Reviewer’s report

Title: Baseline Low ALT Activity, a Marker of Sarcopenia and Frailty, is Associated with Increased Long-Term Mortality after COPD Exacerbations. Historic Prospective Cohort Study.

Version: 0 Date: 07 Dec 2019

Reviewer: Susannah Bloch

Reviewer's report:

07/12/2019

Dear Editors,

Review of manuscript "Pre-Hospital Low ALT Activity, a Marker of Sarcopenia and Frailty, is associated with Increased Long-Term Mortality after COPD Exacerbations"

Thank you for asking me to review this manuscript. The association between muscle mass/muscle dysfunction and muscle loss in COPD and COPD exacerbations and mortality is an important topic and is widely discussed in the literature. In this paper Lasman et al aim to persuade us that a low blood ALT level, as a marker of sarcopenia, is associated with mortality in COPD patients who have had an exacerbation. If true this is an interesting observation, but I have some comments and questions about the manuscript.

Background

1) The aim of the study is to examine the link between ALT and mortality in COPD patients. The authors presume that the readers accept that low ALT represents sarcopenia - but this could be better explained perhaps by reviewing references 15-18 more explicitly. I am not sure that it has been shown that ALT is a biomarker for sarcopenia in COPD. Why this has been accepted by the authors should be explained.

2) The authors do not state why they chose to examine this association or why it might be clinically interesting

3) There are several spelling/grammatical errors in the text

Patients and methods

1) Statistical method - this should be reviewed by a statistician
Results

1) A consort diagram would be useful to demonstrate how patients were screened and then how many were excluded for example for an ALT &gt; 40IU

2) I am not aware that the Norton score is widely used in the UK literature in COPD patients, there are several components to it which include activity and mobility - these clearly have relevance when considering sarcopenia and the manuscript might benefit from an explanation of what the Norton score is and also a comment in the discussion about the relationship of it to sarcopenia and potential impact on the results.

3) The authors do not make it clear when the "Baseline ALT" is from - were these routine blood tests or at the time of a prior exacerbation? Why were they taken and what was the relation to the ALT during the admission?

4) This group as a whole have a high mortality - some information on GOLD stage, severity of exacerbation - (type 2 respiratory failure? Need for NIV etc…) would be useful and is very important as it may confound the results.

5) Tables - it should be explicit from the table legend what statistical tests were used to calculate the p values.

Discussion

1) The first paragraph should be re written as the point of it is not clear.

2) I'm not sure that the statement "In the current study we show that similarly to other patients' groups, COPD patients can also be classified as sarcopenic and frail, according to their baseline ALT values" has actually been proven by this study - this study claims an association between low baseline ALT and mortality - it does not show that these patients are definitively sarcopenic or frail as no other measures of muscle function or mass are mentioned.

3) The authors should discuss critically the limitations of their study

4) "Future, prospective, interventional studies should aim at evaluation of different therapies and rehabilitation programs, concentrated at the sarcopenic and frail COPD patients." This is true but I'm not sure that low ALT levels add to this at the moment.

Overall comments

The authors aim to show that low ALT could be used to predict poor outcomes in the COPD population. Although they touch on the fact that low ALT can be used as a surrogate for other assessments of sarcopenia they do not assess muscle mass or strength or other markers of muscle
dysfunction in this paper, other than in the Norton score (which includes activity and mobility). It has not been shown explicitly that in COPD patients ALT is a biomarker for sarcopenia this should be reviewed more fully. Most importantly the manuscript must contain some description of COPD severity both at baseline and during the index exacerbation between the different groups.

The English could be improved throughout to make it easier to read and understand. The statistics should be reviewed by a statistician to ensure that they agree that they have used valid statistical methodology.

Thank you for asking me to review this manuscript. It is interesting but would need significant work, statistical review and additional information prior to publication.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Unable to assess

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

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