

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	The Diagnostic Value of Triglyceride-Glucose Index and Related Parameters in Metabolism-associated Fatty Liver Disease in a Chinese Population: A cross-sectional study
AUTHORS	Yu, Rong; Xie, Weijiang; Peng, Hwei; Lu, Lili; Yin, Shuo; xu, shanghua; Hu, Zhijian; Peng, Xian-E

VERSION 1 – REVIEW

REVIEWER	Cui, Weiwei Jilin University School of Public Health, Department of Nutrition and Food Hygiene
REVIEW RETURNED	07-Jul-2023

GENERAL COMMENTS	<p>The aim of this cross-sectional study is to explore the diagnostic value of TyG and its related parameters in MAFLD. At present, research on the diagnostic value of the TyG index in MAFLD has received widespread attention. However, enthusiasm is diminished by the following:</p> <ol style="list-style-type: none">1. English-language need to be extensively checked and improved.2. Missing exclusion criteria for patients in study subjects and design.3. lines 12-13, the authors use overweight or obesity (BMI \geq 23.0kg/m²) and metabolic dysregulation among non-overweight individuals (BMI < 23.0kg/m²) as one of the diagnosis for MAFLD. However, the diagnostic standard for overweight or obesity is BMI > 24.0kg/m² in China, and WHO \geq 25.0 kg/m². Which standard did you used ?4. Corresponding references should be attached to the diagnostic criteria for hypertension and diabetes (line 40-47 of page 7).5. The study design is a cross-sectional study. Can we conclude that the TyG index and its related parameters are risk factors for MAFLD and have great predictive value for MAFLD?6. Please verify the study design of this article. Lines 52-54 of page 5, the study is indicated as a cohort study, while in other parts of the manuscript, it is considered as a cross-sectional study.7. In the discussion section, it is recommended to reduce the repetitive statements about the background and results, and focus on finding the reasons and possible mechanisms for the occurrence of results, or comparing with the current research status.
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REVIEWER	Perseghin, Gianluca Università degli Studi di Milano-Bicocca, Department of Medicine and Surgery
REVIEW RETURNED	08-Jul-2023

GENERAL COMMENTS	<p>In the present manuscript, Yu R et al wanted to assess the association between the TyG in MAFLD. They used a cross-sectional approach taking advantage of a data-base related to a medical checkup in Nanping City, between 2015 and 2017. 2605 subjects were included and were segregated according to whether they had MAFLD.</p> <p>They basically report a strong association also when adjusting for many variable</p> <p>Major comments</p> <p>1) The authors need to put more emphasis on the novelty of their work when compared with the previous reported literature, especially when a longitudinal study in a Chinese population has been previously reported, about same sample size</p> <p>2) The authors states that the performance of TyG is better than FLI, but based on the data presented in the table about sensitivity and specificity it is difficult to detect some sort of superiority. Please comment</p> <p>3) The same is when a comparison is attempted when FLI is compared to the TyG related parameters. Please comment</p> <p>4) To be honest I have the feeling that waist and BMI per se in this setting perform in a non-different fashion that TyG. Please comment</p> <p>5) the figure comparing AUROC is very difficult to understand and again the curves apparently are superimposable</p> <p>6) The authors need to better clarify the reasons of the screening strategy in this cohort of individuals; it is difficult to understand whether these subjects may be representative of the entire population or whether they may be differing somehow because of the employment of some other risk factors</p>
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REVIEWER	Kilonzo, Semvua Catholic University Health and Allied Science PO BOX 1464
REVIEW RETURNED	10-Jul-2023

GENERAL COMMENTS	<p>1) The title should change to reflect the study aim and results. The words "utility" or diagnostic value" can be used instead of "Application"</p> <p>2) The components used for diagnosis of MAFLD were not clearly described., e.g. Abdominal ultrasound: how was hepatic steatosis diagnosed by U/S? which criteria was used? What were the cut-off values for all metabolic disorders? (WC, BP, TG, HDL, etc.</p> <p>3) It would be very interesting to know the ratio of patients with underlying liver diseases and/or risk of chronic liver disease (hepatitis, etc)</p> <p>4) The authors didn't do much to compare their findings from other studies, and to criticise the differences or similarities that were observed in the discussion section</p>
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REVIEWER	Gao, Xiao-Ming Department of Cardiology of the First Affiliated Hospital of Xinjiang Medical University
REVIEW RETURNED	19-Jul-2023

GENERAL COMMENTS	<p>Yu et al investigated the diagnostic value of TyG index and its related parameters for MAFLD in a community-based population study. This study involved over 2600 subjects who were divided into two subgroups, one with MAFLD and one not. They found that</p>
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	<p>TyG and its related parameters (TyG-WC, TyG-BMI and TyG-WHR) are useful markers for identification and prediction of MAFLD, and TyG-WC is the most powerful index with the largest AUC for MAFLD.</p> <p>There are many studies have been published to investigate the diagnostic value of TyG index and its related parameters for MAFLD, the problem of the current study is the lack of novelty and analysis, what is the strength and weakness compared other similar clinical studies with substantial larger, similar or smaller study population? Author should provide critical analysis.</p> <p>In addition, there are some technique issue need to be fixed.</p> <ol style="list-style-type: none"> 1. Many abbreviations were not defined in abstract, related tables and figures. 2. Definitions of many of clinical parameters were not clearly stated or incomplete, such as HDL, LDL etc. 3. For TyG index, glucose is FPG or random glucose (page 6)? 4. Especially, what are the diagnostic standards for metabolic disorders? 5. As MAFLD or NAFLD are primarily diagnosed by imaging techniques such as ultrasonography or MRI. There was not description of the latest ultrasonographic method and diagnostic criteria of hepatic steatosis. Author should provide the incidence of hepatic steatosis detected by ultrasound and TyG and its-related indices. 6. The reason for use RCS analysis in this study should be provided compared with other traditional methods. NRI and IDI analyses did not explained in the statistical section. 7. Suppl Table 1 and 2 should be included in the main text part. 8. In page 10, the author stated that “The new parameters TyG-BMI, TyG-WC, and TyG-WHR combine the above indices and appear to be more reflective of IR status in MAFLD”, although TyG and its related parameters is able to reflect IR status, IR is a only risk parameter, the study is focused on MAFLD, not IR, the logical rationale need to be modified.
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VERSION 1 – AUTHOR RESPONSE

Reply to Reviewer 1

Prof. Weiwei Cui, Jilin University School of Public Health

Comments to the Author:

The aim of this cross-sectional study is to explore the diagnostic value of TyG and its related parameters in MAFLD. At present, research on the diagnostic value of the TyG index in MAFLD has received widespread attention. However, enthusiasm is diminished by the following

Response:

Many thanks to the reviewers for taking the time and effort to help us improve our paper. We took the comments we received very seriously and corrected and responded to each one individually.

Question 1:

English-language need to be extensively checked and improved.

Response:

We thank the reviewers for pointing out this problem. We apologize for the deficiencies in the English language presentation and have amended some sentences.

Question 2:

Missing exclusion criteria for patients in study subjects and design.

Response:

Many thanks for the reviewer's constructive suggestions. As suggested, we added subject exclusion criteria to the study subjects and design module as described below: "Subjects with malignant tumors, incomplete data, or pregnant or lactating women were excluded."

Question 3:

lines 12-13, the authors use overweight or obesity ($BMI \geq 23.0 \text{ kg/m}^2$) and metabolic dysregulation among non-overweight individuals ($BMI < 23.0 \text{ kg/m}^2$) as one of the diagnosis for MAFLD. However, the diagnostic standard for overweight or obesity is $BMI > 24.0 \text{ kg/m}^2$ in China, and WHO $\geq 25.0 \text{ kg/m}^2$. Which standard did you used ?

Response:

Many thanks for the carefulness of the reviewer. According to previous studies, for the diagnosis of MAFLD, overweight or obesity is defined as $BMI \geq 25 \text{ kg/m}^2$ for Caucasians and $BMI \geq 23 \text{ kg/m}^2$ for Asians. Therefore, in this study, the Asian definition of the criteria was chosen to define those with a BMI over 23 as overweight or obese.

Question 4:

Corresponding references should be attached to the diagnostic criteria for hypertension and diabetes (line 40-47 of page 7).

Response:

Many thanks to the reviewers for their attentiveness. References on diagnostic criteria for hypertension and diabetes mellitus have been inserted into the corresponding positions in the paper (line 147-149 of page 6).

Question 5:

The study design is a cross-sectional study. Can we conclude that the TyG index and its related parameters are risk factors for MAFLD and have great predictive value for MAFLD?

Response:

Thank you for pointing out this problem in the manuscript. I apologize for my inappropriate expression. The study design method of cross-sectional analysis only allowed us to conclude that there is a correlation between the TyG index and its related parameters and the risk of developing MAFLD, which has a greater diagnostic value for MAFLD. Again, we apologize for our error. We have corrected the statements in the paper related to these issues.

Question 6:

Please verify the study design of this article. Lines 52-54 of page 5, the study is indicated as a cohort study, while in other parts of the manuscript, it is considered as a cross-sectional study.

Response:

Many thanks for your suggestion. We apologize for our carelessness. The research design of this paper is a cross-sectional study, we have changed "The diagnosis of fatty liver disease (FLD) in this cohort was primarily based on ultrasonographic findings rather than a liver biopsy" to "The diagnosis of fatty liver disease (FLD) in this study was primarily based on ultrasonographic findings rather than a liver biopsy".

Question 7:

In the discussion section, it is recommended to reduce the repetitive statements about the background and results, and focus on finding the reasons and possible mechanisms for the occurrence of results, or comparing with the current research status.

Response:

We gratefully appreciate for your valuable suggestion. Based on the suggestions, we have amended the related description in the discussion section. Repetitive statements of context and results have

been deleted. We compared the results of the analysis of this study with the same type of articles to analyze the differences. Also, the reasons for the results of this study and possible mechanisms are discussed.

Reply to Reviewer 2

Prof. Gianluca Perseghin, Università degli Studi di Milano-Bicocca, Policlinico Di Monza Casa Di Cura Privata

Comments to the Author:

In the present manuscript, Yu R et al wanted to assess the association between the TyG in MAFLD. They used a cross-sectional approach taking advantage of a data-base related to a medical checkup in Nanping City, between 2015 and 2017. 2605 subjects were included and were segregated according to whether they had MAFLD.

They basically report a strong association also when adjusting for many variable

Response:

Many thanks to the reviewers for taking the time and effort to help us improve our paper. We took the comments we received very seriously and corrected and responded to each one individually.

Question 1:

The authors need to put more emphasis on the novelty of their work when compared with the previous reported literature, especially when a longitudinal study in a Chinese population has been previously reported, about same sample size.

Response:

We gratefully appreciate for your valuable suggestion. We have compared our finding with the previous reported literature, and discussed the differences between them in the discussion section (page 10-12). Compared with previously reported longitudinal studies on Chinese populations, the present study has the advantage of collecting more comprehensive data on confounders other than gender and age, such as smoking, alcohol and tea consumption, dietary habits, and social life situations such as marital status and income. Thus, the association of TyG index and its related parameters with MAFLD was less affected by confounders. Meanwhile, we have critically re-analyzed the strengths and weaknesses of this study and the related description were added in the discussion section (page 12).

Question 2:

The authors states that the performance of TyG is better than FLI, but based on the data presented in the table about sensitivity and specificity it is difficult to detect some sort of superiority. Please comment.

Response:

Many thanks for your kindly comment. There are a number of indicators that can be used to diagnose MAFLD, such as the Fatty Liver Index (FLI) and the Hepatic Steatosis Index (HSI). The FLI is calculated from BMI, waist circumference, triglycerides, and gamma-glutamyltransferase. The HSI is comprised of BMI, diabetes mellitus, and the alanine aminotransferase (ALT)/aspartate aminotransferase (AST) ratio. The specific formula is as follows:

$$FLI = \frac{e^{0.953 \ln(TG) + 0.139 \cdot BMI + 0.718 \ln(GGT) + 0.053 \cdot WC - 15.745}}{(1 + e^{0.953 \ln(TG) + 0.139 \cdot BMI + 0.718 \ln(GGT) + 0.053 \cdot WC - 15.745})} \times 100;$$

$$HSI = 8 \cdot ALT/AST + BMI (+2 \text{ if type 2 diabetes, } +2 \text{ if female}).$$

Both indices are more complex to calculate and involve more features and indicators. The ideal noninvasive test should be simple, easy to use, economical, efficient, and convenient for detecting and identifying people at risk for MAFLD. Although the TyG index and its associated parameters do not differ significantly from the diagnostic performance of the FLI. However, TyG index and its related parameters well balance the above requirements. Therefore, this study considered that TyG index and its related parameters can be used as a reference index for early diagnosis of MAFLD. The related description was added in the discussion section (page 11).

Question 3

The same is when a comparison is attempted when FLI is compared to the TyG related parameters. Please comment.

Response:

Many thanks for your kindly comment. As stated in question 2, the traditional MAFLD diagnostic index has problems such as involving more indicators and more complicated calculations. The use of the TyG index and its related parameters does not require the involvement of too many laboratory test indicators and the calculation process is much simpler. Therefore, this study concluded that TyG and its related parameters can also be used as a reference index for early diagnosis of MAFLD. The related description was added in the discussion section(page 11).

Question 4:

To be honest I have the feeling that waist and BMI per se in this setting perform in a non-different fashion that TyG. Please comment.

Response:

Thank you for your kindly comment. WC and BMI are indicators of physical condition that can be obtained by measurement and do not require any laboratory testing. These indicators are subjected to measurement error and measurement bias is inevitable if they are used alone. The TyG index is a combination of triglycerides and fasting plasma glucose, which provides a more accurate description of the subject's physical condition. Combining this with the TyG index will make the results more stable and reasonable.

Question 5:

the figure comparing AUROC is very difficult to understand and again the curves apparently are superimposable.

Response:

Many thanks for the reviewer's constructive suggestions. Based on the suggestions, we have made some adjustments to the AUROC diagram. We kept TyG and its related parameters as well as WC, BMI, FLI, and HSI indicators in the graph, and added the area under the ROC curve for these eight indicators. At the same time, we adjusted the color of the curves so that the curves can be better distinguished from each other. The changed "Figure 2 ROC curves of TyG and its related parameters and biochemical indexes" have been re-uploaded.

Question 6:

The authors need to better clarify the reasons of the screening strategy in this cohort of individuals; it is difficult to understand whether these subjects may be representative of the entire population or whether they may be differing somehow because of the employment of some other risk factors.

Response:

Many thanks for your suggestion. Nanping city is located in the north of Fujian Province, China. Red meat is the main protein source of local population, and local population are prefer to heavier taste(1), which may increase the risk of NAFLD.(2) Our previous study also reported that the prevalence of NAFLD (32.8%) in the population of medical checkups in Nanping is higher than other city of Fujian(1, 3). Therefore, we chose the physical examination population of the First Hospital of Nanping City as our study population to better understand the diagnostic performance of TyG index and its related parameters in a higher risk population of Fujian. We have added related description in the discussion section(page 12).

1. Peng H, Xie X, Pan X, Zheng J, Zeng Y, Cai X, et al. Association of meat consumption with NAFLD risk and liver-related biochemical indexes in older Chinese: a cross-sectional study. *BMC Gastroenterol.* 2021;21(1):221.
2. Hashemian M, Merat S, Poustchi H, Jafari E, Radmard AR, Kamangar F, et al. Red Meat Consumption and Risk of Nonalcoholic Fatty Liver Disease in a Population With Low Meat Consumption: The Golestan Cohort Study. *Am J Gastroenterol.* 2021;116(8):1667-75.
3. Peng X, Huang Z, Lin J, Lu Q, Lin J, Lin X. Analysis of the prevalence and influencing factors of non-alcoholic fatty liver disease in staff. *China Public Health.* 2009;25(10):1235-7.

Reply to Reviewer 3

Dr. Semvua Kilonzo, Catholic University Health and Allied Science PO BOX 1464

Many thanks to the reviewers for taking the time and effort to help us improve our paper. We took the comments we received very seriously and corrected and responded to each one individually.

Question 1:

The title should change to reflect the study aim and results. The words "utility" or diagnostic value" can be used instead of "Application".

Response:

Many thanks for the reviewer's constructive suggestions. As suggested, we have replaced the word "Application" with "Diagnostic Value" in the title.

Question 2:

The components used for diagnosis of MAFLD were not clearly described., e.g. Abdominal ultrasound: how was hepatic steatosis diagnosed by U/S? which criteria was used? What were the cut-off values for all metabolic disorders? (WC, BP, TG, HDL, etc.

Response:

Thank you for your nice suggestion. As suggested, I have added criteria for the diagnosis of starvation by ultrasonography of fatty liver, detailed diagnostic criteria for metabolic disorders, including critical values for each of these indicators, in the Methods section. The specific expressions are as follows:

"Diagnostic of FLD: Liver ultrasonography is used to diagnose fatty liver. The presence of criteria (i) and any of criteria (ii) through (iv) indicates the presence of fatty liver: (i) Diffuse enhancement of the near-field echoes of the liver and gradual attenuation of the far-field echoes of the liver; (ii) Mild to moderate hepatomegaly with rounded obtuse borders; (iii) unclear structure of intrahepatic ducts; (iv) Reduced hepatic blood flow signal".

"Metabolic disorder was defined as the presence of at least two of the following metabolic risk abnormalities: (1) WC \geq 90 cm for Asian men and 80 cm for Asian women; (2) BP \geq 130/85 mmHg or specific drug treatment; (3) TG \geq 1.70 mmol/L or specific drug treatment; (4) HDL-c $<$ 1.0 mmol/L for men and $<$ 1.3 mmol/L for women; (5) prediabetes; (6) HOMA-IR \geq 2.5; and (7) C-reactive protein (CRP) $>$ 2 mg/L".

Question 3:

It would be very interesting to know the ratio of patients with underlying liver diseases and/or risk of chronic liver disease (hepatitis, etc).

Response:

We gratefully appreciate for your valuable suggestion. Based on the data collected, we calculated the prevalence of FLD in the subjects of this study, which was 28.68%. We also estimated the prevalence of chronic viral hepatitis B in this population, which was 8.73%. We have added related description in the result section(line200 of page 8).

Question 4:

The authors didn't do much to compare their findings from other studies, and to criticise the differences or similarities that were observed in the discussion section.

Response:

Many thanks to the reviewer for the constructive suggestions. Based on the suggestions, we have overhauled the discussion section. Repetitive statements of context and results have been deleted. We compared the results of the analysis of this study with the same type of articles to analyze the differences. Also, the reasons for the results of this study and possible mechanisms are discussed.

Reply to Reviewer 4

Dr. Xiao-Ming Gao, Department of Cardiology of the First Affiliated Hospital of Xinjiang Medical University

Comments to the Author:

Yu et al investigated the diagnostic value of TyG index and its related parameters for MAFLD in a community-based population study. This study involved over 2600 subjects who were divided into two subgroups, one with MAFLD and one not. They found that TyG and its related parameters (TyG-WC, TyG-BMI and TyG-WHR) are useful markers for identification and prediction of MAFLD, and TyG-WC is the most powerful index with the largest AUC for MAFLD. There are many studies have been published to investigate the diagnostic value of TyG index and its related parameters for MAFLD, the problem of the current study is the lack of novelty and analysis, what is the strength and weakness compared other similar clinical studies with substantial larger, similar or smaller study population? Author should provide critical analysis.

Response:

Many thanks to the reviewers for taking the time and effort to help us improve our paper. We took the comments we received very seriously and corrected and responded to each one individually. Based on your suggestions, we have critically reanalyzed the strengths and weaknesses of this study. Also, we have completely revised the discussion section. The analytical results of this study were compared with the same type of articles and the differences between them were analyzed.

Question 1:

Many abbreviations were not defined in abstract, related tables and figures.

Response:

Many thanks for the carefulness of the reviewer. We are so sorry for these errors. Based on the reviewers' suggestions, we have scrutinized and revised the abbreviations in the abstract, related tables, and figures.

Question 2:

Definitions of many of clinical parameters were not clearly stated or incomplete, such as HDL, LDL etc.

Response:

Thank you for your rigorous consideration. We feel sorry for the inconvenience brought to the reviewer. In this study, clinical parameters such as HDL were analyzed as continuous variables. Therefore, they were not clearly defined. In response to this omission, I have added information on the units of each variable in the original article to clarify these parameters. The specific formulation is as follows:" The clinical variables collected were height (m), weight (kg), waist circumference (WC, cm), hip circumference (HC, cm), Waist-to-Hip Ratio (WHR), diastolic blood pressure (DBP, mmHg), and systolic blood pressure (SBP, mmHg), serum triglyceride (TG, mg/dL), total cholesterol (TC, mmol/L), low-density lipoprotein (LDL, mmol/L), and high-density lipoprotein (HDL, mmol/L), fasting plasma glucose (FPG, mg/dL), Gamma-glutamyltransferase (GGT, U/L) alanine transaminase (ALT, U/L), and aspartate aminotransferase (AST, U/L)". The specific values of some of the indicators used to diagnose MAFLD are also listed in detail in the article "Diagnosis of MAFLD". The amendments are as follows: "Metabolic disorder was defined as the presence of at least two of the following metabolic risk abnormalities: (1) WC \geq 90 cm for Asian men and 80 cm for Asian women; (2) BP \geq 130/85 mmHg or specific drug treatment; (3) TG \geq 1.70 mmol/L or specific drug treatment; (4) HDL-c $<$ 1.0 mmol/L for men and $<$ 1.3 mmol/L for women; (5) prediabetes; (6) HOMA-IR \geq 2.5; and (7) C-reactive protein (CRP) $>$ 2 mg/L".

Question 3:

For TyG index, glucose is FPG or random glucose (page 6)?

Response:

Thank you for your rigorous consideration. We apologize for our omission. The TyG index, calculated as $TyG\ index = \ln [fasting\ triglyceride\ (mg/dl) \times fasting\ plasma\ glucose\ (mg/dl)/2]$, is a composite indicator composed of fasting triglyceride (TG) and fasting plasma glucose (FPG) levels. The complete TyG index formula has been updated in the paper.

Question 4:

Especially, what are the diagnostic standards for metabolic disorders?

Response:

Many thanks to the reviewer for the question. Metabolic disorder was defined as the presence of at least two of the following metabolic risk abnormalities: (1) WC \geq 90 cm for Asian men and 80 cm for Asian women; (2) BP \geq 130/85 mmHg or specific drug treatment; (3) TG \geq 1.70 mmol/L or specific drug treatment; (4) HDL-c $<$ 1.0 mmol/L for men and $<$ 1.3 mmol/L for women; (5) prediabetes; (6) HOMA-IR \geq 2.5; and (7) CRP $>$ 2 mg/L. The diagnosis of MAFLD was further refined in the methodology based on the reviewers' suggestions.

Question 5:

As MAFLD or NAFLD are primarily diagnosed by imaging techniques such as ultrasonography or MRI. There was not description of the latest ultrasonographic method and diagnostic criteria of hepatic steatosis. Author should provide the incidence of hepatic steatosis detected by ultrasound and TyG and its-related indices.

Response:

Thank you for your valuable comments. We have added detailed diagnostic criteria for ultrasound for fatty liver in the "Methods" module. The details are as follows: "Liver ultrasonography is used to diagnose fatty liver. The presence of criteria (i) and any of criteria (ii) through (iv) indicates the presence of fatty liver: (i) Diffuse enhancement of the near-field echoes of the liver and gradual attenuation of the far-field echoes of the liver; (ii) Mild to moderate hepatomegaly with rounded obtuse borders; (iii) unclear structure of intrahepatic ducts; (iv) Reduced hepatic blood flow signal". We again apologize for the omission. Unfortunately, however, due to the lack of data on hepatic steatosis, the analysis related to hepatic steatosis could not be completed in this study.

Question 6:

The reason for use RCS analysis in this study should be provided compared with other traditional methods. NRI and IDI analyses did not explained in the statistical section.

Response:

Many thanks to the reviewer for the constructive comments. Traditional analysis methods such as logistic regression require continuous variables to be transformed into categorical variables, but the selection of the number of categories of categorical variables and the location of nodes is generally subjective, and categorical variables lose some information. However, restricted cubic spline plots can directly fit the nonlinear relationship between independent variables and dependent variables. Therefore, this study also analyzed the nonlinear relationship between TyG and its related parameters and MAFLD using RCS. Additionally, thank you very much for careful check. Explanations of the NRI and IDI analyses have been added in detail in the paper. Add the following to the statistical analysis section: "The Net Reclassification Index (NRI) and the Integrated Discrimination Improvement Index (IDI) were used to reflect the overall improvement of the predictive model". The following has been added to the results section: "Based on the results of NRI, it can be seen that the accuracy of TyG-WC, TyG-BMI and TyG-WHR were improved by 26.4%, 18.7% and 12.5%, respectively, compared with TyG (all $P < 0.001$). Moreover, the IDI values of TyG-WC, TyG-BMI, and TyG-WHR were 0.148, 0.125, and 0.071, respectively, which were all greater than 0, indicating that the predictive ability of the TyG-related parameters improved compared with the TyG index alone. Specific results are shown in Supplementary Table 1".

Question 7:

Suppl Table 1 and 2 should be included in the main text part.

Response:

Thank you so much for your careful check. As suggested, supplementary tables 1 and 2 have been placed in the text. Supplementary table 1 has been renamed Table 1 and supplementary table 2 has been renamed Table 2. Former Tables 1 and 2 have been renamed Tables 3 and 4.

Question 8:

In page 10, the author stated that "The new parameters TyG-BMI, TyG-WC, and TyG-WHR combine the above indices and appear to be more reflective of IR status in MAFLD", although TyG and its

related parameters is able to reflect IR status, IR is a only risk parameter, the study is focused on MAFLD, not IR, the logical rationale need to be modified.

Response:

We totally understand the reviewer's concern. As suggested, we have reorganized the relationship between MAFLD, IR and TyG in our discussion. At the same time, we have completely revised the discussion section to make it more readable.

VERSION 2 – REVIEW

REVIEWER	Cui, Weiwei Jilin University School of Public Health, Department of Nutrition and Food Hygiene
REVIEW RETURNED	09-Aug-2023

GENERAL COMMENTS	No comments.
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REVIEWER	Kilonzo, Semvua Catholic University Health and Allied Science PO BOX 1464
REVIEW RETURNED	13-Aug-2023

GENERAL COMMENTS	NONE
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