Author’s response to reviews

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

Authors:
Xunliang Tong (tongxunliang@163.com)
Anqi Cheng (angle1990419@126.com)
Hongtao Xu (taotao200703@sina.com)
Jin Jin (jinjinwlw@126.com)
Yimeng Yang (d860@sina.com)
Sainan Zhu (zhusainan77@163.com)
Yanming Li (lymyl@263.net)

Version: 2 Date: 06 Nov 2017

Author’s response to reviews:

Editor

BMC Pulmonary Medicine

Nov 06, 2017

Re: Manuscript No. PULM-D-17-00280R2

Dear Professor Fabiano Di Marco,

Attached please find our revised manuscript entitled “Aspergillus fumigatus during COPD exacerbation: A pair-matched retrospective study”.
We highly appreciate all the valuable comments from you and the reviewers. In the following pages we have included our point-by-point responses to each of the comments from you and the reviewers.

Based on the reviewers’ suggestion, we revised expression with the help of a native speaker, in order to improve its clarity and readability. We also made some information, which shown in revised manuscript, as reviewer’s suggestion. We hope that the revised manuscript and our accompanying responses will be sufficient to make our manuscript suitable for publication in the BMC Pulmonary Medicine.

We look forward to hearing from you at your earliest convenience.

Sincerely,

Yanming Li, M.D.

Vice Professor, Beijing Institute of Respiratory Medicine, Beijing Hospital,

#1 Dahua Road, DongCheng District, Beijing 100730, China

Phone: 0086-10-85136242

E-mail: lymyl@263.net

Responses to Editor Comments:
Comment 1: Since Authors stated in the accompanying letter that “The data used in this study was part of our project "Study on Aspergillus of COPD patients", which was approved by the ethics committee of Beijing Hospital”, I do not why in the paper is still present the statement that “As a retrospective study, no ethical approval was needed for this study”. If there is an ethical committee approval, why Authors state the opposite in the paper?

Response: Thanks for your kind suggestion. Due to the data used in this study from the project of "Study on Aspergillus of COPD patients", which was approved by the ethics committee of Beijing Hospital, we deleted the sentence of “As a retrospective study, no ethical approval was needed for this study” in the revised version.

Comment 2: Both in abstract and in the whole paper the subject (AC or COPD patient) has to be careful evaluated. For instance “asymptomatic AC” cannot be accepted (I’m sure Authors mean: asymptomatic COPD patients with AC”. The same for “the clinical feature of AC in the airways …”: Authors have to refer to “patients’ clinical feature with AC”. Moreover, since the abbreviation “AC” is not usual I suggest do not use it.

Response: Thanks for your kind suggestion. We revised the sentences expression with the help of a native speaker, in order to improve its clarity and readability. The expression of Aspergillus colonization was used instead of the abbreviation of “AC” in revised version.

Comment 3: Abstract: “Recently identification of Aspergillus colonization (AC) in the airway of patients of chronic obstructive pulmonary disease (COPD) was rising”: probably Authors mean “Recently the awareness of the importance of Aspergillus colonization (AC) in the airway of patients of chronic obstructive pulmonary disease (COPD) was rising”, if I’m right please modify.

Response: Thanks for your kind suggestion. The sentence was modified as “Recently awareness of the importance of Aspergillus colonization in the airway of patients of chronic obstructive pulmonary disease (COPD) was rising” as your suggestion in the revised version.
Comment 4: “This study provides new insight for clinicians managing patients with fungal colonization.” This comment is not informative for readers, I suggest to delete it.

Response: Totally agree with you. The sentence above was deleted in revised version.

Responses to the Reviewer’s comments:

Reviewer #1

Silvia Terraneo, MD

Abstract

Comment 1: The abstract, as the whole manuscript would improve by English editing. The aims of the paper must be improved: the short-term outcomes, for example, were one important aim and has to be reported. I suggest making whole abstract more linear.

Response: As your suggestion, we invited a native speaker helping us in language modification to improve its clarity and readability and we revised the abstract to highlight the key points and make it more linear.

Method

Comment 2: The most important point about the whole paper is: how did you diagnose Aspergillus colonization? I mean, how did you exclude the possibility of ABPA? CPA? Simple aspergilloma? Did you search the presence of clinical symptoms suggestive of CPA or ABPA? Did you perform chest X-rays and how were its findings?

Response: Aspergillus colonization was defined in “Inclusion criteria” of Methods section in revised version (line 138). All the patients recruited in this research were under evaluation of
chest CT scan for exclusion of ABPA, CPA and simple aspergilloma. The laboratory examination was performed of detecting the level of IgE, IgG, IgM and so on. The combination of clinical symptom, laboratory results and radiologic findings could help us in excluding the diagnosis of ABPA, CPA and simple aspergilloma.

Comment 3: I suggest bettering explaining where did you find patients’ data. What are "patients' data files"? Did you follow the patients after the exacerbation?

Response: Thanks for your kind suggestion. All patients enrolled in this research were admitted patients in Department of Respiratory and Critical Care Medicine of our hospital. Their data was collected and all restored in the electronic medical records system in our hospital. We followed these patients for more than a year and the information was analyzed for further investigation.

Comment 4: Within how many days were LRT samples collected?

Response: When patients admitted into hospital, their LRT samples were delivered for microbiological examination the next day.

Ethical

Comment 5: retrospective studies need ethical approval. In the response to editors you wrote that the data used in this study were part of another project, which was approved by your ethic committee. This needs to be reported in the paper, in methods section. Is this a retrospective analysis of a prospectic database?

Response: It is a retrospective analysis of a prospective research. Due to the data used in this study from the project of "Study on Aspergillus of COPD patients", which was approved by the ethics committee of Beijing Hospital, we corrected our expression and added in methods section and the declaration section in revised version. And the approval was agreed by ethic committee of Beijing Hospital and the related documents had been attached in former submitted version.
Results

Comment 6: The figure about "the study group" belongs to Results section and needs a figure capture.

Response: Thanks for your suggestion. We moved the figure about "the study group" to the Results section and added a figure capture as your suggestion.

Comment 7: I could not find Results about multivariate analysis of risk factors for the isolation of Aspergillus, and survival curves. Why?

Response: We added results about risk factors for Aspergillus colonization by multivariate analysis and remission time curve by Kaplan-Meier analysis in the revised version.

Table 1

Comment 8: I suggest reporting all class GOLD.

Response: As your suggestion, we added all GOLD severity classification of patients in the revised version.

Table 2

Comment 9: in which day were laboratory examination collected? At admission?

Response: At admission, the LRT samples were collected for laboratory examination. When patients admitted into hospital, their LRT samples were delivered for microbiological examination the next day.

Comment 10: I could not understand FiO2 results. Did you mean Pa/Fi?
Response: We have corrected the related expression in revised version.

Table 3

Comment 11: what does "combination identification of pathogens" mean? Was a microorganism isolated only in 12/23 patients? I suggest reporting p value also for single pathogens.

Response: Special attention was paid to identification of pathogenic bacteria and other fungi from LRT sample from COPD patients. After LRT sample cultivation, some of these samples were reported positive by identification of pathogens, some were not. As your suggestion, p value for single pathogen was analyzed in revised version. This original table was moved to Supplemental Table 1.

Table 4

Comment 12: do you have any data about the class of the antibiotics? I suggest to explicit them in table 4 (what does it mean ≥1?). I suggest reporting p value also for single steroid therapy (systemic and ICS). I am not sure that combination between im/ev and inh could be an interesting information. Dose: I suggest inserting the route of administration in "dose of usage" (im, inhaled).

Response: We only counted the numbers of antibiotic classes in this research and we corrected the expression to “more than 1 class”. Some patients needed combination use of antibiotics in their initial treatment and some patients needed escalation antibiotics therapy for adjustment after clinical evaluation. Therefore, "more than 1 class" meant combination and/or escalation antibiotics therapy. As your kind suggestion, we inserted the route of administration in "dose of usage" (iv, inhaled) and p value for single steroid therapy was analyzed, respectively. The data of combination use of steroid therapy was deleted in the revised version.
Comment 13: How do you define "remission time"? It must be cleared in Methods. I suggest verifying the unit of measurement of bronchodilators.

Response: Remission time was defined as the duration of stabilization of clinical symptoms and disappearance of signs, like the typical symptoms of cough, sputum, wheeze, and the typical signs of wheezing rale. As your suggestion, we added the definition of remission time in the Methods section. We also verified the unit of measurement of bronchodilators.

Discussion

Comment 14: The first part of the discussion needs to summarize the main results of the paper. In addition the discussion is not fluent. After the results, novelty and comparison with literature should be addressed in a clearer way.

Response: Thanks for the kind suggestion. The part of discussion was revised in the new version. At the same time, the novelty and comparison with literature according to our results are addressed in discussion part.

Table 1

Comment 15: FEV1% (OQR) I think there is an error. Are functional values pre or post bronchodilators?

Response: As your suggestion, the error was revised. The functional values were post bronchodilators and were revised in the new version.