Christos S Katsouras, MD, PhD Second Department of Cardiology, University Hospital of Ioannina, University of Ioannina, Ioannina, Greece. Email: chkatsou@uoi.gr

Ioannina, 29 June 2021

Dear Editor,

with the present letter we would like to resubmit the revised manuscript entitled "Elderly patients with non-cardiac admissions and elevated high-sensitivity troponin: the prognostic value of renal function." (Manuscript ID: 67099) for publication in World Journal of Cardiology.

We would like to thank the reviewer and the editor for their thorough and constructive review of our manuscript. We have carefully read their comments and we have addressed each of them according to their suggestions.

Please find a detailed list of changes according to the reviewer's and editor's specific comments:

<u>Reviewer #1</u>

Specific Comments to Authors: The author investigated the in-hospital prognosis of elderly patients admitted to the Internal Medicine Department with acute non-cardiac events and increased high-sensitivity cardiac troponin I (hs-cTnI) levels in this study. 1. In this study, receiver Operating Characteristic analysis of hs-cTnI and creatinine for predicting in-hospital mortality. The area under the curve was only 0.527 for hs-cTnI. What is the clinical implication? 2.In Research perspectives section, the author should clarify who are the "this group of patients".

 In the revised version of the manuscript, we included in the discussion section, the clinical implication regarding the value (0.527) for hs-cTnI in the ROC analysis

The paragraph "Our study showed that although elderly patients with noncardiac events and hs-cTnl \geq 100 ng/L have a high risk of in-hospital death, individuals who died did not have higher hs-cTnl levels compared with those who were discharged alive. Similarly, Frencken, et al.⁵ also showed that troponin release beyond hs-cTnl plasma concentrations of ~ 100 ng/L does not carry an additional mortality risk in patients with sepsis. This non-linear relationship between troponin levels and mortality may be present even in patients with revascularized acute coronary syndromes¹². The nonlinear relationship with mortality is difficult to explain. It is possible that in patients with non-cardiac acute events, the presence of myocardial injury (and not the extent of injury) maybe a marker of increased mortality." was changed as follows:

The paragraph "Our study showed that although elderly patients with non-cardiac events and hs-cTnl \geq 100 ng/L have a high risk of in-hospital death, individuals who died did not have higher hs-cTnl levels compared with those who were discharged alive. Similarly, Frencken, et al.⁵ also showed that troponin release beyond hs-cTnl plasma concentrations of ~ 100 ng/L does not carry an additional mortality risk in patients with sepsis. This non-linear relationship between troponin levels and mortality may be present even in patients with revascularized acute coronary syndromes¹². The nonlinear relationship with mortality is difficult to explain. It is possible that in patients with non-cardiac acute events, the presence of myocardial injury (and not the extent of injury) maybe a marker of increased mortality. This hypothesis is supported from our ROC analysis, since the area under the curve for hs-cTnI was approximately 0.5, thereby indicating that the level of the troponin (the level of myocardial injury) has no discrimination capacity for further distinguish the risk of in-hospital death.

2. In Research perspectives section, the author should clarify who are the "this group of patients".

We clarified the group of patients. We stated that

"Our results emphasize the need for more aggressive monitoring and treatment in elderly patients with severe renal impairment admitted to the hospital for noncardiac reasons in order to avoid complications and death."

Editorial office's comments

 Summary of the Peer-Review Report: The author should explain the clinical implication of area under the curve 0.527 for hs-cTnl. The meaning of "group of patients" need to be clarify. The questions raised by the reviewers should be answered

We answered the questions raised by the reviewers

 The authors did not provide original pictures. 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;

We provided the original pictures (using Power Point)

 PMID and DOI numbers are missing 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;

We provided the PubMed numbers and DOI citation numbers to the reference list and all authors of the references.

The authors need to fill out the STROBE checklist with page numbers.
We filled out the STROBE checklist with page numbers.

Finally, we would like to thank the reviewer for his comments and the editorial office for the consideration of our manuscript and we hope that you will find it worth publishing, interesting and helpful for your readers.

Yours sincerely,

Christos S Katsouras, MD, PhD