Reviewer's report

Title: Aspergillus fumigatus during COPD exacerbation: A pair-matched retrospective study

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Reviewer: Néstor Soler

Reviewer's report:

This study aims to investigate the clinical features and short-term outcomes of COPD patients with Aspergillus spp during exacerbations. It is a very interesting topic and has maximum therapeutic relevance. However, I believe that their exacerbated limitations prevent obtaining valid conclusions.

Major comments:

First, the number of valid respiratory samples with positive isolations for Aspergillus is scarce and insufficient to consider an analysis of outcomes.

Second, the authors assume that a single positive isolation already defines colonization. In many cases, the isolates for Aspergillus and other fungi are transient and have no significance.

Third, the authors point out the treatment with high doses of inhaled corticosteroids (1000 mcg of beclomethasone or equivalent) as the main risk factor for colonization by Aspergillus. Although in previous studies this possibility has been suggested, there is no evidence to demonstrate this association and the pathogenic mechanism is not clear either. The authors also suggest that the presence of Aspergillus spp. in the lower airway may have an impact on episodes of exacerbation of COPD. This statement can not be derived from the findings of the study since it would require a significant relationship between the persistent isolation of Aspergillus spp in the stable patient and an increase in the frequency of exacerbations. Only a long-term follow-up study of a cohort with repeated cultures could demonstrate this hypothesis.

Fourth, although the finding that patients of Aspergillus group require more intensive treatment with systemic corticosteroids is attractive, it is not clear that a greater degree of inflammatory response of the airway area during the exacerbation is a consequence of the direct effect of the
fungus. In my opinion, the potential colonization by Aspergillus spp may be a mere indicator of the severity of the underlying disease and this condition could demonstrate the longer duration of hospital admission and a longer remission time.

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

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

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.
No

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