Author's response to reviews

Title: Clinical course and complications following diagnostic bronchoalveolar lavage in critically ill mechanically ventilated patients

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Author's response to reviews: see over
List of changes to the manuscript: “Clinical course following diagnostic bronchoalveolar lavage in critically ill mechanically ventilated patients”

Dear editor,

Thank you for giving us the opportunity to further improve our paper. We received valuable advice. We cite the statement of the reviewer first and subsequently give our comment and describe revisions.

Title: I would change in “Complications and Clinical course following diagnostic bronchoalveolar lavage in critically ill mechanically ventilated patients”?

We agree that adjusting the title can better highlight the focus of the paper. The title was changed as requested.

Methods: information about the relationship between the calibre of the bronchoscope and that of the endotracheal tube are lacking; this is a very crucial detail as it is determinants of severe respiratory mechanic changes (i.e. airways resistance and air trapping..)

The requested information was added to the method section.

Results: As the core of the paper is the safety of a potentially useful invasive procedure, I suggest to calculate the incidence of the overall complications in the studied population (respiratory and haemodynamic) that should be separated in complication(+) and complication(-). These two groups should be compared in terms of the main variables (admission diagnosis, comorbidities, ABG, apache II, SOFA, etc) with the aims of identifying predicting factors of complications (with logistic regression eventually)

Patients were divided into two groups: hemodynamic complications / no hemodynamic complications and respiratory complications / no respiratory complications. Those two groups were compared with regard to various demographic and clinical items: age, gender, APACHE II, SOFA, diagnoses at admission, severe sepsis, co-morbidities. The odds ratios with 95% confidence interval were calculated. The results are presented in 2 additional figures and described in the result section.

PaCO2 and pH data are lacking: I believe that the analysis and time course of these vital data, expression of lung function, must be included

The data were added as requested. (Table 3, results)

Non-infectious Interstitial lung diseases (ILD): ?further 7% of patients computer tomography of the thorax and lung biopsies were helpful in the diagnosis of interstitial lung diseases (bronchiolitis obliterans organizing pneumonia, usual interstitial pneumonia, graft versus host disease of the lung)? . The Authors should specify in the text when and why they performed lung biopsies (through bronchoscopy? in all pts?) and should empathize that to get to these non-infectious ILDs BAL is not enough!

In 64 out of 164 patients BAL fluid analysis could confirm a bacterial pneumonia (VAP). When BAL fluid analysis rejected the diagnosis of bacterial pneumonia, additional steps
followed to determine an alternative diagnosis. In 7% of patients a further workup included CT thorax and lung biopsy. This lead to the diagnosis of interstitial lung disease. The lung biopsies were not taken via bronchoscopy. The diagnosis of interstitial lung disease was based on findings from the lung biopsy pathology and not on results from BAL analysis.

**SOFA:** I do not see the usefulness of SOFA as marker of BAL-correlated complications; so I suggest to remove it from this analysis

The SOFA score as a parameter to indicate the clinical course following BAL was removed from the manuscript.

**Duration of complications:** in the results (both abstract, main text) the length of respiratory and haemodynamic changes has to be inserted (eg. reversibility after 1 and 24 hrs)

The duration was added to the sections.

**Table 1:** number are not readable because over-written. I would separate Hospital from ICU mortality; BAL positive: I would specify for a microbiological etiology. I would add length of stay in ICU/Hospital.

The ICU mortality was added to table. The microbiological etiology of VAP is mentioned in the result section.

**Table 4:** I suggest to put median and quartile values in the same row for drugs

Quartile values were put into the same row of the table.

**Limitations:** further limitation is the lack of the measurement of respiratory mechanic before, during and after FFB. Part of the included cases are retrospectively collected: this point has to be reported

These facts were added to the limitations.

**Discussion:** Table 5 provides an overview of the literature. [13-20] The studies differ in patient population, setting, applied diagnostic technique and length of observation. In general the authors judged the risk to gain ratio favourable?. These sentence is not clearly supported by the quoted studies. Please mitigate these statement.

The statement with regard to the existing literature was changed and mitigated.

**Usefulness of BAL for guide and deescalate antibiotic therapy:** I suggest to largely reduce this part in the discussion, as the authors did not show data about this issue; the digression is purely speculative

The discussion of this topic was reduced in size.

**Conclusions:** I do not agree with the conclusions as they are not supported by the findings of this non-controlled study. Please mitigate the conclusions (both in the abs and in the main text), and, at the same time, highlight the need for a controlled study (i.e. pts managed with FFB vs those managed with non-invasive strategy)

The conclusions were mitigated. The need for a controlled study was highlighted following the limitation remarks.