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: 19 Feb 2020

Reviewer: Tomas Mikal Eagan

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PULM-D-19-00703

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

There are a number of studies published recently that point to low ALT levels being indicators of low muscle mass and increased mortality. COPD patients are quite often cachectic, and cachexia is a known predictor of mortality in COPD. Thus it would be likely that low ALT levels also predicted mortality in COPD patients, and that is the study question of this study, whose study design is not completely clear.

Major comments

1. This is not a thoroughly worked out manuscript; rather it feels unfinished.

Examples of simple text errors:

"huge health expanses", "have been descried", "Survival and COPD mortality are negatively influenced by ..." [which is it that is negatively influenced, survival or mortality - this is nonsensical], "Vellas and co. (12) relate to COPD" [this is just not a good phrase]. These examples are from the first page only, there are several more. If foreign language is the challenge, I suggest using professional editing help prior to submission.

2. The study design is under-described. Why include patients hospitalized for exacerbation who had ALT measured within the last three months prior to hospitalization? This sounds ambiguous, where the inclusion of patients from the steady state population, or during an exacerbation event? Is it possible that ALT levels were influenced by an ongoing exacerbation. How was the main outcome - mortality - recorded? Could mortality events have been missed? Where the mortality data from a national register?

What was the definition of "Metabolic disorder"? - or any of the other "background diagnoses"? What is Norton score, and how was it calculated?
Using the STROBE checklist would enhance this draft vastly:


3. Several references I would expect to see (and which it takes 30 seconds on PubMed to find), were not present, for example:


4. The authors fail to convince me that ALT has added value to other known parameters of mortality. Stable state FEV1 is not included, which I think would be appropriate, also body composition, at the very least in terms of BMI. If one adjusts for both BMI and FEV1 - is ALT still an independent predictor of mortality?

Minor comments

5. Why was a forward stepwise regression modelling strategy used? - this is arguably the most criticized approached by statisticians. If a stepwise strategy is to be used (which is in itself debatable), probably a backward approach is more prudent.

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

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

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