Author's response to reviews

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

Authors:

Ronny Schnabel (r.schnabel@mumc.nl)
Kim van der Velden (kim.vander.velden@mumc.nl)
Aart Osinski (aart_osinski@hotmail.com)
Gernot Rohde (r.rohde@mumc.nl)
Paul Roekaerts (p.roekaerts@mumc.nl)
Dennis Bergmans (d.bergmans@mumc.nl)

Version: 3
Date: 24 July 2015

Author's response to reviews: see over
Dear editor,

We received valuable critical comments from two reviewers on our manuscript. We thank you for giving us the opportunity to change parts of our article to improve on substance, clarity and readability. We cite the statement of the reviewer first and subsequently give our comment and describe textual revisions. We hope that we can provide you convincing arguments to present our findings to the readers of Biomedcentral Pulmonary Medicine.

Yours sincerely,
Ron Schnabel

The choice to separate analysis of patients with positive results or negative results of BAL is unclear for me. Table 4 should be clarified.

We agree that our considerations for separate analysis were speculatory. We revised our manuscript and present the data un-separated and improved on clarity of Table 4.

In the results, we lacked specific information concerning clinical characteristics of patients (comorbidities, immunosuppressed host, cardiac and respiratory chronic failure...) we need to know if baseline PaO2/FiO2 ratio are significantly different (202 vs 225) as well as FiO2 (data not shown), Hemodynamic (data not shown), vasopressors and concentrations of drugs used for sedation.

The paragraph was revised and the requested information added.

In Table 1 (patients demographics) co-morbidities (cardiovascular, respiratory, chronic renal failure, immunocompromised patients, patients with active malignancy, chronic hepatic failure) were added. The definitions of co-morbidty items were added to the methods section in the main document. The percentage of patients with severe sepsis following the Surviving Sepsis Campaign criteria were added. Since a separate analysis of BAL+ and BAL- patients have been waived we now report the percentage of BAL+ patients in Table 1. FiO₂ data were added to Table 4.

Why did the authors not consider hypertension and heart rhythm disturbances as cardiovascular complications? The authors should better describe the hemodynamic changes that occurred.
The definition of “hemodynamic instability” was revised and better described. Paragraphs in the method section, result section and tables were revised.

Figure 1 was added to the manuscript for better illustration showing hemodynamic and respiratory parameters before BAL, one hour and 24 hours after BAL.

**Information about non-infectious and not determined etiology subsets of patients should be better detailed: e.g. what diagnosis of interstitial lung disease means?**

The paragraph was revised and information added to the result section.

*In further 7% of patients computer tomography of the thorax and lung biopsies aided in the diagnosis of interstitial lung diseases (bronchiolitis obliterans organizing pneumonia, usual interstitial pneumonia, graft versus host disease of the lung).*

**Concerning BAL technics, 120 ml of saline were injected for BAL but we lacked information about the quality of this sampling (volume of recovery, cytologic information …).**

Information about the quality of BAL sampling were collected and added to the method section.

*The BAL fluid was regarded non-representative if the volume of recovery was <20mL, the total cell count was < 60.000/mL, the presence of squamous epithelial cells was >1%, the presence of bronchial epithelial cells was>5% or in the presence of extensive amounts of debris and damaged cells. Further BAL workup in the laboratory included: a differential cell count, microscopic investigation of a Gram-stained preparation, quantitative bacterial and fungal culture.*

*I am not convinced that SOFA score is relevant to assess the tolerance of fiberoptic bronchoscopy (renal failure is a very unusual complication of FOB).*

SOFA score is an established tool and frequently used to compare the diurnal clinical course of patients. We agree that it has its limitations in this context. Certainly no change in renal, liver or central nervous system function can be expected after BAL except in case of severe clinical deterioration with persisting shock.

**The introduction is not focused on BAL tolerance but mainly on the role of BAL in ICU, which may not appropriate for the topic of the study.**

The role of BAL as a diagnostic tool in ICU had been questioned. To justify the use of BAL in critical care patients we have to trade off benefits against risks. Therefore we talk about the role of BAL in ICU. In the current revision of the introduction we focus more on “BAL tolerance” to make it more appropriate.

*In order to evaluate FFB and BAL as a diagnostic tool in ICU patients, it is necessary to balance benefits with potential hazards caused by the invasiveness of the technique. The focus of the present study is on the clinical tolerance of FFB and BAL. The clinical course of critically ill mechanically ventilated patients after a diagnostic FFB and BAL was investigated.*

**Table 4 : although kPa is the international unit of pressure, it is more usual to give the results of PaO2/FiO2 ratio in mmHg.**
The results in mmHg were added for readers more accustomed to this scale.

**Table 5 : to complete the list of studies, it should be added the study of Turner et al, Crit Care Med 1994 Feb;22(2):259-64.**

Compared to the other cited studies in the literature overview, the study by Turner monitored the complication rate of fiberoptic bronchoscopy in both therapeutic and diagnostic procedures. Out of 147 procedures in 107 patients only 23 procedures were bronchial brushes in pulmonary infiltrations. Nevertheless, the study was added to the overview of literature as suggested.

**There are several typos in the manuscript.**

The manuscript was scrutinised to eliminate typos.

**Limitations of the study should be added to the discussion.**

A paragraph dealing with the limitations of the present study were added to the discussion.

*Limitation of the study is its observational design of FFB and BAL as standard of care in a single centre without a randomized control group. In the assessment of a long term clinical course it might be difficult to differentiate the natural course of the underlying disease from the impact of the bronchoscopic intervention.*