

3 SCIENTIFIC QUALITY

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, and **highlighted the revised/added contents with yellow color in the revised manuscript**. 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)

Novelty of This Manuscript: Grade B (Good)

Language Quality: Grade B (Minor language polishing)

Creativity or Innovation of This Manuscript: Grade A (Excellent)

Scientific Significance of the Conclusion in This Manuscript: Grade B (Good)

Conclusion: Minor revision

Specific Comments to Authors: The authors of this study aimed to investigate the CA199, CA242, and CEA expression in T2DM and its clinical implications. To do this, they analyzed the level of FBG, tumor markers (CA199, CEA, and CA242), HbA1c, and other metabolic indicators in 82 T2DM patients and 51 individual who underwent health examinations at their hospital. For diagnosis accuracy, they used the receiver operating curve (ROC) curve to test tumor markers in patients with high HbA1c (>9%). The methods of data analysis are very clear, and the results are presented well. The manuscript is written clearly and I do agree with them about the limitations of retrospective studies. However, some issues have to be addressed: 1. How are the expected differences in tumor markers determined between patients with T2DM and controls? 2. The main inclusion criteria also need to be listed, for example, the age range of enrollment, etc. Thank you for giving the opportunity to review this manuscript.

Reply: We greatly appreciate these positive comments our study.

The sample size calculation of this study is based on the expected differences in tumor markers (CA199, CA242, and CEA) between T2DM patients and the control group. The expected difference size assumes a moderate effect size of ($d=0.5$), with a significance level is 0.05, and the expected power is 80%. The settings of these parameters refer to similar studies in the past.

The inclusion criteria set for this study are: ① age ≥ 18 years old; ② Conform to the diagnostic criteria for T2DM in the Guidelines for the Prevention and Treatment of Type 2 diabetes in China (2020 Edition) formulated by the diabetes Branch of the Chinese Medical Association, including newly diagnosed patients and patients who have been previously diagnosed but have poor blood glucose control; ③ Informed consent of patients and their families. Exclusion criteria: ① patients with heart, liver, kidney and lung dysfunction, diabetes acute complications, infectious diseases, autoimmune diseases, acute and chronic inflammatory reactions, and malignant tumors; ② Long term use of glucocorticoids and their impact on blood sugar and lipid levels; ③ Pregnant or lactating women; ④ Exclude diseases such as acute and chronic pancreatitis, liver cirrhosis, hepatitis, colitis, gallstones, and obstructive jaundice that can cause benign elevation of serum CA199 or CEA; ⑤ Incomplete clinical information or inaccurate data.

Reviewer #2:

Scientific Quality: Grade C (Good)

Novelty of This Manuscript: Grade B (Good)

Creativity or Innovation of This Manuscript: Grade B (Good)

Scientific Significance of the Conclusion in This Manuscript: Grade B (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: The topic of this work is interesting. Epidemiological studies have shown that the risk of certain malignancies,

including hepatoma, hepatocellular carcinoma, colorectal cancer, and bladder cancer, is elevated in patients with T2DM. However, the correlation between their expression levels and blood glucose levels in T2DM patients is unknown. I would like to thank the authors for their efforts in evaluating serum tumor marker expression (CA199, CA242, and CEA) in T2DM and its clinical implications. It is well written and highly interesting. The study is well designed and presented with optimal analysis, discussion, tabulation and graphic display of data. Thank you for giving opportunity to review this study. However, the following points must be considered before publication. In my opinion, the background is too simple, and I recommend providing more evidence that diabetes boosts specific serum tumor markers. Also, the conclusion section needs to be more explicit. Besides, this study identified that HbA1c and FBG correlate with CA199, CEA, and CA242. Incorporating routine CA199, CEA, and CA242 assessments in patients with T2DM care might provide clinicians with valuable insights, aiding in therapeutic decisions, especially for those struggling with blood sugar management. I suggest that it could be published early on WJD.

Reply: We appreciate it very much for this good comment. We have made modifications to the background and discussion sections according to your suggestion.

If the picture is 'original', the author needs to add the following copyright information to the bottom right-hand side of the picture in PowerPoint (PPT): Copyright ©The Author(s) 2023. Authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden.