Reviewer’s report

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

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Reviewer: Nicole Hamblett

Reviewer’s report:

This is a cross-sectional study aimed at correlating systemic inflammatory outcomes with key clinical parameters in CF including lung function and hospitalization. While the overall study design and data collection are straightforward and sound, I have some major issues with the presentation and interpretation of the results.

(1) The study would be much cleaner if the primary emphasis was on correlating the markers with FEV at the time of their collection.

(2) Emphasizing any association between hospitalizations in the prior 5 years and the markers or other covariates is extremely problematic in this study. While the limitations section touches on the issues of causality and directionality, the limitations are serious enough that they should prevent drawing attention to these associations. Specifically,

a. The term “risk factor for hospitalization” is used throughout the manuscript. This term can only be used in a prospective study correlating markers with subsequent risk of hospitalization. Correlating a marker with hospitalization in the prior 5 years in no way implies that it is a risk factor for hospitalization.

b. The hypothesis is that systemic inflammation may be an important risk factor for poor health outcome in CF and the intent of this study is to investigate this. However, this cross sectional study with retrospective hospitalization data is not designed to answer this question. Hospitalization in the prior 5 years should be treated as a covariate (eg in table 1) but not an outcome. Table 1 should show differences in the inflammatory markers by each patient characteristic (eg age group, gender, hospitalized in last 5 years) and removing columns for hosp/non hosp, and table 2 should be removed as well as Figure 1.

c. The discussion is currently written that the data suggest that these markers are good candidates for health outcome/ risk factors for disease progression. Although potentially true, the study results are unable to support these conclusions.

Minor comments

• Multivariate analysis should be “multivariable”

• Methods – definition of “chronically colonized” does not seem appropriate with just one positive culture for Pa needed to meet the definition
• The term risk factor should be removed throughout unless the study is redone to look at hospitalizations after assessment of the inflammatory markers.

• There should be a multivariable model exploring which set of markers is associated with FEV, as they are highly correlated.

• Results refer to a false positive result – this is not informative and fails to address the complexity of the data.

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

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

'I declare that I have no competing interests