Medicine Insights

Article

Prognostic Role of the Triglyceride Glucose Index on All-Cause, Cardiovascular, and Cause-Specific Mortality in Adult Gastric Cancer Patients

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Abstract: Objective: To evaluate the link between the triglyceride-glucose index (TyG) and the risk of death in adults diagnosed with gastric cancer, utilizing data from the National Health and Nutrition Examination Survey (NHANES). Method: To understand the relationship between TyG levels and mortality outcomes in gastric cancer patients, we applied Cox proportional hazards models, Kaplan-Meier curves, and restricted cubic spline analyses. Result: Our findings indicated that participants in the highest TyG quartile showed a significant rise in mortality from all causes, heart-related deaths, and gastric cancer compared to those in the lowest quartile. There was a linear correlation between TyG and both all-cause and cardiovascular mortality, underscoring TyG's potential as a prognostic marker. Conclusion: The research highlights a strong link between TyG and mortality rates in adults with gastric cancer, indicating that keeping track of TyG could be vital for clinical management and risk assessment in this group. Future investigations need to delve deeper into the biological mechanisms behind these associations.

Keywords: gastric cancer; triglyceride glucose index (TyG); mortality; cardiovascular diseases; prognostic analysis

1. Introduction

One of the most frequently occurring malignant tumors worldwide is gastric cancer (GC), especially in East Asia, where both its incidence and mortality are considerably elevated. According to worldwide cancer data, about 780,000 people die from gastric cancer annually, positioning it as the third leading cause of death due to cancer [1-2]. Even with improvements in diagnostic and treatment methods, the outlook for gastric cancer is still bleak, mainly because it is often diagnosed at a late stage and is highly aggressive [3]. In advanced stages, the effectiveness of current treatments, including surgery, chemotherapy, and targeted therapy, is limited, pointing to the need for innovative prognostic markers and therapeutic targets [4-5].

Researchers investigated the relationship between the Triglyceride-glucose index (TyG) and mortality rates, including all-cause, cardiovascular, and specific causes, in adults with gastric cancer. As a metabolic marker, the TyG index is based on triglyceride and fasting blood glucose levels and is connected to insulin resistance and cardiovascular risk [6-7]. Research indicates that high TyG levels could be linked to higher mortality rates across diverse populations, suggesting its potential as a prognostic marker in cancer patients [8-9]. Moreover, factors like age, gender, and existing health conditions can affect the link between TyG and patient outcomes, emphasizing the complexity of this relationship [10]. Comprehending these dynamics is vital for designing specific interventions aimed at boosting survival rates in gastric cancer patients, particularly those at high risk [11]. Annually, gastric cancer affects approximately 1 million people, making

Received: 11 July 2026
Revised: 25 August 2026
Accepted: 09 September 2026
Published: 12 September 2026

it a significant global health challenge. It is the fifth most common cancer worldwide and the third leading cause of cancer-related deaths, causing over 700,000 deaths [12]. Even with improvements in treatment, the outlook for individuals with advanced gastric cancer is bleak, with less than 30% surviving beyond five years. The effectiveness of current diagnostic and therapeutic strategies, like endoscopic screening and surgical intervention, is often limited by late-stage detection and the disease's aggressiveness, pointing to the pressing need for novel biomarkers [13-14].

In the context of GC, the TyG index has surfaced as a potential biomarker for measuring insulin resistance and predicting cardiovascular risk [11]. Earlier research has shown a link between higher TyG levels and a greater risk of death in different groups, indicating it could be a useful prognostic indicator for GC patients [15]. The connection between TyG and clinical outcomes in GC is further influenced by multiple confounding elements, such as age, gender, race, and comorbidities like diabetes and hypertension [16]. Comprehending these relationships is vital for revealing the underlying mechanisms between TyG and GC outcomes and for formulating targeted interventions [17]. The purpose of this study was to investigate the links between TyG and overall mortality, cardiovascular mortality, and mortality from specific causes, thus adding to the expanding research on the impact of metabolic factors in GC patients.

The study relied on data from the National Health and Nutrition Examination Survey (NHANES), which was conducted by the Disease Control and Prevention (CDC). Using a range of statistical analysis approaches, like Cox proportional hazards models, Kaplan-Meier curves, and restricted cubic splines, the study aimed to investigate the connection between TyG and mortality risk in GC patients. It is expected that the study's findings will highlight the potential importance of TyG in clinical strategies for GC prevention and management, contributing to better patient outcomes and informing medical practice.

2. Materials and Methods

2.1. Data Sources

The NHANES data, collected by the CDC from 1999 to 2018, was utilized in this cross-sectional study. Using a stratified multistage probability sampling approach, the NHANES database is a survey that represents the nation and assesses the nutritional and health status of people in the U.S.

2.2. Participant Selection

Only adults with a gastric cancer diagnosis were included to examine the association between the TyG index and outcomes like all-cause mortality, ardiovascular diseases (CVD), and gastric cancer. Throughout 10 survey cycles spanning from 1999 to 2018, a total of 101,316 participants were evaluated. Once participants under 18 were excluded, 59,204 participants remained. After excluding 54,038 non-gastric cancer participants, 5,166 gastric cancer patients remained. Further removal of 2,750 individuals with incomplete or missing laboratory data reduced the cohort to 2,416 GC patients. Ultimately, 2,377 participants with complete follow-up data were included in this analysis after excluding 39 individuals with missing death data or accidental deaths (Figure 1).

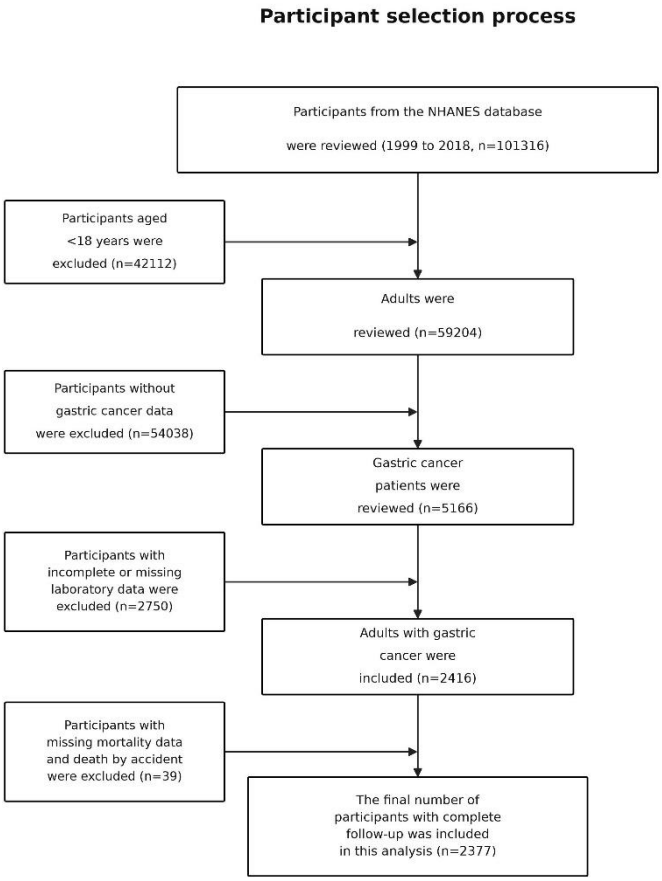

Figure 1. Flowchart of the Study Design.

2.3. Definition of Gastric Cancer

We described the history of GC based on participants' responses to the question in the NHANES database: " Have you ever received a diagnosis of GC or any type of cancer from a doctor or health professional?" Trained interviewers conducted these questions in participants' homes using a computer-assisted personal interview system. To minimize errors in data entry, the system had built-in consistency checks.

2.4. Definition of TyG and Covariates

Peripheral blood tests measuring triglycerides (TG) and fasting blood glucose (FBG) were used to determine TyG, considering previous glucose readings. Investigations have demonstrated its role in measuring insulin resistance and predicting cardiovascular conditions like hypertension, diabetes, and atherosclerosis. The calculation formula is: LN [triglycerides (mg/dl) * plasma glucose (mg/dl)/2]. Among the socioeconomic variables considered in this study was age (classified into 10-year intervals ranging from 18 to 80 years), sex (male versus female), educational attainment (college degree or higher, high school graduate or equivalent, and less than high school education), race/ethnicity (Hispanic, non-Hispanic White, non-Hispanic Black, and other racial groups), the poverty income ratio (PIR) with classifications of less than 1.3, between 1.3 and 1.8, and greater than 1.8, and marital status (categorized as married, unmarried, or cohabiting). Moreover, lifestyle practices and comorbidities were analyzed, including weekly physical activity frequency (never, occasional, or regular),alcohol consumption (categorized as never, moderate, or heavy), , sleep disorders (no, yes), smoking status (never, current, or former smoker) and the presence of comorbidities such as hypertension, osteoporosis, type 2 diabetes, chronic kidney disease (CKD), CVD, and bone cancer (no, yes). Physical and laboratory evaluations were part of the study, encompassing measurements of weight, height, waist circumference, and body mass index (BMI), Additionally, the evaluation

encompassed energy intake, determined as the average kilocalories derived from two 24-hour dietary recall interviews, and the analysis of serum biomarkers such as albumin, C-reactive protein levels, aspartate aminotransferase, glycated hemoglobin, triglycerides, total cholesterol, alanine aminotransferase, glomerular filtration rate, and high-density lipoprotein.

2.5. Outcome Measurement

The primary endpoint of the study was the mortality rate from all causes in gastric cancer patients. Cardiovascular mortality and mortality specific to gastric cancer were secondary outcomes in this group. The 10th Revision of the International Classification of Diseases (ICD-10) was employed to classify death causes. Death data from 1999 to 2018 were obtained from the NHANES follow-up cohort. By December 31, 2019, these data were available in the NHANES public-use mortality data file.

2.6. Statistical Analysis

To compute group-specific weights, the recommended weights from the NHANES database were applied. This research applied sample weights, clustering, and stratification to estimate variance accurately, thus ensuring the national representativeness of the U.S. adult GC population. Histogram distributions, Q-Q plots, and the Kolmogorov-Smirnov test were used to assess the normality of each variable. The Kruskal-Wallis test was used to compare continuous variables between those who survived and those who did not. The comparison of categorical variables was done using the Chi-square test. Continuous variables, not following a normal distribution, were displayed as medians and interquartile ranges. Numbers with weighted percentages were used to present categorical variables.

To evaluate the connection between TyG and several mortality outcomes, including all-cause, cardiovascular, and GC-specific mortality, in GC patients, Cox proportional hazards models were utilized. The choice of covariates for this analysis was guided by previous relevant studies [17]. The development included three models: Model 1 without adjustments, Model 2 with adjustments for sex, age, and race, and Model 3 fully adjusted for sex, age, marital status, race, PIR, education, smoking status, energy intake, physical activity, C-reactive protein, alcohol consumption, hypertension, sleep disorders, diabetes, osteoporosis, CKD, cardiovascular disease, high-density lipoprotein, alanine aminotransferase, glomerular filtration rate, serum albumin, and aspartate aminotransferase. The predictive accuracy of TyG for mortality was assessed using the concordance index (C-index) [18]. Kaplan-Meier (KM) curves illustrated survival data and compared survival patterns among different TyG quartiles in GC patients. The dose-response relationship between TyG and outcomes, including all-cause mortality, cardiovascular mortality, and GC mortality, was assessed using restricted cubic spline (RCS) transformations. Minimizing the Akaike information criterion (AIC) helped decide the number of knots for the RCS curves. Subgroup interaction analyses were also conducted, categorized by variables such as gender, race, age, education, PIR, BMI, marital status, alcohol consumption, hypertension, smoking status, and type 2 diabetes. The goal of these analyses was to further establish the link between TyG and all-cause mortality in GC patients and to assess the predictive significance of TyG in specific demographic and clinical subgroups. Version 4.5.2 of R software was employed for performing statistical analyses.

3. Results

3.1. Baseline Characteristics of Adult Gastric Cancer Patients

A total of 2,377 gastric cancer patients were part of this study conducted between 1999 and 2018. Participants had a median age of 64 years (range: 53.0 - 75.0), with a median body weight of 78.3 kg, a median height of 166.5 cm, a median waist size of 99.9 cm, a BMI of 27.5 kg/m2, and a median daily caloric intake of 1,801 kcal. With 1,270 females (59.3%)

and 1,107 males (40.7%), the study population was predominantly female. The majority of the patients, 1,637 (85.7%), were non-Hispanic White. Also, 39.7% of the participants, totaling 1,122, had reached a high school education or beyond. Of these, 37.2% (947 individuals) were active smokers, and 24.9% (577 individuals) were active drinkers. Among the participants, 667 (30.6%) had a history of sleep disorders, and 624 (31.2%) did not participate in weekly physical activity. Moreover, 18% of the participants were diagnosed with Diabetes Mellitus, 61.6% with hypertension, 10.9% with osteoporosis, 15.9% with cardiovascular diseases, and 19.3% with CKD. Remarkably, the median TyG was 8.69. During a median follow-up of 107 months, there were 875 deaths from all causes, 432 due to cardiovascular issues, and 624 related to GC. The majority of non-survivors were male, over the age of 60, possessed higher educational attainment, were married, had moderate income levels, and frequently presented with hypertension. Additionally, they tended to consume alcohol, were current smokers, did not engage in physical exercise, had a lower BMI, and exhibited elevated TyG index levels in comparison to survivors, with all associated P values being less than 0.05, as detailed in Table 1.

Table 1. Demographic Characteristics of Adult Gastric Cancer Patients.

Variables	Total (n=2377)	Survivors (n=1502,74.1%)	Non-survivors (n=875,25.9%)	P
Age (years), n (%)	64.00 (53.00 - 75.00)	60.00 (49.00 - 70.00)	75.00 (67.00 - 80.00)	<0.001
18-29	54 (3.0%)	50 (3.6%)	4 (1.4%)	
30-39	104 (6.6%)	101 (8.7%)	3 (0.6%)	
40-49	175 (10.5%)	154 (13.1%)	21 (2.7%)	
50-59	310 (17.9%)	264 (21.7%)	46 (6.9%)	
60-69	569 (25.6%)	412 (27.6%)	157 (19.9%)	
70-80	1,165 (36.5%)	521 (25.3%)	644 (68.4%)	
Sex, n (%)				<0.001
Male	1,107 (40.7%)	613 (37.4%)	494 (56.5%)	
Female	1,270 (59.3%)	889 (62.6%)	381 (43.5%)	
Race, n (%)				0.266
Hispanic	310 (5.4%)	240 (5.9%)	70 (4.0%)	
Non-Hispanic white	1,637 (85.7%)	956 (85.1%)	681 (87.5%)	
Non-Hispanic black	323 (5.6%)	214 (5.2%)	109 (6.7%)	
Other races	107 (3.3%)	92 (3.8%)	15 (1.9%)	
Education status, n (%)				<0.001
More than high school	1,122 (39.7%)	625 (34.9%)	497 (53.4%)	
High school or equivalent	663 (28.3%)	456 (29.2%)	207 (25.7%)	
Less than high school	588 (31.9%)	418 (35.8%)	170 (20.9%)	
Not recorded	4 (0.1%)	3 (0.1%)	1 (0.1%)	
Marital status, n (%)				<0.001
Married	1,378 (64.1%)	902 (67.7%)	476 (53.7%)	
Not married	898 (31.6%)	528 (27.9%)	370 (42.1%)	
Living with partner	87 (3.9%)	67 (4.3%)	20 (2.9%)	
Not recorded	14 (0.4%)	5 (0.1%)	9 (1.3%)	
PIR (%)				<0.001
<1.3	526 (14.3%)	307 (11.6%)	219 (22.0%)	
1.3-1.8	884 (34.1%)	509 (30.8%)	375 (43.7%)	
>1.8	755 (43.8%)	551 (49.8%)	204 (26.9%)	
Not recorded	212 (7.7%)	135 (7.8%)	77 (7.4%)	
Daily alcohol drinking status, n (%)				<0.001

Non-drinkers	300 (10.6%)	179 (9.1%)	121 (14.7%)	
Moderate-drinkers	305 (11.1%)	193 (10.7%)	112 (12.3%)	
Heavy-drinkers	272 (13.8%)	212 (16.1%)	60 (7.3%)	
Not recorded	1,500 (64.5%)	918 (64.1%)	582 (65.6%)	
Smoking, n (%)				<0.001
Never	1,062 (46.3%)	723 (49.0%)	339 (38.8%)	
Now	947 (37.2%)	529 (34.2%)	418 (45.6%)	
Ever	365 (16.4%)	247 (16.7%)	118 (15.6%)	
Not recorded	3 (0.1%)	3 (0.1%)	0 (0.0%)	
Sleep disorder, n (%)				<0.001
No	1,710 (69.4%)	1,019 (66.3%)	691 (78.1%)	
Yes	667 (30.6%)	483 (33.7%)	184 (21.9%)	
Physical activity, n (%)				<0.001
Inactive	624 (31.2%)	405 (26.7%)	219 (54.4%)	
Less active or Active	927 (68.8%)	765 (73.3%)	162 (45.6%)	
History of diabetes, n (%)				0.001
No	1,703 (82.0%)	1,114 (83.9%)	589 (76.7%)	
Yes	550 (18.0%)	321 (16.1%)	229 (23.3%)	
History of hypertension, n (%)				<0.001
No	762 (38.4%)	568 (44.5%)	194 (20.9%)	
Yes	1,615 (61.6%)	934 (55.5%)	681 (79.1%)	
History of osteoporosis, n (%)				<0.001
No	2,109 (89.1%)	1,351 (91.1%)	758 (83.7%)	
Yes	268 (10.9%)	151 (8.9%)	117 (16.3%)	
Bone cancer, n (%)				<0.001
No	1,882 (84.1%)	1,275 (88.8%)	607 (70.7%)	
Yes	473 (15.9%)	217 (11.2%)	256 (29.3%)	
CKD, n (%)				<0.001
No	1,806 (80.7%)	1,203 (84.8%)	603 (69.2%)	
Yes	571 (19.3%)	299 (15.2%)	272 (30.8%)	
Weight (kg)	78.3 (66.1 - 92.3)	79.2 (66.8 - 92.5)	75.1 (63.9 - 91.2)	0.003
Standing height (cm)	166.5 (160.0 - 174.7)	166.4 (16.4 - 174.7)	166.9 (159.3 - 174.6)	0.643
Waist circumference (cm)	99.9 (88.9 - 110.7)	99.8 (88.5 - 110.7)	100.1 (89.6 - 110.9)	0.611
BMI (Kg/m2), n (%)	27.5 (24.1 - 32.3)	27.7 (24.2 - 32.9)	26.9 (23.8 - 31.3)	0.005
<25	655 (31.2)	374 (29.6)	281 (35.9)	
25-30	759 (32.2)	494 (33.2)	265 (29.3)	
>30	787 (34.8)	552 (36.1)	235 (31.2)	
Not recorded	52 (1.7)	15 (1.1)	37 (3.6)	
Daily energy (kcal)	1,801.0 (1,335.0-2,286.0)	1,821.0 (1,396.0 - 2,309.0)	1,665.0 (1,120.0 - 2,203.0)	<0.001
ALB (g/L)	20.0 (16.0 - 27.0)	20.0 (16.0 - 28.0)	19.0 (15.0 - 24.0)	<0.001
ALT (U/L)	42.0 (40.0 - 44.0)	42.0 (40.0 - 44.0)	41.0 (39.0 - 44.0)	<0.001
AST (U/L)	23.0 (19.0 - 27.0)	23.0 (19.0 - 27.0)	23.0 (20.0 - 28.0)	0.05
HDL (mg/dL)	54.00 (45.00 - 65.00)	54.00 (45.00 - 65.00)	54.00 (45.00 - 67.00)	0.669
TG (mmol/L)	1.28 (0.89 - 1.84)	1.23 (0.87 - 1.81)	1.39 (0.98 - 1.95)	<0.001
TC (mmol/L)	5.04 (4.40 - 5.79)	5.07 (4.42 - 5.82)	4.97 (4.27 - 5.66)	0.014

eGFR (mL/min/1.73 m2)	82.01 (67.34 - 95.45)	84.64 (70.48 - 97.78)	71.63 (54.06 - 85.03)	<0.001
Glycohemoglobin (%)	5.6 (5.3 - 5.9)	5.5 (5.3 - 5.9)	5.7 (5.4 - 6.0)	<0.001
CRP (mg/dL)	0.28 (0.12 - 0.83)	0.26 (0.10 - 0.83)	0.28 (0.15 - 0.83)	<0.001
TyG	8.69 (8.29 - 9.11)	8.64 (8.26 - 9.08)	8.78 (8.44 - 9.17)	<0.001

TyG, Triglyceride glucose index; PIR, Poverty income ration; CKD, Chronic kidney disease; BMI, Body mass index; ALB, Serum albumin level; AST, Aspartate aminotransferase; HDL, High-density lipoprotein; TG, CRP, C-reaction protein; Triglyceride; ALT, Alanine aminotransferase; TC, Total cholesterol; eGFR, Glomerular filtration rate. The median and the first and third quartiles (M, Q1, Q3) are used to present variables with a non-normal distribution. Categorical variables are expressed as numbers with weighted percentages (n; %). When p<0.05, statistical significance is shown by bold values.

3.2. Association between TyG and Mortality Outcomes in Adult Gastric Cancer Patients

The high TyG quartile subgroup showed significantly increased all-cause, cardiovascular, and GC mortality compared to the low quartile subgroup among unweighted participants, as indicated in Figures 2A, 2C, and 2E ($P < 0.05$). Likewise, participants in the high TyG quartile, when weighted, showed notably higher rates of all-cause mortality (Figure 2B), cardiovascular mortality (Figure 2D), and GC mortality (Figure 2F) compared to those in the low quartile subgroup ($P < 0.05$). The fourth quartile of TyG was found to be significantly associated with all-cause mortality risk in the multivariable-adjusted Cox regression analysis, with an adjusted hazard ratio (aHR) of 1.369 (95% CI: 1.051–1.782, $P = 0.02$) (Figure 3A). Also, elevated TyG quartile levels were significantly associated with cardiovascular mortality in adult GC patients, with a TyG-aHR of 1.37 (95% CI: 1.058–1.774, $P = 0.017$) (Figure 3B). The study did not find a significant relationship between higher TyG quartile levels and GC mortality, with a TyG-aHR of 1.206 (95% CI: 0.536–2.716, $P = 0.651$) (Figure 3C). For predicting all-cause mortality, the C-index of TyG was 0.519, while it was 0.575 for cardiovascular mortality and 0.552 for GC mortality. The prediction accuracy for all-cause mortality, measured by the c-index, improved to 0.820, and for cardiovascular mortality to 0.814, when TyG was used alongside other clinical factors.

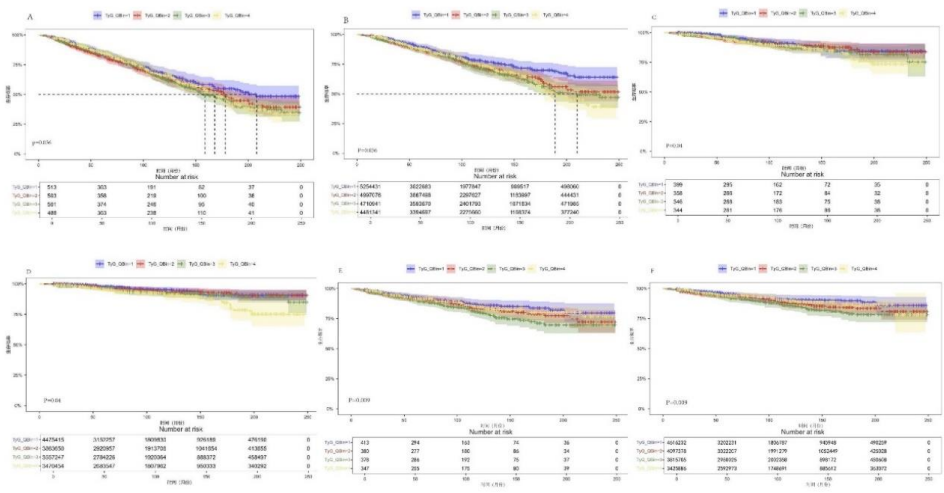

Figure 2. Survival patterns in adult gastric cancer patients across different TyG quartiles are shown by Kaplan-Meier curves. A (unweighted)-B (weighted) represent all-cause mortality at various TyG quartile levels. Cardiovascular mortality in adult GC patients at different TyG quartile levels is represented by C (unweighted) and D (weighted). GC mortality in these patients at various TyG quartile levels is shown by E (unweighted) and F (weighted). TyG, Triglyceride-Glucose Index; Q, Quartile.

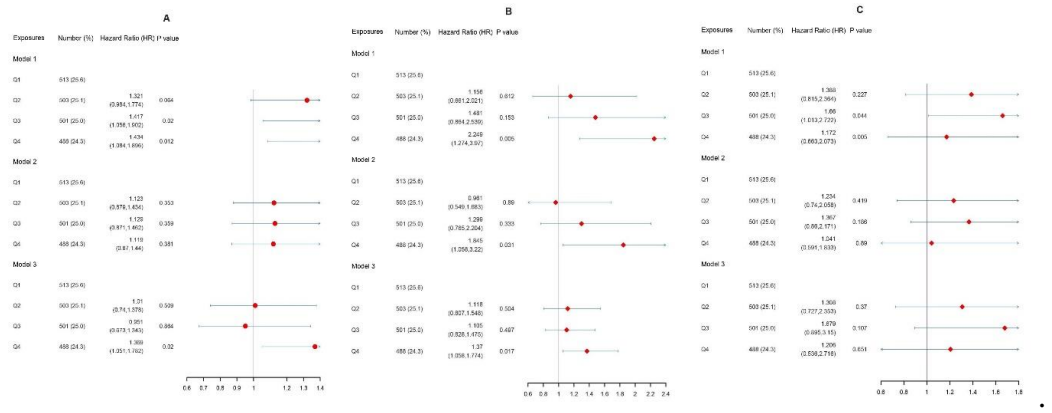

Figure 3. Forest Plot A presents the correlation between TyG and all-cause mortality among adult GC patients, and Forest Plot B shows the relationship with cardiovascular mortality. Forest Plot C demonstrates how TyG is associated with cancer mortality among adults with gastric cancer. Model 1: Unadjusted; Model 2: Adjusted for Race; Sex, Age, Model 3: Adjusted for Age, Race, Sex, Education, PIP, Energy Intake, Marital Status, Alcohol Consumption, Physical Activity, Diabetes, Smoking Status, Sleep Disorders, Osteoporosis, Hypertension, Cardiovascular Disease, Serum Albumin Level, Alanine Aminotransferase, Aspartate Glomerular Filtration Rate, High-Density Lipoprotein, C-reactive Protein, Aminotransferase and Chronic Kidney Disease.

3.3. Linear Trends of TyG Index with Mortality Outcomes in Adult Gastric Cancer Patients

In GC patients, TyG showed a linear correlation with all-cause mortality and cardiovascular mortality (P for overall effect < 0.005, P for nonlinearity > 0.05) (Figures 4A and 4B). Conversely, the RCS plot, which accounted for various covariates, showed that TyG did not have a statistically significant impact on gastric cancer mortality (P for overall effect = 0.195, P for nonlinearity = 0.121) (Figure 4C). Elevated TyG levels appear to be connected with a significantly increased risk of both all-cause and cardiovascular mortality among the GC population.

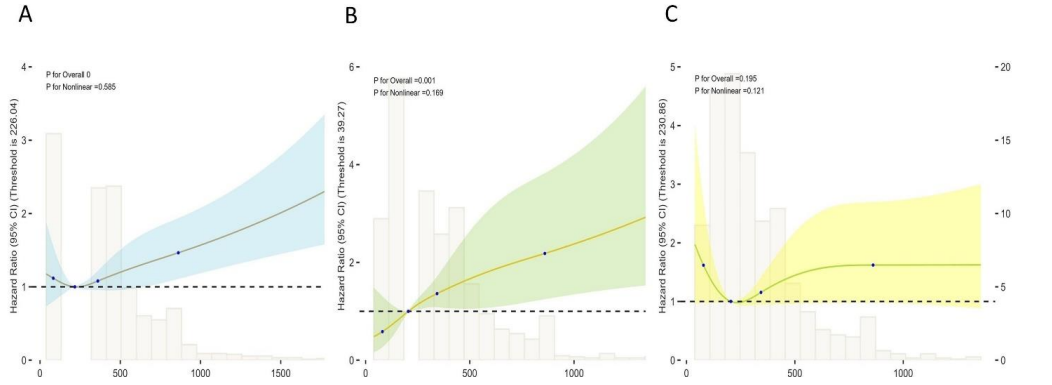

Figure 4. A: The dose-response relationship between TyG and all-cause mortality in adult GC patients is depicted by a restricted cubic spline. B: The dose-response relationship between TyG and cardiovascular mortality in adult GC patients is also depicted by a restricted cubic spline. C: In adult GC patients, a restricted cubic spline illustrates the connection between TyG levels and cancer mortality.

3.4. Subgroup Interaction Analysis

The fully adjusted model's subgroup interaction analysis in adult GC patients revealed no significant differences in the interaction results between the TyG index and gender, race, PIR, hypertension, marital status, alcohol consumption history and type 2 diabetes mellitus. The interaction P values for age, education level, BMI, and smoking status were all found to be less than 0.05, signifying a significant enhancement in the predictive efficacy of TyG within these specific subgroups. Notably, this enhancement

was observed among individuals aged 60 to 69 years, those possessing a high school education level, individuals with a BMI ranging from 25 to 30, and both current and former smokers. These findings imply that the integration of TyG with covariates is positively associated with an increased risk of all-cause mortality among gastric cancer patients aged 60 to 69 years and those who are current or former smokers. Conversely, the combination of TyG with covariates is negatively associated with an increased risk of all-cause mortality in gastric cancer patients who have a high school education level and those with a BMI between 25 and 30 (Figure 5).

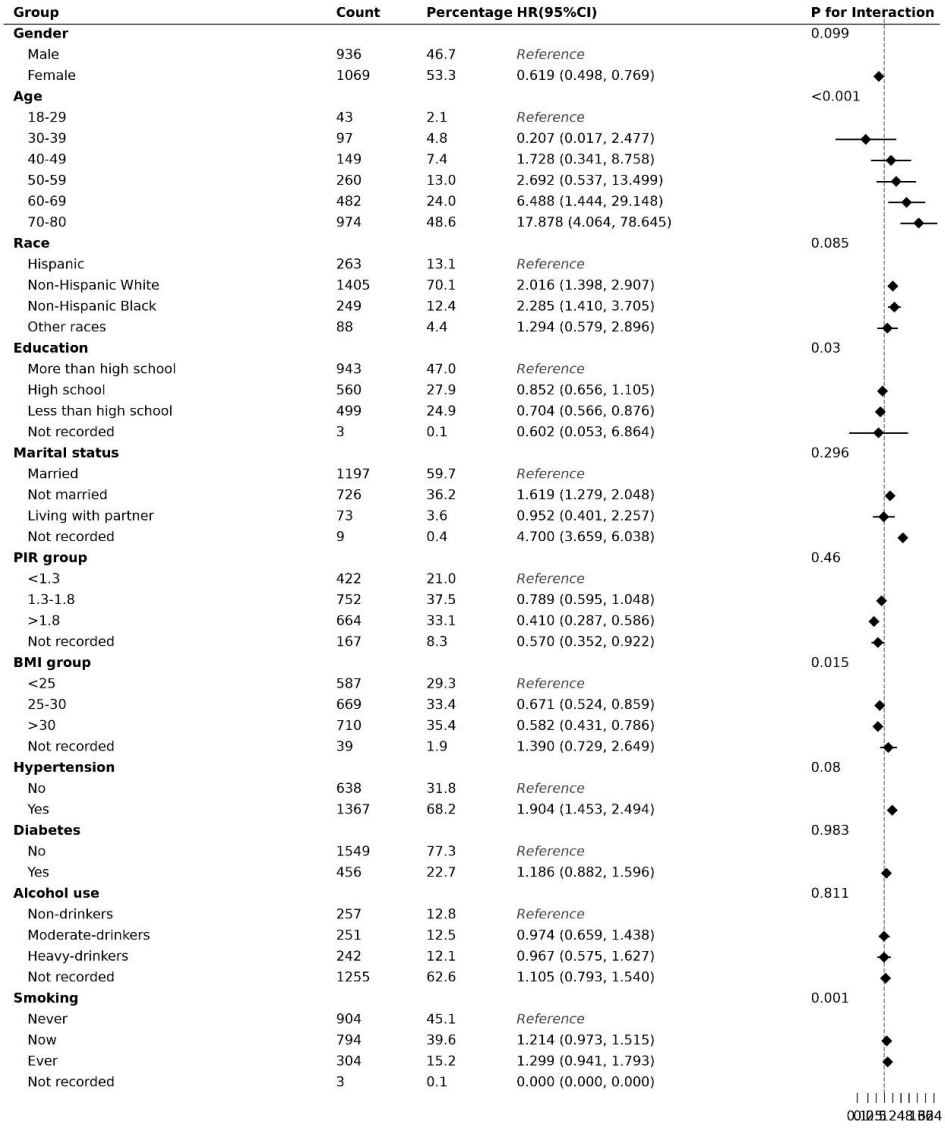

Figure 5. Subgroups Were Defined Based on Race, Education, Age, Marital Status, PIR, Body Mass Index, Smoking, Diabetes, Alcohol Consumption, Hypertension and gender. The purpose was to investigate the connection between TyG and all-cause mortality among adult GC patients in diverse subgroups. PIR, Poverty income ration; BMI, Body Mass Index.

4. Discussion

The advanced stages of GC are associated with high mortality rates, making it a significant issue worldwide. This investigation points out the crucial association between the triglyceride-glucose index and both all-cause and cardiovascular mortality in adult GC patients. Our study focuses on the TyG index as a composite biomarker, differing from previous research that concentrated on individual risk factors, indicating its potential utility as a prognostic tool in clinical settings. Monitoring TyG levels is crucial in the

treatment of gastric cancer patients, as indicated by the findings, to potentially improve results. Our analysis using the NHANES database found that elevated TyG levels are significantly linked to increased risks of overall and cardiovascular mortality in GC patients. Importantly, this link remained even after accounting for different confounding variables, indicating that TyG might offer extra predictive insights beyond standard clinical measures. Integrating TyG monitoring into everyday clinical practice is recommended by these results, as it can enhance risk evaluation and assist in making treatment decisions for this susceptible patient population.

Research findings demonstrate a strong positive correlation between TyG and all-cause as well as cardiovascular mortality in GC patients, pointing to TyG as a vital prognostic biomarker. This outcome corresponds with previous studies, such as a cohort study of 1,040 patients with locally advanced GC, which identified the TyG index as an independent predictor of overall survival, suggesting its potential clinical utility [18]. A study with 2,377 participants found that higher TyG levels are linked to increased mortality risk, highlighting TyG as an important marker for metabolic dysfunction and cancer prognosis [19]. A meta-analysis also showed that elevated TyG levels are associated with negative cardiovascular outcomes across various populations [20]. However, a study of 3,614 hypertensive individuals found no significant link between TyG and cardiovascular mortality after adjusting for confounders, suggesting discrepancies due to differences in study design or population [21]. Overall, this study supports TyG as a key prognostic factor for gastric cancer and emphasizes the need for more research to clarify its role in different patient groups and clinical settings [22].

This study utilized a range of statistical methodologies, including Cox proportional hazards models, Kaplan-Meier survival curves, and restricted cubic splines, to thoroughly investigate the association between the TyG index as an exposure variable and mortality outcomes in adult patients with gastric cancer. The analysis using the Cox proportional hazards model revealed that individuals in the highest quartile of the TyG index exhibited a statistically significant association with increased all-cause mortality, with an adjusted hazard ratio (aHR) of 1.369 (95% confidence interval [CI]: 1.051–1.782, P = 0.020). This result was corroborated by Kaplan-Meier survival analyses, which illustrated distinct survival trajectories corresponding to different TyG quartiles. Additionally, the application of restricted cubic spline analysis reinforced the presence of a linear relationship between TyG levels and mortality risk, suggesting a dose-response effect. The Cox proportional hazards model provided a robust framework for evaluating the impact of the TyG index on mortality. Complementary analyses, including Kaplan-Meier survival estimates and spline regression techniques, further enhanced the validity of our findings by confirming the consistency of results across diverse statistical methodologies. Collectively, these models demonstrate a positive linear association between TyG levels and mortality outcomes, thereby reinforcing the conclusion that elevated TyG levels are linked to an increased risk of mortality within this patient cohort. The integration of multiple statistical approaches not only fortifies the evidence supporting the association between TyG and mortality but also underscores the importance of employing various analytical perspectives in the assessment of health risks in clinical research. This multifaceted approach underscores the potential of TyG as a significant biomarker for predicting mortality in patients with GC, advocating for its application in clinical settings to identify high-risk individuals and tailor interventions accordingly.

The TyG index, a key metabolic biomarker, impacts the prognosis of GC patients by linking insulin resistance and inflammation to increased mortality risk [23]. This suggests metabolic issues may worsen the tumor environment and affect treatment. Studies highlight immune cell subtypes like tumor-associated macrophages and regulatory T cells, which promote inflammation, tumor progression, and immune evasion, leading to poor treatment outcomes [24-26]. This observation matches prior research, such as a cohort study with 1,040 patients with locally advanced GC, which pinpointed the TyG index as an independent predictor of overall survival, highlighting its potential for clinical application.

This study elucidates significant findings concerning the relationship between the TyG index and mortality among adult GC patients. Nonetheless, several limitations warrant consideration. Firstly, the absence of wet-laboratory experiments constrains the capacity to ascertain causal mechanisms underlying the observed associations. Additionally, the sample size may be inadequate for extrapolating the findings to diverse populations, which could compromise the robustness of the results. Furthermore, the lack of clinical validation analyses raises questions regarding the applicability of the TyG index in practical clinical contexts. The utilization of multiple datasets may introduce batch effects, thereby complicating the interpretation of results and potentially leading to certain biases.

5. Conclusion

The results of our study demonstrate that adult GC participants in the highest TyG index quartile exhibit significantly higher rates of all-cause, cardiovascular, and cancer-related mortality compared to those in the lowest quartile. A linear relationship was observed between TyG levels and both all-cause and cardiovascular mortality. These findings suggest that the TyG index could be a critical metabolic biomarker influencing survival outcomes in GC patients. Future research should aim to validate these findings in larger and more diverse cohorts, as well as to investigate the underlying biological mechanisms. Such efforts may ultimately enhance clinical management strategies and improve prognostic outcomes for the adult GC population.

Data Availability Statement: The datasets presented in this study can be found in the following publicly accessible online repositories. The individual-level data were obtained from the NHANES, available at https://wwwn.cdc.gov/nchs/nhanes/.

Institutional Review Board Statement: Not applicable. Only publicly available summary statistics were used.

Author Contributions: Rongxiang Sun: conceptualization, methodology, writing–original draft, funding acquisition. Zhifeng Mo: writing–review & editing, investigation, formal analysis. Guo Huilong: writing–original draft, supervision, validation. Qinglong Jian: writing–review & editing, data curation, project administration, funding acquisition.

Funding: This study was supported by Pre-hospital Emergency Care Financial Reward-based Subsidy Fund from the Seventh Affiliated Hospital, Sun Yat-sen University (00403000002).

Acknowledgments: We would like to thank the researchers and participants of the NHANES.

Conflicts of Interest: The authors declare that they have no competing interests.

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