Author’s response to reviews

Title: Dynamics of microbiota during mechanical ventilation in aspiration pneumonia

Authors:

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Author’s response to reviews:

Dear, Dr. James Edwards and Dr. Tamara Hughes

Thank you for carefully reading our manuscript entitled “Dynamics of microbiota during mechanical ventilation in aspiration pneumonia” (PULM-D-19-00238) and for considering forward for acceptance our manuscript. We have read the editor’s and reviewer’s comments very carefully, and have revised our manuscript. We are hereby sending a revised version of our manuscript.

Our point-by-point responses to the editor’s and reviewer’s comments are below.

We hope that our manuscript is now acceptable for publication in BMC Pulmonary Medicine. We are looking forward to your favorable consideration.

Sincerely yours,

Ken Otsuji M.D.

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Responses to the editor comments:

1. Reviewer comments/copy edit

-- Please address the remaining comments from reviewer 1, seen below. We recommend that you ask a native English speaking colleague to help you copyedit the paper. If this is not possible, you may need to use a professional language editing service. Use of an editing service is neither a requirement nor a guarantee of acceptance for publication.

Response 1.
We addressed the comments from reviewer 1. Please check “Responses to the Reviewer’s (Reviewer #1) comments”. We have corrected English writing of our manuscript by native English speaking colleague.

2. Consent to participate

-- In your “ethical approval and consent to participate” section of your declarations please confirm if an ethics committee approved the procedure for verbal consent, and why they felt the need for written consent was not necessary for this study. Please also detail how you documented the consent.

Response 2.
We rephrased the content following your comment. Page 17, line 357-360. “This study was approved by the Ethics Committee of Medical Research, University of Occupational and Environmental Health, Japan (No. H27-233). Since no new invasive procedures were required to participate in the study, consent to participate in the research was obtained orally from patient or their families and these contents were recorded in the electronic medical record.”

3. Authors’ contributions

-- Please provide further clarification on the individual contributions of KO.

Response 3.
We corrected author’s contribution following your comment. Page 16, 350-351. “KO is corresponding author which contributed for study design, data collection, data analysis, statistical analysis, literature search and writing.”

4. Funding

-- In the Funding section, please also describe the role of the funding body in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript.
Response 4.
We corrected the content following your comment. Page 16, 341-343. “The design, performance, data analysis of this study and writing the manuscript were funded by a Grant-in-Aid for Young Scientists (B) (grant no. 17K17078) from the Japan Society for the Promotion of Science (JSPS).”

5. Corresponding author

-- Please note that the corresponding author emails addresses in your manuscript file differ from those entered in the submission system - please correct so they are consistent with each other.

Response 5.
We have corrected the email address of my personal information in BMC to “otsujiken@clnc.uoeh-u.ac.jp” so as to consistent with the manuscript.

6. Clean copy

-- At this stage, please upload your manuscript as a single, final, clean version that does not contain any tracked changes, comments, highlights, strikethroughs or text in different colours. All relevant tables/figures/additional files should also be clean versions. Figures (and additional files) should remain uploaded as separate files. Please ensure that all figures, tables and additional/supplementary files are cited within the text.

Response 6.
We performed following your suggestion.

Dear Dr. Gisli G Einarsson (Reviewer #1),

Thank you for carefully reading our manuscript entitled “Dynamics of microbiota during mechanical ventilation in aspiration pneumonia” (PULM-D-19-00238) and for considering forward for acceptance our manuscript. We have read the editor’s and reviewer’s comments very carefully, and have revised our manuscript. We are hereby sending a revised version of our manuscript.

Our point-by-point responses to your comments are indicated below.

We hope that our manuscript is now acceptable for publication in BMC Pulmonary Medicine. We are looking forward to your favorable consideration.

Sincerely yours,

Ken Otsuji M.D.

Responses to the Reviewer’s (Reviewer #1) comments:
Reviewer #1: Gisli G Einarsson (Reviewer 1): In general, Otsuji et al. have addressed my points raised during first round of review. I find that the authors have addressed the main limitations related to the current study in a sufficient manner. However, I do find the manuscript somewhat hard to follow in places and some attention might be required regarding sentence structure etc. Below are few examples that require attention.

General points:

Comment 1
Page 1, line 20, stating "...urgent social problem...", I think that "social problem" would in general more refer to problems such as crime and poverty etc. I would suggest that the authors would consider revising this statement and frame this somewhere along the lines of high economic and health-related impact or cost.

Response 1
We rephrased the sentence following your suggestion. Page 1, line 20, “The emergence of multi-drug resistant pathogens is an urgent health-related problem, and the appropriate use of antibiotics is imperative.”

Comment 2
Page 3, lines 56-57, stating "Although more than 700 bacterial species or phylotypes have been detected in the oral cavity by genetic analysis, 30-60% of them have not been cultured [12,13].". This sentence is a bit confusing, as either 70% or 30% of anaerobes have not been cultured according to this statement. I would suggest that for clarity the authors would omit the numbers and instead say something such as "large number of anaerobic species have yet to be detected by culture using conventional methodologies".

Response 2
We rephrased the sentence following your suggestion. Page 3, line 57-59. “Although over 700 bacterial species/phylotypes have been detected in the oral cavity by genetic analysis, a large number of anaerobic species have yet to be detected by culture using conventional methodologies [12,13].”

Comment 3
Page 5, lines 104-105, stating "The tracheal aspirate (B) were culture microaerobically...", would suggest to change this to "...were cultured under microaerophilic conditions..."

Response 3
We changed the sentence following your suggestion.

Comment 4
Page 6, line 119, "RDP (ribosomal data project)..." should be "database" not "data".
Response 4
We collected the sentence following your suggestion.

Comment 5
Page 6, line 120, stating "The sequences less than 90% value were deemed unclassified", the authors need to state what this value denotes. Is this "confidence threshold" or "similarity cut-off"?

Response 5
Confidence threshold was used. We corrected the sentence following your suggestion. Page 6, Line 120-122. “The highly accurate sequences were classified into the level of genus with RDP (ribosomal database project) classifier (confidence threshold 90%) [26]. The sequences of less than 90% confidence threshold value were deemed unclassified.”

Comment 6
Page 7, description of PCA plots. The authors need to state which R package (and package version) was used to produce the plot. The cited paper by Morotomi et al. (2011) gives a brief explanation of the justification for doing PCA plots, but does not provide specific information regarding the R package used.

Response 6
We rephrased the sentence as follows. Page 7, line 132. “R software version 3.4.0. (http://cran.r-project.org/) was used for the PCA as described previously [27].”

Comment 7
Page 8, line 163, stating "The culture results and phylotypes detected by clone library method in each case were shown in Table 2". Suggest to change "…were shown…” to "are shown".

Response 7
We rephrased the content following your suggestion.

Comment 8
Page 9, line 175, remove white-space between "PC 1"

Response 8
We removed white-space following your suggestion.