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Associations of modified triglyceride-glucose indices and the triglyceride/high-density lipoprotein ratio with all-cause and cause-specific mortality in the general population: an analysis of the UK biobank database

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Abstract

Background This study investigates the associations between modified triglyceride-glucose (TyG) indices and the triglyceride-to-high-density lipoprotein (TG/HDL) ratio, which are recognized as simple surrogate indicators of insulin resistance, with all-cause and cause-specific mortality.

Methods A cohort of 410,515 participants from the UK Biobank was analyzed. Cox proportional hazard models and restricted cubic spline regression analyses were employed to examine the relationships between the TyG index, TyG-body mass index (TyG-BMI), TyG-waist circumference (TyG-WC), TG/HDL ratio, and all-cause and cause-specific mortality. Structural equation modeling was employed to elucidate the associations between the TyG index, TG/HDL ratio, inflammation, metabolism, and mortality.

Results The TyG index, TyG-WC, and TG/HDL ratio were associated with an increased risk of all-cause mortality by 3.7% (HR 1.037 [1.016, 1.059]), 0.1% (HR 1.001 [1.024, 1.031]), and 1.5% (HR 1.015 [1.006, 1.025]), respectively. Restricted cubic spline regression models revealed nonlinear trends in the TyG index, TyG-BMI, TyG-WC, and TG/HDL ratio in relation to both all-cause and cause-specific mortality (P for nonlinearity < 0.05). TyG index and TG/HDL ratio exhibited a J-shaped relationship with all-cause mortality as well as mortality from cancer, cardiovascular diseases, and respiratory diseases. Similarly, TyG-BMI demonstrated an L-shaped association with all-cause mortality and mortality due to cancer, cardiovascular diseases, and respiratory diseases. Additionally, TyG-WC was associated with a progressively increasing mortality risk once it exceeded a certain threshold. Structural equation modeling demonstrated that the TyG index and TG/HDL ratio influenced mortality through inflammation and lifestyle factors.

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Conclusions In conclusion, TyG, TyG-BMI, TyG-WC, and TG/HDL ratio are significantly associated with all-cause and cause-specific mortality in the general population.These associations appear to be linked to inflammation and lifestyle.

Keywords TyG index, TG/HDL ratio, All-cause mortality, Cause-Specific mortality, UK biobank

Introduction

Metabolic abnormalities and insulin resistance (IR) play key roles in the initiation and progression of many diseases [1, 2]. Metabolic abnormalities may cause IR by interfering with glucose and lipid metabolism [3]. IR, a prominent manifestation of metabolic abnormalities, is closely associated with diseases like diabetes and obesity [4, 5]. Furthermore, it can influence systemic inflammation levels through multiple pathways [6, 7]. Given that all-cause and cause-specific mortality are crucial indicators reflecting the overall impact of disease on an individual, a thorough investigation into their relationship with metabolism and inflammation could offer valuable insights for future precision medicine and health management.

The triglyceride-glucose (TyG) index and triglyceride/high-density lipoprotein (TG/HDL) ratio, serving as measures of metabolism and IR, collectively reflect the overall metabolic profile [8]. The TyG index, which takes into account two important biomarkers, triglycerides and glucose, excels in the assessment of IR, with a high degree of sensitivity and specificity. Besides, some studies suggest that modified TyG indices, such as TyG-body mass index (TyG-BMI), TyG-waist circumference (TyG-WC) may better predict diabetes and cardiovascular diseases [9, 10]. Compared to the TyG index alone, the modified TyG indices may provide better predictive ability for mortality risk [11]. Additionally, the modified TyG indices and TG/HDL are both simple and cost-effective. Compared to invasive and costly tests like the insulin tolerance test, the modified TyG indices and TG/HDL are more convenient and practical for large-scale studies [12–14].

Findings from the MIMIC database found that an elevated TyG index was associated with a significantly increased risk of hospitalization and ICU death, but the database focuses on critically ill patients, limiting the generalizability of the conclusions [15, 16]. In contrast, data from the National Health and Nutrition Examination Survey showed significant correlations between TyG index and all-cause and cardiovascular mortality in the general population, but the association between TG/HDL and death was not examined [17]. We utilized the broad participation and diverse demographic characteristics of the UK Biobank database to investigate the associations between modified TyG indices and TG/HDL with all-cause and cause-specific mortality. By analyzing both metrics comprehensively, we hope to gain a fuller understanding of their role in metabolic disorders and inflammation.

Method

Study population

Investigators from the UK Biobank sent out postal invitations to 9,238,453 individuals aged 40–69, who were registered with the National Health Service in the UK and resided within approximately 25 miles (40 km) of one of the 22 assessment centers in England, Wales, and Scotland [18]. From 2006 to 2010, a total of 502,488 individuals consented to participate and completed a thorough questionnaire, encompassing socio-demographic, lifestyle, and health-related information. Following a medical examination, participants furnished blood, urine, and saliva samples [19]. Exclusions were made for individuals lost to follow-up until November 2023, those who died within six months of enrollment, and participants with missing fasting glucose, triglycerides, HDL, BMI, WC and covariates, resulting in a total of 410,515 individuals enrolled in the study. The UK Biobank study received approval from the National Health and Social Care Information Management Board and the NHS North West Multi-centre Research Ethics Committee. All participants provided consent through electronically signed forms.

Exposure assessment

TG, HDL, glucose and other blood biochemistry and blood count data were obtained from the baseline assessment (2006–2010). Biomarker assay quality procedures are provided in open source documentation. Blood count samples collected in 4 ml ethylenediaminetetraacetic acid (EDTA) vacuum containers were analysed using a Beckman Coulter LH750 instrument.

The TyG index was calculated using the formula: ln [triglycerides (mg/dL) × glucose (mg/dL)/2] [20]. The TyG-BMI was calculated by multiplying the TyG index by BMI, while the TyG-WC was derived by multiplying the TyG index by WC [21]. The TG/HDL ratio was calculated as TG (mg/dL) divided by HDL (mg/dL) [22].

Covariates

Data on covariates were collected at baseline. Potential confounders, including age, sex(Male, Female), ethnicity (White, Non-white), education (college or university degree, advanced/advanced subsidiary levels or equivalent, ordinary/advanced subsidiary levels or

equivalent, certificate of secondary educations or equivalent, national vocational qualification/ higher national diploma/higher national certificate equivalent, Other professional qualifications), smoking (no, yes), alcohol consumption (Never, former, current), Townsend Deprivation Index (TDI, referring to an area-based measure of socioeconomic deprivation), diabetes, cardiovascular disease, use of anti-diabetic, lipid-lowering, and antihypertensive medications.

Mortality ascertainment

Vital status, date of death, and underlying primary cause of death were provided by the NHS Information Centre (England and Wales) and the NHS Central Register (Scotland). Detailed information on the linkage procedure is available online (http://biobank.ctsu.ox.ac.uk/crystal/ukb/docs/DeathLinkage.pdf). The specific causes of death were defined using codes from the 10th edition of the International Classification of Diseases and Related Health Problems (ICD-10). The primary causes of death include respiratory diseases, cardiovascular diseases, tumors, digestive diseases, infections, mental disorders, endocrine diseases, musculoskeletal diseases, neurological diseases, hematologic diseases, congenital disorders, urinary system diseases, skin diseases, diseases not otherwise classified, and other unspecified diseases.

Statistical analyses

Study population characteristics were stratified according to modified TyG indices quartiles and TG/HDL ratio quartiles, respectively, using analysis of variance or Kruskal-Wallis test for continuous variables and test for categorical variables.

We used Kaplan-Meier survival analyses, and log-rank tests to assess the incidence of all-cause and cause-specific deaths between groups with different levels of modified TyG indices and TG/HDL ratio. Hazard ratios (HR) and 95% confidence intervals (CI) between modified TyG indices and TG/HDL ratio and all-cause and cause-specific mortality were examined using multivariate Cox proportional risk models adjusted for multiple models. Model 1 did not adjust for any covariates, while Model 2 adjusted for age, sex, ethnicity, Townsend deprivation score, education, smoking, drinking status, diabetes, cardiovascular disease, and the use of anti-diabetic, lipid-lowering, and anti-hypertensive medications. To evaluate the discriminative ability of the models, we reported the C-index for both Model 1 and Model 2. The Akaike Information Criterion (AIC) was used to determine the optimal number of knots in the restricted cubic spline (RCS) model. The knot configuration with the lowest AIC value was selected to fit the Cox proportional hazards regression model and analyze the association between adjusted modified TyG indices, TG/HDL ratio, and mortality.

Structural equation modeling (SEM) was used to explore the relationship between lifestyle, inflammation, modified TyG indices, and TG/HDL ratio. First, validated factor analysis was performed to test potential latent variables in SEM, including inflammation and lifestyle. Neutrophil count (N), lymphocyte count (L), monocyte count (M), platelet count (P), and C-reactive protein (CRP) were identified as significant indicators of inflammation (β-values: 0.85, 0.99, 0.99, 0.52, and 0.93, respectively; $P<0.05$). The latent variable lifestyle was represented by smoking, alcohol consumption, education, and Townsend deprivation index (TDI) (β-values: 0.86, 0.98, 0.95, and 0.82, respectively; $P<0.001$).

All statistical analyses were performed using R 4.2.0, and statistical significance was defined as $P<0.05$.

Result

Baseline characteristics

We included 410,515 individuals from the UK Biobank database, with a mean age of 56.48 ± 8.07 years. Among them, 54.1% were female ($n=222,274$). Over a follow-up period of 16.5 years, a total of 33,004 deaths were recorded. The leading causes of death were tumors (52.1%), cardiovascular diseases (21.3%), respiratory diseases (7.2%) and neurological diseases (4.5%). For the TyG index, all-cause mortality increased progressively from quartile 1 (Q1) to Q4, with significant differences observed among the four quartiles. Regarding cause-specific mortality, individuals in the higher TyG quartiles (Q3 and Q4) had higher mortality rates than those in the lower quartiles (Q1 and Q2). Participants across different quartiles exhibited significant differences in age, smoking status, alcohol consumption, TDI, diabetes, cardiovascular disease, and the use of anti-diabetic, lipid-lowering, and antihypertensive medications ($P<0.001$) (Table 1). Additionally, fasting blood glucose, lipid levels, BMI, and WC increased across the quartiles, whereas HDL levels gradually decreased. Similar trends were observed for TyG-BMI, TyG-WC, and TG/HDL (Supplementary Tables S1–S3).

Association between modified TyG indices and TG/HDL ratio with all cause-morality

The Kaplan-Meier survival curves for all-cause mortality across quartiles of TyG, TyG-BMI, TyG-WC, and TG/HDL are presented in Fig. 1. A statistically significant difference in mortality between groups was observed (Log-rank $P<0.0001$) over the 16.5-year follow-up period. Table 2 presents the Cox proportional hazards analysis examining the association between modified TyG indices, TG/HDL, and all-cause mortality. In the unadjusted model, for each unit increase in TyG, TyG-BMI, TyG-WC, and TG/HDL (as continuous variables), the risk of all-cause mortality increased by 50.2% (HR: 1.502 [1.475,

Table 1 Characteristics and outcomes of participants categorized by TyG index

Variance	Overall	Q1	Q2	Q3	Q4	*p*
Number	410,515	102,629	102,629	102,628	102,629	
Age (years)	56.48 (8.07)	54.23 (8.28)	56.71 (8.00)	57.51 (7.79)	57.46 (7.74)	< 0.001
sex (%)						< 0.001
Female	222,274 (54.1)	69,044 (67.3)	60,297 (58.8)	51,896 (50.6)	41,037 (40.0)	
Male	188,241 (45.9)	33,585 (32.7)	42,332 (41.2)	50,732 (49.4)	61,592 (60.0)	
Ethnicity (%)						< 0.001
Non-white	20,434 (5.0)	6497 (6.3)	4770 (4.6)	4450 (4.3)	4717 (4.6)	
white	390,081 (95.0)	96,132 (93.7)	97,859 (95.4)	98,178 (95.7)	97,912 (95.4)	
smk (%)						< 0.001
No	367,616 (89.5)	93,847 (91.4)	92,630 (90.3)	91,694 (89.3)	89,445 (87.2)	
Yes	42,899 (10.5)	8782 (8.6)	9999 (9.7)	10,934 (10.7)	13,184 (12.8)	
Drink(%)						< 0.001
Never	17,222 (4.2)	3875 (3.8)	4164 (4.1)	4402 (4.3)	4781 (4.7)	
Former	14,385 (3.5)	3217 (3.1)	3380 (3.3)	3616 (3.5)	4172 (4.1)	
Current	378,908 (92.3)	95,537 (93.1)	95,085 (92.6)	94,610 (92.2)	93,676 (91.3)	
TDI	-1.36 (3.06)	-1.38 (3.06)	-1.44 (3.01)	-1.41 (3.03)	-1.20 (3.12)	< 0.001
Education (%)						< 0.001
College or university degree	69,451 (16.9)	12,381 (12.1)	16,739 (16.3)	19,137 (18.6)	21,194 (20.7)	
A/AS levels or equivalent	110,895 (27.0)	27,426 (26.7)	27,757 (27.0)	27,747 (27.0)	27,965 (27.2)	
O/AS levels or equivalent	46,454 (11.3)	12,657 (12.3)	11,774 (11.5)	11,268 (11.0)	10,755 (10.5)	
CSEs or equivalent	21,535 (5.2)	4892 (4.8)	5350 (5.2)	5595 (5.5)	5698 (5.6)	
NVQ/HND/HNC equivalent	27,259 (6.6)	5353 (5.2)	6435 (6.3)	7330 (7.1)	8141 (7.9)	
Other professional qualifications	134,921 (32.9)	39,920 (38.9)	34,574 (33.7)	31,551 (30.7)	28,876 (28.1)	
Living state						< 0.001
Alive	377,511 (92.0)	96,519 (94.0)	95,062 (92.6)	93,949 (91.5)	91,981 (89.6)	
Death	33,004 (8.0)	6110 (6.0)	7567 (7.4)	8679 (8.5)	10,648 (10.4)	
Death Reason						< 0.001
Alive	377,511 (92.0)	96,519 (94.0)	95,062 (92.6)	93,949 (91.5)	91,981 (89.6)	
Other diseases	962 (0.2)	213 (0.2)	243 (0.2)	213 (0.2)	293 (0.3)	
Respiratory diseases	2390 (0.6)	511 (0.5)	546 (0.5)	647 (0.6)	686 (0.7)	
Neoplasms	17,196 (4.2)	3210 (3.1)	4022 (3.9)	4641 (4.5)	5323 (5.2)	
Cardiovascular diseases	7025 (1.7)	1160 (1.1)	1514 (1.5)	1835 (1.8)	2516 (2.5)	
Digestive diseases	1311 (0.3)	237 (0.2)	308 (0.3)	315 (0.3)	451 (0.4)	
Infectious	246 (0.1)	40 (0.0)	65 (0.1)	74 (0.1)	67 (0.1)	
Mental disorders	388 (0.1)	86 (0.1)	86 (0.1)	104 (0.1)	112 (0.1)	
Endocrine diseases	378 (0.1)	55 (0.1)	67 (0.1)	57 (0.1)	199 (0.2)	
Musculoskeletal diseases	180 (0.0)	34 (0.0)	41 (0.0)	49 (0.0)	56 (0.1)	
Neurological diseases	1498 (0.4)	334 (0.3)	390 (0.4)	384 (0.4)	390 (0.4)	
Uncertain diseases	1017 (0.2)	152 (0.1)	209 (0.2)	275 (0.3)	381 (0.4)	
Hematologic diseases	82 (0.0)	19 (0.0)	22 (0.0)	19 (0.0)	22 (0.0)	
Congenital diseases	51 (0.0)	14 (0.0)	9 (0.0)	16 (0.0)	12 (0.0)	
Urinate system diseases	225 (0.1)	39 (0.0)	37 (0.0)	42 (0.0)	107 (0.1)	
Skin diseases	55 (0.0)	6 (0.0)	8 (0.0)	8 (0.0)	33 (0.0)	
Diabetes (%)						< 0.001
No	390,164 (95.0)	100,840 (98.3)	100,055 (97.5)	98,271 (95.8)	90,998 (88.7)	
Yes	20,351 (5.0)	1789 (1.7)	2574 (2.5)	4357 (4.2)	11,631 (11.3)	
CVD (%)						< 0.001
No	374,604 (91.3)	95,548 (93.1)	94,252 (91.8)	93,423 (91.0)	91,381 (89.0)	
Yes	35,911 (8.7)	7081 (6.9)	8377 (8.2)	9205 (9.0)	11,248 (11.0)	
Medicine (%)						< 0.001
No	300,269 (73.1)	85,561 (83.4)	78,389 (76.4)	72,457 (70.6)	63,862 (62.2)	
Yes	110,246 (26.9)	17,068 (16.6)	24,240 (23.6)	30,171 (29.4)	38,767 (37.8)	
TG (mg/dl)	1.74 (1.02)	0.84 (0.18)	1.27 (0.19)	1.80 (0.30)	3.07 (1.11)	< 0.001

Table 1 (continued)

Variance	Overall	Q1	Q2	Q3	Q4	*p*
Glucose (mg/dl)	5.12 (1.22)	4.73 (0.56)	4.93 (0.61)	5.07 (0.78)	5.73 (2.02)	< 0.001
HDL (mg/dl)	1.45 (0.38)	1.68 (0.40)	1.52 (0.36)	1.38 (0.32)	1.22 (0.28)	< 0.001
BMI (Kg/m2)	27.41 (4.77)	25.15 (4.02)	26.83 (4.48)	28.13 (4.66)	29.53 (4.76)	< 0.001
WC (cm)	90.24 (13.43)	82.50 (11.69)	88.14 (12.41)	92.65 (12.39)	97.66 (12.32)	< 0.001

Continuous variables are expressed as mean (SD). Categorical variables are expressed as frequency (percentage)

Abbreviations: TG/HDL,triglyceride/high-density lipoprotein ratio; TyG index, triglyceride glucose index; CVD, cardiovascular disease; BMI, Body mass index; WC, waist circumference; A/AS, advanced/advanced subsidiary; CSE, certificate of secondary education; HNC, higher national certificate; HND, higher national diploma; NVQ, national vocational qualification; O/AS, ordinary/advanced subsidiary; Q1/2/3/4/, quintiles 1/2/3/4/

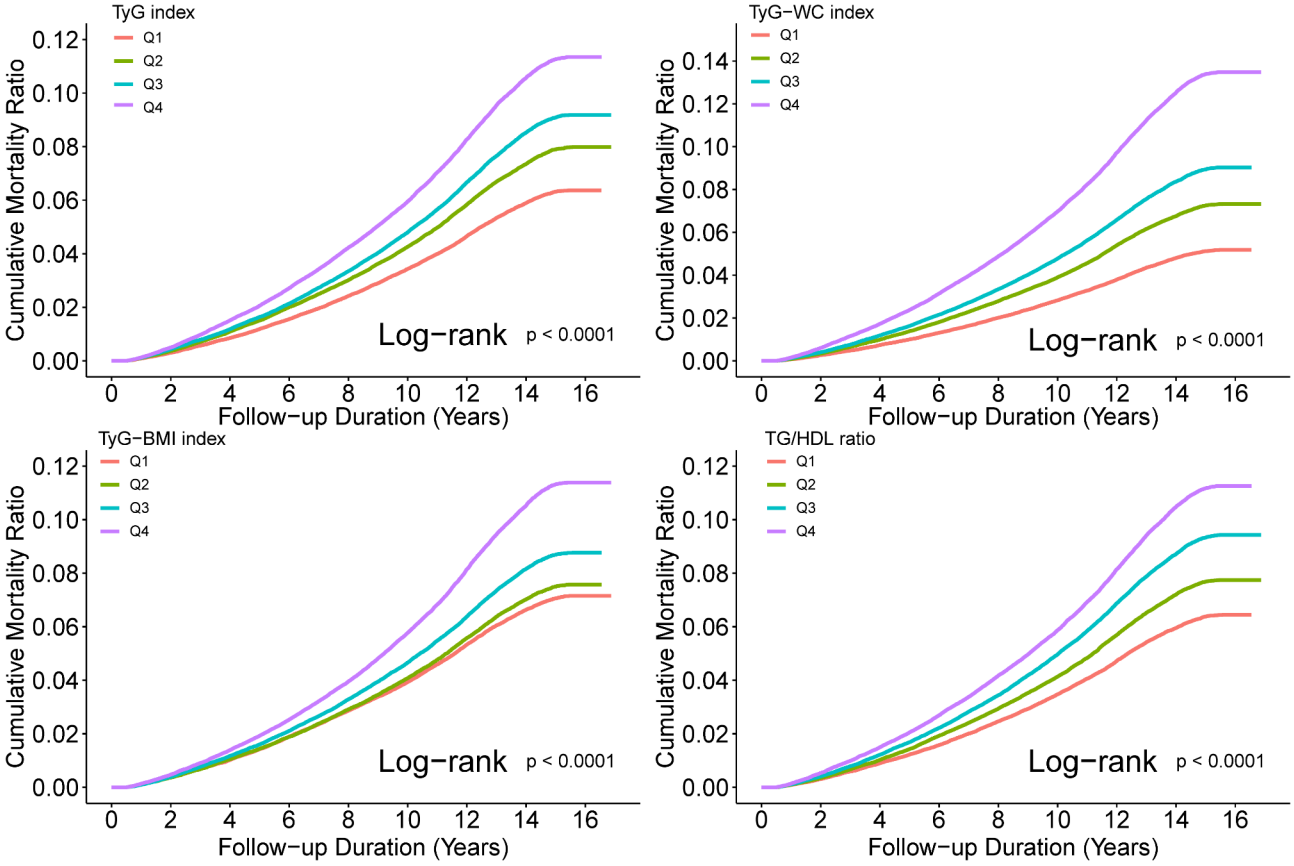


Fig. 1 Kaplan–Meier survival analysis curves for all-cause mortality. Kaplan–Meier curves showing the cumulative probability of all-cause mortality according to groups based on TyG, TyG-BMI, TyG-WC, and TG/HDL ratio

1.530]), 0.4% (HR: 1.004 [1.004, 1.004]), 0.2% (HR: 1.002 [1.002, 1.003]), and 14.5% (HR: 1.145 [1.136, 1.153]), respectively (Supplementary Table S4). After adjusting for covariates, each unit increase in TyG, TyG-WC, and TG/HDL was associated with a 3.7% (HR: 1.037 [1.016, 1.059]), 0.1% (HR: 1.001 [1.001, 1.001]), and 1.5% (HR: 1.015 [1.006, 1.025]) increase in mortality risk, respectively, while TyG-BMI showed no significant association with all-cause mortality. (Table 2) When categorized into quartiles, all-cause mortality risk was lower in Q2 and Q3 compared to Q1 for TyG and TG/HDL. In contrast, for TyG-BMI, mortality risk decreased in Q2–Q4, whereas for TyG-WC, the Q4 group exhibited an increased risk of all-cause mortality (Table 2). These findings suggest a potential nonlinear association between modified TyG indices and the TG/HDL ratio.

The restricted cubic spline (RCS) results further support this nonlinear relationship. The TyG index and TG/HDL exhibited a J-shaped association with all-cause mortality, with the lowest risk observed at 8.86 and 1.08, respectively. TyG-BMI showed an approximately L-shaped relationship, with the lowest risk observed at 217.6, while TyG-WC demonstrated a gradual increase in mortality risk beyond 780.3 (Fig. 2).

Additionally, in the unadjusted model, the C-index values for TyG, TyG-BMI, TyG-WC, and TG/HDL were

Table 2 Cox proportional hazard ratios for all-cause and Cause-Specific mortalities

Categories	TyG index		TyG-BMI index		TyG-WC index		TG/HDLRatio	
	HR(95%CI)	*P*	HR(95%CI)	*P*	HR(95%CI)	*P*	HR(95%CI)	*P*
All-cause mortality								
Continuous	1.037 (1.016, 1.059)	< 0.001	1.000 (1.000, 1.001)	0.277	1.001 (1.001, 1.001)	< 0.001	1.015 (1.006, 1.025)	0.002
Quartile2	0.945 (0.914, 0.978)	0.001	0.840 (0.811, 0.870)	< 0.001	0.977 (0.940, 1.015)	0.236	0.919 (0.888, 0.951)	< 0.001
Quartile3	0.942 (0.911, 0.974)	< 0.001	0.824 (0.794, 0.857)	< 0.001	0.975 (0.935, 1.017)	0.244	0.932 (0.901, 0.965)	< 0.001
Quartile4	0.993 (0.961, 1.027)	0.692	0.884 (0.841, 0.930)	< 0.001	1.151 (1.095, 1.210)	< 0.001	0.967 (0.935, 1.001)	0.060
Other diseases								
Continuous	0.943 (0.836, 1.063)	0.334	1.000(0.996, 1.004)	0.887	1.000 (0.999, 1.001)	0.458	0.966 (0.912, 1.024)	0.250
Quartile2	0.796 (0.654, 0.968)	0.023	0.699 (0.558, 0.876)	0.002	0.823 (0.648, 1.046)	0.111	0.814 (0.671, 0.987)	0.036
Quartile3	0.931 (0.768, 1.127)	0.462	0.844 (0.622, 1.146)	0.277	0.916 (0.685, 1.225)	0.555	0.793 (0.650, 0.966)	0.021
Quartile4	1.032 (1.023, 1.042)	< 0.001	1.032 (1.023, 1.041)	< 0.001	1.032 (1.023, 1.042)	< 0.001	1.032 (1.023, 1.041)	< 0.001
Respiratory diseases								
Continuous	0.858 (0.793, 0.927)	< 0.001	1.001 (0.999, 1.004)	0.313	1.001 (1.001, 1.002)	< 0.001	0.926 (0.890, 0.963)	< 0.001
Quartile2	0.787 (0.699, 0.887)	< 0.001	0.626 (0.543, 0.721)	< 0.001	0.741 (0.635, 0.863)	< 0.001	0.743 (0.659, 0.838)	< 0.001
Quartile3	0.700 (0.620, 0.791)	< 0.001	0.791 (0.655, 0.954)	0.014	0.867 (0.722, 1.041)	0.126	0.634 (0.559, 0.719)	< 0.001
Quartile4	1.142 (1.133, 1.150)	< 0.001	1.142 (1.133, 1.151)	< 0.001	1.142 (1.133, 1.151)	< 0.001	1.141 (1.132, 1.150)	< 0.001
Neoplasms								
Continuous	1.075 (1.044, 1.107)	< 0.001	1.000 (0.999, 1.001)	0.407	1.001 (1.001, 1.002)	< 0.001	1.035 (1.022, 1.049)	< 0.001
Quartile2	1.013 (0.967, 1.061)	0.290	0.930 (0.882, 0.981)	0.007	1.071 (1.012, 1.134)	0.018	1.005 (0.959, 1.053)	0.831
Quartile3	1.074 (1.025, 1.126)	0.003	0.987 (0.919, 1.061)	0.732	1.318 (1.230, 1.412)	< 0.001	1.076 (1.026, 1.129)	0.003
Quartile4	1.098 (1.095, 1.101)	< 0.001	1.099 (1.096, 1.101)	< 0.001	1.098 (1.095, 1.100)	< 0.001	1.098 (1.096, 1.101)	< 0.001
Cardiovascular diseases								
Continuous	1.059 (1.014, 1.106)	< 0.001	1.001 (0.999, 1.002)	0.469	1.001 (1.001, 1.002)	< 0.001	1.019 (1.000, 1.038)	0.055
Quartile2	0.918 (0.852, 0.99)	0.026	0.792 (0.727, 0.862)	< 0.001	0.985 (0.892, 1.088)	0.767	0.908 (0.84, 0.981)	0.014
Quartile3	0.975 (0.906, 1.05)	0.507	0.841 (0.755, 0.936)	0.002	1.128 (1.007, 1.263)	0.037	0.943 (0.873, 1.018)	0.134
Quartile4	1.105 (1.100, 1.109)	< 0.001	1.105 (1.100, 1.109)	< 0.001	1.104 (1.099, 1.109)	< 0.001	1.104 (1.100, 1.109)	< 0.001
Disestive diseases								
Continuous	0.955 (0.862, 1.057)	0.372	0.999 (0.996, 1.002)	0.626	1.002 (1.001, 1.003)	< 0.001	0.945 (0.900, 0.993)	0.025
Quartile2	0.803 (0.676, 0.955)	0.013	0.673 (0.556, 0.814)	< 0.001	1.261 (1.006, 1.579)	0.044	0.652 (0.549, 0.774)	< 0.001
Quartile3	0.903 (0.763, 1.067)	0.230	0.817 (0.642, 1.040)	0.101	1.479 (1.141, 1.918)	0.003	0.685 (0.578, 0.811)	< 0.001
Quartile4	1.082 (1.073, 1.092)	< 0.001	1.082 (1.073, 1.092)	< 0.001	1.080 (1.071, 1.090)	< 0.001	1.082 (1.073, 1.092)	< 0.001
Infectious								
Continuous	0.883 (0.696, 1.121)	0.307	0.999 (0.991, 1.006)	0.732	1.001 (0.999, 1.002)	0.468	0.930 (0.824, 1.051)	0.244
Quartile2	1.194 (0.805, 1.771)	0.379	0.524 (0.333, 0.824)	0.005	0.860 (0.538, 1.374)	0.528	0.877 (0.591, 1.302)	0.515
Quartile3	0.877 (0.579, 1.329)	0.537	0.772 (0.440, 1.354)	0.367	1.007 (0.575, 1.763)	0.981	0.883 (0.591, 1.320)	0.544
Quartile4	1.091 (1.069, 1.114)	< 0.001	1.093 (1.071, 1.116)	< 0.001	1.093 (1.071, 1.116)	< 0.001	1.092 (1.070, 1.115)	< 0.001
Mental disorders								
Continuous	1.032 (0.848, 1.255)	0.755	0.997 (0.991, 1.004)	0.385	1.001 (0.999, 1.002)	0.239	0.991 (0.898, 1.092)	0.850
Quartile2	0.838 (0.625, 1.124)	0.238	0.551 (0.386, 0.787)	0.001	0.758 (0.524, 1.096)	0.141	0.945 (0.705, 1.268)	0.708
Quartile3	0.856 (0.634, 1.155)	0.308	0.545 (0.329, 0.901)	0.019	0.743 (0.468, 1.181)	0.209	0.880 (0.644, 1.201)	0.42
Quartile4	1.200 (1.174, 1.228)	< 0.001	1.200 (1.174, 1.227)	< 0.001	1.201 (1.174, 1.228)	< 0.001	1.200 (1.173, 1.227)	< 0.001
Endocrine								
Continuous	1.255 (1.064, 1.480)	0.007	1.000 (0.994, 1.005)	0.977	1.002 (1.001, 1.003)	< 0.001	1.012 (0.940, 1.089)	0.750
Quartile2	0.549 (0.376, 0.802)	0.001	0.582 (0.400, 0.847)	0.005	0.616 (0.401, 0.945)	0.026	0.555 (0.396, 0.777)	< 0.001
Quartile3	1.069 (0.775, 1.474)	0.686	0.529 (0.340, 0.822)	0.005	0.738 (0.464, 1.174)	0.199	0.699 (0.509, 0.961)	0.027
Quartile4	1.057 (1.040, 1.074)	< 0.001	1.056 (1.039, 1.073)	< 0.001	1.057 (1.040, 1.074)	< 0.001	1.057 (1.040, 1.074)	< 0.001
Musculoskeletal diseases								
Continuous	1.035 (0.784, 1.367)	0.806	1.009 (1.000, 1.017)	0.043	1.001 (1.000, 1.003)	0.128	0.979 (0.853, 1.124)	0.768
Quartile2	0.918 (0.586, 1.438)	0.709	0.665 (0.387, 1.143)	0.140	0.898 (0.512, 1.577)	0.709	1.272 (0.792, 2.044)	0.320
Quartile3	0.883 (0.561, 1.390)	0.591	0.963 (0.495, 1.873)	0.911	0.799 (0.405, 1.578)	0.518	1.158 (0.706, 1.897)	0.561
Quartile4	1.100 (1.072, 1.129)	< 0.001	1.100 (1.072, 1.129)	< 0.001	1.100 (1.072, 1.129)	< 0.001	1.099 (1.071, 1.127)	< 0.001
Neurological diseases								
Continuous	0.876 (0.791, 0.970)	0.011	1.001 (0.998, 1.004)	0.636	1.000 (0.999, 1.001)	0.611	0.983 (0.933, 1.035)	0.514

Table 2 (continued)

Categories	TyG index		TyG-BMI index		TyG-WC index		TG/HDLRatio	
	HR(95%CI)	*P*	HR(95%CI)	*P*	HR(95%CI)	*P*	HR(95%CI)	*P*
Quartile2	0.843 (0.725, 0.980)	0.026	0.881 (0.734, 1.058)	0.176	0.789 (0.655, 0.951)	0.013	0.839 (0.721, 0.977)	0.024
Quartile3	0.846 (0.724, 0.989)	0.036	0.939 (0.725, 1.215)	0.630	0.874 (0.692, 1.104)	0.259	0.867 (0.739, 1.016)	0.078
Quartile4	1.141 (1.131, 1.152)	< 0.001	1.141 (1.130, 1.151)	< 0.001	1.142 (1.131, 1.153)	< 0.001	1.141 (1.130, 1.152)	< 0.001
Uncertain diseases								
Continuous	1.158 (1.034, 1.297)	0.011	1.000 (0.996, 1.003)	0.961	1.002 (1.001, 1.003)	< 0.001	1.058 (1.01, 1.107)	0.017
Quartile2	1.011 (0.827, 1.237)	0.912	0.972 (0.768, 1.230)	0.813	1.411 (1.061, 1.877)	0.018	1.240 (0.993, 1.550)	0.058
Quartile3	1.100 (0.904, 1.340)	0.341	1.001 (0.755, 1.327)	0.995	1.698 (1.240, 2.327)	< 0.001	1.363 (1.093, 1.701)	0.006
Quartile4	1.113 (1.101, 1.125)	< 0.001	1.113 (1.101, 1.125)	< 0.001	1.111 (1.099, 1.123)	< 0.001	1.113 (1.101, 1.125)	< 0.001
Hematologic diseases								
Continuous	0.964 (0.636, 1.462)	0.864	0.998 (0.984, 1.012)	0.750	1.002 (0.999, 1.004)	0.294	1.026 (0.843, 1.247)	0.800
Quartile2	0.769 (0.399, 1.480)	0.431	1.000 (0.449, 2.227)	0.999	1.291 (0.545, 3.055)	0.561	1.290 (0.669, 2.486)	0.447
Quartile3	0.790 (0.407, 1.533)	0.486	2.409 (0.867, 6.695)	0.092	1.954 (0.704, 5.424)	0.198	0.934 (0.453, 1.926)	0.854
Quartile4	1.087 (1.050, 1.125)	< 0.001	1.087 (1.050, 1.125)	< 0.001	1.084 (1.047, 1.122)	< 0.001	1.085 (1.048, 1.123)	< 0.001
Congenital diseases								
Continuous	1.138 (0.659, 1.968)	0.642	1.013 (0.996, 1.031)	0.143	1.004 (1.000, 1.008)	0.056	1.086 (0.852, 1.385)	0.504
Quartile2	1.150 (0.543, 2.435)	0.715	1.543 (0.498, 4.785)	0.452	0.745 (0.248, 2.232)	0.598	1.768 (0.744, 4.199)	0.197
Quartile3	0.924 (0.401, 2.129)	0.853	7.697 (1.966, 30.141)	0.003	1.940 (0.555, 6.790)	0.300	1.837 (0.737, 4.577)	0.192
Quartile4	1.015 (0.976, 1.057)	0.455	1.016 (0.977, 1.058)	0.426	1.015 (0.975, 1.057)	0.459	1.014 (0.974, 1.055)	0.490
Urinate system diseases								
Continuous	1.287 (1.020, 1.624)	0.034	0.994 (0.987, 1.001)	0.107	1.003 (1.001, 1.004)	< 0.001	1.102 (1.015, 1.198)	0.021
Quartile2	0.519 (0.333, 0.809)	0.004	0.747 (0.458, 1.218)	0.243	1.033 (0.560, 1.907)	0.916	0.883 (0.564, 1.381)	0.585
Quartile3	0.916 (0.621, 1.351)	0.659	0.471 (0.259, 0.859)	0.014	1.351 (0.696, 2.621)	0.374	0.914 (0.587, 1.425)	0.693
Quartile4	1.150 (1.120, 1.181)	< 0.001	1.149 (1.118, 1.180)	< 0.001	1.147 (1.117, 1.178)	< 0.001	1.148 (1.118, 1.179)	< 0.001
Skin diseases								
Continuous	1.690 (1.051, 2.719)	0.030	0.999 (0.985, 1.013)	0.867	1.005 (1.002, 1.008)	< 0.001	1.140 (0.967, 1.343)	0.118
Quartile2	0.653 (0.223, 1.911)	0.437	0.454 (0.177, 1.162)	0.099	0.527 (0.179, 1.552)	0.245	1.055 (0.420, 2.646)	0.910
Quartile3	2.094 (0.842, 5.203)	0.111	0.437 (0.152, 1.259)	0.125	0.940 (0.302, 2.921)	0.915	1.289 (0.520, 3.195)	0.584
Quartile4	1.115 (1.063, 1.170)	< 0.001	1.117 (1.065, 1.171)	< 0.001	1.116 (1.064, 1.171)	< 0.001	1.115 (1.063, 1.170)	< 0.001

All factors were adjusted for, including age, sex, ethnicity, Townsend deprivation score, education, smoking, drinking status, diabetes, cardiovascular disease, and the use of anti-diabetic, lipid-lowering, and anti-hypertensive medications

Abbreviations: HR, hazard ratio; CI, confdence interval; TG/HDL, triglyceride/high-density lipoprotein ratio; TyG index, triglyceride glucose index; BMI, Body mass index; WC, waist circumference

0.564, 0.555, 0.605, and 0.562, respectively, with TyG-WC showing the highest C-index among the unadjusted models. After adjusting for covariates, the C-index values improved, reaching 0.744, 0.745, 0.745, and 0.744, respectively, indicating enhanced discriminative ability of these models (Supplementary Table S5).

Association between modified TyG indices and TG/HDL ratio with cause-specific morality

Among all deaths, 52.1% were attributed to tumors. Each unit increase in TyG, TyG-WC, and TG/HDL was associated with a 7.5% (HR: 1.075 [1.044, 1.107]), 0.1% (HR: 1.001 [1.001, 1.002]), and 3.5% (HR: 1.035 [1.022, 1.049]) increase in mortality risk, respectively. Compared to individuals in the Q1, those in the Q4 of TyG, TyG-BMI, TyG-WC, and TG/HDL had a 9.8% (HR: 1.098 [1.095, 1.101]), 9.9% (HR: 1.099 [1.096, 1.101]), 9.8% (HR: 1.098 [1.095, 1.100]), and 9.8% (HR: 1.098 [1.096, 1.101]) higher mortality risk, respectively. A nonlinear association was observed between TyG and TyG-BMI and mortality risk, with the lowest risk was observed when TyG was around 8.5 and TyG-BMI was approximately 218 (Fig. 3). Additionally, mortality risk began to increase when TyG-WC exceeded 778 and TG/HDL exceeded 0.76. Among the four indices, TyG-WC demonstrated the highest discrimination ability, with a C-index of 0.719.

Cardiovascular diseases ranked as the second leading cause of death, accounting for 21.3% of total deaths. Compared to individuals in the Q1, those in the Q4 of TyG, TyG-BMI, TyG-WC, and TG/HDL had an increased risk of cardiovascular mortality by 10.5% (HR: 1.105 [1.100, 1.109]), 10.5% (HR: 1.105 [1.100, 1.109]), 10.4% (HR: 1.104 [1.100, 1.109]), and 10.4% (HR: 1.104 [1.100, 1.109]), respectively (Table 2). Additionally, all four indices exhibited a nonlinear association with cardiovascular disease mortality risk. The lowest mortality risk was observed when TyG was around 8.9, TyG-BMI was approximately 224, and TG/HDL was close to 1.08,

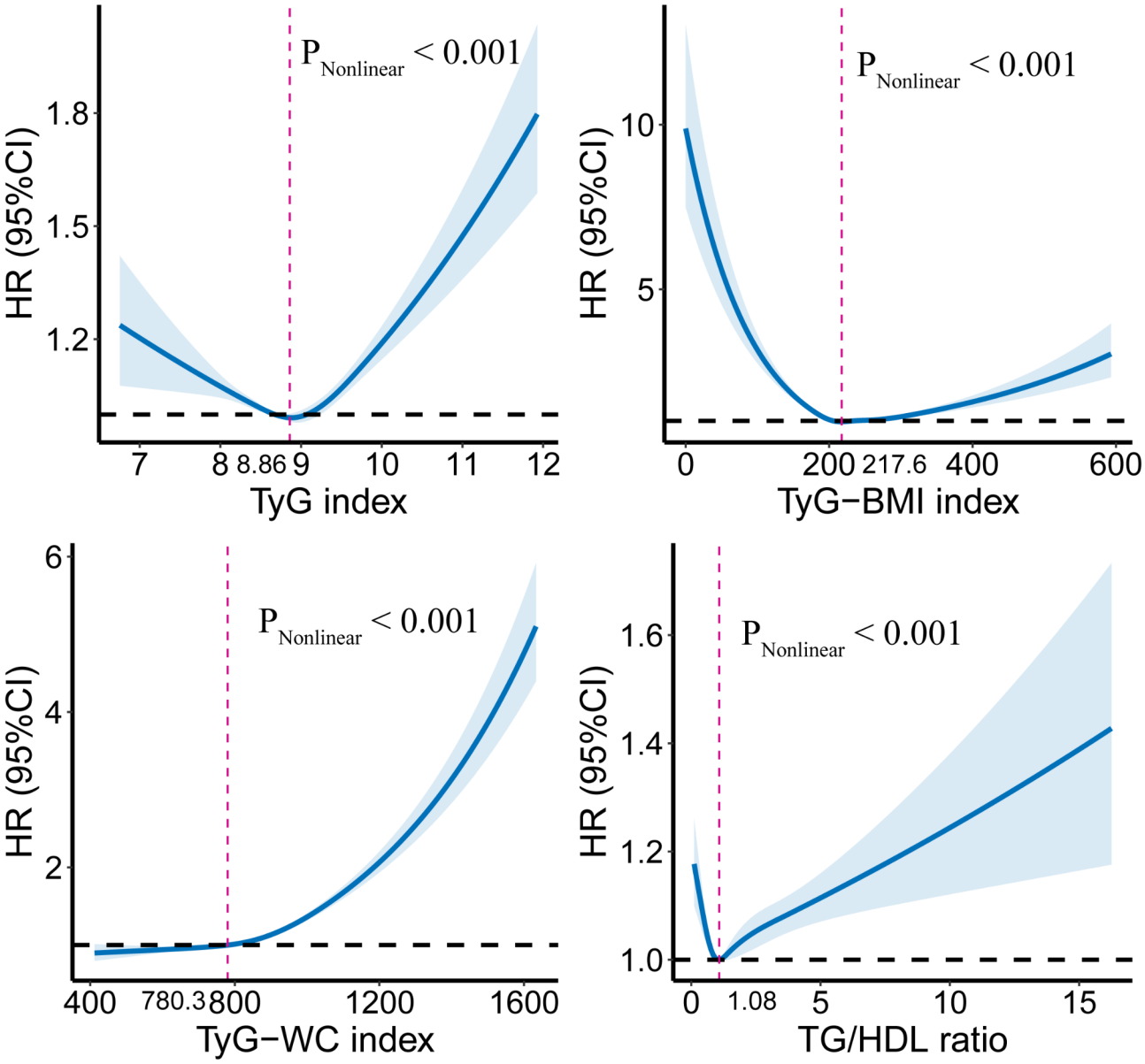


Fig. 2 The association of TyG, TyG-BMI, TyG-WC, and TG/HDL ratio with all-cause mortality. All factors were adjusted for age, sex, ethnicity, Townsend deprivation score, education, smoking, drinking status, diabetes, cardiovascular disease, and the use of anti-diabetic, lipid-lowering, and antihypertensive medications. Abbreviations: HR, hazard ratio; CI, confdence interval; TG/HDL, triglyceride/high-density lipoprotein ratio; TyG index, triglyceride glucose index; BMI, Body mass index; WC, waist circumference

whereas mortality risk began to increase when TyG-WC exceeded 781(Fig. 3). Compared to tumor-related mortality, these four IR indices demonstrated greater discrimination ability for cardiovascular mortality.

Respiratory diseases and neurological diseases were the third and fourth leading causes of death, accounting for 7.2% and 4.5% of total deaths, respectively. When TyG was treated as a continuous variable, each unit increase was associated with a 14.2% decrease in the risk of death from respiratory diseases (HR: 0.858 [0.793, 0.927]) and a 12.4% decrease in the risk of death from neurological diseases (HR: 0.876 [0.791, 0.970]). Compared to the Q1, individuals in the Q4 had an increased risk of death from respiratory diseases by 14.2% (HR: 1.142 [1.133, 1.150]) and from neurological diseases by 14.1% (HR: 1.141 [1.131, 1.521]), suggesting that higher TyG levels may be associated with an elevated mortality risk (Table 2). Furthermore, RCS results further supported the nonlinear associations between TyG, TyG-BMI, TyG-WC, and TG/HDL and mortality risk from respiratory and neurological diseases (Fig. 3).

Excluding deaths from congenital diseases, mortality risk for all other diseases increased in the Q4 of TyG, TyG-BMI, TyG-WC, and TG/HDL compared to the Q1

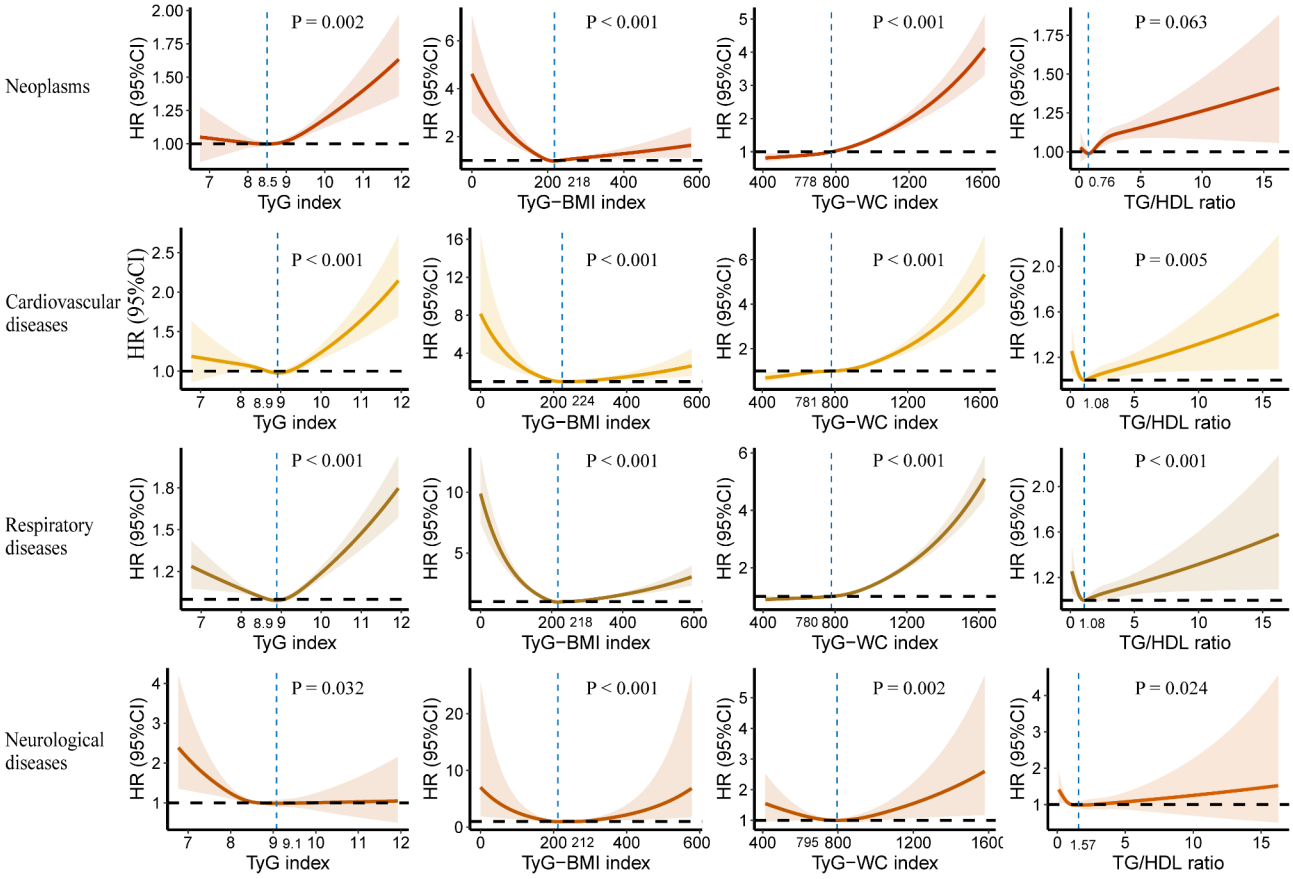


Fig. 3 The association of TyG, TyG-BMI, TyG-WC, and TG/HDL ratio with cause-specific mortality. All factors were adjusted for age, sex, ethnicity, Townsend deprivation score, education, smoking, drinking status, diabetes, cardiovascular disease, and the use of anti-diabetic, lipid-lowering, and antihypertensive medications. Abbreviations: HR, hazard ratio; CI, confdence interval; TG/HDL, triglyceride/high-density lipoprotein ratio; TyG index, triglyceride glucose index; BMI, Body mass index; WC, waist circumference

(Table 2). Moreover, these four IR indices demonstrated strong discrimination ability in identifying high-risk individuals for mortality due to respiratory diseases, cardiovascular diseases, mental disorders, endocrine diseases, urinary system diseases, and skin diseases, with C-index values ranging from 0.80 to 0.90 (Supplementary Table S5).

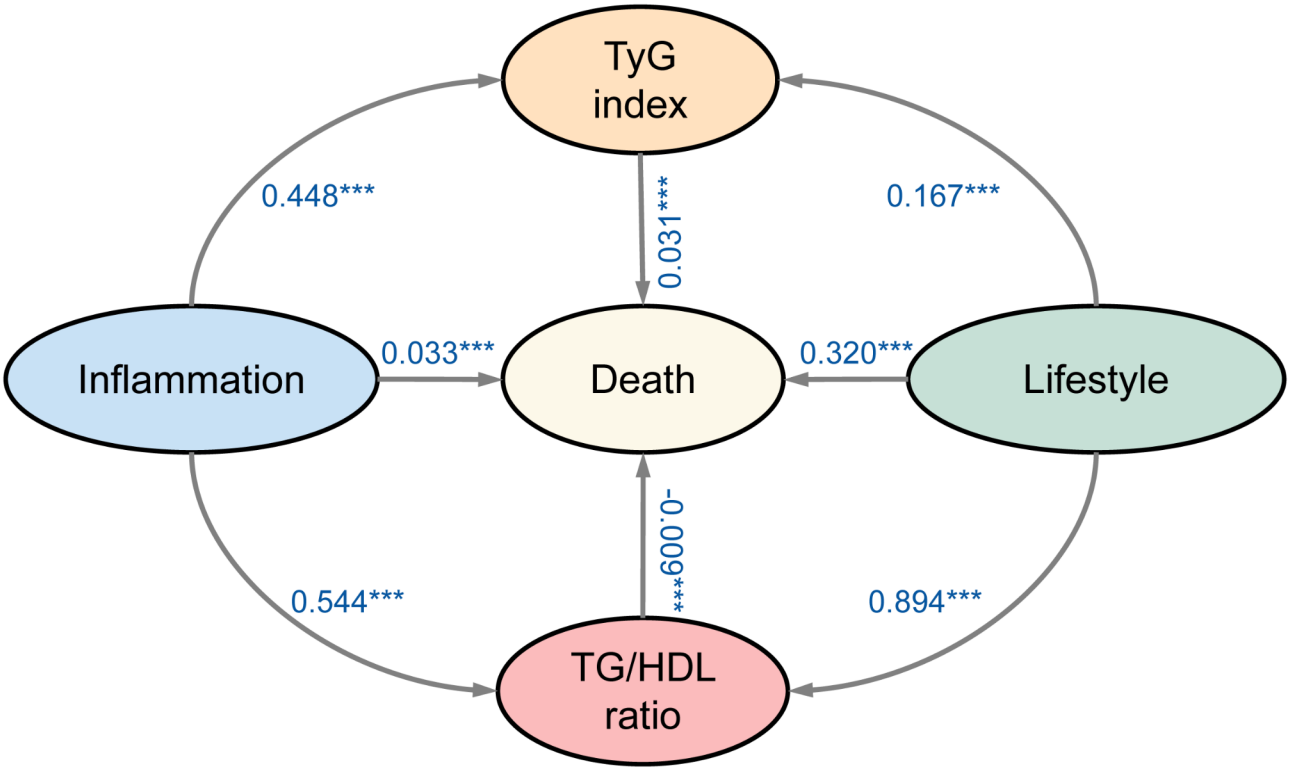
Structure equation model

We employed structural equation modeling to analyze the relationships among TyG index, TG/HDL ratio, inflammation, lifestyle and mortality. The results showed that TyG index (β = 0.031, $P < 0.001$), TG/HDL ratio (β=-0.009, $P < 0.001$), inflammation (β = 0.033, $P < 0.001$), and lifestyle (β = 0.320, $P < 0.001$) were all associated with mortality. Inflammation can influence death by affecting TyG index (β = 0.448, $P < 0.001$) and TG/HDL (β = 0.544, $P < 0.001$) ratio. Lifestyle can also influence death by affecting TyG index (β = 0.167, $P < 0.001$) and TG/HDL (β = 0.894 $P < 0.001$) ratio. (Fig. 4).

Discussion

To our knowledge, this study is the first to investigate the relationship between modified TyG indices and TG/HDL ratio and all-cause and cause-specific mortality in the general population in a large cohort of more than 410,000 people over a 16.5 years. The results revealed that elevated levels of modified TyG indices and TG/HDL ratios were associated with an increased risk of all-cause mortality. Similarly, compared to lower levels of modified TyG indices and TG/HDL ratio, higher levels were associated with an increased risk of cause-specific mortality, excluding deaths from congenital diseases.

Previous studies in the MIMIC database indicated an elevated risk of all-cause mortality associated with the TyG index [15, 16, 23]. However, the database primarily consists of patient records from intensive care units, which predominantly capture ICU mortality, in-hospital mortality, or short-term (e.g., 28-day) mortality. As such, it may not accurately reflect the impact of the TyG index on mortality in the general population. Cohort studies conducted in the general population of the United States also reported an elevated risk of all-cause mortality and



cfi	nfi	ifi	rmsea	srmr
0.965	0.965	0.965	0.036	0.026

Fig. 4 Structural equation model. Nfi, cfi, and ifi indices approach 1, indicating a higher model fit, with values ≥ 0.95 considered as a good fit. Rmsea and srmr should be as low as possible, with values ≤ 0.05 indicating a good fit. Abbreviations: TG/HDL, triglyceride/high-density lipoprotein ratio; TyG index, triglyceride glucose index; nfi, normed fit index; cfi, comparative fit index; ifi, incremental fit index; rmsea, root mean square error of approximation;srmr, standardized root mean square residual. ***$P < 0.001$

cardiovascular disease deaths associated with the TyG index. However, after adjusting for covariates, higher TyG index levels did not remain independently associated with increased mortality risk when compared to levels in Q1 [17]. A study conducted in the general population of Iran found an association between the TyG index and all-cause mortality. However, after adjusting for factors such as diabetes, this association was no longer significant [24]. Chen et al. [17] identified a non-linear relationship between the TyG index and all-cause and CVD deaths, reporting HRs of 1 when the TyG index was between 8.757 and 8.975. Similarly, a study in the United States found that all-cause mortality risk was lowest when the TyG index was around 8.88 [25]. In our study, we also observed a J-shaped relationship between the TyG index and all-cause mortality risk, which remained significant even after adjusting for diabetes status and the use of antidiabetic and lipid-lowering medications.

Previous studies have suggested that combining the TyG index with obesity indicators (such as BMI and WC) may provide greater advantages in assessing IR and the risk of cardiometabolic diseases compared to the TyG index alone [21, 26]. Our study found that TyG-BMI followed an L-shaped association with all-cause mortality, with the lowest risk at approximately 217.6. This finding is consistent with previous research on critically ill patients with atrial fibrillation, which also observed an L-shaped relationship between TyG-BMI and all-cause mortality [27]. Furthermore, multiple studies have demonstrated that TyG-WC outperforms the TyG index in predicting adverse health outcomes, particularly in studies related to metabolic syndrome and cardiovascular diseases [28]. We also observed that when TyG-WC exceeded 780.3, the risk of all-cause mortality significantly increased. This threshold suggests that excessive visceral adiposity accumulation beyond a critical level may accelerate metabolic dysfunction, leading to heightened mortality risk.

The TyG index and its modified indices (TyG-BMI and TyG-WC) are closely associated with cause-specific mortality risk. Our study found that the TyG index exhibited

a J-shaped nonlinear relationship with mortality from cancer, cardiovascular diseases, and respiratory diseases, with the lowest mortality risk observed at 8.5, 8.9 and 8.9, respectively. This finding is consistent with the study by He et al. [29], which showed that in diabetic patients, the TyG index above 9.04 was significantly associated with an increased risk of all-cause and cardiovascular mortality. Additionally, Chen et al. reported a significant association between the TyG index and cancer-related mortality, potentially mediated by chronic inflammation, oxidative stress, and metabolic disorders [30]. Our study found that TyG-BMI exhibited an L-shaped nonlinear relationship with mortality from cancer, cardiovascular diseases, and respiratory diseases, with the lowest risk observed at 218, 224, and 218, respectively. This could be related to the role of BMI in modulating IR and metabolic function. While high BMI is often considered a risk factor for metabolic syndrome, it may also reflect better nutritional status and greater muscle mass, which could confer some protective effects, particularly in the elderly population [21]. Moreover, when TyG-WC exceeded 778, 781, and 780, the mortality risk significantly increased. Excessive abdominal fat accumulation may contribute to increased chronic inflammation, exacerbated IR, and vascular damage, thereby accelerating the progression of cardiovascular diseases and metabolic disorders, ultimately leading to increased mortality [31]. Therefore, maintaining a healthy level of abdominal fat may be an important strategy for reducing mortality risk.

Notably, our study also found that TyG-BMI and TyG-WC exhibited a U-shaped relationship with mortality from neurological diseases, suggesting that IR may play a complex role in the development of neurodegenerative diseases. Previous studies have demonstrated that high IR levels can promote neurodegeneration by impairing insulin signaling, increasing neuroinflammation, and exacerbating oxidative stress [32]. However, other studies have indicated that excessively low IR levels may lead to insufficient energy metabolism, which could impair neuronal survival [33]. Therefore, maintaining the TyG index and its modified indices within an optimal range may be crucial for preserving neurological health.

Studies investigating the impact of TG/HDL ratios on all-cause mortality remain limited. While TG/HDL ratios have been proposed as a reliable surrogate for IR, existing research has primarily focused on their association with the incidence of cardiovascular disease [13]. The study within the UK Biobank cohort found that elevated TG/HDL ratios increased the risk of CVD and CHD (HR 1.12 [1.10–1.13], HR 1.15 [1.13–1.18], respectively), with unclear associations with stroke (HR 1.00 [0.96–1.04]) [22].Our study identified a J-shaped relationship between the TG/HDL ratio and all-cause mortality, as well as cancer-, cardiovascular-, and respiratory-related mortality. Specifically, we found that the lowest mortality risk was observed at 1.08 for all-cause, cardiovascular, and respiratory deaths, and at 0.76 for cancer mortality, with risk increasing beyond these thresholds. A higher TG/HDL ratio reflects IR, promotes atherosclerosis, and increases the risk of cardiovascular events. However, an excessively low TG/HDL ratio may indicate frailty or underlying metabolic deficiencies, which aligns with previous studies linking lower TG/HDL levels to an increased risk of cardiovascular disease and all-cause mortality [34]. A low TG/HDL ratio may be associated with muscle loss, malnutrition, or chronic wasting conditions, leading to impaired immune function and reduced resilience against disease [35]. Additionally, HDL plays a critical role in cholesterol metabolism, cell membrane stability, and signal transduction, and excessively low HDL levels may impair normal cellular functions, contributing to increased mortality risk [36].

The association between TyG, TyG-BMI, TyG-WC, and TG/HDL with all-cause and cause-specific mortality is likely mediated through multiple interrelated pathways, including insulin signaling dysregulation, oxidative stress, and cytokine-mediated inflammation. A high TyG index is a recognized marker of IR, which disrupts glucose metabolism and leads to hyperinsulinemia, contributing to endothelial dysfunction and lipid dysregulation [37]. Prolonged IR reduces insulin-mediated suppression of lipolysis, leading to elevated levels of free fatty acids and oxidized lipids, which promote lipotoxicity, increase oxidative stress, and contribute to atherosclerosis and dyslipidemia [38, 39]. These metabolic disturbances significantly increase the risk of cardiovascular diseases and all-cause mortality. Impaired lipid metabolism is also a crucial factor contributing to mortality risk, as it exacerbates oxidative stress and endothelial dysfunction. Specifically, an elevated TG/HDL ratio reflects compromised reverse cholesterol transport, leading to cholesterol accumulation in macrophages and vascular walls, thereby accelerating the development of atherosclerosis [40, 41]. Additionally, an increased TyG-WC indicates excessive visceral fat accumulation, which is closely associated with chronic low-grade inflammation, further aggravating IR and metabolic syndrome progression [42]. Besides metabolic disorders, chronic inflammation and oxidative stress also play a crucial role. IR and lipid accumulation can activate inflammatory signaling pathways, particularly nuclear factor-κB, c-Jun N-terminal kinase, and mitogen-activated protein kinase, thereby inducing the release of pro-inflammatory cytokines such as IL-6 and TNF-α [43]. These cytokines promote systemic inflammation, leading to vascular remodeling, atherosclerosis, and an increased risk of thrombosis [44]. Moreover, chronic inflammation is closely linked to tumorigenesis, as pro-inflammatory cytokines can enhance tumor

cell proliferation, survival, and metastasis [45]. Elevated levels of oxidized low-density lipoprotein and free fatty acids can generate excessive reactive oxygen species, further inhibiting insulin signaling pathways, impairing mitochondrial function, and inducing endothelial dysfunction [46]. These oxidative damage processes accelerate neurodegenerative changes. Excessive oxidative stress disrupts DNA repair mechanisms, increasing genomic instability, which may further contribute to the risk of cancer-related mortality [47].

Strengths and limitations

The present study demonstrates several strengths. We identified a significant association between the TG/HDL ratio and all-cause as well as cause-specific mortality in a large cohort. Furthermore, our findings suggest that inflammation and lifestyle play crucial roles as underlying factors influencing mortality. However, it is important to acknowledge certain limitations in our study. Firstly, the retrospective design poses challenges in establishing causality. Moreover, the post hoc nature of our analyses limited our ability to fully mitigate remaining confounders. Additionally, traditional Cox models assume that exposure remains constant throughout the follow-up period, which may lead to misclassification bias and an inaccurate estimation of risk. In contrast, time-dependent Cox regression can account for variations in exposure over time, providing a more precise assessment of its impact on outcomes. Lastly, our study lacked continuous monitoring of changes in the TyG index.

Conclusion

Both modified TyG indices and TG/HDL ratio demonstrated significant associations with all-cause and cause-specific mortality in the general population. Lifestyle and inflammation may influence mortality risk by regulating TyG and TG/HDL. Additionally, a threshold effect may exist between these metabolic indices and mortality, and maintaining an appropriate range could serve as a potential target for reducing mortality risk.

Abbreviations

HR	Hazard ratio
CI	Confdence interval
TG/HDL	Triglyceride/high-density lipoprotein ratio
TyG	Index triglyceride glucose index
BMI	Body mass index
WC	Waist circumference

Supplementary Information

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Supplementary Material 1

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Author contributions

L-T contributed to the conception or design of the work. All authors were responsible for the acquisition, analysis and interpretation of data. ZH-Z drafted the manuscript. All author agreed with the content of the article to be submitted. All authors reviewed and approved the final manuscript.

Data availability

Raw data supporting the obtained results are available at the corresponding author.

Declarations

Competing interests

The authors declare no competing interests.

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