Dear Reviewers,

Thank you very much for your valuable feedback on our study. We greatly appreciate your comments, and we have addressed them accordingly. Please find our responses below.

The following is the answer to Reviewer 1(ID:03767650):

1. Comment 1: Please provide a clear definition of polyps in the Methods section. Do polyps in this study include hyperplastic or hamartomatous polyps? The reviewer imagines that a variety of polyps are included in this study, but in general, adenomas occupy an important place among polyps as precancerous lesions. Thus, the association between the presence of adenoma and TyG index is significant. Please analyze the assotiation. A similar analysis for serrated polyps, such as hyperplastic polyp, SSL, and TSA, would be meaningful.

Response 1:
Thank you for your valuable feedback and questions. In response, we would like to address your concerns regarding the definition of polyps and the inclusion of different types of polyps in our study.

In the Methods section of our paper, we have provided a clear definition of polyps, explicitly stating that it encompasses both adenomatous and non-adenomatous polyps. We have highlighted this distinction for clarity. It is important to note that adenomatous polyps are considered significant precancerous lesions. Therefore, we conducted further analysis to explore the association between the TyG index and the presence of adenomatous polyps. As you mentioned, the results indeed demonstrated a significant correlation between the TyG index and the risk of adenomatous polyps, as outlined in Tables 1 and 2.

However, we did not specifically analyze the association with other types of polyps, such as hyperplastic polyps, serrated polyps (such as SSL and TSA), or hamartomatous polyps. While we acknowledge the potential significance of such analysis, our study primarily focused on colorectal polyps and adenomatous polyps. This choice was based on the fact that this study represents the first exploration of the relationship between the TyG index and colorectal polyps, as well as adenomatous polyps. Moreover, adenomatous polyps are widely recognized as the most common precursors of colorectal cancer, making them a crucial focus for investigation in this context.

We appreciate your suggestion and believe that further research exploring the association between the TyG index and various types of polyps would be meaningful. We will consider this aspect for future investigations.

2. Comment 2: The number of colorectal adenomas is associated with the risk of CRC. Can you present the association between more than 3 adenomas and TyG index, since more than 3 adenomas are classified as high risk adenomas?

Response 2:
Thank you for your comment and suggestion. We agree that the number of colorectal adenomas is associated with an increased risk of colorectal cancer (CRC). We appreciate your interest in exploring the association between more than 3 adenomas, classified as high-risk adenomas, and the TyG index.

However, we regret to inform you that due to limitations in our data collection process, we were

unable to obtain detailed records of the specific number of adenomas for each participant. As a result, we were unable to conduct a specific analysis focusing on the association between more than 3 adenomas and the TyG index.

We acknowledge that investigating this aspect would provide valuable insights into the relationship between high-risk adenomas and the TyG index. We encourage future studies to explore this association in more detail, taking into account the specific number of adenomas and their implications for CRC risk.

Thank you once again for your thoughtful feedback. We appreciate your understanding regarding the limitations of our study.

3. Comment 3: Polyp detection has been shown to have association with endoscopist experience and endoscopic equipment "literature". If you can adjust for them, please provide the relationship.

Response 3:
Thank you for your comment and inquiry regarding the potential influence of endoscopist experience and endoscopic equipment on polyp detection. In response to your suggestion, we would like to clarify that, although we were unable to directly adjust for these factors in our analysis, we did provide detailed descriptions of our endoscopic equipment and the experience level of our endoscopists in the methods section of our study.

We acknowledge that endoscopist experience and endoscopic equipment are important factors that may affect polyp detection rates. However, in this particular study, we were unable to conduct a specific analysis adjusting for these variables due to limitations in our data collection process.

Nonetheless, we firmly believe that our study findings contribute valuable insights into the relationship between the TyG index and colorectal polyps, specifically adenomatous polyps. We hope that our detailed descriptions of our endoscopic equipment and endoscopist experience will provide readers with a clear understanding of the potential limitations and impact of these factors on our study results.

We appreciate your thoughtful comments and suggestions, and we will certainly take them into consideration for future research.

4. Comment 4: Please explain why you adjusted for the factors, such as TC, LDL-C and HDL-C, but not Glu and ALT.

Response 4:
Thank you for your valuable feedback on our study. We appreciate your suggestions and will make the necessary revisions accordingly.

Regarding the adjustment of factors, such as TC, LDL-C, and HDL-C, but not Glu and ALT, we based our decision on existing literature and the specific research question addressed in our study.

Total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C) have been extensively studied and established as important risk factors for various health conditions, including cardiovascular diseases and metabolic disorders. As such, we included these lipid-related factors in our analysis to account for their potential confounding effects.

On the other hand, Glucose (Glu) and Alanine aminotransferase (ALT) are indeed relevant to metabolic health, but their direct association with the risk of colorectal polyps is less well-established.

While Glu is a component of the TyG index, it is not the focus of our study, which primarily aimed to investigate the relationship between the TyG index and colorectal polyp detection. Similarly, ALT, an enzyme related to liver function, has limited evidence linking it directly to the risk of colorectal polyps.

We acknowledge that Glu and ALT could potentially be important confounders or factors of interest in certain contexts. However, based on the scope and objectives of our study, we made the decision not to adjust for Glu and ALT in our analysis.

Once again, we appreciate your feedback.

5. Comment 5: I believe it is better to show the sensitivity, specificity, positive predictive value and negative predictive value with a cutoff of 2.31MinorPlease delete Characteristics and Colonoscopic findings in the first row from Table 1.

Response 5:

Thank you for your feedback on our study.

The purpose of our study was to investigate the relationship between TyG index and colorectal polyps. Therefore, we employed multivariable logistic regression analysis, smooth curve fitting, and saturated threshold effect analysis, which do not involve ROC curves. Sensitivity, specificity, positive predictive value, and negative predictive value are important components of ROC curves, primarily used to assess the accuracy of X in predicting Y. We believe that they are not applicable in this study.

For reference, we have included relevant articles on smooth curve fitting and saturated threshold effect analysis that employ similar statistical methods and table content[1-2]. We recommend reviewing these references. However, we acknowledge the value of your suggestion to include sensitivity, specificity, positive predictive value, and negative predictive value, and we plan to incorporate them in our future research.

Additionally, we have made the necessary adjustments to Table 1 based on your suggestion. We are grateful for your valuable input.

[1] Zhao L, Sun Y, Liu Y, Yan Z, Peng W. A J-shaped association between Dietary Inflammatory Index (DII) and depression: A cross-sectional study from NHANES 2007-2018. J Affect Disord. 2023 Feb 15;323:257-263. doi: 10.1016/j.jad.2022.11.052. Epub 2022 Nov 30. PMID: 36462606.

[2] Xie R, Liu M. Relationship Between Non-Alcoholic Fatty Liver Disease and Degree of Hepatic Steatosis and Bone Mineral Density. Front Endocrinol (Lausanne). 2022 Mar 14;13:857110. doi: 10.3389/fendo.2022.857110. PMID: 35360054; PMCID: PMC8964007.

The following is the answer to Reviewer 2(ID:04163041):

6. Comment 1: It is presumed that this retrospective study is a sub analysis of data that were collected from patients who underwent screening colonoscopy, but the article is described as though it is a prospective study.

Response 1:

Thank you for your comment. We apologize for any confusion caused by the description of our study.

Indeed, this is a retrospective study, and we appreciate your suggestion to clarify this point. We have made the necessary revisions to clearly state in the title and methods section that our study is a retrospective analysis based on data collected from patients who underwent screening colonoscopy.

7. Comment 2: It is not mentioned in this study how the patients were selected for screening colonoscopy. In this study patients above 17 years are included but it is not mentioned why they were subjected to screening colonoscopy.

Response 2:
This study is a retrospective analysis that collected data from a group of healthy individuals who underwent routine health check-ups. Screening colonoscopy was performed as part of the comprehensive health examination protocol. As such, patients above 17 years of age were included in this study because colonoscopy was a routine component of the health check-up program.

We appreciate your comment and have now added this information to the methods section of our manuscript to provide a better understanding of how the patients were selected for screening colonoscopy.

8. Comment 3: Patients were grouped as those with or without polyps – but those with polyps are not categorised as per the polyps' histopathological data and analysed. All polyps were considered as potential precursors of malignancy.

Response 3:
Thank you for your continued feedback on our study. We apologize for any confusion caused and appreciate the opportunity to clarify our research methodology.

In our study, we included both adenomatous and non-adenomatous polyps in the classification of colorectal polyps. We have addressed this issue by providing additional information in the methods section of our manuscript, clearly specifying the inclusion of the type of polyps. We have also made sure to highlight these modifications for better clarity.

Furthermore, recognizing the importance of adenomatous polyps as significant precursors to malignancy, we conducted additional analyses to explore the relationship between the TyG index and adenomatous polyps. We aimed to investigate whether the TyG index could serve as a potential biomarker for identifying individuals at risk for developing colorectal polyps and adenomatous polyps, which are known to be important precursors to colorectal cancer.

We appreciate your attention to detail and your valuable comments.

9. Comment 4: If the patients underwent screening colonoscopy, did they undergo the specific blood tests also so that TyG index can be calculated? If so what is the explanation for doing these blood tests in all these patients, that too without informed consent. The role of AST and ALT in these patients is not indicated.

Response 4:
Thank you for your comments on our study. We appreciate your interest and would like to address your questions.

All the patients who underwent screening colonoscopy in our study were part of a health examination group, and blood tests were a routine part of this check-up. The blood tests, including those that enabled calculation of the TyG index, were performed to assess the metabolic status and blood glucose levels of the patients. It is important to note that these blood tests were not specifically

conducted for our study but were part of the standard clinical evaluation of the patients in the health examination group.

Regarding the concern about informed consent, we would like to clarify that the data used in our study came from an existing database that had de-identified patient information to protect their privacy. Thus, we did not directly interact with the patients or obtain their informed consent. In such cases, the ethical committee approved the waiver of informed consent. We have made a statement about this in the method section of our manuscript.

Lastly, regarding the role of AST and ALT, we understand your concern. However, in our study, these indicators were not directly associated with the risk factors of colorectal polyps, and thus, we did not include them in the analysis. AST and ALT are commonly used to assess liver function, which is not the focus and objective of our study.

We hope this explanation clarifies any misunderstandings, and we thank you again for your valuable feedback.

10. Comment 5: It is unlikely that the Ethical committee would have waived informed consent for the screening program. if the authors conclusively prove that it is a retrospective study, this point may be accepted.

Response 5:
Thank you for your feedback regarding the issue of informed consent in our study. We agree with your concern that the ethical committee would have unlikely waived informed consent for this type of screening program.

We want to clarify that our study is retrospective and used data collected from a preexisting database. We did not directly interact with patients, and all patient data was deidentified to protect confidentiality. As such, we did not obtain informed consent from patients, and the ethical committee approved the waiver of consent.

Nevertheless, we understand the importance of informed consent in research and will work to provide more clarity on this issue in the manuscript. We will include a statement in the methods section explaining that the data used in this study were obtained from a pre-existing database, and that the use of the data was approved by the ethical committee with a waiver of informed consent.

Thank you again for your feedback and for taking the time to review our manuscript.

11. Comment 6: The variables included were only age and sex, but smoking, alcohol use, physical activity, BMI , diabetes, etc were not discussed.

Response 6:
Thank you for pointing out the mistake in my previous response. I apologize for the confusion caused. I appreciate the opportunity to clarify.

In our study, we indeed only adjusted for two demographic characteristics - age and gender, and did not adjust for other factors such as body mass index (BMI), smoking status, alcohol consumption, physical activity, and family history of colorectal cancer (CRC). Due to limitations in data collection, we were unable to provide adjustment results for these factors.

We acknowledge that these factors may play important roles in the detection of colorectal polyps. Considering and adjusting for these potential confounding factors in future research would provide

more accurate and comprehensive analysis results.

Thank you for pointing out this oversight and providing your suggestions. We will take note of them and make improvements in future studies.

12. Comment 7: The significance of TyG in predicting IR is not detailed, except stating that it is better than HOMA IR index.

Response 7:
Thank you for your comment. In our revised manuscript, we have addressed your concerns by providing additional details and references in the discussion section on the significance of the TyG index in predicting insulin resistance (IR). Specifically, we have highlighted that the TyG index has been validated as a reliable and simple estimate index for IR, comparable to the euglycemic-hyperinsulinemic clamp method, which is considered the gold standard for evaluating IR ([19]Guerrero-Romero F, Simental-Mendía LE, González-Ortiz M, Martínez-Abundis E, Ramos-Zavala MG, Hernández-González SO, Jacques-Camarena O, Rodríguez-Morán M. The product of triglycerides and glucose, a simple measure of insulin sensitivity. Comparison with the euglycemic-hyperinsulinemic clamp. J Clin Endocrinol Metab. 2010 Jul;95(7):3347-51. doi: 10.1210/jc.2010-0288. Epub 2010 May 19. PMID: 20484475.)

We appreciate your feedback and we hope that these revisions demonstrate our respect for your comments and input.