

Please resolve all issues in the manuscript based on the peer review report and make a point-by-point response to each of the issues raised in the peer review report. Note, authors must resolve all issues in the manuscript that are raised in the peer-review report(s) and provide point-by-point responses to each of the issues raised in the peer-review report(s); these are listed below for your convenience:

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: In this retrospective study, the authors aimed at exploring the value of mALB, mALB/U-CR, U-CR,  $\beta$ 2MG and RBP in early detection of Diabetic retinopathy (DR). The authors used observation indicators and correlation analysis to verify the hypothesis of them. The results showed that the levels of mALB,  $\beta$ 2MG, RBP, mALB/U-CR, and U-CR in the PDR group were higher than those in the NPDR and NDR groups ( $P < 0.05$ ), and the difference was statistically significant. So, in my opinion, this study is well-written. The experimental design is reasonable, and the results reflects the conclusion as well. I recommend its acceptance after the minor revision. The detailed comments are: -a. The authors have showed that the combination of mALB,  $\beta$ 2MG, RBP, mALB/U-CR, and U-CR can be used to predict the progression of DR, my point is, can we use one or some of these factors to realize the same goal to simplify the diagnostic procedure? -b. I have noticed that HbA1c in the PDR group is higher than that in the NPDR and NDR groups, how about use it as a diagnostic basis of DR?

Thanks for your helpful suggestion.

a. The AUC of one indicator (mALB, mALB/U-CR, U-CR,  $\beta$ 2MG, and RBP) predicting the progression of DR was 0.641, 0.726, 0.757, 0.748, 0.807 respectively. They are lower than the AUC of combination prediction.

b. In the revised manuscript, we added the ROC analysis of HbA1c to predict the progression of DR, whose AUC was 0.710. They were lower than the combination prediction of mALB, mALB/U-CR, U-CR,  $\beta$ 2MG, RBP, HbA1c, whose AUC was 0.958. The result showed that the combination prediction ability was higher than the single indicator prediction ability, suggesting that it is efficient to choose the combination detection to predict the progression of DR.

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade A (Priority publishing)

Conclusion: Minor revision

Specific Comments to Authors: Diabetic retinopathy (DR) is an irreversible blindness-causing disease that lacks of effective early diagnosis and treatment. Here, Song et al. demonstrated the predictive role of the combined detection of mALB, mALB/U-CR, U-CR,  $\beta$ 2MG and RBP in DR. Moreover, the authors found that the disease duration, HbA1c, mALB,  $\beta$ 2MG, RBP, mALB/U-CR and U-CR were risk factors for the development of DR. In general, this study is instructive, and the experimental methods and data can support the conclusion of this paper

very well. I have only two minor concerns about this paper: 1) Since glycated hemoglobin A1c (HbA1c) in the PDR group is higher than that in the NPDR and NDR groups ( $P < 0.05$ ), why HbA1c is not a predictive factor of DR? 2) The authors have demonstrated that the combination of mALB, mALB/U-CR, U-CR,  $\beta$ 2MG and RBP has predictive value for proliferative DR. So, how much of the accuracy rate was increased using all these factors compared with that of using only one factor? 3) This paper should be polished before publishing.

Thanks for your valuable suggestion.

(1) As your opinion, HbA1c could be a predictive factor. In the revised manuscript, we added the ROC analysis of HbA1c to predict the progression of DR, whose AUC was 0.710.

(2) The accuracy rate of one indicator (mALB, mALB/U-CR, U-CR,  $\beta$ 2MG, RBP and HbA1c) predicting the progression of DR was 71.24%, 73.85%, 75.58%, 79.84%, 79.38%, 63.11% respectively. The accuracy rate of combination (mALB, mALB/U-CR, U-CR,  $\beta$ 2MG, RBP, HbA1c) prediction was 96.72%. The result showed that the combination predicting is 33.61%-16.88% higher than single factor predicting.

(3) After careful examination and modification, the language has been improved.