Author's response to reviews

Title: The impact of anemia in heart failure patients' clinical characteristics and overall prognosis. A retrospective cohort study

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Author’s response to reviews:

Juan Gagliardi (Reviewer 1):

1. It is unclear why asymptomatic patients were excluded from admission. It should be specified why patients in functional class II were not included. This could mean a greater number of patients included and therefore greater representativeness of the sample.

Authors’ reply: We intended to study the impact of anemia in patients with severe HF and as such we included patients with NYHA functional class III and IV. Therefore, we excluded patients with NYHA functional class II (as the Mozaffarian et al study). However we have now re-written the title and objective of the study to indicate that this study is about patients with severe HF not all HF patients as follows:

Title: Anemia in Severe Heart Failure Patients: Does it predict prognosis?

Objective: The aim of this study was to evaluate the prevalence of anemia in patients with severe HF, to compare baseline clinical characteristic and outcomes of severe HF patients with and without anemia admitted to Gondar University Referral Hospital (GURH).

2. Establishing survival status from last hospital discharge or medication refill as a subrogant to establish survival time is not usual and implies a major limitation. This topic should be included limitations of the study.

Authors’ reply: Thank you for your valuable comment. We now included the following sentence in the limitation section of the manuscript: “Finally, last hospital discharge or medication refill
was used to determine time for survival analysis and this could be affected by documentation or loss to follow-up.”

3. In turn, it is better to express the follow-up time as median (IQR) than as mean ± SD. The "Methods" section seems to incomplete (page 4)

Authors’ reply: Thank you for your insight. We now expressed the follow-up time as mean (IQR) instead of the previous statement of mean ± SD as follows. “The median (IQR) duration of follow up was 18 (8-36) months.”

In addition, we rephrased the sentence stated as “Continuous variables were revealed as mean ± standard deviation and discrete variables presented as percentage.” in the methodology section in to “Continuous variables were revealed as mean ± standard deviation and median (IQR) and discrete variables presented as percentage.”

4. In the Results section, it is shown that hemoglobin was statistically different between both groups, however, this should be in methodology since it was the criterion used to define the groups.

Authors’ reply: We have already stated that hemoglobin was used as a criterion to define the groups in the methodology section as follows: “According to hemoglobin level on hospital admission, patients were categorized into anemic and non-anemic groups. Hemoglobin concentration of less than 13 g/dl for male and less than 12 g/dl for female was used to define anemia according to the world health organization (WHO) criteria (20).”

However, in the results section, we performed statistical analysis to determine the significance of difference between the two groups and to see the mean difference among groups.

5. It is clearly observed that, although anemia is a significant risk marker, it is not an independent predictor of mortality. This should be emphasized both in the results and in the discussion and conclusions.

Author’s reply: We appreciate the reviewer’s comment and we have emphasized the statement in the result, discussion and conclusion section of the manuscript.

Authors’ reply:

Ricardo Perez de la Hoz, Ph.D. (Reviewer 2):

6. However, since the article shows certain limitations due to its retrospective approach, I'd suggest to do some extra work to clear up some topics, thus fostering stronger conclusions. For instance, it would be important to specify the higher degree of anemia among rural population as well as the age of patients included vs the etiology of cardiac insufficiency
Authors’ reply: We appreciate the reviewer’s comments. However, as we already tried to state in Table 1.0, there was no statistically difference in anemia between people from rural areas or urban areas. Also, none of the etiologies, other than cor pulmonale, were statistically different between patients with anemia and without anemia. On the other hand, there was a statistically difference in age between patients on either groups where patients who were in the anemia group were older. This issue was already addressed in the first, second, and sixth paragraphs of the discussion section.

7. Another interesting step would be considering if the worse cardiac insufficiency progression and insufficient treatment had any relation with actual renal dysfunction or if constituted a free association with the presence of anemia.

Authors’ reply: we appreciate the reviewer’s comment. However, as described in the objective/aim of the study, we only focused on the impact of anemia on the prognosis of severe HF patients and considered creatinine as a variable of independent factor in the overall mortality. In this regard, we are restricted on the objective of the study.