Peer Review File

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Reviewer A

Duan et al used statistical analyses to identify variables associated with complex febrile seizure that could predict secondary seizures. The conceptual basis of the study is sound but the description of the analyses omitted key details that make it difficult to know how they were carried out. The disparity in the sample size and the sample size used for training and validation were concerning. There may be a legitimate reason for this, but it was not explained. Coupled with the poor justification for the tests and the limited discussion of the results, the manuscript generates more skepticism than enthusiasm. This is unfortunate as the results could be very important for predicting which children that experience complex febrile seizures could be at risk for secondary seizures as well as point to a mechanistic connection between the two. Below I offer some suggestions as to how the article can be improved:

Reply 1: We thanks for your positive feedback.

1A) The nomogram predictive model is new to this reviewer. How is this analysis different from or coupled with the ROC curve analysis? Logistic regression analyses were also used but this test was also not described. A poor description of these tests and how they were carried out created a great deal of confusion. As stated above, the differences in the sample size and that used in analysis was a serious concern.

Reply 1: We have added the description of the test in the methods section.

1B) Who were the controls in the study?

Reply 2: Children with complicated febrile seizures but did not suffer from secondary epilepsy were the controls. We have stated it in the methods section.

2) This is a minor point, but while ‘complicated seizures’ has been used it really should be ‘complex seizures. If a problem is complex, it means that it has many components. Complexity does not evoke difficulty. On the other hand, complicated refers to a high level of difficulty. If a problem is complicated, there might be or might not be many parts, but it will difficult to solve. This manuscript aims to sort out which components lead to secondary seizure. Therefore, ‘complex’ is a more appropriate term.

Reply 2: We have changed the 'complicated' to 'complex' in the entire text.

3) The terms “growth and development” were used throughout the study but never defined. No elements of the Gessel Development Scale were described.

Reply 3: The Gesell Development Scale score was provided in the test. We have added some content in the discussion in the revised version.

4) The manuscript suffers from a lack of appropriate references. Very few of the references address outcomes from Febrile Seizures or Febrile Status Epilepticus. There are many large studies that address this (i.e., FEBSTAT study) as well as several animal models, and none are mentioned here. The majority of the references seem tangential, to the point of being random. The reduction of systemic seizures to "excessive excitement" suggests the authors have a great deal of reading to do.
Reply 4: We have added reference 21 (FEBSTAT study).

Reviewer B

First of all, my major concern for this study is the present study has three research focuses, risk factors, accuracy of prediction model, and the prognostic role of secondary epilepsy, which is too many. In fact, a clinical study is suitable for answering one clinical question only. The authors need to consider to report the one which is clinically important and more suitable for the current data.
Reply 1: We thanks for your feedback. We hope to keep these three parts, thank you.

Second, the title did not describe the clinical research design of this study, i.e., a retrospective cohort study.
Reply 2: We have added it in the title.

Third, the abstract needs some revisions. The background did not describe the knowledge gaps on and the clinical significance of this research focus. The methods did not describe the inclusion of subjects, the assessment of baseline clinical factors, follow up procedures, the generation of training and validation samples, and outcome assessment of secondary epilepsy and development. The results need to briefly summarize the characteristics of the study sample, quantify the findings by reporting OR and P values, and the sensitivity and specificity parameters of the model. In the conclusion, please have more detailed comments for the clinical implications of the findings.
Reply 3: We thanks for your positive feedback. We have revised it accordingly. However, we failed added all the content to the abstract due to the limitations of the words.

Fourth, the introduction of the main text is not adequate, the authors did not review what has been known on the factors associated with, the available prediction models for, and the prognostic role of secondary epilepsy in children with complicated febrile seizures, did not have

comments on the limitations and knowledge gaps of prior studies, and importantly, what the potential clinical significance of this research focus is.

Reply 4: We have added.

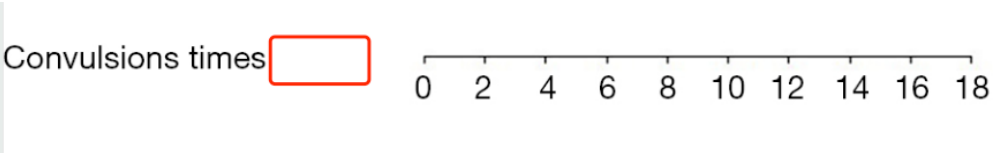
Fifth, in the methodology of the main text, please accurately describe the clinical research design, sample size estimation, follow up procedures, how the training and validation samples were generated, details of the Gesell developmental scale, and diagnosis of secondary epilepsy. In statistics, please describe the detailed procedures of multiple logistic regression analysis and the calculation of sensitivity and specificity of the prediction model. The authors should not rely on AUC only to assess the accuracy of the predictive model because sensitivity and specificity are more important, which should be at least 0.75. The authors need to do multiple regression analysis to ascertain the independent effect of secondary epilepsy on growth and development, the current analysis on this is univariate analysis only.

Reply 5: We have revised the methods accordingly.

Reviewer C

1. Figure 3

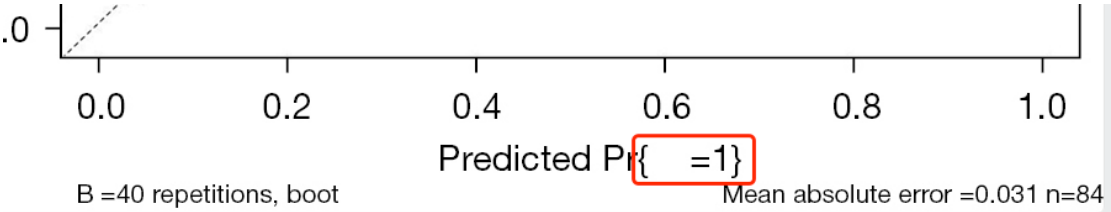
Please provide the unit here.



Reply: We have revised figure 3.

2. Figure 4

Please double check if here is correct.



Reply: We have revised the figure 4, see the attached files.

3. Table 1

Please explain EEG in the table footnote.

Reply: We have added the explanation in the footnote of table 1.