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ORIGINAL RESEARCH

Association of the Triglyceride-Glucose Index and Obesity Indicators with Multiple Chronic Diseases: A Longitudinal Cohort Study Based on CHARLS

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Objective: To explore the relationship between triglyceride glucose (TyG) and the obesity combined indexes and the occurrence of multiple chronic diseases (MCD), which will help to provide a basis for the prevention and treatment of this condition.

Methods: 3037 participants in the China Health and Retirement Longitudinal Study, which was conducted from 2011 to 2015 were selected for this study. They were divided into four groups (Q1, Q2, Q3, Q4) based on the quartiles of TyG, TyG-BMI, TyGWC and TyGWHtR in the baseline data. A Cox proportional hazard model was used to analyze the risk of MCD associated with TyG and its obesity-related combined indicators. Dose-response relationships were analyzed using restricted cubic spline regression, and the predictive ability for detection of MCD was analyzed using ROC curve.

Results: At the end of the follow-up in 2015, 473 new cases of MCD were observed among the study population, with an incidence rate of 15.6%. After adjusting for confounding factors, the risk of MCD significantly increased in the Q4 TyG, TyG-BMI, TyG-WC and TyG-WHtR index groups compared to the Q1 groups ($p<0.001$ in all cases). A linear dose-response relationship was observed between the TyG index and the risk of MCD, indicating increased risks of CKD with higher TyG indexes. However, the TyG-BMI, TyG-WC and TyG-WHtR indexes exhibited nonlinear dose-response relationships with the risk of MCD (P-nonlinearity <0.0001 in all cases), indicating higher indexes were associated with higher risks of MCD. The areas under the ROC curves for the Cox regression models of TyG, TyG-BMI, TyG-WC and TyG-WHtR indices were 0.610, 0.590, 0.590 and 0.607, respectively.

Conclusion: The TyG, TyG-BMI, TyG-WC and TyG-WHtR indexes were found to be positively correlated with increased risk of developing MCD. Measurements and regulation of these indexes can be used to prevent and control the occurrence of MCD.

Keywords: triglycerides-glucose, multiple chronic diseases, chronic disease comorbidity, CHARLS

Multiple chronic diseases (MCD) refer to the condition when individuals suffer from two or more chronic diseases simultaneously, and it is characterized by complex mechanisms with high correlation and it can involve several influencing factors.[1] MCD can have a more serious negative impact on health than a single disease.[2] It can drastically reduce the quality of life of patients, often placing huge economic burden to their families resulting in economic pressures for the whole society. Studies have found that MCD have become the most common epidemic feature of

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middle-aged and elderly people in China, and the prevalence rate among these population groups over 50 years old is approximately 42.4%.[3]

The degree of insulin resistance can render abnormal insulin metabolism in the body, and this can lead to glucose and lipid metabolism disorders, including hyperglycemia, hyperlipidemia and other problems, these problems can promote the development of metabolic syndrome. Metabolic syndrome[4] is a clinical syndrome characterized by the simultaneous presence of multiple metabolic abnormalities, including insulin resistance, hyperglycemia, obesity, hypertriglyceridemia, and low high-density lipoprotein cholesterol. Among them, the relationship between insulin resistance and obesity and oxidative stress is the closest.[5] On the one hand, insulin resistance and obesity can increase the levels of inflammation and oxidative stress in the body, which can cause a decrease in the activity of antioxidant substances such as superoxide dismutase (SOD) or catalase (CAT) and an increase in the level of reactive oxygen species (ROS), thereby reducing the body's antioxidant capacity and leading to damage to tissue and organs such as the kidneys, cardiovascular system, and liver.[6] On the other hand, oxidative stress and chronic inflammation can damage pancreaticβ-cell function, interfere with insulin signal transduction, and cause systemic mitochondrial dysfunction, thereby promoting the occurrence and development of insulin resistance.[7] Additionally, an elevated oxidative stress level will stimulate the generation of an excessive amount of ROS in the body. Furthermore, an elevated oxidative stress level will stimulate the production of an excessive amount of ROS in the body. These ROS will react with the lipids and proteins in lipoproteins, thereby modifying the structure and properties of lipoproteins and promoting the development of hypertension, dyslipidemia, and the occurrence and progression of atherosclerosis.[8] This is likely to lead to the occurrence of various diseases. The euglycemic-hyperinsulinemic clamp technique is currently the gold standard for measuring insulin resistance. However, this method is costly and operationally complex, presenting significant limitations in practical applications.[9] The Homeostasis Model Assessment (HOMA) is the most widely used method at present. However, due to the high cost of measuring fasting insulin, as this method requires insulin blood testing, the testing cost is relatively high, which to a certain extent limits its widespread application.[10] Therefore, it is necessary to find insulin resistance measurement indicators that are simple to operate, low in cost, and effective. Studies[11] have demonstrated that TyG is associated with MCD. In addition, there are also studies[12] which found that the combination of TyG and obesity indexes together with Ty G-BMI, Ty G-WC and Ty G-WHtR indexes were also associated with chronic diseases such as diabetes, hypertension and high uric acid. However, studies on TyG and its association with obesity indicators and the occurrence of MCD are relatively rare. Therefore, this study explored the relationship between TyG and its obesity combined indicators as well as MCD by using data from the CHARLS survey project. The potential use of these indicators as auxiliary diagnostic factors to identify people at high risk of MCD was assessed this will provide a basis for the prevention and treatment of MCD.

Participants and Methods

Study Population

The data for this study were obtained from the China Health and Retirement Longitudinal Study (CHARLS), which were downloaded from the CHARLS official website after obtaining authorization. CHARLS was China's first national longitudinal survey project targeting middle-aged and elderly individuals. The baseline survey was conducted from July 2011 to March 2012, using a stratified multi-stage random sampling method to select residents over 45 years old from 28 provinces (autonomous regions and municipalities directly under the central government) consisting of 150 counties and 450 villages across the country for follow-up visits.[13] Computer-Assisted Personal Interviewing (CAPI) technology was employed to gather information on the socioeconomic status and personal health status of the respondents, and it covered aspects related to personal family, health, medical care and other relevant information. Follow-up surveys have been conducted every 2 to 3 years, and so far, the second (2013), third (2015), fourth (2018) and fifth (2020) rounds of surveys have been completed.[14] Blood samples were tested for some disease indicators in the baseline survey conducted in 2011 as well as in the third-round follow-up survey in 2015, and these could be used to objectively and accurately reflect disease status of individuals. In this study, we selected survey data from these two periods for analysis, and this involved collection of data from 11,176 participants who were assessed in both of these surveys. After

excluding 595 participants with missing basic demographic information, 3599 with missing data on lifestyle habits and chronic disease questionnaires, 777 with missing physical examination data, 2103 with missing blood biochemistry examination data and 1065 with MCD at baseline, 3037 participants were ultimately included in the study (Figure 1). This study has been approved by the Ethics Committee of Youjiang Medical University for Nationalities (IRB2024022601), and all participants have signed the informed consent form before the start of the study.

The inclusion criteria for this study were: (1) the participants who participated in the 2011 baseline survey and the follow-up survey in 2015, (2) complete physical examination and blood biochemical data and (3) no chronic disease or only one chronic disease at the baseline survey. All the included participants had complete data with respect to their basic population information, living habits and health status questionnaires.

Study Methods

Basic Information Collection

Data collection primarily involved questionnaires to gather social demographic information (gender, age, marital status and education level), basic physical examinations (such as height, weight, waist circumference and blood pressure),

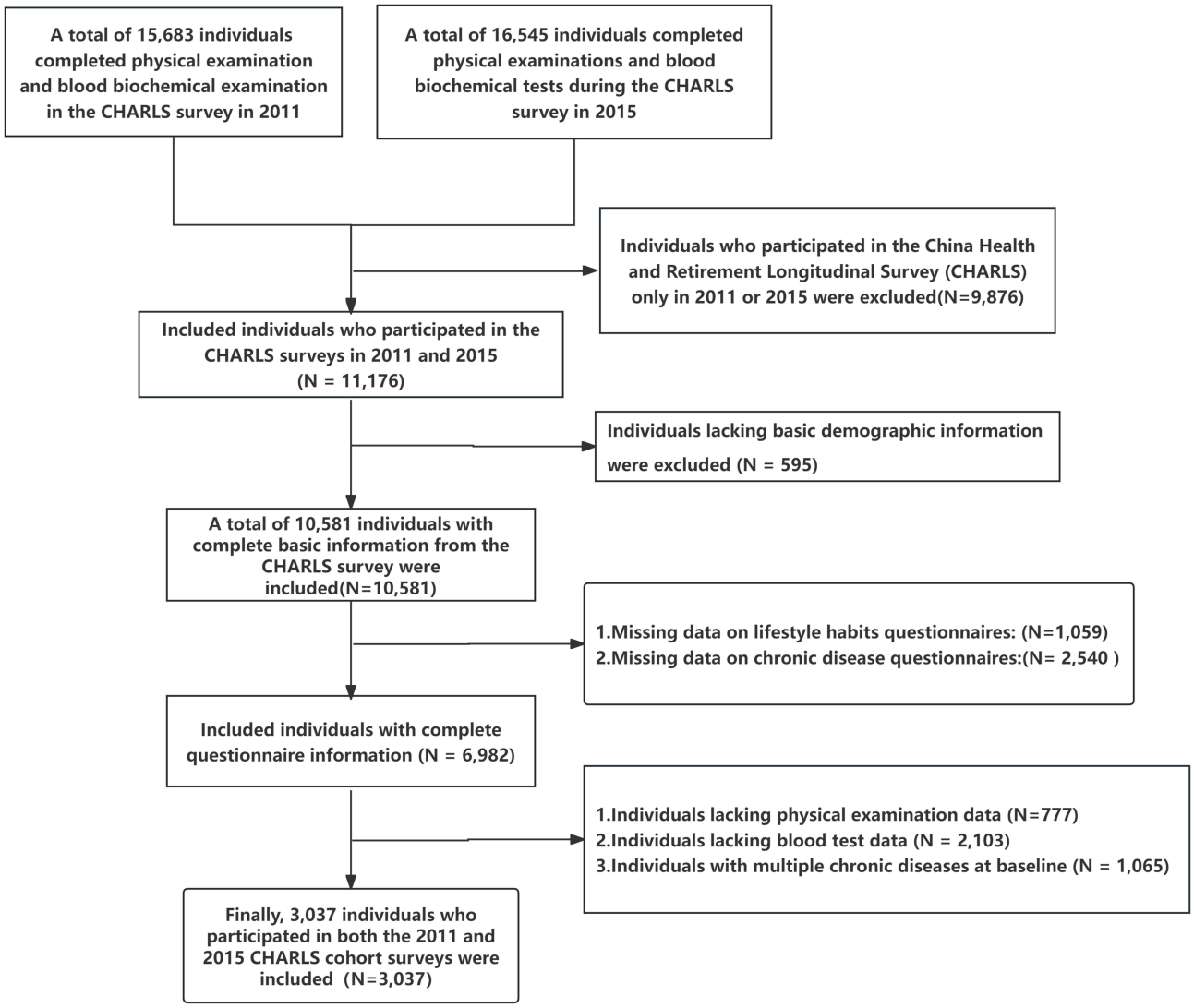

Figure 1 A flow chart of the data extraction protocol used in this study.

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lifestyle and health status questionnaires (smoking, alcohol consumption, sleep duration and chronic disease status) and blood biochemical examination data from the study participants.

Definition of Relevant Indicators

In the CHARLS questionnaire survey, there are inquiries regarding 14 common chronic diseases, including hypertension, dyslipidemia, diabetes, malignant tumors such as cancer (excluding mild skin cancer), chronic lung diseases, liver diseases, heart diseases, stroke, kidney diseases, stomach and digestive system diseases, emotional and mental problems, memory-related diseases, arthritis or rheumatism as well as asthma.[15] Information regarding the prevalence of chronic diseases was collected based on the self-reporting as well as physician-diagnosed diseases of the respondents. According to a guideline on the assessment and management of patients with multiple chronic diseases issued by the National Institute for Health and Care Excellence (NICE) in the UK, MCD[16] are defined as the presence of two or more chronic diseases. Meanwhile, referring to the research,[17] we define the participants with two or more chronic diseases as patients with multiple chronic diseases.

Measurements and Calculations of Different Indexes

Staff from various counties and districts who were trained by the Chinese Center for Disease Control and Prevention (CDC), conducted the physical examinations and blood pressure sample collections. For weight measurements, participants were instructed to remove their shoes, and measurements were taken to an accuracy of 0.01 kg. Height measurements were taken using a vertical stadiometer to an accuracy of 0.1 cm. Waist circumference was measured at the level of the umbilicus, also to an accuracy of 0.1 cm. Prior to blood collection, all subjects were in a 12-hour fasting state. After collection, blood samples were stored at −20°C and transported to the CDC in Beijing within two weeks, where laboratory personnel measured fasting blood glucose (FBG), glycated hemoglobin A1c (HbA1c), triglycerides (TG), total cholesterol (TC), and high-density lipoprotein cholesterol (HDL-C). The body mass index (BMI), TyG, TyG-BMI, TyG-waist circumference (TyG-WC) and TyG-waist-to-height ratio (TyG-WHtR) indexes were calculated using the following formulas based on previous related studies:[14,18]

$$BMI = \frac{Weight(kg)}{Height^2}$$

$$WHtR = \frac{Waist\ circumference}{Height}$$

$$TyG = Ln[TG(mg/dL) \times FBG(mg/dL)/2]$$

$$TyG - BMI = TyG \times BMI$$

$$TyG - WC = TyG \times Waist\ circumference$$

$$TyG - WHtR = TyG \times WHtR$$

Statistical Analysis

In this study, statistical analysis of the data was performed using R software (version 4.4.1). Sample data were be tested for normality by using the Shapiro–Wilk test. Means ± standard deviations (SD) were used for continuous variables that conformed to normal distribution, and comparisons between groups were made using either the Student's *t*-test or analysis of variance (ANOVA). Median (interquartile range) were used for continuous variables that did not conform to a normal distribution, and comparisons between groups were made using either the Mann–Whitney U or Kruskal–Wallis tests. Count data were expressed as frequencies and proportions (n(%)), and comparisons between groups were made using the chi-square (χ^2) test. Cox regression analysis was used to examine the relationship between the TyG, TyG-BMI, TyG-WC, and TyG-WHtR indexes and the risk of the incidence of MCD. Additionally, restricted cubic spline (RCS) curves were plotted to visually illustrate the dose-response relationship between TyG, TyG-BMI, TyG-WC, and TyG-

WHtR and the risk of the incidence of MCD. Three Cox regression models were used for assessment of the data. Model 1 had no adjustments made. In Model 2, the data was adjusted for gender and age and for Model 3 adjustments were made for gender, age, marital status, education, BMI, smoking, drinking and sleep time. Receiver operating characteristic (ROC) curves were used to evaluate the predictive ability of the Cox regression models, which incorporated the TyG, TyG-BMI, TyG-WC and TyG-WHtR indexes for MCD risk. A statistical difference of $p < 0.05$ was considered to be significant.

Results

Participant Characteristics

3037 individuals were included in the study cohort, with 1397 (46%) males and 1640 (54%) females. The median age (interquartile range) of the cohort was 57 (50, 63) years. The population was divided into four groups (Q1, Q2, Q3, and Q4) based on the quartiles of the baseline TyG, TyG-BMI, TyG-WC and TyG-WHtR indexes. At the end of the follow-up survey period in 2015, 473 cases of incident MCD were identified, with an incidence rate of 15.57%. The incidence of MCD increased with the increase in quartiles of TyG, TyG-WC and TyG-WHtR, and the differences between groups were statistically significant ($p<0.01$; Table 1).

Univariate Analysis of Patients with and without Newly Developed MCD

Based on the presence and absence of MCD at the 2015 CHARLS follow-up survey, the population was divided into an incident and a non-incident MCD group for comparison. There were statistically significant differences ($p<0.05$) between

Table 1 Comparison of the Incidence Rates of Multiple Chronic Diseases Among Patients with Different Quartiles of TyG, TyG-WC, TyG-BMI and TyG-WHtR

Characteristic	N	*MCD*	X^2	p-value
TyG			16.154	**0.001**
Q1	760	99 (13.03)		
Q2	759	100 (13.17)		
Q3	759	127 (16.73)		
Q4	759	147 (19.36)		
TyG-BMI			36.887	**<0.001**
Q1	760	95 (12.50)		
Q2	759	109 (14.36)		
Q3	759	99 (13.03)		
Q4	759	170 (22.39)		
TyG-WC			34.417	**<0.001**
Q1	760	90 (11.84)		
Q2	759	97 (12.77)		
Q3	759	119 (15.67)		
Q4	759	167 (22.0)		
TyG-WHtR			37.277	**<0.001**
Q1	760	91 (11.97)		
Q2	759	96 (12.64)		
Q3	759	118 (15.54)		
Q4	759	168 (22.13)		

Notes: Data are present as N(%); The incidence of multiple chronic diseases in different quantile groups was compared using Pearson's Chi-squared test; For easier reading, when the analysis is statistically significant ($P < 0.05$), we bold the font.

Abbreviations: TyG, Triglyceride glucose index; TyG-BMI, Triglyceride glucose-body mass index; TyG-WC, Triglyceride glucose-waist circumference index; WHtR, waist-to-height ratio; TyG -WHtR, Triglyceride-glucose-waist-to-height ratio index; Q, quartile; MCD, Multiple chronic diseases.

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the two groups with respect to age, marital status, alcohol consumption, weight, waist circumference, BMI, blood glucose, triglycerides as well as the TyG, TyG-BMI, TyG-WC and TyG-WHtR indexes. No differences (p>0.05) were observed between the two groups in terms of gender, education level, sleep duration, smoking and height (Table 2).

Association Between TyG, TyG-BMI, TyG-WC and TyG-WHtR and Emerging Incidence of MCD

For Cox regression analysis, the occurrence of MCD was used as the dependent variable (no =1, yes =2), and the TyG, Ty G-BMI, Ty G-WC and Ty G-WHTR indexes were taken as independent variables. In the Cox regression model with unadjusted covariates (Model 1), the risk of MCD was significantly increased in the TyG index Q3 and Q4 groups, TyG-BMI Q4 group and TyG-WHtR index when compared with the Q1 group. After the results were fully adjustment for covariates (Model 3), the risk of MCD was significantly increased in the Q3 and Q4 groups compared with the Q1 group with respect to all the indexes. In addition, when compared with the Q1 group of the TyG-BMI index, the risk of the Q3

Table 2 Analysis of the Influencing Factors in Patients with and without Newly Diagnosed Multiple Chronic

Characteristic	Newly Diagnosed N = 473	Non-Diagnosed N = 2564	X^2/z	P-value
Gender			0.924	0.336
Male	208 (44)	1189 (46)		
Female	265 (56)	1375 (54)		
Age	63.0 (56.0, 69.0)	60.0 (54.0, 66.0)	4.277	**<0.001**
Education			0.769	0.680
Primary school and below	330 (70)	1768 (69)		
Junior middle school	104 (22)	552 (22)		
High school and above	39 (8.2)	244 (9.5)		
Marriage status			6.210	**0.013**
Married	377 (80)	2162 (84)		
Other	96 (20)	402 (16)		
Sleep status			1.374	0.503
<7	226 (48)	1164 (45)		
7–8	101 (21)	540 (21)		
>8	146 (31)	860 (34)		
Smoking status			0.251	0.616
Smokers	191 (40)	1067 (42)		
Non smokers	282 (60)	1497 (58)		
Alcohol consumption			4.596	**0.032**
Drinkers	148 (31)	934 (36)		
Non drinkers	325 (69)	1630 (64)		
Height	157 (151, 163)	157 (152, 164)	−1.192	0.233
Body weight (kg)	60 (52, 67)	58 (51, 65)	2.973	**0.003**
Waist circumference (cm)	87 (80, 94)	84 (78, 91)	4.569	**<0.001**
BMI (Kg/m^2)	24.1 (21.5, 26.6)	23.2 (20.9, 25.5)	4.536	**<0.001**
Blood Glucose (mg/dL)	95 (88, 106)	94 (88, 103)	2.453	**0.014**
Triglycerides (mg/dL)	122 (89, 174)	110 (80, 160)	4.465	**<0.001**
TyG	8.69 (8.32, 9.14)	8.55 (8.22, 9.00)	4.563	**<0.001**
TyG-BMI	212 (185, 239)	200 (175, 226)	5.566	**<0.001**
TyG-WC	761 (667, 842)	724 (649, 805)	5.284	**<0.001**
WHtR	0.56 (0.50, 0.60)	0.54 (0.49, 0.58)	4.788	**<0.001**
TyG-WHtR	4.84 (4.27, 5.46)	4.62 (4.09, 5.12)	5.513	**<0.001**

Notes: Data are present as Interquartile Range (IQR) or N (%),; Use Pearson's Chi-squared test or Wilcoxon rank sum test to conduct a comparative analysis between the newly diagnosed group and the undiagnosed group; For easier reading, when the analysis is statistically significant (P < 0.05), we bold the font.

Abbreviations: TyG, Triglyceride glucose index; TyG-BMI, Triglyceride glucose-body mass index; TyG-WC, Triglyceride glucose-waist circumference Index; WHtR, waist-to-height ratio; TyG -WHtR, Triglyceride-glucose-waist-to-height ratio; M, median; Q, quartile.

and Q4 groups of the TyG-BMI index was significantly increased. Compared with the Q1 group of the TyG-WC index, the risk of developing MCD was significantly increased in the Q4 of the TyG-WC index. Compared with the Q4 group, the Q1 group of the Ty G-WHtR index, the Q 4 group of the TyG-WHtR index (Table 3).

RCS Curves to Evaluate the Risk of TyG, TyG-BMI, TyG-WC and TyG-WHtR in Patients with MCD

In this study, RCS curves were used to visualize the relationship between the TyG, TyG-BMI, TyG-WC and TyG-WHtR indexes and the risk of MCD. The results showed that after adjusting for gender, age, education, the risk of marriage, BMI, sleep duration and smoking and the risk of MCD ($p_{non\text{-}linear}$=0.536) (Figure 2A), the higher the TyG index, the higher the risk of developing MCD. An increase of the TyG-BMI index was linked to a slow decline in the risk of severe chronic diseases and this increased when the TyG-BMI index > 171 ($p_{non\text{-}linear}$<0.0001) (Figure 2B). There was also a significant non-linear relationship between the risk of severe chronic diseases and the TyG-WC index ($p_{non\text{-}linear}$<0.0001) (Figure 2C), such that when the TyG-WC index > 609, the risk of developing these diseases increased with the increasing TyG-WC index. The risk of serious chronic diseases showed a non-linear relationship that first slowly decreased and then rapidly increased when the TyG-WHtR > 3.83 ($p_{non\text{-}linear}$=0.0052) (Figure 2D) as show in Figure 2.

ROC Curves of the TyG, TyG-BMI, TyG-WC and TyG-WHtR Indexes Cox Regression Analysis

ROC curves were constructed to further evaluate the predictive performance of the Cox regression models for TyG, TyG-BMI, TyG-WC, and TyG-WHtR indexes. After adjusting for confounding factors, the area under the ROC curve (AUC) for the Cox regression models of the TyG, TyG-BMI, TyG-WC, and TyG-WHtR indexes were 0.610, 0.590, 0.590, and

Table 3 Association of TyG, TyG-BMI, TyG-WC and TyGWHtR with the Incidence of Newly Diagnosed Patients with Multiple Chronic Diseases

Variable	Model 1			Model 2			Model 3		
	HR	95% CI	p-value	HR	95% CI	p-value	HR	95% CI	p-value
TyG									
Q1	—	—		—	—		—	—	
Q2	1.05	0.79, 1.39	0.735	1.04	0.78, 1.38	0.798	1.03	0.77, 1.36	0.860
Q3	1.48	1.14, 1.93	**0.003**	1.49	1.14, 1.94	**0.003**	1.48	1.14, 1.93	**0.004**
Q4	1.62	1.25, 2.10	**<0.001**	1.64	1.26, 2.13	**<0.001**	1.63	1.25, 2.12	**<0.001**
TyG-BMI									
Q1	—	—		—	—		—	—	
Q2	1.01	0.76, 1.35	0.930	1.09	0.82, 1.45	0.563	1.09	0.82, 1.46	0.555
Q3	1.27	0.97, 1.66	0.087	1.40	1.06, 1.85	**0.017**	1.40	1.06, 1.85	**0.017**
Q4	1.88	1.46, 2.42	**<0.001**	2.18	1.67, 2.83	**<0.001**	2.17	1.66, 2.84	**<0.001**
TyG-WC									
Q1	—	—		—	—		—	—	
Q2	0.80	0.60, 1.07	0.138	0.82	0.61, 1.10	0.178	0.83	0.62, 1.11	0.200
Q3	1.26	0.97, 1.64	0.083	1.30	1.00, 1.69	0.054	1.28	0.98, 1.67	0.066
Q4	1.72	1.34, 2.20	**<0.001**	1.79	1.40, 2.30	**<0.001**	1.79	1.39, 2.30	**<0.001**
TyG -WHtR									
Q1	—	—		—	—		—	—	
Q2	1.06	0.80, 1.40	0.693	1.09	0.82, 1.44	0.561	1.09	0.82, 1.44	0.567
Q3	1.15	0.87, 1.52	0.321	1.21	0.91, 1.61	0.185	1.20	0.91, 1.60	0.201
Q4	1.95	1.52, 2.51	**<0.001**	2.03	1.56, 2.64	**<0.001**	2.01	1.54, 2.62	**<0.001**

Notes: Model 1: no adjustment; Model 2: adjust for gender and age; Model 3: adjust for gender, age, marital status, education, BMI, smoking, drinking, sleep time; For easier reading, when the analysis is statistically significant (P < 0.05), we bold the font.
Abbreviations: TyG, triglyceride glucose index; TyG-BMI, triglyceride glucose - body mass index; TyG-WC, triglyceride glucose - waist circumference index; TyG -WHtR, triglyceride-glucose-waist-to-height ratio; HR, Hazard Ratio; CI, confidence interval; Q, quantile.

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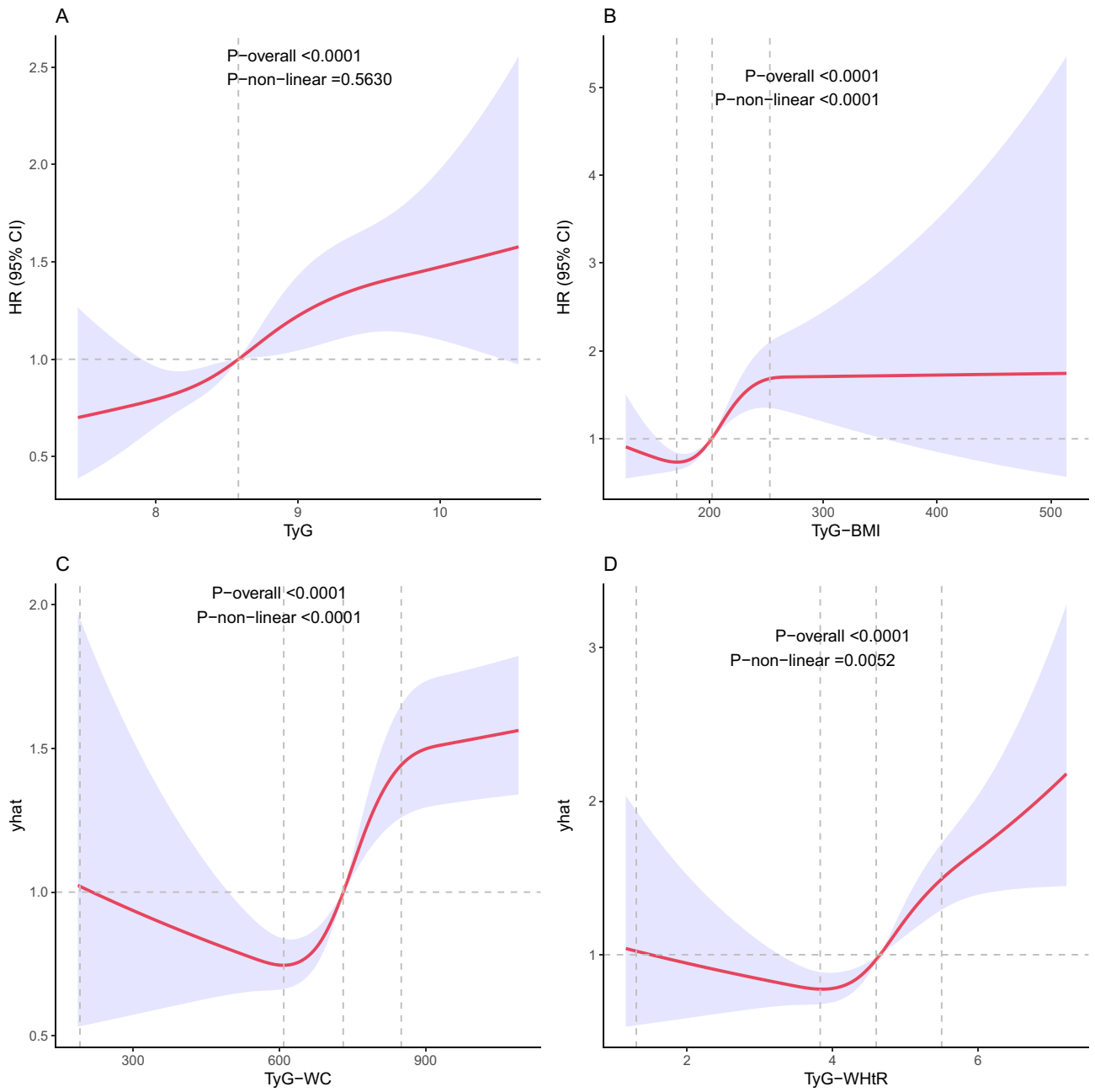

Figure 2 Dose-response relationship between TyG, TyG-BMI, TyG-WC and TyG-WHtR and the risk of multiple chronic diseases.(**A**) represents the restricted cubic spline model for the relationship between the TyG index and the risk of multiple chronic diseases after adjusting for gender, age, marriage, education, BMI, smoking, drinking, and sleep duration. (**B**) represents the restricted cubic spline model for the relationship between the TyG-BMI index and the risk of multiple chronic diseases after adjusting for gender, age, marriage, education, BMI, smoking, drinking, and sleep duration. (**C**) represents the restricted cubic spline model for the relationship between the TyG-WC index and the risk of multiple chronic diseases after adjusting for gender, age, marriage, education, BMI, smoking, drinking, and sleep duration. (**D**) represents the restricted cubic spline model for the relationship between the TyG-WHtR index and the risk of multiple chronic diseases after adjusting for gender, age, marriage, education, BMI, smoking, drinking, and sleep duration.

0.607, respectively (Figure 3). The optimal cut-off values for predicting the incidence of MCD using the Cox regression models for TyG, TyG-BMI, TyG-WC, and TyG-WHtR indexes were 0.248, 0.219, 0.115, and 0.132, respectively (Table 4). These optimal cut-off values can potentially serve as reference points for identifying individuals at greater risk of developing MCD based on their respective indexes.

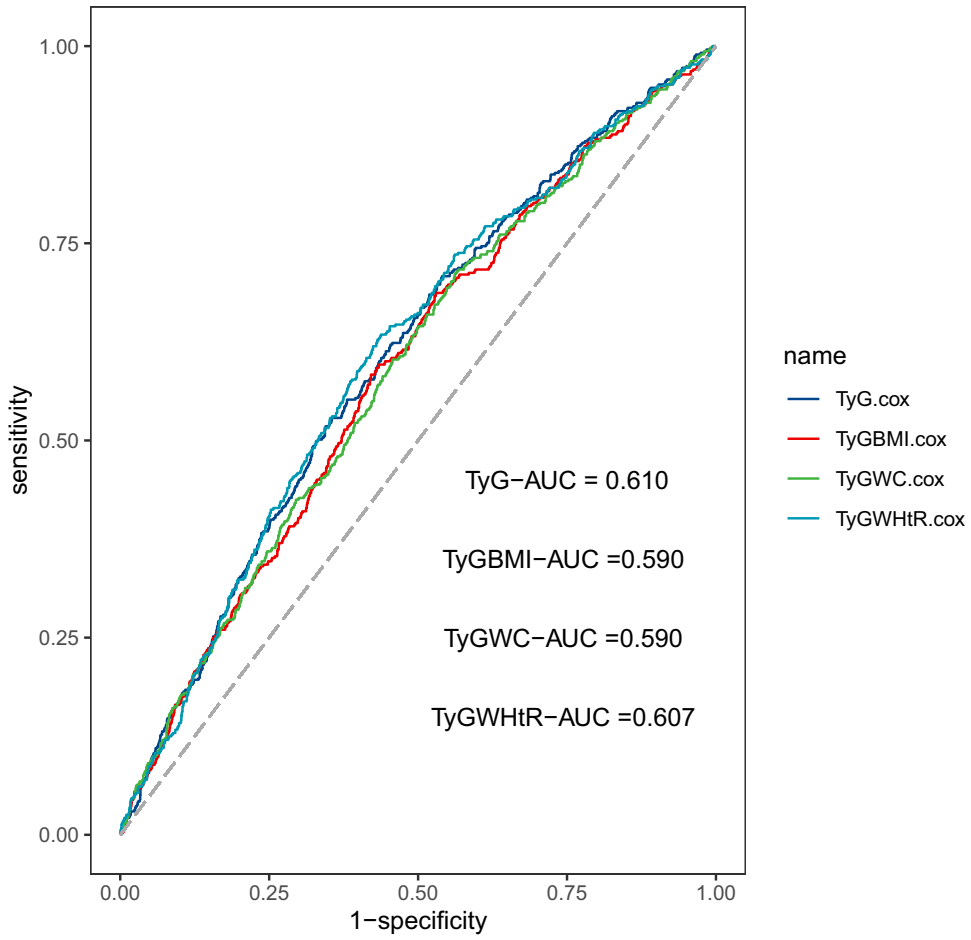

Figure 3 ROC curves for the TyG, TyG-BMI, TyG-WC and TyG-WHtR indexes Cox regression models.

Discussion

The most remarkable observation result of this study is that triglyceride-glucose and its obesity-related combined index are associated with an increased risk of multiple chronic diseases. Furthermore, we also found that the triglyceride-glucose index shows a linear dose-response relationship with the risk of multiple chronic diseases. The combined index of triglyceride-glucose and obesity shows a non-linear dose-response relationship with the risk of multiple chronic diseases.

With the improvement of the level of healthcare, the increase in the prevalence of chronic diseases, and the continuous intensification of aging, multiple chronic diseases have become relatively common.[19] If the problems of obesity and insulin resistance are not effectively addressed in the treatment of chronic diseases, the occurrence of multiple chronic diseases will be more common.[20,21] The underlying mechanisms of various chronic diseases include obesity-induced hyperinsulinemia, activation of the sympathetic nervous system, chronic inflammation, and changes in

Table 4 The Areas Under the Receiver Operating Characteristic Curves and Cut-off Points for TyG and the Other Indexes

Variable	Cut-off value	Sensitivity	Specificity	AUC	95% CI	P-value
TyG	0.248	0.529	0.645	0.610	0.579–0.634	<0.001
TyG-BMI	0.219	0.584	0.579	0.590	0.562–0.618	<0.001
TyG-WC	0.115	0.712	0.437	0.590	0.563–0.618	<0.001
TyG-WHtR	0.132	0.634	0.562	0.607	0.582–0.637	<0.001

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adipocytokine factors.[22] Insulin resistance refers to a reduced biological responsiveness of insulin-sensitive target tissues or organs (such as the liver, skeletal muscle cells, and adipose tissue) to the promotion of glucose uptake by insulin, which can lead to an imbalance in the body's glycolipid metabolism,[23] causing the adipose tissue to secrete a large amount of pro-inflammatory cytokines (such as TNF-α, IL-1β, IL-6, resistin, leptin, PAI-1, and MCP-1, etc). These cytokines will activate inflammatory signaling pathways, thereby triggering systemic chronic inflammation.[24] Here exists a complex interaction among insulin resistance, inflammation, mitochondrial dysfunction, and oxidative stress, which is the key pathological basis for the pathogenesis of many chronic diseases.[25]

Research[26] indicates that oxidative stress and inflammatory oxidative stress induce an increase in the formation of superoxide and free radicals in blood vessels, resulting in structural and functional damage to endothelial cells and a reduction in the bioavailability of nitric oxide (NO), causing endothelial dysfunction and promoting the occurrence and development of cardiovascular diseases such as hypertension and atherosclerosis. The results of a 9-year population cohort study in China show that there is a longitudinal relationship between the risk of new-onset hypertension (HTN) and TyG is an independent predictor of new-onset hypertension.[27] In addition, an increase in TyG levels is also associated with an increased risk of chronic kidney disease and shows a non-linear dose-response relationship.[28] A cross-sectional study involving 3316 Chinese elderly people aged ≥ 60 years reported that the TyG index has a linear relationship with hypertension-diabetes comorbidity and mainly mediates the association between the visceral obesity index and hypertension-diabetes comorbidity, partially mediates the association of hypertension or diabetes, and completely mediates the association of diabetes.[29] Another Chinese cohort study also reported that the TyG index has a linear relationship with the risk of developing hypertension-diabetes comorbidity and mediates the relationship between BMI and waist circumference and hypertension, diabetes, and hypertension-diabetes comorbidity.[30] Different from the above studies, the definition of multiple chronic diseases in our study includes a wider range of diseases. We explored the association between TyG and its obesity-related combined indicators with the risk of multiple chronic diseases. We found that the risk of multiple chronic diseases for TyG also shows a linear correlation, while the risk of multiple chronic diseases for TyG-BMI, TyG-WC, and TyG-WHtR shows a non-linear relationship.

Similar to our results, Feng et al[31] evaluated the relationship between 17 obesity or insulin resistance indicators and hypertension, dyslipidemia, T2DM, and multimorbidity. It was found that the predictive ability of TyG based on triglyceride and glucose concentrations is the best. The results of a recent study comparing the predictive ability of TyG and the homeostasis model assessment for metabolic syndrome show that when distinguishing between the presence and absence of metabolic syndrome, the area under the receiver operating characteristic curve (AUC) of TyG is 0.827, slightly higher than that of HOMA-IR (AUC = 0.847) and HOMA-β (AUC = 0.614).[32] In the population of patients with multiple chronic diseases, the prevalence of dyslipidemia is high, and elevated TG is the most common form,[33] while fasting blood glucose is the gold standard for reflecting an individual's current blood glucose level and can accurately reflect the body's glucose metabolism.[34] Therefore, TyG is a comprehensive indicator that can reflect an individual's current glycolipid metabolism and is of great practical significance for evaluating insulin resistance and predicting the risk of multiple chronic diseases. In the study by Mirr et al[12] evaluating the diagnostic accuracy of indirect insulin resistance indicators such as TG/HDLc, METS-IR, TyG, TyG-BMI, TyG-WC, and TyG-WHtR for metabolic syndrome, all indicators achieved significant diagnostic accuracy, among which the area under the curve (AUC) of TyG was the highest. The study by Raimi et al[35] compared the predictive effects of indicators such as TyG, TyG-BMI, TyG-WC, TyG-WHpR, and TyG-WHtR on metabolic syndrome and found that all indicators had a good predictive effect on metabolic syndrome, among which TyG-WHtR had the best detection effect on metabolic syndrome. In the study by Lim et al,[36] the TyG obesity index had a better effect on insulin resistance than TyG, and the predictive effect of TyG-BMI was the best. Metabolic syndrome is the result of the interaction between insulin resistance and obesity, usually accompanied by oxidative stress and chronic low-grade inflammation.[37] And oxidative stress and chronic low-grade inflammation are the core of the occurrence and development of many chronic diseases.[38] This provides a basis for the correlation between indicators such as TyG, TyG-BMI, TyG-WC, and TyG-WHtR and the risk of occurrence of various chronic diseases, suggesting that triglycerides and their obesity-related combined indicators are potential biomarkers for predicting the occurrence and development of MCD.

The TyG, TyG-BMI, TyG-WC, and TyG-WHtR indexes show varying degrees of correlation with the incidence of MCD in middle-aged and elderly populations. After adjusting for confounding factors, the risk of the incidence of MCD was significantly higher in the fourth quartile compared to the first quartile for all the indexes examined in this study. The TyG index exhibited a linear relationship with the risk of MCD, while TyG-BMI, TyG-WC and TyG-WHtR indexes showed nonlinear relationships. These indexes demonstrated predictive ability for MCD. However, the mechanisms underlying the associations between TyG and its obesity-combined indices with MCD are not fully understood, and this study, being a retrospective cohort study, has certain limitations.

In conclusion, TyG, TyG-BMI, TyGWC, and Ty G-WHTR showed different degrees of correlation with MCD in middle-aged and elderly people. After the exclusion of confounding factors, the risk of MCD in the fourth array was significantly higher than the first quartile array, and TyG index showed a linear relationship with the risk of MCD, while TyG-BMI, Ty GWC, and TyG-WHtR showed a non-linear relationship with the risk of MCD. TyG, TyG-BMI, TyGWC and Ty G-WHtR have certain predictive ability for detecting MCD and as they are relatively easy to obtain in the general population with limited resources, they can be useful in predicting more serious health issues.

Data Sharing Statement

Data will be made available on reasonable request from the corresponding author.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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