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Investigation of TyG-based metabolic indices and colorectal tumor risk: Evidence from the CHARLS and NHANES cohorts

Running Title: TyG indices and colorectal tumor risk

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Declarations

Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki. The CHARLS and NHANES surveys were approved by the institutional review boards of their respective institutions, and all participants provided written informed consent. The present study was a secondary analysis of fully anonymized, publicly available datasets; therefore, no additional ethical approval or consent was required for this study.

Human Ethics and Consent to Participate declarations

not applicable.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analysed during the current study are publicly available. The National Health and Nutrition Examination Survey (NHANES) data from the 1999–2018 cycles are available in the U.S. Centers for Disease Control and Prevention repository, <https://wwwn.cdc.gov/nchs/nhanes/>, and the China Health and Retirement Longitudinal Study (CHARLS) data from the 2011–2018 waves are available in the CHARLS official repository, <https://charls.charlsdata.com/>. All other data relevant to the study are included in the article and its supplementary information files..

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Lyu Jin, Xu Jin, and Wang Zhi performed the literature search and drafted the initial manuscript. Xu Mu contributed to data organization and assisted in manuscript revision. Lyu Jin conceived the study, supervised the overall work, and critically revised the manuscript. All authors read and approved the final version of the manuscript.

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Abstract

Background: Metabolic dysfunction and insulin resistance contribute to colorectal tumorigenesis, yet simple markers for early risk assessment remain limited. The triglyceride–glucose (TyG) index and its derivative indices capture key metabolic disturbances, but their associations with colorectal tumor risk across populations remain unclear.

Methods: Participants from CHARLS (n=9,293) and NHANES (n=2,839) were included. TyG-related indices were calculated from standard formulas. Associations with colorectal tumor risk were estimated using logistic regression. Subgroup effects and predictive performance were assessed using ROC analyses.

Results: All TyG-related indices were significantly higher in tumor cases than non-tumor participants in both cohorts. In CHARLS, fully adjusted models showed strong associations for TyG (OR = 3.98, 95% CI: 2.66–5.94), TyG-CI (OR = 2.00, 95% CI: 1.60–2.50), TyG-HGB (OR = 1.28, 95% CI: 1.20–1.36), and TyG-WWI (OR = 1.08, 95% CI: 1.06–1.11). Similar but weaker effects were observed in NHANES. RCS models demonstrated significant nonlinear relationships in both cohorts (all P for overall < 0.001), with clear metabolic thresholds (e.g., TyG: 10.88 in CHARLS; 9.93 in NHANES). Above these breakpoints, risk increased sharply. ROC analyses showed moderate discrimination in CHARLS (AUCs 0.767–0.786) and lower performance in NHANES (AUCs 0.570–0.587). Subgroup findings were broadly consistent across age, sex, lifestyle, and metabolic strata.

Conclusions: TyG and its derivative indices are consistently and nonlinearly linked to colorectal tumor risk across populations. Their metabolic thresholds suggest usefulness for early detection and risk stratification, supporting these indices as simple, low-cost markers for colorectal tumor risk.

Keywords: TyG; colorectal tumor; CHARLS; NHANES

Introduction

Colorectal tumor represents one of the most common gastrointestinal neoplasms worldwide and remains a leading contributor to cancer-related morbidity and mortality[1,2]. Despite advances in screening and treatment, a substantial proportion of individuals are diagnosed at a later stage, highlighting ongoing gaps in early identification and prevention strategies[2,3]. Increasing evidence suggests that metabolic abnormalities, including insulin resistance, lipid dysregulation, and chronic low-grade inflammation, play important roles in the initiation and progression of colorectal neoplasia[2,4–6]. However, easily obtainable metabolic markers that reliably capture these underlying processes and are suitable for population-level risk assessment are still limited.

The triglyceride-glucose (TyG) index has emerged as a simple, cost-effective surrogate marker of insulin resistance and metabolic dysfunction[7,8]. Beyond the traditional TyG index, several TyG-derived indices-such as TyG-CI, TyG-HGB, and TyG-WWI-combine additional anthropometric or hematologic parameters, thereby enhancing their ability to reflect adiposity distribution, inflammation, and cardiometabolic risk[9]. These indices have demonstrated strong predictive ability for metabolic disorders, cardiovascular diseases, nonalcoholic fatty liver disease, and certain malignancies[10]. However, the associations between TyG-based metabolic markers and colorectal tumor risk remain insufficiently understood, and it is unclear whether nonlinear or threshold patterns exist across different populations.

Most previous studies have focused on linear associations or single-cohort analyses, limiting the understanding of potential dose-response or threshold effects[11–13]. Moreover, the generalizability of TyG-related indices across populations with different ethnic backgrounds, lifestyles, and metabolic profiles has not been systematically examined[14]. Whether elevated TyG or its derivative indices are consistently linked to colorectal tumor risk in both Asian and Western populations-and whether such associations exhibit nonlinear characteristics-remains largely unknown[15,16]. Addressing these gaps requires robust cross-population evidence and advanced statistical approaches.

Therefore, the present study aimed to investigate the associations of TyG, TyG-CI, TyG-HGB, and TyG-WWI with colorectal tumor risk using two nationally representative cohorts: the China Health and Retirement Longitudinal Study (CHARLS) and the U.S. National Health and Nutrition Examination Survey (NHANES)[17]. We evaluated both linear and nonlinear relationships using restricted cubic spline models, explored potential threshold effects through segmented regression, examined predictive ability via ROC analysis, and assessed effect modification across clinically relevant subgroups. By integrating findings from two large cross-population datasets, this study provides comprehensive epidemiological evidence on the metabolic signatures captured by TyG-based indices and their relevance for colorectal tumor risk assessment.

Methods

Study design and populations

This study was based on two nationally representative cohorts: the CHARLS and the U.S. NHANES. CHARLS is an ongoing longitudinal survey of middle-aged and older adults in China, using multistage probability sampling across 28 provinces[18,19]. Data from the 2011-2018 waves were combined to construct a cross-sectional analytic dataset. NHANES is a continuous U.S. nationwide survey that integrates interviews, physical examinations, and laboratory assessments; we included public data from the 1999-2018 cycles[20,21]. For both cohorts, participants were eligible if they had complete information on colorectal tumor status and laboratory measurements required to compute TyG and TyG-derived indices. Individuals were excluded for missing tumor outcomes, incomplete triglyceride or glucose measurements, missing anthropometric or hematologic indicators required for derivative indices, or missing covariates. After applying these criteria, 9,293 CHARLS participants and 2,839 NHANES participants were included in the final analyses.

Across the combined 1999 – 2018 NHANES cycles, the numbers of eligible participants ranged from 12,160 to 16,211 per 2-year cycle, with interview response rates of 61 – 84% and examination response rates of 59 – 80%. The reduction from the originally sampled population to the final analytic sample of 2,839 participants reflects the sequential application of the prespecified exclusion criteria for missing data on

outcome, key exposures, and covariates, which is a common and well-accepted analytical approach for secondary analyses of NHANES data.

Assessment of TyG and TyG-derived metabolic indices

The TyG index was calculated as $\ln[\text{fasting triglycerides (mg/dL)} \times \text{fasting glucose (mg/dL)} / 2]$, which has been widely validated as a surrogate marker of insulin resistance. To capture multidimensional metabolic disturbances, three additional TyG-derived indices were constructed following established formulas: TyG-WWI, which integrates waist circumference and weight to better reflect adiposity distribution; TyG-HGB, which incorporates hemoglobin to capture metabolic-inflammatory interactions; and TyG-CI, which combines TyG with cardiometabolic parameters to enhance sensitivity to metabolic dysfunction[22]. All laboratory indicators were obtained under standardized protocols in both cohorts, with NHANES measurements performed at CDC-certified laboratories and CHARLS assays conducted at nationally accredited testing centers.

Outcome assessment

In CHARLS, colorectal tumor status was based on participants' self-reported physician diagnosis of cancer and corresponding system codes indicating colorectal location. NHANES colorectal tumor status was determined using standardized medical condition questionnaires administered by trained interviewers, supplemented by medical condition files indicating self-reported cancer site. In both cohorts, colorectal tumor status was dichotomized as "YES" (presence of colorectal tumor) or "NO" (no colorectal tumor).

Covariates

Covariates were selected based on recognized risk factors for colorectal tumors, metabolic diseases, and potential confounders of TyG-related indices. These included demographic variables (age, sex, marital status, and education level), lifestyle behaviors (smoking and alcohol consumption), and clinical factors such as body mass index (BMI), hypertension, and diabetes status. Laboratory biomarkers-including fasting glucose, lipid profiles, uric acid, liver enzymes, and creatinine-were included when available to minimize residual confounding. All covariates were harmonized across datasets to ensure comparability between CHARLS and NHANES.

Statistical analysis

Continuous variables were expressed as medians with interquartile ranges and compared using the Mann-Whitney U test, while categorical variables were described as counts and percentages and compared using chi-square tests. Logistic regression models were applied to estimate the adjusted odds ratios (ORs) and 95% confidence intervals for the associations between each TyG-related index and colorectal tumor risk. Three models were constructed: Model 1 (unadjusted), Model 2 (adjusted for age and sex), and Model 3 (fully adjusted for all demographic, lifestyle, and clinical covariates). To explore potential nonlinear dose-response patterns, restricted cubic spline (RCS) models with three knots were used. Threshold effects were examined using segmented logistic regression, where inflection points were estimated iteratively, and likelihood ratio tests were used to compare segmented versus linear models. Subgroup analyses were conducted to evaluate effect modification across key clinical strata-age (<60/≥60 years), sex, BMI categories, hypertension, diabetes, smoking, and alcohol intake-by estimating stratum-specific ORs and interaction P-values. Discriminatory performance of each TyG-related index was evaluated using receiver operating characteristic (ROC) curves, from which the area under the curve (AUC), optimal cutoff values (Youden index), sensitivity, and specificity were extracted. Pairwise comparisons of AUCs were conducted using the DeLong test. Sensitivity analyses were additionally performed by modifying covariate structures and excluding extreme TyG values to ensure robustness. All analyses were performed separately in CHARLS and NHANES to allow cross-population comparison.

Ethical considerations

Both CHARLS and NHANES obtained approval from their respective institutional review boards, and all participants provided written informed consent. The present study was a secondary analysis of fully anonymized public datasets and therefore required no additional ethical review.

Results

Characteristics of study participants

A total of 9,293 participants from the 2011-2018 CHARLS waves and 2,839 participants from the 1999-2018 NHANES cycles were included after applying the prespecified exclusion criteria (**Figure 1**). In CHARLS, individuals were excluded for

missing colorectal tumor status, incomplete metabolic indicators, or missing covariates, resulting in 9,270 participants without colorectal tumor (99.75%) and 23 with colorectal tumor (0.25%). In NHANES, exclusions were based on missing colorectal tumor status, metabolic indicators, or covariates, yielding 2,646 participants without colorectal tumor (93.20%) and 193 with colorectal tumor (6.80%). These flowcharts outline the derivation of the analytic samples and ensure consistency in the population selection process across cohorts.

Baseline characteristics of participants in the CHARLS cohort are presented in **Table 1**. Individuals with colorectal tumors had significantly higher levels of fasting glucose, triglycerides, SBP, DBP, and all TyG-related indices (TyG, TyG-WWI, TyG-HGB, TyG-CI) than those without tumors ($P < 0.05$). By contrast, HDL-C, LDL-C, BUN, and creatinine levels were lower among participants with colorectal tumors. No significant differences were observed in age, BMI, cholesterol, uric acid, WBC count, or platelet count. Among categorical variables, the prevalence of hypertension and diabetes was higher in the tumor group, while age category, sex, marital status, smoking, and drinking status showed no statistically significant differences. Baseline characteristics of NHANES participants are summarized in **Table 2**. Compared with participants without colorectal tumors, those with tumors exhibited significantly higher waist circumference, systolic blood pressure, fasting glucose, triglycerides, uric acid, GGT, creatinine, and TyG-related indices ($P < 0.05$). Most hematological and hepatic parameters (WBC, platelet count, AST, ALT, LDH) were similar between groups. In categorical comparisons, older age (≥ 60 years), lower education, living alone, hypertension, and diabetes were more common among participants with colorectal tumors, whereas sex, alcohol use, and smoking status did not differ significantly.

Associations between TyG-related indices and colorectal tumor risk

Multivariable logistic regression analyses demonstrated consistent positive associations between TyG-related metabolic indices and colorectal tumor risk in both the CHARLS and NHANES cohorts (**Table 3**). In the CHARLS cohort, all TyG-derived indices showed significant associations across crude and adjusted models. For TyG, the association remained strong after full adjustment (Model 3: OR = 3.98, 95% CI: 2.66-5.94). Similar patterns were observed for TyG-CI (OR = 2.00, 95% CI: 1.60-2.50) and

TyG-HGB (OR = 1.28, 95% CI: 1.20-1.36), while TyG-WWI also showed a modest but statistically significant association (OR = 1.08, 95% CI: 1.06-1.11). These findings indicate that higher levels of TyG and its derivative indices were robustly associated with increased colorectal tumor risk in the Chinese population. Consistent associations were observed in the NHANES cohort. Higher TyG levels were associated with elevated colorectal tumor risk (Model 3: OR = 1.69, 95% CI: 1.34-2.12), and positive associations were also identified for TyG-CI (OR = 1.24, 95% CI: 1.09-1.41), TyG-HGB (OR = 1.22, 95% CI: 1.16-1.29), and TyG-WWI (OR = 1.02, 95% CI: 1.01-1.04). Although effect estimates in NHANES were comparatively smaller than those in CHARLS, the associations remained consistent and statistically significant across all adjusted models.

Nonlinear dose-response relationships

Restricted cubic spline analyses revealed clear nonlinear dose-response relationships between TyG-related indices and colorectal tumor risk across both the CHARLS and NHANES cohorts (**Figure 2A-H**). In the CHARLS cohort, all four indices (TyG, TyG-CI, TyG-HGB, TyG-WWI) showed significant overall and nonlinear associations (all P for overall < 0.001; P for nonlinear < 0.05). Corresponding two-piecewise logistic regression models further confirmed distinct inflection points (TyG: 10.88; TyG-CI: 14.63; TyG-HGB: 15.66; TyG-WWI: 93.54) (**Supplementary Table S1**). Below these thresholds, the associations were weak or nonsignificant (e.g., TyG < 10.88: OR = 0.98, 95% CI: 0.48-2.03; TyG-CI < 14.63: OR = 0.97, 95% CI: 0.69-1.37), whereas above the thresholds, risk increased markedly (TyG-CI $\geq$ 14.63: OR = 1.40, 95% CI: 0.72-2.72; TyG-WWI $\geq$ 93.54: OR = 1.10, 95% CI: 1.07-1.13), with all likelihood ratio tests supporting significant threshold effects (all P < 0.001).

Similar nonlinear patterns were observed in the NHANES cohort, where overall and nonlinear associations were statistically significant for all indices (all P for overall < 0.001; P for nonlinear < 0.05), and the spline curves showed sharp risk elevation at higher index levels (**Figure 2E-H**). Consistently, two-piecewise models identified comparable inflection points (TyG: 9.93; TyG-CI: 13.90; TyG-HGB: 12.78; TyG-WWI: 119.76) (**Supplementary Table S2**). Below each threshold, associations were minimal or nonsignificant (e.g., TyG < 9.93: OR = 1.16, 95% CI: 0.88-1.54; TyG-CI < 13.90: OR = 1.07, 95% CI: 0.93-1.23), while above the thresholds, risk increased sharply (TyG $\geq$ 9.93:

OR = 202.54, 95% CI: 27.31-1502.19; TyG-CI ≥ 13.90 : OR = 3.72, 95% CI: 2.03-6.81; TyG-HGB ≥ 12.78 : OR = 1.56, 95% CI: 1.31-1.85; TyG-WWI ≥ 119.76 : OR = 1.17, 95% CI: 1.08-1.27), with robust statistical evidence for threshold effects (all P for likelihood tests < 0.01). Collectively, these findings indicate that colorectal tumor risk remains stable at lower TyG-related index levels but rises sharply once cohort-specific metabolic thresholds are surpassed.

Discriminatory ability of TyG-related indices

Receiver operating characteristic analyses showed that TyG-related indices demonstrated moderate discriminatory performance for identifying colorectal tumors in the CHARLS cohort (**Figure 3A**). The AUC values were 0.786 for TyG, 0.773 for TyG-WWI, 0.767 for TyG-HGB, and 0.770 for TyG-CI, with sensitivities around 0.609 and specificities ranging from 0.931 to 0.985. These results indicate that all four indices had comparable and moderately accurate classification ability in the Chinese population. In contrast, the discriminatory accuracy was lower in the NHANES cohort (**Figure 3B**). The corresponding AUC values were 0.570 for TyG, 0.580 for TyG-WWI, 0.587 for TyG-HGB, and 0.579 for TyG-CI, with sensitivities ranging from 0.197 to 0.415 and specificities between 0.731 and 0.933. Although all AUCs were statistically higher than 0.5, the overall predictive performance in NHANES was noticeably weaker than in CHARLS, suggesting cohort-specific differences in discrimination ability.

Subgroup analyses

Subgroup analyses in the CHARLS cohort demonstrated that the positive associations between TyG-related indices and colorectal tumor risk were generally consistent across major demographic and clinical strata (**Figure 4A-D**). For TyG, the association remained significant in both younger (<60 years) and older participants (≥ 60 years), with a stronger effect observed in the older group (OR = 2.50, 95% CI: 1.61-3.88). Similar patterns were seen across marital status, gender, drinking behavior, hypertension, and diabetes, with ORs ranging approximately from 2.22 to 5.64 in different subgroups, although some interaction P-values suggested modest heterogeneity (e.g., P for interaction = 0.024 for hypertension). For TyG-CI, subgroup-specific ORs consistently indicated a positive association, particularly among participants drinking alcohol (OR = 2.82, 95% CI: 1.90-4.16) and those with diabetes (OR = 2.60, 95% CI:

1.74-3.89), with significant interactions for age and drinking (P for interaction = 0.001 and 0.012, respectively). TyG-HGB and TyG-WWI also showed stable associations across most subgroups, albeit with relatively smaller effect sizes; higher risks were observed among females, hypertensive individuals, and participants aged <60 years for TyG-HGB, and among drinkers and diabetic participants for TyG-WWI. Overall, although some subgroup interactions reached statistical significance, none reversed the direction of effect, indicating that the relationship between TyG-related metabolic alterations and colorectal tumor risk remained robust across diverse population subgroups.

Subgroup analyses in the NHANES cohort showed that the associations between TyG-related indices and colorectal tumor risk were largely consistent across demographic and clinical subgroups (**Figure 5A-D**). For TyG, elevated risk was observed in both age groups (<60 and $\geq$ 60 years), with stronger effects in younger participants (OR = 2.36, 95% CI: 1.51-3.70) compared with older adults (OR = 1.64, 95% CI: 1.29-2.07). Similar patterns were seen across marital status and gender, with ORs ranging from approximately 1.63 to 1.97 in different strata. For TyG-CI, the association remained significant in all subgroups, including drinkers (OR = 1.34, 95% CI: 1.17-1.53) and individuals with diabetes (OR = 1.64, 95% CI: 1.34-2.01), while interaction tests indicated modest heterogeneity for age (P = 0.066) and diabetes (P = 0.004). The TyG-HGB index showed stable associations across age, sex, marital status, and lifestyle factors, with effect sizes clustering between OR = 1.18 and 1.27 in most subgroups. For TyG-WWI, consistent positive associations were also observed, with slightly stronger effects among individuals with hypertension (OR = 1.03-1.05) and diabetes (OR = 1.05, 95% CI: 1.03-1.08). Although several interaction P -values suggested minor subgroup differences, none of the associations reversed direction, and all four indices maintained significant relationships with colorectal tumor risk across the NHANES population.

Discussion

In this large cross-population analysis incorporating nationally representative data from CHARLS and NHANES, we found that TyG and three TyG-derived metabolic indices (TyG-CI, TyG-HGB, TyG-WWI) were consistently and positively associated

with colorectal tumor risk. These associations persisted across diverse demographic and clinical subgroups and exhibited clear nonlinear dose-response patterns with identifiable metabolic thresholds. Collectively, our findings provide new evidence supporting the role of TyG-related metabolic dysfunction in colorectal tumorigenesis and suggest their potential utility as accessible markers for population-level metabolic risk stratification.

Our results complement and extend the growing literature linking metabolic dysregulation to colorectal neoplasia. Insulin resistance, hyperinsulinemia, and chronic low-grade inflammation have long been recognized as key biological mechanisms promoting colorectal epithelial proliferation, angiogenesis, and tumor progression[23]. Prior studies have shown that higher TyG levels are associated with increased risks of colorectal adenoma, colorectal cancer, and interval colorectal cancer. However, most existing research has relied on small, single-center, or homogenous populations, and the evidence for TyG-derived indices remains sparse[24–26]. By analyzing two large cohorts from different ethnic and metabolic backgrounds, our study demonstrates that not only the traditional TyG index but also the TyG-derived indices—TyG-CI, TyG-HGB, and TyG-WWI—consistently reflect colorectal tumor risk. The stronger associations observed in CHARLS relative to NHANES may reflect population differences in baseline metabolic burden, lifestyle patterns, genetic susceptibility, or cancer detection pathways, yet the overall direction of association remained robust.

A key contribution of this study is the identification of nonlinear and threshold relationships between TyG-related markers and colorectal tumor risk[26,27]. Unlike previous studies assuming linearity, our restricted cubic spline analyses revealed that risk remained relatively stable at lower levels of each index but increased sharply beyond population-specific inflection points. For example, risk sharply escalated when TyG exceeded 10.88 in CHARLS and 9.93 in NHANES, corresponding to metabolically adverse ranges known to reflect pronounced insulin resistance. These findings underscore that the metabolic transition from relatively healthy to high-risk states may occur over narrow ranges and that TyG-based indices may serve as early warning indicators before overt metabolic disease develops. The consistent identification of thresholds across both Asian and Western populations supports the biological plausibility of these inflection

points and provides quantitative cutoffs that could inform future risk-based screening strategies[28,29].

Subgroup analyses further strengthened the credibility of our findings. The associations between TyG-related indices and colorectal tumor risk were largely preserved across age, sex, marital status, drinking behavior, hypertension, and diabetes strata. The stronger associations observed in participants with diabetes, hypertension, or central obesity align with mechanistic studies showing synergistic interactions among insulin resistance, adipose dysfunction, and inflammation in colorectal carcinogenesis[30]. Although certain subgroups demonstrated modest heterogeneity-such as younger participants in NHANES showing stronger associations-none of the interactions reversed the direction of effect. This suggests that TyG-related metabolic stress is a broadly relevant tumor-promoting mechanism, independent of traditional risk factors.

This study has several limitations. First, both CHARLS and NHANES ascertain colorectal tumor status primarily through self-reported physician diagnoses, which may lead to under-reporting or misclassification, although such bias is likely nondifferential[31,32]. Second, the cross-sectional design precludes causal inference, and reverse causality cannot be fully excluded-metabolic disturbances could both precede and result from tumor presence. Third, although we adjusted for a comprehensive panel of covariates, residual confounding from unmeasured factors such as dietary patterns, physical activity, microbiome composition, or genetic predisposition may persist. Fourth, the relatively small number of tumor cases in CHARLS limited statistical power for certain subgroup analyses. Finally, TyG-derived indices incorporate different anthropometric or hematologic variables across populations, which may introduce measurement variability between CHARLS and NHANES.

In conclusion, this cross-population study demonstrates that TyG and TyG-based metabolic indices are consistently associated with increased colorectal tumor risk, exhibit nonlinear dose-response patterns with identifiable thresholds, and maintain predictive value across diverse population subgroups. These findings highlight the relevance of accessible metabolic indices for identifying individuals at elevated risk for colorectal tumors and underscore the importance of metabolic health in colorectal cancer

prevention. Future prospective studies are warranted to validate the observed thresholds, elucidate underlying biological pathways, and evaluate the clinical utility of integrating TyG-related markers into risk prediction and screening strategies.

Abbreviations

AUC: Area under the curve
BMI: Body mass index
BUN: Blood urea nitrogen
CDC: Centers for Disease Control and Prevention
CHARLS: China Health and Retirement Longitudinal Study
CI: Confidence interval
DBP: Diastolic blood pressure
GGT: Gamma-glutamyl transferase
HDL-C: High-density lipoprotein cholesterol
IR: Insulin resistance
LDH: Lactate dehydrogenase
LDL-C: Low-density lipoprotein cholesterol
NHANES: National Health and Nutrition Examination Survey
OR: Odds ratio
RCS: Restricted cubic spline
ROC: Receiver operating characteristic
SBP: Systolic blood pressure
TG: Triglycerides
TyG: Triglyceride-glucose index
TyG-CI: Triglyceride-glucose index-cardiometabolic index
TyG-HGB: Triglyceride-glucose index-hemoglobin index
TyG-WWI: Triglyceride-glucose index-weight-adjusted waist index

References

- [1] A. Maharati, M. Moghbeli, PI3K/AKT signaling pathway as a critical regulator of epithelial-mesenchymal transition in colorectal tumor cells, *Cell Commun Signal* 21 (2023) 201. <https://doi.org/10.1186/s12964-023-01225-x>.

- [2] W.H. Fridman, I. Miller, C. Sautès-Fridman, A.T. Byrne, Therapeutic Targeting of the Colorectal Tumor Stroma, *Gastroenterology* 158 (2020) 303–321. <https://doi.org/10.1053/j.gastro.2019.09.045>.
- [3] N.M. Hogan, R.M. Dwyer, M.R. Joyce, M.J. Kerin, Mesenchymal stem cells in the colorectal tumor microenvironment: recent progress and implications, *Int J Cancer* 131 (2012) 1–7. <https://doi.org/10.1002/ijc.27458>.
- [4] Y. Chen, Z. Ma, X. Gong, LEF1 Suppresses Ferroptosis in Colorectal Cancer Cells by Targeted Promotion of SLC7A11 Transcription, *FASEB J* 39 (2025) e71231. <https://doi.org/10.1096/fj.202502018R>.
- [5] F. Cong, J. Zhang, W. Pao, P. Zhou, H. Varmus, A protein knockdown strategy to study the function of beta-catenin in tumorigenesis, *BMC Mol Biol* 4 (2003) 10. <https://doi.org/10.1186/1471-2199-4-10>.
- [6] Y. Li, J. Zhou, H. Luo, S. Li, Y. Shi, D. Chen, X. Hu, Prognostic value of platelet to lymphocyte ratio in patients with colorectal cancer undergoing chemotherapy: a systematic review and meta-analysis, *Front Immunol* 16 (2025) 1642181. <https://doi.org/10.3389/fimmu.2025.1642181>.
- [7] Y. Zhang, R. Yuan, D. Li, Association between triglyceride-glucose index and risk of chronic kidney disease: a meta-analysis, *Ren Fail* 47 (2025) 2572356. <https://doi.org/10.1080/0886022X.2025.2572356>.
- [8] S. Peng, C. Wang, Q. Liu, Q. Luo, The association of triglyceride-glucose index with cancer incidence and mortality: a systematic review and meta-analysis of cohort studies, *Front Endocrinol (Lausanne)* 16 (2025) 1682062. <https://doi.org/10.3389/fendo.2025.1682062>.
- [9] M. Du, L. Chen, Y. Li, L. Xia, Y. Liu, M. Guo, Z. Zhang, Y. Li, Association between sedentary behavior, physical activity, and the triglyceride glucose index and its derived indices: evidence from NHANES 2013-2018, *J Exerc Sci Fit* 23 (2025) 451–461. <https://doi.org/10.1016/j.jesf.2025.10.003>.
- [10] M. Chen, J. Guo, Y. Shangguan, Z. Sun, X. He, Q. Tu, Q. Yan, Association of the triglyceride-glucose index combined with a body shape index with all-cause and cardiovascular mortality in individuals with cardiovascular-kidney-metabolic syndrome stage 0-3: findings from two prospective cohorts, *Cardiovasc Diabetol* 24 (2025) 366. <https://doi.org/10.1186/s12933-025-02921-3>.
- [11] N. Zhang, J. Wu, Q. Wang, Y. Liang, X. Li, G. Chen, L. Ma, X. Liu, F. Zhou, Global burden of hematologic malignancies and evolution patterns over the past 30 years, *Blood Cancer J* 13 (2023) 82. <https://doi.org/10.1038/s41408-023-00853-3>.
- [12] Y. Fan, D. Ye, K. Zhou, L. Cai, L. Yu, The novel triglyceride–glucose-weighted adjusted waist index as a supplementary diagnostic tool for heart failure: evidence of improved reclassification beyond traditional TyG-related indices from a cross-sectional study, *Cardiovasc Diabetol* 24 (2025) 329. <https://doi.org/10.1186/s12933-025-02896-1>.
- [13] N. Zhang, Q. Wang, G. Chen, L. Liu, Z. Wang, L. Ma, Y. Liang, J. Wu, X. Li, X. Liu, F. Zhou, Jab1 promotes immune evasion and progression in acute myeloid leukemia models under oxidative stress, *J Clin Invest* 135 (2025) e183761. <https://doi.org/10.1172/JCI183761>.
- [14] Y. Li, Z. Luo, Z. Zhang, N. Huang, L. Xiao, J. Li, K. Zou, J. Wang, Exploring the mediating role of TyG-related indicators in the relationship between biological aging

- and late-stage cardiovascular-kidney-metabolic in middle-aged and older adults, *Diabetes Res Clin Pract* 230 (2025) 112988. <https://doi.org/10.1016/j.diabres.2025.112988>.
- [15] Z.-K. Wei, C.-Y. Li, Z.-Y. Liu, B.-L. Wang, C. Wang, Y. Liu, T.-J. Ba, L. Kong, F.-H. Zhang, Nonlinear association between TyG-related Indices and motoric cognitive risk syndrome in depressive individuals: evidence from the CHARLS study, *Front Psychiatry* 16 (2025) 1622973. <https://doi.org/10.3389/fpsyt.2025.1622973>.
- [16] R. Jiang, S. Xing, X. Wang, S. Chen, S. Wu, Association between TyG-related indices and colorectal cancer risk: A prospective cohort study, *Int J Cancer* (2025). <https://doi.org/10.1002/ijc.70222>.
- [17] M.-Y. Tan, Z.-N. Jiang, Y.-Q. Li, Z.-Y. Li, B. Niu, Association of estimated glucose disposition rate with aging acceleration and mortality risk in individuals with cardiovascular-kidney-metabolic syndrome: evidence from two large national population-based studies, *Cardiovasc Diabetol* 24 (2025) 402. <https://doi.org/10.1186/s12933-025-02940-0>.
- [18] Z. Zhao, S. Cheng, S. Li, Dynamic patterns of depression and their association with stroke: insights from CHARLS, ELSA, and HRS, *Int J Surg* (2025). <https://doi.org/10.1097/JS9.0000000000003909>.
- [19] Y. Yang, A. Liu, Associations of cumulative exposure and dynamic trajectories of the C-reactive protein-triglyceride-glucose index with incident stroke in middle-aged and older Chinese adults: a longitudinal analysis based on CHARLS, *Cardiovasc Diabetol* 24 (2025) 386. <https://doi.org/10.1186/s12933-025-02945-9>.
- [20] R.O. Almadfaa, Racial and socioeconomic disparities in the utilization of diabetes medication: A comprehensive analysis of NHANES 2011-2023, *Res Social Adm Pharm* (2025) S1551-7411(25)00493-0. <https://doi.org/10.1016/j.sapharm.2025.10.013>.
- [21] E. Pyo, R. Haardörfer, L. Aguayo, M. Vos, M.B. Weber, J.A. Welsh, Associations of Acculturation With Added Sugars Intake and Weight Status Among Mexican American Adolescents in the United States, NHANES, 2009-2018, *Pediatr Obes* (2025) e70063. <https://doi.org/10.1111/ijpo.70063>.
- [22] Z. Li, Y. Ban, M. Hu, L. Deng, X. Xie, Joint association of triglyceride-glucose index and obesity indicators with stroke risk: a nationwide prospective cohort study, *Sci Rep* 15 (2025) 37276. <https://doi.org/10.1038/s41598-025-21331-9>.
- [23] C. Xie, Y. Yuan, Y. Wang, C. Qi, W. Wang, C. An, A. Aikepaer, Y. Zhang, G. Zhang, X. Feng, H. Gao, Beyond Discrete Diagnoses: Conceptualizing Obesity-associated Metabolic Disorders as a Unified, Dynamic Continuum, *Curr Obes Rep* 14 (2025) 81. <https://doi.org/10.1007/s13679-025-00673-5>.
- [24] C. Göbl, A. Dardano, G. Daniele, A. Tura, Is It Worth Assessing the Prevalence of Sarcopenia in Pregnant Women? Should Any Impact on Pregnancy Outcomes Be Expected?, *Nutrients* 17 (2025) 2682. <https://doi.org/10.3390/nu17162682>.
- [25] A.M. Cybulska, K. Rachubińska, E. Grochans, M. Bosiacki, D. Simińska, J. Korbecki, A. Lubkowska, M. Panczyk, M. Kuczyńska, D. Schneider-Matyka, Systemic Inflammation Indices, Chemokines, and Metabolic Markers in Perimenopausal Women, *Nutrients* 17 (2025) 2885. <https://doi.org/10.3390/nu17172885>.

- [26] M.P. Narayanan, A. Sehrawat, B. Goyal, P. Kumar, S. Bansal, S. Gupta, A. Gupta, A.A. Mirza, D. Sundriyal, S. Gupta, Association between insulin resistance biomarkers and metastatic prognosis in treatment-naïve colorectal cancer patients: a pilot study, *BMC Cancer* 25 (2025) 1711. <https://doi.org/10.1186/s12885-025-14669-w>.
- [27] Z. Wu, J. Yang, Z. Ma, Y. Chen, M. Han, Q. Wu, C. Zhang, S. Huang, B. Hou, Q. Zhou, Associations between triglyceride-glucose related indices and the risk of incident pancreatic cancer: a large-scale prospective cohort study in the UK Biobank, *BMC Cancer* 25 (2025) 327. <https://doi.org/10.1186/s12885-025-13718-8>.
- [28] GBD 2023 Causes of Death Collaborators, Global burden of 292 causes of death in 204 countries and territories and 660 subnational locations, 1990-2023: a systematic analysis for the Global Burden of Disease Study 2023, *Lancet* 406 (2025) 1811–1872. [https://doi.org/10.1016/S0140-6736\(25\)01917-8](https://doi.org/10.1016/S0140-6736(25)01917-8).
- [29] N. Zhang, P. Zhang, Y. Chen, S. Lou, H. Zeng, J. Deng, Clusterization in acute myeloid leukemia based on prognostic alternative splicing signature to reveal the clinical characteristics in the bone marrow microenvironment, *Cell Biosci* 10 (2020) 118. <https://doi.org/10.1186/s13578-020-00481-5>.
- [30] D.A. Lamabadusuriya, H. Jayasena, A.K. Bopitiya, A.D. De Silva, P. Jayasekera, Obesity-driven inflammation and cancer risk: A comprehensive review, *Semin Cancer Biol* 114 (2025) 256–266. <https://doi.org/10.1016/j.semcancer.2025.07.007>.
- [31] Y. Deng, F. Chen, Y. Xiong, S. Li, Q. Zhang, M.T. Knopf, J. Li, Z. Ye, Identifying gender-specific treatment targets for depression in cancer survivors: Evidence from NHANES, *Eur J Oncol Nurs* 80 (2025) 103030. <https://doi.org/10.1016/j.ejon.2025.103030>.
- [32] J. Tang, W. Gu, M. Wang, J. Liu, Y. Chen, X. Zhang, Association between extreme temperature events and multimorbidity among older adults: evidence from the CHARLS, *BMC Med* 23 (2025) 625. <https://doi.org/10.1186/s12916-025-04456-6>.

Table 1. Baseline demographic and metabolic characteristics of CHARLS participants with and without colorectal cancer.

Variables	Total 9293)	(n =	NO (n = 9270)	YES (n = 23)	Stati stic	P	
Age, M (Q1, Q3)	61.00 68.00)	(53.00,	61.00 68.00)	(53.00,	61.00 65.00)	(56.50, Z=- 0.30	0.7 68
Bmi, M (Q1, Q3)	23.74 26.31)	(21.39,	23.74 26.31)	(21.38,	23.82 25.73)	(22.37, Z=- 0.40	0.6 88
Glucose 31, M (Q1, Q3)	95.50 104.50)	(88.29,	95.50 104.50)	(88.29,	106.31 123.42)	(96.40, Z=- 3.24	0.0 01
Cholesterol 33, M (Q1, Q3)	181.85 206.18)	(160.23,	181.85 206.18)	(160.23,	192.28 232.63)	(166.02, Z=- 1.43	0.1 53
Hdl 34, M (Q1, Q3)	49.81 57.53)	(43.24,	49.81 57.53)	(43.24,	44.02 52.32)	(36.68, Z=- 2.86	0.0 04
Ldl 35, M (Q1, Q3)	101.54 120.08)	(83.01,	101.54 120.08)	(83.01,	84.56 106.56)	(65.64, Z=- 2.70	0.0 07
Tg 36, M (Q1, Q3)	112.39 164.60)	(81.42,	112.39 164.60)	(81.42,	500.00 500.00)	(118.58, Z=- 4.75	<.0 01
Bun 37, M (Q1, Q3)	14.85 17.93)	(12.32,	14.85 17.93)	(12.32,	13.73 14.57)	(11.48, Z=- 2.05	0.0 4
Creatine 38, M (Q1, Q3)	0.76 0.89)	(0.65,	0.76 0.89)	(0.65,	0.68 0.77)	(0.56, Z=- 2.19	0.0 29
Uricacid 39, M (Q1, Q3)	4.80 5.70)	(3.90,	4.80 5.70)	(3.90,	4.90 6.20)	(4.10, Z=- 0.91	0.3 61
Wbc 44, M (Q1, Q3)	5.70 6.81)	(4.73,	5.70 6.81)	(4.73,	5.73 6.90)	(4.88, Z=- 0.41	0.6 82
Platelet 46, M (Q1, Q3)	201.00 244.00)	(160.00,	201.50 244.00)	(160.00,	174.00 267.00)	(132.50, Z=- 1.08	0.2 8
SBP 59, M (Q1, Q3)	127.33 142.00)	(114.67,	127.33 142.00)	(114.67,	143.00 157.00)	(127.83, Z=- 3.15	0.0 02
DBP 63, M (Q1, Q3)	75.00 85.00)	(68.00,	75.00 85.00)	(68.00,	85.00 95.00)	(72.00, Z=- 3.15	0.0 02

Q3)	83.00)	83.00)	92.17)	2.76	06
TyG 115, M (Q1, Q3)	8.75 (8.11, 9.51)	8.75 (8.11, 9.51)	11.74 (8.86, 11.74)	Z=-4.75	<.001
TyGWWI, M (Q1, Q3)	98.19 (88.09, 109.68)	98.14 (88.08, 109.60)	130.82 (104.08, 135.50)	Z=-4.54	<.001
TyG-HGB, M (Q1, Q3)	8.47 (7.39, 10.30)	8.46 (7.39, 10.29)	17.43 (9.35, 21.21)	Z=-4.43	<.001
TyGCI, M (Q1, Q3)	11.30 (10.17, 12.60)	11.30 (10.17, 12.60)	14.97 (11.61, 15.67)	Z=-4.48	<.001
Agefenji, n(%)				$\chi^2=0.69$	0.407
<60	4027 (43.33)	4019 (43.35)	8 (34.78)		
≥ 60	5266 (56.67)	5251 (56.65)	15 (65.22)		
Marryfenji, n(%)				$\chi^2=0.06$	0.8
Live alone	1632 (17.56)	1627 (17.55)	5 (21.74)		
Live with partner	7661 (82.44)	7643 (82.45)	18 (78.26)		
Gender, n(%)				$\chi^2=0.39$	0.534
1	4249 (45.72)	4237 (45.71)	12 (52.17)		
2	5044 (54.28)	5033 (54.29)	11 (47.83)		
Drinkl, n(%)				$\chi^2=0.78$	0.377
0	6067 (65.29)	6054 (65.31)	13 (56.52)		
1	3226 (34.71)	3216 (34.69)	10 (43.48)		
Smoken, n(%)				$\chi^2=0.33$	0.564
0	6777 (72.93)	6759 (72.91)	18 (78.26)		

1	2516 (27.07)	2511 (27.09)	5 (21.74)		
Diaht1, n(%)				$\chi^2=7.70$	0.006
0	6172 (66.42)	6163 (66.48)	9 (39.13)		
1	3121 (33.58)	3107 (33.52)	14 (60.87)		
Diabe1, n(%)				$\chi^2=3.23$	0.072
0	7289 (78.44)	7275 (78.48)	14 (60.87)		
1	2004 (21.56)	1995 (21.52)	9 (39.13)		

Z: Mann-Whitney test, χ^2 : Chi-square test

M: Median, Q1: 1st Quartile, Q3: 3rd Quartile

Table 2. Comparison of demographic and metabolic characteristics between participants with and without colorectal tumors in the NHANES cohort

Variables	Total 2839)	(n =	NO (n = 2646)	YES (n = 193)	Statistic	P
High, M (Q1, Q3)	167.00 (159.80, 174.40)		166.90 (159.90, 174.30)	167.80 (158.80, 174.70)	Z=-0.00	0.99
Weight, M (Q1, Q3)	78.80 (67.20, 92.50)		78.60 (67.20, 92.30)	80.70 (67.20, 95.70)	Z=-1.31	0.192
WC, M (Q1, Q3)	101.50 (91.60, 111.20)		101.30 (91.32, 111.07)	103.50 (93.40, 115.20)	Z=-2.25	0.024
BMI, M (Q1, Q3)	28.00 (24.51, 32.36)		27.93 (24.39, 32.30)	28.70 (25.70, 33.30)	Z=-1.95	0.051
SBP, M (Q1, Q3)	127.33 (115.33, 141.33)		126.67 (115.33, 140.67)	132.67 (120.00, 148.00)	Z=-3.53	<0.01
DBP, M (Q1, Q3)	68.67 (60.67, 76.00)		68.67 (60.67, 76.00)	67.33 (60.00, 74.67)	Z=-1.78	0.074
WBC, M (Q1, Q3)	6.90 (5.60, 8.30)		6.90 (5.60, 8.30)	6.60 (5.50, 8.20)	Z=-1.37	0.17
Plt, M (Q1, Q3)	231.00 (192.75, 275.00)		232.00 (193.00, 275.00)	227.00 (187.00, 270.00)	Z=-1.06	0.29
Danguchun, M (Q1, Q3)	191.00 (162.00, 221.00)		191.00 (163.00, 221.00)	188.00 (152.00, 221.00)	Z=-1.14	0.255
Creatinine, M (Q1, Q3)	0.92 (0.77, 1.10)		0.91 (0.76, 1.10)	0.99 (0.80, 1.13)	Z=-2.42	0.016
Glu, M (Q1, Q3)	97.00 (89.00, 111.00)		97.00 (88.00, 110.00)	102.00 (92.00, 127.00)	Z=-5.00	<0.01
TG, M (Q1, Q3)	129.00 (88.00, 189.00)		128.00 (88.00, 187.00)	140.00 (96.00, 216.00)	Z=-2.16	0.031
Uricacid, M (Q1, Q3)	5.50 (4.60, 6.50)		5.50 (4.60, 6.50)	5.70 (4.90, 6.60)	Z=-2.17	0.03
AST, M (Q1, Q3)	23.00 (20.00, 23.00)		23.00 (20.00, 23.00)	23.00 (20.00, 23.00)	Z=-	0.4

Q3)	27.00)	27.00)	28.00)	0.72	75
ALT, M (Q1, Q3)	20.00 (16.00, 26.00)	20.00 (16.00, 26.00)	21.00 (16.00, 26.00)	Z=-1.00	0.316
LDH, M (Q1, Q3)	135.00 (118.00, 154.00)	135.00 (118.00, 154.75)	132.00 (115.00, 153.00)	Z=-0.82	0.409
GGT, M (Q1, Q3)	20.00 (15.00, 30.00)	20.00 (15.00, 29.75)	22.00 (16.00, 38.00)	Z=-2.74	0.006
TyG, M (Q1, Q3)	8.78 (8.35, 9.22)	8.77 (8.34, 9.20)	8.95 (8.46, 9.44)	Z=-3.24	0.001
TyGWWI, (Q1, Q3) M	100.29 (92.33, 108.15)	100.14 (92.20, 107.90)	102.63 (94.91, 112.49)	Z=-3.70	<.001
TyG-HGB, (Q1, Q3) M	7.98 (7.00, 9.38)	7.94 (6.99, 9.32)	8.46 (7.28, 10.66)	Z=-4.03	<.001
TyGCI, (Q1, Q3) M	11.90 (10.98, 12.81)	11.87 (10.96, 12.79)	12.14 (11.21, 13.34)	Z=-3.65	<.001
Educationfeji, n(%)				$\chi^2=18.88$	<.001
<high school	240 (8.45)	211 (7.97)	29 (15.03)		
>high school	1599 (56.32)	1515 (57.26)	84 (43.52)		
high school	1000 (35.22)	920 (34.77)	80 (41.45)		
Marriagefenji, n(%)				$\chi^2=4.55$	0.033
live alone	1104 (38.89)	1015 (38.36)	89 (46.11)		
live with partner	1735 (61.11)	1631 (61.64)	104 (53.89)		
Sex, n(%)				$\chi^2=1.37$	0.242
Female	1498 (52.77)	1404 (53.06)	94 (48.70)		
Male	1341 (47.23)	1242 (46.94)	99 (51.30)		

Agefenji60, n(%)				$\chi^2=11.96$	$<.001$
<60	808 (28.46)	774 (29.25)	34 (17.62)		
≥ 60	2031 (71.54)	1872 (70.75)	159 (82.38)		
Alcohol, n(%)				$\chi^2=2.11$	0.147
0	770 (27.12)	709 (26.80)	61 (31.61)		
1	2069 (72.88)	1937 (73.20)	132 (68.39)		
Smoking, n(%)				$\chi^2=1.74$	0.187
0	1247 (43.92)	1171 (44.26)	76 (39.38)		
1	1592 (56.08)	1475 (55.74)	117 (60.62)		
Hypertation, n(%)				$\chi^2=11.51$	$<.001$
0	1229 (43.29)	1168 (44.14)	61 (31.61)		
1	1610 (56.71)	1478 (55.86)	132 (68.39)		
Diabetes, n(%)				$\chi^2=10.70$	0.001
0	2197 (77.39)	2066 (78.08)	131 (67.88)		
1	642 (22.61)	580 (21.92)	62 (32.12)		

Z: Mann-Whitney test, χ^2 : Chi-square test

M: Median, Q1: 1st Quartile, Q3: 3st Quartile

Table 3. Multivariable logistic regression of TyG-related indices and colorectal tumor risk in the CHARLS and NHANES cohorts

Cohort	Variables	Model1		Model2		Model3	
		OR (95%CI)	P	OR (95%CI)	P	OR (95%CI)	P
CHARLS	TyG	3.67 (2.49 ~ 5.39)	<.001	3.90 (2.64 ~ 5.77)	<.001	3.98 (2.66 ~ 5.94)	<.001
	TyGCI	1.93 (1.56 ~ 2.39)	<.001	1.97 (1.59 ~ 2.44)	<.001	2.00 (1.60 ~ 2.50)	<.001
	TyG-HGB	1.12 (1.08 ~ 1.18)	<.001	1.13 (1.08 ~ 1.18)	<.001	1.28 (1.20 ~ 1.36)	<.001
	TyGWI	1.08 (1.05 ~ 1.10)	<.001	1.08 (1.06 ~ 1.11)	<.001	1.08 (1.06 ~ 1.11)	<.001
	TyG	1.80 (1.46 ~ 2.21)	<.001	1.80 (1.46 ~ 2.23)	<.001	1.69 (1.34 ~ 2.12)	<.001
NHANES	TyGCI	1.33 (1.19 ~ 1.48)	<.001	1.29 (1.15 ~ 1.44)	<.001	1.24 (1.09 ~ 1.41)	0.001
	TyG-HGB	1.20 (1.15 ~ 1.25)	<.001	1.21 (1.15 ~ 1.26)	<.001	1.22 (1.16 ~ 1.29)	<.001
	TyGWI	1.03 (1.02 ~ 1.05)	<.001	1.03 (1.02 ~ 1.04)	<.001	1.02 (1.01 ~ 1.04)	0.002

OR: Odds Ratio, CI: Confidence Interval

Model1: Crude

Model2: Adjust: marriage, sex, age

Model3: Adjust: marriage, sex, alcohol, smoking, hypertension, diabetes, age, BMI

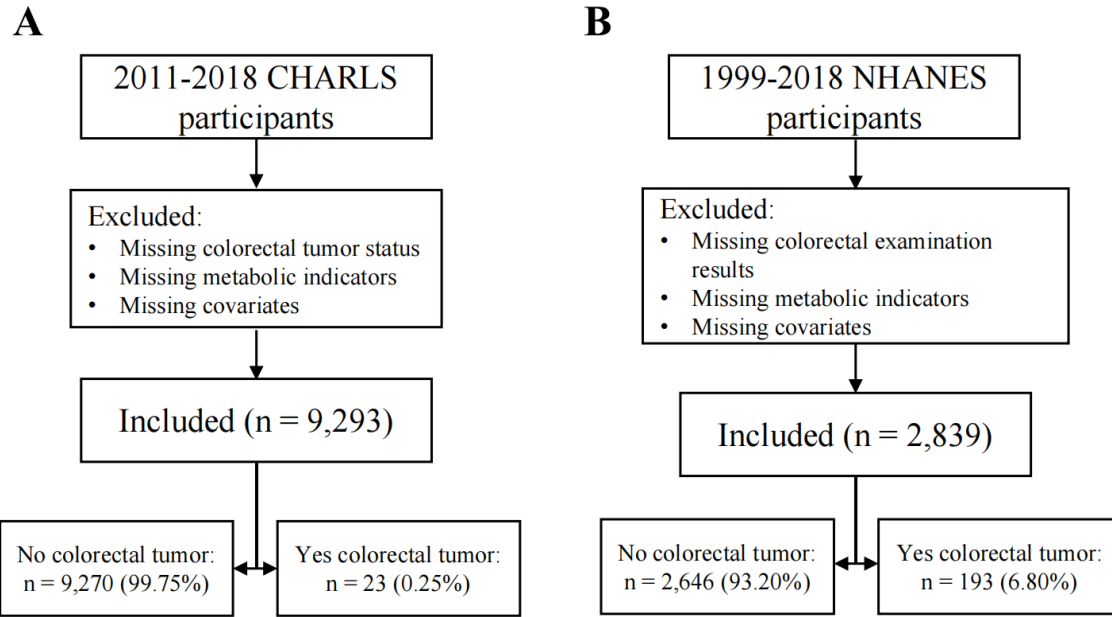


Figure 1. Flowchart of participant selection in the CHARLS and NHANES cohorts.

(A) CHARLS cohort. After excluding individuals with missing colorectal tumor status, metabolic indicators, or covariates, 9,293 participants were included (9,270 without colorectal tumor; 23 with colorectal tumor).

(B) NHANES cohort. After removing participants with missing colorectal tumor status, metabolic indicators, or covariates, 2,839 participants remained (2,646 without colorectal tumor; 193 with colorectal tumor).

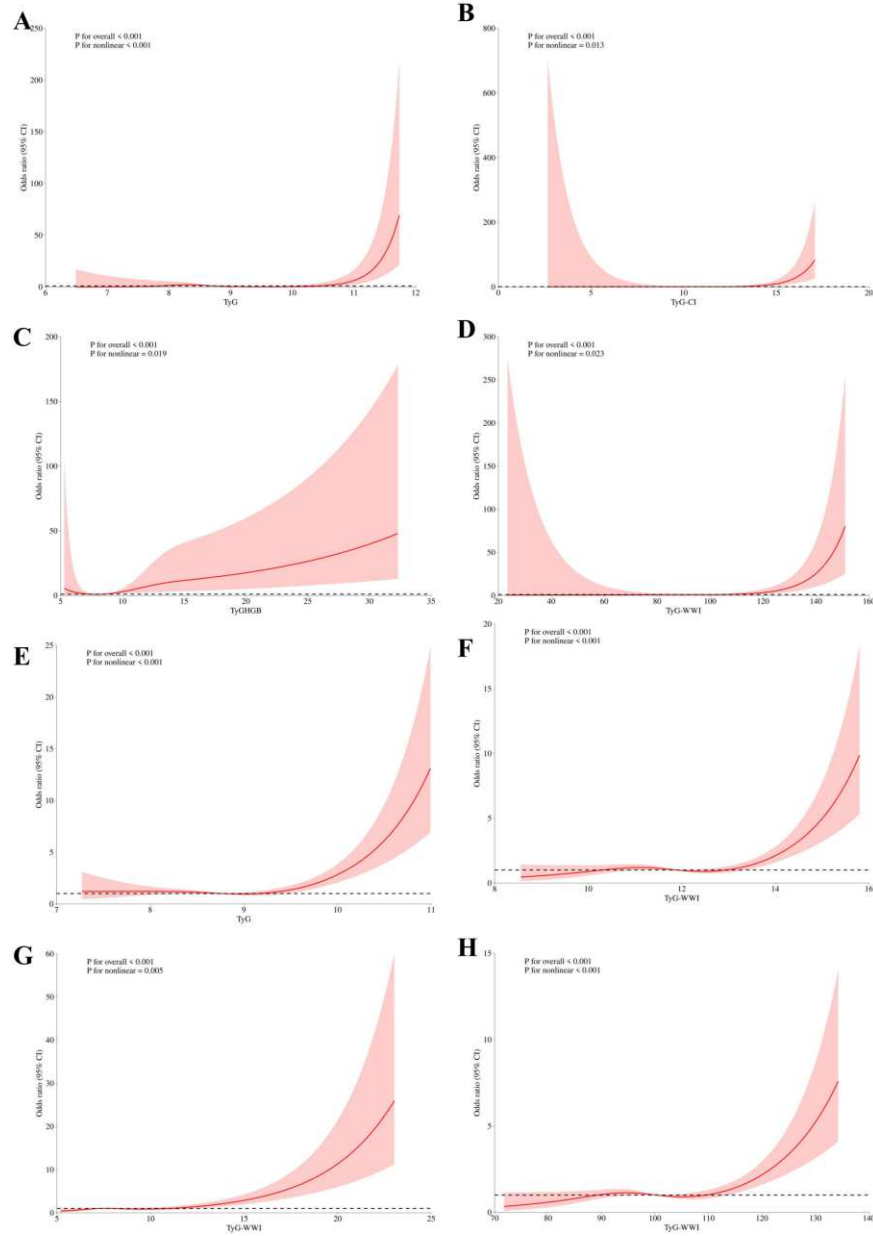


Figure 2. Restricted cubic spline (RCS) analyses of TyG-related indices and colorectal tumor risk in the CHARLS and NHANES cohorts.

(A) TyG, (B) TyG-CI, (C) TyG-HGB, and (D) TyG-WWI in the CHARLS cohort, each showing a significant nonlinear association with colorectal tumor risk. (E) TyG, (F) TyG-CI, (G) TyG-HGB, and (H) TyG-WWI in the NHANES cohort, demonstrating similar nonlinear dose-response patterns. The red line indicates the adjusted odds ratio and the shaded area represents the 95% confidence interval.

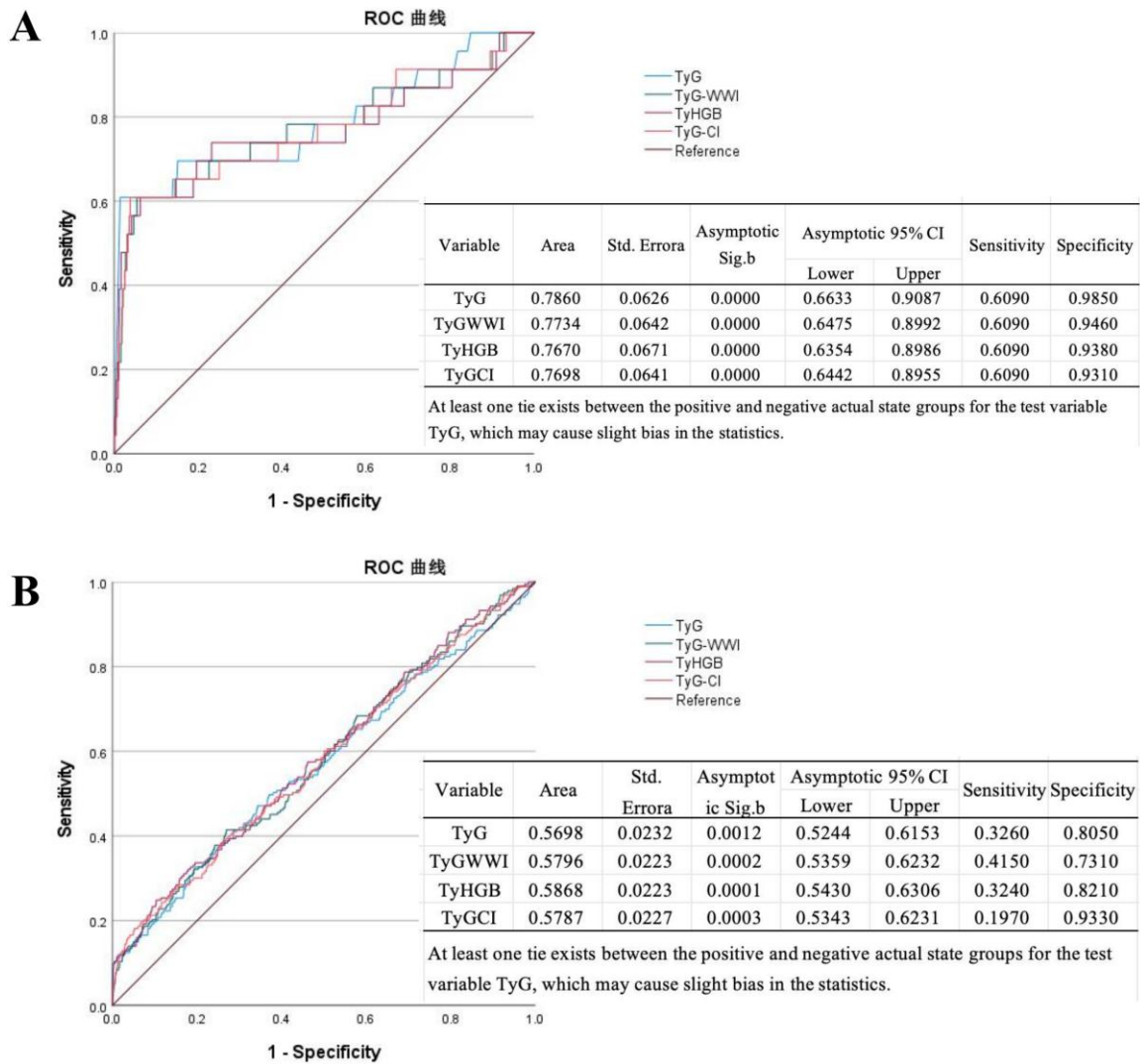


Figure 3. Receiver operating characteristic (ROC) curves of TyG-related indices for predicting colorectal tumor in the CHARLS and NHANES cohorts.

(A) ROC curves for TyG, TyG-WWI, TyG-HGB, and TyG-CI in the CHARLS cohort. The AUC values were 0.786 for TyG, 0.773 for TyG-WWI, 0.767 for TyG-HGB, and 0.770 for TyG-CI.

(B) ROC curves for the same four indices in the NHANES cohort, with corresponding AUC values of 0.570 for TyG, 0.580 for TyG-WWI, 0.587 for TyG-HGB, and 0.579 for TyG-CI.

A CHARLS-TyG					
Variables	n (%)	OR (95%CI)	P	P for interaction	
All patients	9293 (100.00)	3.67 (2.49 ~ 5.39)	<.001		
Age					
<60	4027 (43.33)	Inf (0.00 ~ Inf)	0.911		
≥60	5266 (56.67)	2.50 (1.61 ~ 3.88)	<.001		
Marital status				0.316	
Live alone	1632 (17.56)	2.64 (1.22 ~ 5.69)	0.013		
Live with partne	7661 (82.44)	4.18 (2.63 ~ 6.65)	<.001		
Gender				0.323	
Male	4249 (45.72)	3.11 (1.92 ~ 5.05)	<.001		
Female	5044 (54.28)	4.61 (2.47 ~ 8.60)	<.001		
Drinking				0.005	
NO	6067 (65.29)	2.38 (1.48 ~ 3.82)	<.001		
YES	3226 (34.71)	3.52 (3.46 ~ 21.00)	<.001		
Hypertension				0.024	
NO	6172 (66.42)	2.22 (1.28 ~ 3.86)	0.004		
YES	3121 (33.58)	3.64 (3.00 ~ 10.60)	<.001		
Diabetes				0.007	
NO	7289 (78.44)	2.64 (1.69 ~ 4.13)	<.001		
YES	2004 (21.56)	1.98 (3.33 ~ 43.1)	<.001		

B CHARLS-TyGCI					
Variables	n (%)	OR (95%CI)	P	P for interaction	
All patients	9293 (100.00)	1.93 (1.56 ~ 2.39)	<.001		
Age				0.001	
<60	4027 (43.33)	3.81 (2.19 ~ 6.62)	<.001		
≥60	5266 (56.67)	1.54 (1.19 ~ 1.99)	<.001		
Marital status				0.148	
Live alone	1632 (17.56)	1.45 (0.93 ~ 2.27)	0.103		
Live with partne	7661 (82.44)	2.11 (1.64 ~ 2.71)	<.001		
Gender				0.456	
Male	4249 (45.72)	1.81 (1.35 ~ 2.44)	<.001		
Female	5044 (54.28)	2.13 (1.57 ~ 2.91)	<.001		
Drinking				0.012	
NO	6067 (65.29)	1.55 (1.17 ~ 2.06)	0.002		
YES	3226 (34.71)	2.82 (1.90 ~ 4.16)	<.001		
Hypertension				0.058	
NO	6172 (66.42)	1.43 (1.01 ~ 2.03)	0.046		
YES	3121 (33.58)	2.20 (1.66 ~ 2.92)	<.001		
Diabetes				0.052	
NO	7289 (78.44)	1.63 (1.24 ~ 2.14)	<.001		
YES	2004 (21.56)	2.60 (1.74 ~ 3.89)	<.001		

C CHARLS-TyHGB					
All patients	9293 (100.00)	1.12 (1.08 ~ 1.18)	<.001		
Age				<.001	
<60	4027 (43.33)	1.35 (1.23 ~ 1.47)	<.001		
≥60	5266 (56.67)	1.09 (1.04 ~ 1.13)	<.001		
Marital status				0.766	
Live alone	1632 (17.56)	1.16 (0.98 ~ 1.36)	0.081		
Live with partne	7661 (82.44)	1.13 (1.07 ~ 1.18)	<.001		
Gender				0.034	
Male	4249 (45.72)	1.20 (1.12 ~ 1.27)	<.001		
Female	5044 (54.28)	1.10 (1.05 ~ 1.14)	<.001		
Drinking				0.614	
NO	6067 (65.29)	1.11 (1.05 ~ 1.18)	<.001		
YES	3226 (34.71)	1.14 (1.06 ~ 1.22)	<.001		
Hypertension				0.006	
NO	6172 (66.42)	1.09 (1.05 ~ 1.14)	<.001		
YES	3121 (33.58)	1.22 (1.15 ~ 1.30)	<.001		
Diabetes				0.902	
NO	7289 (78.44)	1.12 (1.05 ~ 1.18)	<.001		
YES	2004 (21.56)	1.12 (1.05 ~ 1.20)	<.001		

D CHARLS-TyGWWI					
All patients	9293 (100.00)	1.08 (1.05 ~ 1.10)	<.001		
Age				<.001	
<60	4027 (43.33)	1.16 (1.09 ~ 1.23)	<.001		
≥60	5266 (56.67)	1.05 (1.02 ~ 1.08)	<.001		
Marital status				0.066	
Live alone	1632 (17.56)	1.03 (0.99 ~ 1.09)	0.172		
Live with partne	7661 (82.44)	1.09 (1.06 ~ 1.12)	<.001		
Gender				0.797	
Male	4249 (45.72)	1.08 (1.04 ~ 1.12)	<.001		
Female	5044 (54.28)	1.09 (1.05 ~ 1.12)	<.001		
Drinking				0.005	
NO	6067 (65.29)	1.05 (1.02 ~ 1.08)	0.002		
YES	3226 (34.71)	1.13 (1.08 ~ 1.18)	<.001		
Hypertension				0.067	
NO	6172 (66.42)	1.04 (1.00 ~ 1.08)	0.050		
YES	3121 (33.58)	1.09 (1.06 ~ 1.12)	<.001		
Diabetes				0.080	
NO	7289 (78.44)	1.06 (1.02 ~ 1.09)	<.001		
YES	2004 (21.56)	1.11 (1.06 ~ 1.15)	<.001		

Figure 4. Subgroup analyses of the associations between TyG-related indices and colorectal tumor risk in the CHARLS cohort.

Subgroup logistic regression analyses were performed for TyG (A), TyG-CI (B), TyG-HGB (C), and TyG-WWI (D). Odds ratios (ORs) and 95% confidence intervals are shown for major subgroups including age (<60/≥60 years), marital status, gender, drinking status, hypertension, and diabetes.

A CHARLS-TyG					
All patients	2839 (100.00)	1.80 (1.46 ~ 2.21)	<.001		
Age					0.158
<60	808 (28.46)	2.36 (1.51 ~ 3.70)	<.001		
≥60	2031 (71.54)	1.64 (1.29 ~ 2.07)	<.001		
Marital status					0.622
Live alone	1104 (38.89)	1.89 (1.41 ~ 2.54)	<.001		
Live with partne	1735 (61.11)	1.70 (1.27 ~ 2.28)	<.001		
Gender					0.376
Male	1498 (52.77)	1.97 (1.47 ~ 2.64)	<.001		
Female	1341 (47.23)	1.63 (1.21 ~ 2.19)	0.001		
Drinking					0.800
NO	770 (27.12)	1.85 (1.30 ~ 2.62)	<.001		
YES	2069 (72.88)	1.75 (1.35 ~ 2.26)	<.001		
Hypertension					0.677
NO	1229 (43.29)	1.63 (1.13 ~ 2.36)	0.010		
YES	1610 (56.71)	1.79 (1.39 ~ 2.32)	<.001		
Diabetes					0.001
NO	2197 (77.39)	1.24 (0.92 ~ 1.66)	0.159		
YES	642 (22.61)	2.58 (1.83 ~ 3.63)	<.001		

B CHARLS-TyGCI					
All patients	2839 (100.00)	1.33 (1.19 ~ 1.48)	<.001		
Age					0.066
<60	808 (28.46)	1.57 (1.24 ~ 1.99)	<.001		
≥60	2031 (71.54)	1.23 (1.08 ~ 1.39)	0.001		
Marital status					0.968
Live alone	1104 (38.89)	1.33 (1.14 ~ 1.55)	<.001		
Live with partne	1735 (61.11)	1.33 (1.15 ~ 1.55)	<.001		
Gender					0.732
Male	1498 (52.77)	1.35 (1.16 ~ 1.56)	<.001		
Female	1341 (47.23)	1.30 (1.10 ~ 1.52)	0.001		
Drinking					0.761
NO	770 (27.12)	1.29 (1.07 ~ 1.56)	0.007		
YES	2069 (72.88)	1.34 (1.17 ~ 1.53)	<.001		
Hypertension					0.636
NO	1229 (43.29)	1.25 (1.04 ~ 1.50)	0.017		
YES	1610 (56.71)	1.32 (1.15 ~ 1.52)	<.001		
Diabetes					0.004
NO	2197 (77.39)	1.14 (0.99 ~ 1.32)	0.065		
YES	642 (22.61)	1.64 (1.34 ~ 2.01)	<.001		

C CHARLS-TyHGB					
All patients	2839 (100.00)	1.20 (1.15 ~ 1.25)	<.001		
Age					0.594
<60	808 (28.46)	1.22 (1.12 ~ 1.33)	<.001		
≥60	2031 (71.54)	1.19 (1.13 ~ 1.25)	<.001		
Marital status					0.907
Live alone	1104 (38.89)	1.19 (1.12 ~ 1.27)	<.001		
Live with partne	1735 (61.11)	1.20 (1.13 ~ 1.28)	<.001		
Gender					0.841
Male	1498 (52.77)	1.19 (1.12 ~ 1.26)	<.001		
Female	1341 (47.23)	1.20 (1.13 ~ 1.28)	<.001		
Drinking					0.696
NO	770 (27.12)	1.18 (1.10 ~ 1.27)	<.001		
YES	2069 (72.88)	1.20 (1.14 ~ 1.27)	<.001		
Hypertension					0.684
NO	1229 (43.29)	1.20 (1.11 ~ 1.30)	<.001		
YES	1610 (56.71)	1.18 (1.12 ~ 1.24)	<.001		
Diabetes					0.006
NO	2197 (77.39)	1.09 (1.00 ~ 1.19)	0.038		
YES	642 (22.61)	1.27 (1.18 ~ 1.35)	<.001		

D CHARLS-TyGWWI					
All patients	2839 (100.00)	1.03 (1.02 ~ 1.05)	<.001		
Age					0.101
<60	808 (28.46)	1.05 (1.02 ~ 1.08)	<.001		
≥60	2031 (71.54)	1.02 (1.01 ~ 1.04)	0.001		
Marital status					0.933
Live alone	1104 (38.89)	1.03 (1.01 ~ 1.05)	<.001		
Live with partne	1735 (61.11)	1.03 (1.01 ~ 1.05)	<.001		
Gender					0.806
Male	1498 (52.77)	1.03 (1.02 ~ 1.05)	<.001		
Female	1341 (47.23)	1.03 (1.01 ~ 1.05)	0.002		
Drinking					0.835
NO	770 (27.12)	1.03 (1.01 ~ 1.05)	0.006		
YES	2069 (72.88)	1.03 (1.02 ~ 1.05)	<.001		
Hypertension					0.595
NO	1229 (43.29)	1.02 (1.00 ~ 1.05)	0.025		
YES	1610 (56.71)	1.03 (1.02 ~ 1.05)	<.001		
Diabetes					0.013
NO	2197 (77.39)	1.02 (1.00 ~ 1.03)	0.047		
YES	642 (22.61)	1.05 (1.03 ~ 1.08)	<.001		

Figure 5. Threshold effect analyses of the associations between TyG-related indices and colorectal tumor risk in the NHANES cohort.

Threshold (segmented) logistic regression analyses were performed for TyG (A), TyG-CI (B), TyG-HGB (C), and TyG-WWI (D). The fitted curves display adjusted odds ratios (ORs) and 95% confidence intervals across the continuous range of each metabolic indicator, with the estimated breakpoint identifying a potential threshold that separates lower-risk and higher-risk segments.

Supplementary Files

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