Author's response to reviews

Title: Non-invasive mechanical ventilation in patients with diffuse interstitial lung diseases.

Authors:

Stefano Aliberti (stefano.aliberti@unimib.it)
Grazia Messinesi (graziamessi@hotmail.com)
Silvia Gamberini (silvia.gamberini85@gmail.com)
Sveva Maggiolini (padme1981@hotmail.it)
Dina Visca (dinavisca@gmail.com)
Vanni Galavotti (vanni.galavotti@aopoma.it)
Fabio Giuliani (fabio.giulian@gmail.com)
Roberto Cosentini (r.cosentini@gmail.com)
Anna Maria Brambilla (brambi.brambi@gmail.com)
Francesco Blasi (francesco.blasi@unimi.it)
Raffaele Scala (raffaele_scala@hotmail.com)
Mauro Carone (Mauro.carone@fsm.it)
Francesca Luisi (francesca.luisi@virgilio.it)
Sergio Harari (sharari@hotmail.it)
Antonio Voza (antonio.voza@humanitas.it)
Antonio Esquinas (antmesquinas@gmail.com)
Alberto Pesci (alberto.pesci@unimib.it)

Version: 3  Date: 30 May 2014

Author's response to reviews:

May 30nd, 2014

Dear Editor,

The authors would like to thank both reviewers for their second analysis of the manuscript. We agree with all comments and recommendations suggested by the reviewers. We have changed the manuscript to comply with reviewers’ recommendations. The following is a detailed response to each reviewer’s recommendations.

Reviewer 1

Major Comment #1

You correctly did not classify patients with acute heart failure for the reasons raised by the reviewers. At this time I think it could be better to not consider at all these patients also in the descriptive analysis of the whole group. For the same reason, in the methods I think you don’t need to define so extensively Acute heart failure.
Reply to major comment #1

We thank the reviewer for her/his suggestion. We agree with her/him and we decided to delete all the informations on acute heart failure from the manuscript. We have changed the following sentence in Materials and Methods: “Patients with acute heart failure were not considered in light of the strong evidence recommending the use of NIV in this population [11].” We have also deleted the definition of acute heart failure in materials and methods. We have re-run all the statistics, although no significant changes appeared in the results. We have changed the results in the abstract, text and tables accordingly.

Major Comment #2

Actually the main result of your study is the better response in term of P/F ratio in the group of exacerbation due to pneumonia. This is also the principal issue of the study discussion. For this reason I think it may be good to better clarify throughout the study the presence of a primary outcome that is the improvement of gas exchanges and the secondary outcome that is the clinical failure. This is not always clear, above all in the "Study group and outcomes" paragraph.

Reply to major comment #2

We agree with the reviewer and we changed the materials and methods accordingly as follows:

“The evaluation of gas exchange was the primary outcome. Clinical failure and length of stay in the hospital (LOS) were secondary clinical outcomes.”

We also decided to cite in the discussion section a recent paper published on Intensive care Medicine [Brambilla AM. ref #15] showing a beneficial effect of helmet CPAP in patients with severe pneumonia in reducing the risk of meeting ETI criteria compared to oxygen therapy. Thus, the following sentence was modified:

“Cosentini et al. demonstrated that the application of non-invasive CPAP improves oxygenation in patients with pneumonia and reduces the risk of meeting ETI criteria in patients with severe hypoxemic ARF due to pneumonia compared to oxygen therapy [10, 15]. “

Major Comment #3.

In the group C there is also one patient with pneumothorax: did you treat also this patient with NIV?

Reply to major comment #3

NIV was applied to a patient with a pneumothorax after the insertion of a pleural drainage.

Minor comment #1.

"study groups and outcomes": the sentence "patients with pneumonia were grouped together…” there is somewhere a mistake inherited by the previous
version of the paper?

Reply to minor comment #1
We thank the reviewer. We have deleted this sentence.

Minor comment #2
Figure 1 Legend still refers to acute heart failure in the group A

Reply to minor comment #1
We thank the reviewer for her/his comment. We have fixed the legend.

Language corrections
We reviewed the text from an English perspective and some minor corrections were fixed along the manuscript.

Reviewer 2

Major Comment #1
Confusing information on the 5 patients with acute heart failure. The authors have eliminated these 5 patients from group A, and it seems that the information of these patients has not been reported in the revised version. However, there are statements in several parts of the manuscript regarding the efficacy of NIV in DILD with heart failure. The authors should clarify better if information of these 5 patients is included or not in the revised version and, if this is not included, all these statements should be revised accordingly. In some places, such as footnote of Figure 1, it seems that the original version has not been revised in this issue.

Reply to major comment #1
We definitely agree with the reviewer. Following the indications of the other reviewer, we decided to delete all the informations concerning acute heart failure. We have changed the following sentence in Materials and Methods: “Patients with acute heart failure were not considered in light of the strong evidence recommending the use of NIV in this population [11].” We have also deleted the definition of acute heart failure in materials and methods. We have re-run all the statistics, although no significant changes appeared in the results. We have changed the results in the abstract, text and tables accordingly.

Major Comment #2
Association of long-term oxygen therapy (LTOT) with clinical success. Table 4 shows a significantly higher rate of LTOT among patients with clinical success; however, this is not mentioned in the results and the discussion. How can they explain this finding? This needs to be stated in the abstract, results and commented in the discussion.
Reply to major comment #2
We understand reviewer’s comment. In the new version of the paper (without the 5 patients with AHF), no significant difference has been detected between the two groups regarding LTOT. Thus, we decided to avoid explanation of this finding.

Major Comment #3
Results, page 1, beginning of 3rd paragraph. "At six hours during NIV treatment...."? or better "Within six hours.....?"

Reply to major comment #3
We agree with the reviewer and we modified the sentence as follows: “At six hours of NIV treatment”.

Major Comment #4
Discussion, page 13, paragraph 2, line 8. Maybe the first time "in terms" appears should be deleted.

Reply to major comment #4
We completely agree. We have fixed this mistake as suggested by the reviewer.

Major Comment #5
Table 2. Please, add the initial FiO2 for PSV, as this information is reported for CPAP.

Reply to major comment #5
We agree with the reviewer and we have added the information as requested

Major Comment #6
Response on the lack of sample size calculation. I agree with the response, but this issue should be added in the limitations section.

Reply to major comment #6
Agree. We added this as a limitation of the study in the Discussion section as follows:
“[...] DILD are rare diseases and NIV is still an emerging treatment in these patients. In light of this, we should also acknowledge as limitation of our study the fact that we were not able to calculate an exact sample size of the study population.”

Language corrections
We reviewed the text from an English perspective and some minor corrections were fixed along the manuscript.