS-VASc risk category, patients tended to be older, a high rate of heart failure, hypertension diabetes and PAD, as a result, they were worse than low risk group patients. It is just one of the aims of our study to distinguish the individuals for high risk of CIN before the procedure. Therefore take measures to prevent CIN. Also in this study, we aimed to investigate a pre-procedural score of CHA2DS2-VASC to predict the incidence of CIN. Total amount of used contrast was acquired post-procedure, there is an inevitable hysteresis for the prediction of CIN, although it plays a vital role in CIN, still we didn’t included it in our study.

4. Please add preprocedural GFR or creatinine and amount of contrast media in to the regression analysis.

Answer: corrected in the manuscript. Thank you for your kind and professional revision.

5. Give the data about change of creatinine or GFR values from baseline to end of the following period according to risk category groups.

Answer: corrected in the manuscript. Thank you for your kind and professional revision.