Author’s response to reviews

Title: Clinical prediction and diagnosis of neurosyphilis in HIV-negative patients: a case-control study

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Reply to the Reviewer

Reviewers' Comments to Author:

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1. The diagnosis of neurosyphilis must be based on the results of lumbar puncture. In line 139, the results of laboratory tests were collected within 90 days before or after the lumbar puncture. If a patient underwent multiple syphilitic serological tests during this long time range, which result would be selected into analysis?

Response: Thank you for your comments. As you said, in such a long period of 180 days, part of patients would take syphilitic serological tests for several times. In this study, if a patient underwent multiple laboratory tests, we selected the results of the first test conducted before treatment into analysis. Because these results have not been affected by the drug before treatment, which could reflect the real situation of these patients. In the included 100 patients, syphilitic serological tests were only conducted once before treatment. We have added a description on Page 8 lines 140-142 in the revised manuscript.

2. How were titer data processed in logistic regression analysis? It should be stated clearly in the statistical analysis section. Besides, in line 214-217, when the CSF TPPA titer, CSF protein, and CSF WBC increased one common unit, patients were 1.004, 1.005, and 1.120-fold more likely to be diagnosed as neurosyphilis. These ORs had statistical significance while the clinical value was little. Why not transform the CSF TPPA titer, CSF protein, and CSF WBC into categorical variables by cutoffs into logistic regression analysis?

Response: Thank you for your suggestions. In our study, TPPA titer and TRUST titer were treat as independent variables of the logistic regression. Before data analysis, we made reciprocal and logarithmic transformation to the titer data. For example, TRUST titer 1:64, after transformation log2(64) =6 [1, 2]. We have added a description on Page 9 lines 167 in the revised manuscript. We transformed the CSF TPPA titer, CSF protein, and CSF WBC into dichotomous variables by cutoff values and then performed logistic regression analysis. The results of multivariable logistic regression also showed neurological symptoms (OR=46.920, 95% CI:2.945-747.637, p = 0.006) , CSF TPPA titer (OR=76.000, 95% CI:16.030-360.323, p&amp;lt;0.001), CSF protein (OR=30.569, 95% CI:2.121-440.487, p = 0.012), and CSF WBC (OR=5.540, 95% CI:1.096-27.995, p = 0.038) were included in the model. We have added a description on lines 248-253 in the revised manuscript.
3. In line 238, when neurological symptoms, CSF protein, and CSF WBC were combined, the sensitivity and specificity were 92.00% and 33.30%, respectively. It should be described in detail how the sensitivity and specificity be calculated in a combination.

Response: Thank you for your suggestion. Because neurosyphilis is seriously harmful, it is clinically necessary to improve the sensitivity of the diagnosis of neurosyphilis. Combination of neurological symptoms, CSF protein, and CSF WBC meant that when the patient had neurological symptoms or any of the indicators (i.e. CSF protein and CSF WBC) exceeded the cutoff values, the patient was considered to be neurosyphilis. Then predictive diagnosis and real diagnosis were used to calculate sensitivity and specificity. The method used to combine neurological symptoms, CSF TPPA, CSF protein, and CSF WBC was similar. We have added a description on Page 13 lines 243-247 in the revised manuscript.

4. In table 1, the meaning of the data in brackets should be described in headings.

Response: Thank you for your suggestion. We have added a description in Table 1 in the revised manuscript.

Reference
