Author’s response to reviews

Title: Low triiodothyronine syndrome and selenium deficiency - undervalued players in advanced heart failure? A single center pilot study.

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Handling Editor
Dr Saverio Muscoli
BMC Cardiovascular Disorders

Dear Dr Muscoli,

We are pleased to submit once again the manuscript entitled: ‘Low triiodothyronine syndrome and selenium deficiency - undervalued players in advanced heart failure? Single center pilot study.’ for renewed consideration.
We are very grateful for your valuable remarks which helped us make the necessary corrections and improve the manuscript. Please consider a revised version to be published in BMC Cardiovascular Disorders.

1. We agree that the sample size of our study group is not large. However, it is substantial for a single center study, given the fact that recruitment and long-term follow-up was quite difficult in patients with severe heart failure. In our opinion, based on the results, the conclusion about the significance of low T3 syndrome in HFrEF is justified. Responding to the comments of the Editor, we have modified the title, adding the information that our research was a single center pilot study (line 1-2). We plan to continue this research in the future in cooperation with other centers, but we think that the current results are worth publishing.

2. Following the Editor’s advice, we have clarified the pathophysiology, especially the mechanisms of oxidative stress accompanying HF. We have also referred to additional articles: Pignatelli et al., Takahashi et al. (line 66-78 and 403-407 of the current text version).

3. At the second Reviewer’s suggestion, we have added the statement “prospective cohort study” in the ‘Methods’ section (line 107 of the current text version).

4. Following the first and third Reviewers comments, we have also clarified the data on participants evaluated at follow-up (line 181-186 of the current text version). The follow-up lasted for 137.53 (±36.49) days. It was not clearly stated in the previous version of the text that the survival follow-up was completed in all patients. The scheduled last ECHO/Lab-test visit was not possible in all group A patients due to the death of 4 participants, and the ongoing hospitalization of one of them in a different hospital. However, all the above events were included in the Kaplan-Meier analysis.

Thus, we apologize for lack of precision in the description of the follow-up that led to a wrong assumption made by the third Reviewer that only 13 participants completed the protocol. Perhaps this misunderstanding resulted also from confusing our results with the quoted research conducted by Holmager et al. in which 13 participants completed study protocol (line 293-297 of the current text version). It is also not correct that only 3 participants from group A were evaluated in the survival analysis at follow-up.

To conclude, in our opinion, we managed to assemble valuable follow-up data. All participants from group A were included in calculations of the most important hard end-points. Occurrence of cardiovascular death in a substantial part of group A (44.4% vs. 0% in group B 0.0%, p=0.0003) made it impossible to assess laboratory and ECHO findings at the third time point.
However, it is an important result for survival analysis, illustrating the severity of disease in Group A. Thus, we hope it is not a major disadvantage. Thank you for the remarks – we hope the description of the follow-up analysis is now clear.

5. We have removed the text: ‘2 patients with initially low T3 syndrome became euthyroid’ (line 224-225 of the current text version) because, even if patients became euthyroid at the follow up visit, according to study protocol they still belonged to group A (the division of group A and B was made during hospitalization and was not changed at follow up).

6. Following the second Reviewer’s comment, wording mistakes were corrected: Line 79-80 of the current text version: lack of TH (thyroid hormones); Line 258 of the current text version: Kozdag et al.

7. Responding to the comments of the first and third Reviewers, we have clarified the discussion (line 267-273, 295 of the current text version). We hope that after refining the description of the follow-up data, the conclusions are adequately supported.

8. Following remarks of Reviewers first and third the final version of the text was also reviewed by the English native speaker expert.

We hope, after the improvements the article is acceptable.

Sincerely,

Corresponding author

Andrzej Gackowski, PhD