

Dear reviewers,

Thank you for your comments and professional advice concerning our manuscript entitled “Clinical study of different prediction models in predicting diabetic nephropathy in patients with type 2 diabetes mellitus”. Those comments and professional advice are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have studied comments and advice carefully and have made correction which we hope meet with approval.

Responds to the reviewer's comments:

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: I think the topic of study is interesting. However, I think that the authors should 1. Explain more about the techniques used in the statistical analysis section. 2. Add a list of abbreviations at the end of the manuscript.

Response: We have added more technical explanations of use have been added to the statistical analysis section, and a list of abbreviations has been added at the end of the document.

Reviewer #2:

Scientific Quality: Grade D (Fair)

Language Quality: Grade A (Priority publishing)

Conclusion: Major revision

Specific Comments to Authors: Dear Authors, Your work is interesting. However, I have many important remarks and comments - you will find them in the attached file. The most important is lack of data regarding other complications of diabetes, both micro- and macrovascular (retinopathy is closely related to nephropathy). And they were not included in the analysis, while probability of diabetic nephropathy is much lower in person without retinopathy. Another remark - Scr and eGFR cannot be used in the multivariate regression analysis because eGFR is estimated based on Scr concentration, age and sex (by the way - which equation did you use?) Other remarks and comments you will find in the manuscript. In summary major revision is required to improve quality and relevancy of your work.

Response: We added the analyses of diabetic retinopathy and coronary heart disease have been added to the paper, and because eGFR was estimated based on Scr concentration, age and sex, we removed eGFR and retained Scr for multivariate regression analysis, and revised the relevant conclusions. Other remarks and comments we have been found in the manuscript and have been revised accordingly. equation:

$$eGFR = 186 \times (Scr)^{-1.154} \times (age)^{-0.203} \times [0.724(\text{female})]$$

Reviewer #2: Comments in the manuscript:

1. "International Diabetes Federation, approximately 463 million people (20-79 years old) worldwide currently have diabetes, and approximately 90-95% of cases are type 2 diabetes"

Newer editions of Diabetes Atlas has been released, so please use the newest one as the reference.

Response: We have revised it according to the new edition of the Diabetes Atlas.

2. "Based on "Standards for the Diagnosis and Treatment of Diabetes (2018 Edition)"

Although diagnostic criteria did not change since 2009, more recent edition should be used, and current Edition is 2023.

Response: The "Diabetes Diagnosis and Treatment Standards (2023 edition)" has been revised and used in the article.

3. ADA "Standards for the Diagnosis and Treatment of Diabetes"

As I wrote previously, more recent edition (2023) should be used.

Response: The "Diabetes Diagnosis and Treatment Standards (2023 edition)" has been revised and used in the article.

4. "Any of the following indicators, lasting for more than three months: ① Renal injury markers: A-albuminuria (AER ≥ 30 mg/24h; urinary albumin/creatinine ratio (ACR) ≥ 30 mg/ g (or ≥ 3 mg/mmol)); B Urine sediment abnormalities; C renal tubular-related lesions; D Histologic abnormalities; E. Structural abnormalities seen on imaging; F Kidney transplant history. ②GFR decreased glomerular filtration rate (eGFR) $< 60\text{mL}/(\text{min} \cdot 1.73\text{m}^2)$."

These are criteria for Chronic Kidney Disease (CKD) and not for diabetic nephropathy.

Response: It has been modified in the text, have been modified into "diabetic patients with renal impairment and urinary microalbumin/creatinine ratio (ACR) ≥ 30 mg/g(or $\geq 3\text{mg}/\text{mmol}$), or patients with glomerular filtration rate (eGFR) $< 60\text{mL}/(\text{min} \cdot 1.73\text{m}^2)$, the total duration of more than 3 months can be diagnosed as DN."

5. "estimated glomerular filtration rate (eGFR),"

How did you calculate eGFR? Which equation was used?

Response: $eGFR = 186 \times (Scr)^{-1.154} \times (age)^{-0.203} \times [0.724(\text{female})]$

6. "A total of 210 patients with T2DM were included in this study, of whom

87 were males and 123 were females. There were 74 patients who had T2DM complicated with DN, and the incidence of DN was 35.24%. There were 74 cases in the DN group with a mean age of (56.01 ± 9.41) years. There were 136 cases in the non-DN group, with a mean age of (57.42 ± 8.15) years."

Did you check presence of other micro- and macrovascular complications (retinopathy, neuropathy, history of MI, stroke or presence of atherosclerosis in coronary, carotid or peripheral arteries)? It is important information because retinopathy usually precedes nephropathy development.

In the ADA Standards of Care it is stated:

"Diabetic kidney disease is usually a clinical diagnosis made based on the presence of albuminuria and/or reduced eGFR in the absence of signs or symptoms of other primary causes of kidney damage. The typical presentation of diabetic kidney disease is considered to include a long-standing duration of diabetes, retinopathy, albuminuria without gross hematuria, and gradually progressive loss of eGFR.

Response: We have added the analyses of diabetic retinopathy and coronary heart disease have been added to the paper.

7. "(there was no collinearity problem between the diagnosed variables)"

I have doubts – in The Chronic Kidney Disease Epidemiology Collaboration CKD-EPI equation eGFR is estimated based on Scr, age and sex, thus, inverse correlation between eGFR and Scr must exist. Due to that, in my opinion, one of these variables must be excluded, preferably Scr (it differs in males and females due to differences in muscle mass), and only eGFR, which better reflects kidney function irrespective of sex, should be included into analysis (moreover, it has higher t/χ^2 ratio as well as higher Wald test value which indicates stronger relationship with DN).

But to ensure these results, please built and check the models with inclusion separately each of these parameters (together with duration of diabetes, FBG and HbA1c). If you have data regarding presence of other diabetic complications, they should be also included into model.

Response: As your eighth suggestion suggests,"eGFR is one of the diagnostic criteria for chronic kidney disease,so including it to the model has no sense (each person with eGFR below this value has chronic kidney disease, irrespective of its cause)", we finally decided to exclude eGFR and retained Scr for multivariate regression analysis, rebuilt the model (Diabetic retinopathy data were added)and modified the discussion, Specific changes can be found in the article.

8. eGFR is estimated upon serum creatinine level – in my opinion the latter should be removed from the model. Moreover, eGFR is one of the diagnostic criteria for chronic kidney disease (<60 ml/min/1.73 m²), so including it to the model has no sense (each person with eGFR below this value has chronic kidney disease, irrespective of its cause)

Response: we finally decided to exclude eGFR and retained Scr for multivariate regression analysis, rebuilt the model (Diabetic retinopathy data were added) and modified the discussion, Specific changes can be found in the article.

9. “FBG (mg/L) ” I think it is in mmol/L

Response: We have corrected it in the article

10. “HbA1c (%) ” Apart of traditional units also SI units should be presented

Response: An introduction has been added to the "Indicators of observation" section of the article.