

Dear Editor,

Thank you for carefully reviewing our manuscript previously titled “**Risk factors of mortality and severe disability in the patients with cerebrovascular diseases treated with perioperative mechanical ventilation**” for possible publication in the World Journal of Clinical Cases. We are grateful to you and your reviewers for their constructive critique. We have revised the manuscript, highlighting our revisions in red. And have attached point-by-point responses detailing how we have revised the manuscript in response to the reviewers' comments below.

Thank you for your consideration and further review of our manuscript. Please do not hesitate to contact us with any further questions or recommendations.

Yours Sincerely,

Kan Xu

Reviewer comments

Reviewer #1:

Title: Follow EQUATOR guidelines as applicable to your study.

Response: Thank you for your important comment.

1. The revised title is “Risk factors of mortality and severe disability in the patients with cerebrovascular diseases treated with perioperative mechanical ventilation”.
2. A background description is added to the Abstract. “Background: The prognosis of cerebrovascular diseases treated with mechanical ventilation during perioperative has not been clearly reported.”

Methods: Mention study period, and data management method Material and Methods Were there any exclusion criteria? If yes, mention How you have reached to the sample size?

Response: Thank you for your insightful comment.

Methods: we rewrite the method part according to the EQUATOR guidelines. This is a big modification, please see the text for detail.

1. Data management: Our study is a retrospective study. We selected all patients from June 2016 to June 2019 based on the inclusion and exclusion criteria.

The inclusion criteria were as follows: 1) patients had neurovascular surgery perioperative ventilator assisted breathing, 2) patients received mechanical ventilation for at least 48 h, and 3) age ≥ 18 years. Patients whose family members gave up treatment or who died of disease were excluded.

2. Sample size: the sample size of this study is based on EPV rule (events per variable) [1]: the number of patients with targeted end points divided by the number of predictor variables considered in developing the risk score (prediction model). EPV rule specifies the minimum requirement of 10 EPV ($EPV \geq 10$) for obtaining the reasonably reliable predictions. The outcome of our study has three categories: good recovery, severe disability, and death. Taking death as an example, there were 50 deaths in the outcome and we included three predictor variables in logistic regression. Therefore, it can be considered to reach the sample size.

[1] Moons KG, Royston P, Vergouwe Y, Grobbee DE, Altman DG. Prognosis and prognostic research: what, why, and how? *BMJ* 2009;338:b375. <https://doi.org/10.1136/bmj.b375>

Please mention Results Table 1: GCS data is better presented in Median and IQR Mention the SAH gradings and include in analysis. Similarly, patients' illness severity scores other than GCS (like SOFA / MODS / APACHE-II or III will be helpful)- include at least one.

Response: Thank you for your constructive comment.

1. GCS data has been presented in median and IQR.
2. We added SAH gradings according to Hunt-Hess method [2] and carried out statistical description and analysis.
3. The assessment of the condition of patients with cerebrovascular disease is mainly the GCS score, and the patients with cardiopulmonary and renal dysfunction will not be operated on, so the GCS score is used in this article.

[2] Fernandez A, Schmidt JM, Claassen J, et al. Fever after subarachnoid hemorrhage: risk factors and impact on outcome. *Neurology*. 2007;68(13):1013-1019. Doi:10.1212/01.wnl.0000258543.45879.f5.

Table 2 shows that 85% of your patients were started on MV in the postoperative period and the causes mentioned are unlikely to be immediate postoperative reason? When these patients required MV? When did the shock (?sepsis) or Pneumonia ? HAP happened? It is very much unclear. Your study will require multivariate logistic regression analysis to accept the result. Best of luck.

Response: We thank the reviewer for this suggestion. We modified the statistical analysis method and added multiple logistic regression. The revised statistical analysis is described as: "Discrete variables were expressed by frequency (%), χ^2 test and fisher exact test were used to compare outcomes of the patients with various features. The Kolmogorov-Smirnov test was used to test the normality of the continuous variables. Continuous variables that fit the normal distribution were expressed by either mean \pm SD otherwise as median and interquartile range

(IQR). Wilcoxon rank sum test or Kruskal-Wallis rank sum test was used to compare outcomes of the patients with various features. Ordinal logistic regression was used to association of mortality and functional outcome in patients with cerebrovascular disease and related factors. R software (R version 4.1.2) was used to perform all analysis and P value < 0.05 was considered as significant.”

Reviewer #2: The article is within the scope of the journal. It is well written and structured. It is easy to read and it is clear on the objectives and methods used to obtain the results. In this sense, the experiment is well designed and executed. The results obtained represent an advance in the area of knowledge. However, it could be improved as follows:

- c) The discussion section is reduced and the article would improve if the results obtained are valued by comparing them with other similar works.

Response: Thank you for your valuable comment. We have reduced the length of the discussion section and have rewritten the discussion section based on the results of multiple logistic regression analysis. In addition, we increased the comparison of similar research results when analyzing the risk factors. As there are many revisions in the discussion section, please refer to the revised manuscript for details.

- b) A paragraph describing future lines of work should be inserted in the conclusions section.

Response: Thank you. We have inserted a paragraph describing future work in the Discussion section. The description is as follows:

“In the future, we will include more samples, fully consider various confounding factors, and conduct a prospective cohort study to verify the causal relationship between various ventilation causes and the poor prognosis of patients with cerebrovascular diseases undergoing perioperative mechanical ventilation.”

- c) The state of the art is very poor. It should be expanded with more bibliography

Response: This point is well taken. We added 20 new references in the revised manuscript to better support our research.

We tried our best to improve the content of the manuscript and made some changes in this manuscript. These changes will not influence the content and framework of the paper. And here we did not list the changes but marked by red in revised paper.

We appreciate for Editors/Reviewers' warm work earnestly, and hope that the correction will meet with approval.

Once again, thank you very much for your comments and suggestions.

Best wishes