Reviewer's report

Title: The relationship of systemic inflammation to hospitalization in adult patients with cystic fibrosis

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Reviewer: Frank Accurso J Accurso

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Report to authors.

Ngan and coworkers examine the hypothesis that systemic inflammation is related to hospitalization and impairment of lung function in Cystic Fibrosis (CF). Systemic inflammation is examined through a panel of biomarkers. This is a valuable study since biomarkers of disease in CF are greatly needed. The authors investigated some biomarkers that have not been investigated previously in CF.

My comments should be taken as major compulsory revisions that each require a response.

1. The question posed by the authors is well defined.
2. Introduction. The last sentence says "by products of Gram-negative pathogens". Actually it is only one by-product. Please change accordingly.
3. I have comments concerning the methods
   a. What were the dates of sampling the patients? In other words, when did the study begin and end?
   b. The manuscript reads as if all patients had nasal potential difference studies. This would be a bit unusual. Please confirm this.
   c. "such as" is used a lot in the description of biomarker assays. It would be better to say exactly what was measured and leave out the "such as" phrase. "Such as" implies that more tests were done.
   d. The coefficients of variation are reported to two decimal places. Would one place be sufficient? It is distracting to the reader to see extra decimal places.
   e. Statistical analysis. How were results below the limit of detection handled?
3. The data are sound but I have questions on the results.
   a. The spread of ages in table 1 would be better reported as ranges rather than standard deviations. The authors give the age range appropriately in the text.
   b. The presentation of the biomarker results is given to two decimal places. Again, are the authors confident of this level of precision?
   c. We should be told the percent of samples below the limit of detection for each biomarker. This could be a figure or a table.
d. I understand that the reviewers do not have controls without CF but it would be helpful if they included the manufacturer's reference ranges or reported reference ranges in Table 2.

e. Most important is that the lung function impairment associations are adjusted for BMI, FEV1 and Pseudomonas status but the way the results read the hospitalization results only take into account BMI, FEV1 and not Pseudomonas. Pseudomonas should be included in the hospitalization analysis. Specifically, do IL-6 and CRP and IL-1beta hold up as different if Pseudomonas is accounted for? The authors should also do the testing within the Pseudomonas group. Perhaps I missed that this was done for the hospitalizations. Please clarify.

f. Please give the c statistics generated by adding IL-6, IL-1beta or LPS mentioned on the bottom of page 8.

4. The manuscript adheres to the relevant standards for reporting and data deposition.

5. The discussion and conclusions are well balanced and adequately supported by the data.

6. Limitations of the work are clearly stated.

8. The title is appropriate. The abstract should reflect the analysis controlling for Pseudomonas for both hospitalization and lung function impairment as mentioned above. 9. The writing is acceptable.

10. Figure legends and tables. Please consider decreasing the extra digits on the p values.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Declaration of competing interests:**

I declare that I have no competing interests.