Author's response to reviews

Title: Outcome of corticosteroid administration in autoimmune pulmonary alveolar proteinosis

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Version: 7 Date: 22 July 2015

Author's response to reviews: see over
July 23th, 2015
BMC Pulmonary Medicine
MS: 116284394165190

Dear Dr. Amit Gaggar

We greatly appreciate for accepting our manuscript. We carefully responded to each item in STROBE checklist as follows.

Title and abstract or the abstract
1 (a) Indicate the study's design with a commonly used term in the title
We add “a retrospective cohort study” in the title.
(b) Provide in the abstract an informative and balanced summary of what was done and what was found
We described an informative and balanced summary of what was done and what was found in the abstract (P3).

Introduction
Background/rationale
2 Explain the scientific background and rationale for the investigation being reported
We clearly explain the scientific background of this study and described the rationale for our investigation (P5-6).

Objectives
3 State specific objectives, including any prespecified hypotheses
In page 6, line 2-8, we state the objectives, including some prespecified hypothesis.

Methods
Study design
4 Present key elements of study design early in the paper
In page 7, we presented key elements of study design.
5 Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection

In page 7, the first paragraph, we described locations (165 major pulmonary centers in Japan) and relevant dates (November 21th 2013 to November 20th 2014) including periods of recruitment, exposure, follow-up, and data collection.

Participants

6 (a) Cohort study—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up

In page 7, line 8-20, we gave the eligibility criteria, and the sources and methods of selection of participants. As the study is a retrospective cohort study, we did not follow-up the participants.

Variables

7 Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable

In page 8, the second paragraph, we defined all outcomes (disease severity scoring). In page 9, the first paragraph (Statistical analysis), we exclude the possibility of exposures, predictors, potential confounders, and effect modifiers. We also described the diagnostic criteria in page 7, the first paragraph.

Data sources/ measurement

8* For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group

In page 8, the second paragraph, we described the sources of data (disease severity score) and details of methods of assessment (definition of disease severity score). Comparability of assessment methods were mentioned at line 15-18 in page 8.

Bias 9 Describe any efforts to address potential sources of bias

In page 14, the second paragraph, we described about selection bias of study
subjects.

Study size 10  Explain how the study size was arrived at
In page 7, the first paragraph, we described the method to determine the number of screened patients.

Quantitative variables 11  Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
In page 12, the third paragraph, we explained how disease severity score were handled. In the same paragraph, we subdivided the study subjects according to the cumulative dose of corticosteroid, because we did not set the control subjects without corticosteroid therapy.

Statistical methods 12
(a) Describe all statistical methods, including those used to control for confounding
We described all statistical methods, including those used to control for confounding in page 9, the first paragraph.

(b) Describe any methods used to examine subgroups and interactions
In page 12, the third paragraph, we subdivided the study subjects according to the cumulative dose of corticosteroid.

(c) Explain how missing data were addressed
In this study, we used complete data.

(d) Cohort study—if applicable, explain how loss to follow-up was addressed
As this study is a retrospective cohort study, we did not followed-up the subjects.

(e) Describe any sensitivity analyses
We did not perform any sensitivity analyses.

Participants 13*
(a) Report numbers of individuals at each stage of study—eg numbers
potentially eligible,
In page 7, the first paragraph and Figure 1, we described the report numbers of individuals at each stage of study.

(b) Give reasons for non-participation at each stage
In page 7, the first paragraph and Figure 1, we gave reasons for non-participation at each stage.

(c) Consider use of a flow diagram
We showed as Figure 1.

Descriptive data 14*
(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
We showed in Table 1.

(b) Indicate number of participants with missing data for each variable of interest
We used complete data in this study.

(c) Cohort study—Summarise follow-up time (eg, average and total amount)
We summarized the follow-up time in the supplemental table 1.

Outcome data 15*
Cohort study—Report numbers of outcome events or summary measures over time
In the supplemental table 1, we reported numbers of outcome events or summary measures over time.

Main results
16 (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
We did not applied unadjusted estimates. We did not make any confounders adjusted.
(b) Report category boundaries when continuous variables were categorized. 
In this study, we used disease severity score that is not continuous variables.

(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period. 
In this study, we did not consider translating estimates of relative risk into absolute risk for a meaningful time period.

Other analyses 17 Report other analyses done—even analyses of subgroups and interactions, and sensitivity analyses. 
In page 12, the third paragraph, we showed the overall cumulative worsening rate using Kaplan-Meyer analysis.

Discussion  
Key results 18 Summarise key results with reference to study objectives. 
We summarised key results with reference to study objectives in page 14, the first paragraph.

Limitations 19 Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias. 
In page 14, the third paragraph, we described difficulty of setting the control subjects in a retrospective study.

Interpretation 20 Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence. 
In page 14, the third paragraph, we described about possibility for the selection bias of the study subjects and reason for subdividing the subjects to low dose and high dose steroid groups.

Generalisability 21 Discuss the generalisability (external validity) of the study results. 
As we did not set any control subjects in this study, we think it is difficult to generalize our finding. However, as we discussed in page 15, the first
paragraph, our results was confirmed by analysis between high and low corticosteroid groups and survey of confounding factors of these two groups.

Other information
Funding

Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based
We gave the source of funding and the role of the funders for the present study.

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