Author's response to reviews

Title: A new prognostic scale for the early prediction of ischemic stroke recovery mainly based on traditional Chinese medicine symptoms and NIHSS score: a retrospective cohort study

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Author's response to reviews: see over
Response to the first reviewer’s comments

Dear reviewer,

Thank you very much for your letter and the comments from the referees about submitted to Research Article titled "A new prognostic scale for the early prediction of ischemic stroke recovery mainly based on traditional Chinese medicine symptoms and NIHSS score: a retrospective cohort study," (MS number 8929410621621626). Now we have revised the manuscript according to the reviewers’ comments. Most of the revisions are in the manuscript. Some explanations of our manuscript are as follows.

Major Compulsory Revisions

1. Introduction should be succinct and focus.
   
   **Answer:** I have modified the introduction part, please look at the revised manuscript.

2. The definition of serious illness, such as liver, kidney, hematopoietic system, endocrine system and osteoarthritis should be clarified.
   
   **Answer:** I have added some description about the definition of serious illness, please look at the revised manuscript.

3. As we know, in most large stroke clinical trials, mRS scale is the most used tool for evaluation of prognosis, why the author choose the BI?
   
   **Answer:** Barthel index (BI) is a kind of activities of daily living (ADL) assessment method commonly used in rehabilitation institutions of the United States. BI evaluation, as a simple method with high reliability and sensitivity, is widely used and most studied to assess the change of quality of daily life of ischemic stroke patients. Returning to life or improving quality of life is the ultimate goal of neural functional recovery for ischemic stroke patients.

4. According to the flowchart of patients recruitment, only 77% patients have full complete the outcome assessments, and it means 23% patients were excluded from the analysis due to incomplete data collection, so the results should be interpreted cautiously. Whether these patients more severe? Or more older? Et al.
   
   **Answer:** To develop a new prognostic scale of ischemic stroke, we performed a retrospective analysis in this study based on the project of Major State Basic Research Development Program of China (973 Program NO.2003CB517102). Data deficiency may affect the efficiency and feasibility of research results, so we screened these patients who full complete the outcome assessments (especially the data of BI on 90th day were completely recorded) rather than avoid these patients more severe and older.

5. Age and NIHSS are the most important predictor of prognosis, the author should provide whether the TCM symptoms or TCM symptoms scores give more
predictive value than age and NIHSS, but not combined them to evaluate. That means whether the TCM symptoms improve the prognostic value of age and NIHSS.

**Answer:** Through statistical analysis, we have found that the scale combined age, NIHSS and TCM symptoms or TCM symptoms scores has higher specificity and sensitivity to predict the 90-day outcomes of ischemic stroke patients than combined application of age and NIHSS. That means the TCM symptoms or TCM symptoms scores improve the prognostic value of age and NIHSS.

6. It seems that TCM symptoms be weighted more scores, such as change in circumrotating during the first 3 days [0(disappear);2(keep);4(appear)], change in tinnitus during the first 3 days [0(disappear);2.5(keep);5(appear)]. Please explain the rationality.

**Answer:** From the clinical perspective of Western medicine, circumrotating and tinnitus are the most common symptoms of posterior circulation ischemic generally considered as a relative dangerous type of ischemic cerebrovascular disease. On the other hand, circumrotating and tinnitus in line with the characteristics of the wind evil of traditional Chinese medicine may quickly change during the first 3 days.

**Minor Essential Revision**

1. How patients be recruited should be more detailed?

**Answer:** This was a retrospective study of developing a new prognostic scale of ischemic stroke on the basis of original experimental data, we have introduced the screening process of ischemic stroke patients met the inclusion criteria in the form of a flowchart in detail. But the process of subjects recruitment should be detailed in the original experimental data rather than in this secondary data analysis.

2. NIHSS, BI should be expressed using median.

**Answer:** Statistically speaking, NIHSS and BI should be expressed in the form of mean ± standard deviation (SD) as measurement data. And many articles collected by SCI are mostly used this form to present.

3. Other prognostic scales should be discussed in the discussion.

**Answer:** I have added this section in the discussion, please look at the revised manuscript.

4. Reference 30 is not China guideline for cerebrovascular disease prevention and treatment.

**Answer:** I am sorry that I made a mistake in this sentence, I have corrected it, please look at the revised manuscript.
5. Diagnostic criteria of ischemic stroke should be listed, because the criteria is not familiar with the western countries.

   Answer: I have added this section in the revised manuscript, please check it.

**Discretionary Revisions**

1. Diagnostic criteria should be forward to data collection.

   Answer: I have adjusted the order of the two parts, please look at the revised manuscript.

2. In the Exclusion criteria section, No.2,6,8 is unnecessary.

   Answer: I agree with the reviewer’s point, No.2,6,8 of the Exclusion criteria section have been removed.

3. ‘However, 16 NIHSS score cannot replace TCM symptoms & signs completely in predicting outcome for stroke patients’ is not suitable.

   Answer: I have revised this sentence. Actually, what I want to express is “NIHSS is one of the most common assessment methods to predict the outcome of ischemic stroke, we found it has some relationship with some TCM symptoms which means TCM symptoms has a predictive value for predicting the outcome of ischemic stroke”.

4. Most references should be updated.

   Answer: Yes, I have updated some references, please see the revised manuscript.
Response to the second reviewer’s comments

Dear reviewer:

Thank you very much for your letter and the comments from the referees about submitted to Research Article titled "A new prognostic scale for the early prediction of ischemic stroke recovery mainly based on traditional Chinese medicine symptoms and NIHSS score: a retrospective cohort study,”(MS number 8929410621621626). We have checked the manuscript and revised it according to the comments. Most of the revisions are in the manuscript. Some explanations regarding the revisions of our manuscript are as follows. If you have any question about this paper, please don’t hesitate to let me know.

Minor essential revisions

1) Table 2 could be sorted in descending values of correlation coefficient values for an easier interpretation of data.
2) Page 4: Please do not start sentences with “And (lines 9 and 19, and several other pates).
3) Page 4, line 15: typo in ‘treatmen’
4) Page 9, line 22: typo in ‘analysisd’
5) Tables 6 and 8 might be merged because their information is quite the same.

Answer: I am sorry that there were many grammar mistakes and spelling mistakes in this article, I have amended in the original manuscript. In addition, thanks a lot for your valuable advice on the above issues (question 1 and question 5), but about question 5, there were some differences between the two tables, the result of the Table 6 was preliminary obtained by screening prognosis factors however the Table 8 presented the final form of the new scale after validation. I have already made revisions as you suggest. Please check them, thank you again.