Author’s response to reviews

Title: Evaluation of peripheral perfusion index and heart rate variability as early predictors for intradialytic hypotension in critically ill patients

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Author’s response to reviews:

Dear editor
We would like to thank the editorial board and the reviewers for the very valuable comments which improved our manuscript. We responded to all the comments and hope to meet the expectations of the reviewers and the editorial board.

Reviewer 2 (Reviewer 2):

REQUESTED REVISIONS:
1) Abstract

This section is well-written, clear and coherent. However, there is no further suggestion to improve the revision.

2) Introduction
The authors provided sufficient background information, placed the study in a broad context and highlight why it is important. Some key and important references on intradialytic hypotension in
critically ill patients with acute kidney injury were reviewed and cited. The authors reviewed the literature very well and did identify some strengths, limitations and controversy that justified the study. In addition, the word count is compatible with journal publications in the medical sciences.

3) Methods
The Methods Section was well-written and detailed. The authors were able to provide adequate description of the subjects, adequate description of the inclusion and exclusion criteria, measurements made as well as variables retrieved. In addition, the Methods are repeatable and can be reproduced. The statistical analysis was fairly well done.

However, there is a concern here.
(i) "Chi-square test was used to compare frequencies between the two groups."
Comment: It is not likely that Chi-square may be applicable here because of the number of cells with expected or observed cells with less than 5 patients mean for a number of this proportions compared, using Fisher's exact test will be more appropriate.
Response
We thank you for this important comment. We repeated the analysis using Fisher’s exact test and corrected this point in the statistical methods section.

4) Results
The Results Section is concise, fairly well-written and reflected the study findings. Currently, there is a correct and well-organized interpretation of the data. The Tables are clear and well-labelled. I have a few revision requests here.

i) Causes of ICU admission included severe sepsis, hemodynamic instability, pulmonary edema, eclampsia, diabetic ketoacidosis, and disturbed conscious level due to head trauma or non-traumatic intracranial hemorrhage.
Comment: Please, provide the number and proportion for cause of ICU admission.
Response
The number and proportion of causes of ICU admission was added in the results section.

ii) "The incidence of intradialytic hypotension was higher in patients admitted to dialysis due to pulmonary edema {odds ratio (95% confidence interval): 13.75(1.4-136)}"  
Comment: This is not correct as the odds ratio here were not based on multivariable logistic regression analysis and the association might be influenced by potential confounders. But, besides the sample size is too small to perform multivariable logistic regression analysis. Also, why was the unadjusted odds ratio for SBP not reported given that is far more significantly associated stable group
Response
We agree with this important comment; therefore, we added in the limitations part in the discussion (limitation number 3) that the study power was not adequate for multivariate analysis. The study was originally powered for AUROC analysis. We also added the odds ratio and 95% CI for systolic blood pressure in the results section.

5) Discussion
The key Results of the study were well-discussed. Also, the authors extensively discussed the study findings which led to an interesting and accurate Conclusion. A good number of old but important studies were cited to discuss the findings of the study. In addition, the authors had excellent description of the limitations of the analysis.
However, for some of the analysis reported (such as Chi-Square test, and reporting unadjusted OR for pulmonary edema and leaving out SBP), the study has inadequate sample size to reach any reasonable statistical conclusion.

Response
The three comments (Fisher’s exact test, odds ratio for SBP, comment on multivariate analysis) we answered. Thank you again

6) References
The number of references cited are adequate and up to date and the authors used a consistent format in writing their references.