Cardiovascular Diabetology

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Association between triglyceride glucose index and biological aging in U.S. adults: National Health and Nutrition Examination Survey

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Abstract

Background Insulin resistance (IR) has been reported to be associated with aging; however, few studies have investigated the relationship between IR and biological age (BA). The Triglyceride–glucose (TyG) index is a recognized marker of IR. Currently, there is insufficient evidence regarding the relationship between the TyG index and biological aging. This study aims to provide deeper insights into the connections between the TyG index and biological aging.

Methods We conducted a cross-sectional study using data from the National Health and Nutrition Examination Survey (NHANES), including 12,074 adults (aged 20 and older) from the 2001–2010 and 2015–2018 cycles. Comprehensive TyG and BA data were extracted for analysis. To explore the relationship between the TyG index and BA, linear regressions were employed, while logistic regression models were used to examine the association between the TyG index and accelerated aging. Additionally, trend tests, subgroup analyses, and smoothed fitted curves were conducted to assess the robustness of the findings.

Results We included 12,074 participants with a mean age of 46.91 years (SD, 16.64); of these, 50.25% were female and 49.75% were male. Each 1-unit increase in the TyG index was associated with a 1.64-year rise in Klemera–Doubal method (KDM) biological age and a 117% higher risk of accelerated aging. Similarly, each 1-unit increase in the TyG index corresponded to a 0.40-year increase in phenotypic age, resulting in a 15% higher risk of accelerated aging. The analysis also revealed nonlinear positive relationships between the TyG index and biological aging, particularly for KDM biological age (P for non-linearity < 0.001) and phenotypic age (P for non-linearity = 0.005), with a turning point at 8.66. Across all subgroups, the TyG index consistently showed a positive correlation with biological aging, even in the presence of significant interactions.

Conclusions There is a significant positive association between the TyG index and biological aging. Higher TyG levels are linked to increased biological age and a greater risk of accelerated aging.

Keywords Triglyceride glucose index, Biological aging, Phenotypic age, NHANES

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Introduction

As the global population ages, understanding the biological processes behind aging and related diseases is increasingly important [1]. Unlike chronological age, which simply counts years, biological age reflects the actual decline in physiological function, providing a more accurate picture of an individual's health and disease risk [2, 3]. This makes biological age a key factor in predicting health outcomes and guiding interventions for healthy aging [4]. Various methods have been developed to measure biological age, using clinical markers, molecular indicators, or composite measures. These methods, such as homeostatic dysregulation (HD) [5], the Klemera–Doubal method (KDM) [6], phenotypic age (PA) [7], and allostatic load (AL) [8], have proven effective in predicting mortality, age-related diseases, and declines in physical function.

Insulin resistance (IR), a key metabolic disturbance in aging, leads to various disorders, including type 2 diabetes and cardiovascular disease [9–15]. IR has also been linked to accelerated aging [16], although the mechanisms are not fully understood. The chronic hyperinsulinemia resulting from IR increases oxidative stress and inflammatory responses, which may contribute to the aging process. The Triglyceride–glucose (TyG) index, derived from fasting triglycerides and glucose levels, has emerged as a practical and reliable marker of IR [17, 18]. Unlike more invasive methods like the euglycemic-hyperinsulinemia clamp or HOMA-IR, the TyG index is simpler and more accessible, making it useful for large-scale studies. While TyG has been shown to correlate with cardiometabolic outcomes such as diabetes and cardiovascular disease [10, 12, 14, 19–21], its relationship with biological aging and mortality is still not well explored.

Given the growing interest in metabolic health as a determinant of aging, it is crucial to understand how the TyG index correlates with biological aging. This study aims to fill this gap by investigating the association between the TyG index and biological age using data from the National Health and Nutrition Examination Survey (NHANES). By examining this relationship, we hope to provide new insights into the role of insulin resistance in the aging process and identify potential markers for early detection of accelerated aging.

Materials and methods

Data source

The National Health and Nutrition Examination Survey (NHANES) is a comprehensive survey conducted by the National Center for Health Statistics (NCHS) to assess the health and nutritional status of the non-institutionalized US population. Using a stratified, multistage probability sampling design, NHANES gathers data through interviews, physical examinations, and laboratory tests. The NHANES protocol is approved by the NCHS research ethics review board, and all participants provided written informed consent. The survey adheres to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines. Further information on NHANES can be accessed at https://www.cdc.gov/nchs/nhanes.

Study population

Our analyses used NHANES data from 2001 to 2010 and 2015 to 2018, focusing on participants aged 20 years and older ($n = 38,872$). Exclusion criteria included missing data for various key components: pregnant participants ($n = 1,136$), components of the TyG index ($n = 21,621$), elements required for calculating Klemera–Doubal method (KDM) biological age and phenotypic age ($n = 1,212$), demographic data ($n = 1,262$), and information on cardiovascular disease history, smoking status, drinking status, BMI, and weights ($n = 1,567$). Finally, a total of 12,074 subjects were included in the study (Fig. 1).

Definitions of TyG

The TyG index measures insulin resistance by combining fasting glucose and triglyceride levels. Fasting blood glucose (FSG) and triglycerides were assessed at baseline using blood samples from participants. The TyG index is calculated using the formula: TyG = ln [triglycerides (mg/dl) × glucose (mg/dl) / 2] [22].

Definition of biological aging

Biological aging (BA) was measured using the Klemera–Doubal method (KDM) and phenotypic age (PA) [7, 23].

The KDM method calculates BA based on eight biomarkers: Ln-C-reactive protein (Ln-CRP), serum creatinine, glycosylated hemoglobin, serum albumin, serum total cholesterol, serum urea nitrogen, serum alkaline phosphatase, and systolic blood pressure. PA is determined using a multivariate mortality hazard model, incorporating ten biomarkers: chronological age (CA), albumin, creatinine, glucose, CRP, lymphocyte percentage, mean cell volume, red cell distribution width, alkaline phosphatase, and white blood cell count. Biological age acceleration is defined when either KDM biological age or PA surpasses CA, and this is treated as a binary variable.

Assessment of covariates

This study identified several key covariates, with data collected through baseline questionnaires administered by trained professionals. Participants provided information on age, gender (female or male), and race (non-Hispanic white, non-Hispanic black, Mexican American, and other). Marital status was categorized as married, living

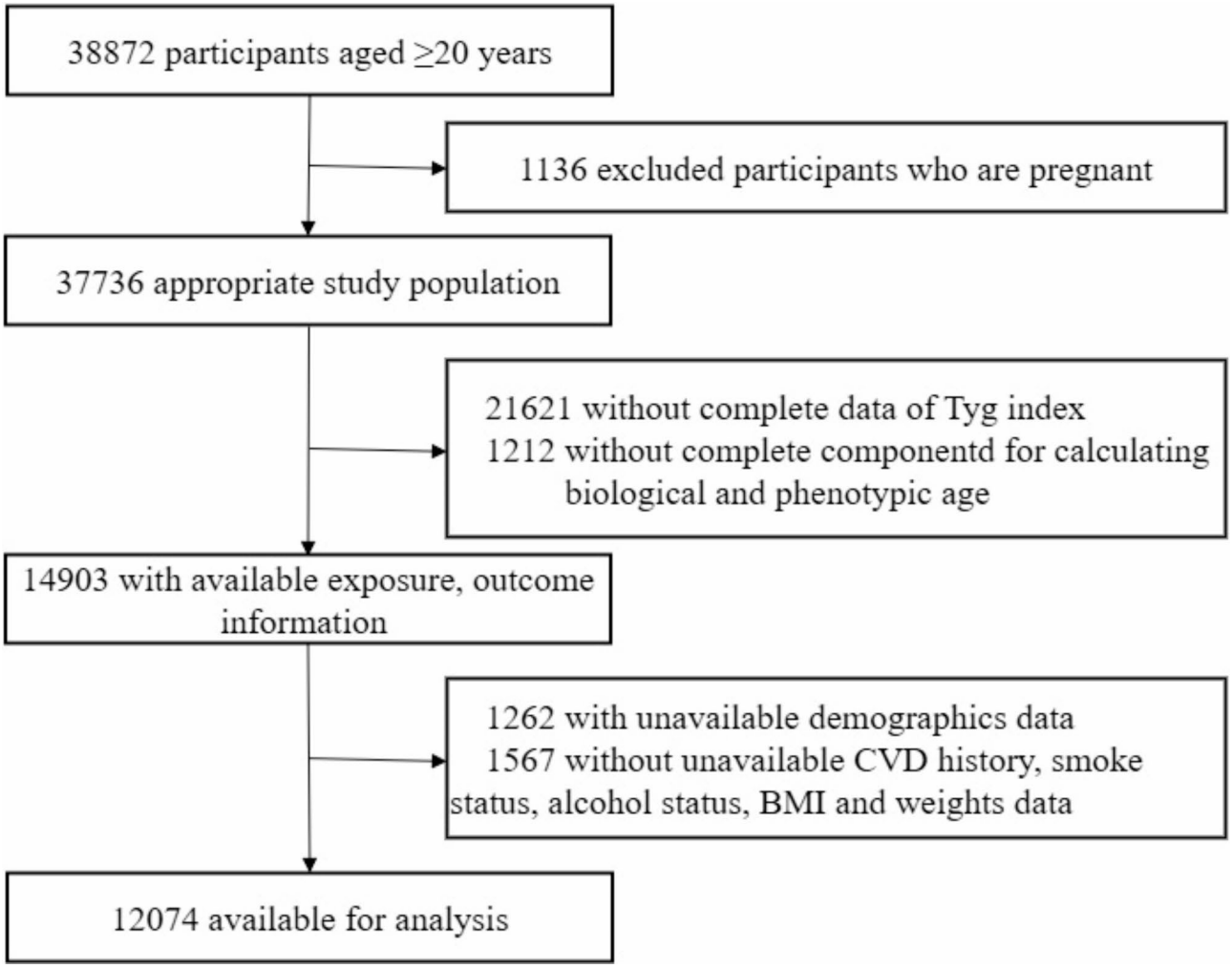

Fig. 1 The study's flow diagram. TyG, triglyceride glucose. CVD, cardiovascular disease. BMI, body mass index

with a partner, or living alone. Education levels were classified as less than 9 years, 9 to 12 years, and more than 12 years. The poverty-to-income ratio (PIR) was grouped into < 1.3, 1.3–3.5, and > 3.5. Smoking status was categorized as current, former, or never smokers, while drinking status was noted as yes or no. Body mass index (BMI) was calculated (weight [kg] / height [m^2]) and classified as < 25, 25–30, or ≥ 30. Physical activity was assessed using the Metabolic Equivalent of Task (MET). Hypertension was diagnosed based on a systolic blood pressure ≥ 140 mmHg, diastolic pressure ≥ 90 mmHg, a doctor's diagnosis, or current use of antihypertensive medication. Diabetes was defined by a doctor's diagnosis, HbA1c ≥ 6.5%, fasting glucose ≥ 7.0 mmol/L, or use of diabetes medication or insulin. Cardiovascular disease (CVD) included congestive heart failure, coronary artery disease, myocardial infarction, angina pectoris, and stroke.

Statistical analysis

Given the complex multistage cluster survey design of the NHANES study, we utilized sample weighting codes "WTSAF4YR" and "WTSAF2YR" for the fasting subsample from 2001 to 2010 and 2015–2018, respectively. The sampling weights were calculated as follows: for the 2001–2002 cycle, the weights were 2/7 × WTSAF4YR, and for the remaining cycles, they were 1/7 × WTSAF2YR.

Participant characteristics were classified according to their TyG index levels. Categorical variables were presented as weighted numbers (weighted percentages), while continuous variables were described as means (standard deviation, SD). To assess differences between TyG groups, we used ANOVA for comparing weighted means of continuous variables and the $\chi 2$ test for comparing weighted percentages of categorical variables. Weighted multivariable linear and logistic regression analyses were performed to determine the β coefficients or odds ratios (OR) and 95% confidence intervals (95%

CIs) for the association between the TyG index and both KDM biological/phenotypic age and their respective age accelerations. Crude models did not include any adjustments for potential confounders. Model 1 adjusted for age and gender. Model 2 further adjusted for race, marital status, and education level. Model 3 included additional adjustments for BMI, smoking status, alcohol consumption, physical activity, hypertension, diabetes, CVD history, and cancer.

To explore potential nonlinear dose-response relationships between the TyG index and biological aging (KDM biological/phenotypic age and their respective accelerations), we employed a restricted cubic spline model, adjusting for variables in Model 3. The TyG index was treated as a continuous variable with four knots at the 5th, 35th, 65th, and 95th percentiles. Based on the smoothing curves, we developed a two-piecewise linear and logistic regression model to identify any threshold effects, with adjustments for potential confounders. Subgroup analyses were conducted by stratifying participants by age group, gender, BMI, smoking status, alcohol consumption, hypertension, diabetes, CVD history, and cancer, following the adjustments in Model 3.

All analyses were conducted using R version 4.2.2 (http://www.R-project.org, R Foundation) and Free Stati stics version 2.0. A *P*-value of less than 0.05 was considered statistically significant.

Results

Baseline characteristics of study subjects

We included 12,074 participants with a mean age of 46.91 years (SD, 16.64); of these, 50.25% were female and 49.75% were male. Table 1 presents the general characteristics of the participants categorized by TyG index. The TyG index was divided into three groups: T1 (≤ 8.34), T2 (8.34–8.89), and T3 (> 8.89). Participants in the T3 group tended to be older, predominantly male, non-Hispanic white, with lower educational attainment and income, and were less likely to consume alcohol compared to those in the T1 group. Additionally, the T3 group had higher rates of hypertension, diabetes, CVD and cancer.

Across all participants, the weighted mean KDM biological age was 46.76 years (SD, 16.21), and the weighted mean phenotypic age was 43.35 years (SD, 17.86). When biological aging was defined using KDM biological age, 47.59% of participants exhibited accelerated aging, compared to 19.69% when defined using phenotypic age. Notably, participants in the T3 group had higher phenotypic and biological ages and were more likely to experience accelerated biological aging.

Association between TyG and biological aging

After adjusting for confounding factors in Model 3, each 1-unit increase in the TyG index was associated with a 1.64-year increase in KDM biological age and a 117% higher risk of accelerated aging (Tables 2 and 3). Similarly, a 1-unit increase in the TyG index corresponded to a 0.40-year increase in phenotypic age, leading to a 15% higher risk of accelerated aging (Tables 2 and 3). When categorizing the TyG index into tertiles, with the T1 group as the reference, the T3 group showed a 159% higher risk of accelerated aging based on biological age and a 10% higher risk based on phenotypic age (Table 3). Moreover, the analysis revealed nonlinear positive relationships between the TyG index and biological aging, particularly for KDM biological age (*P* for non-linearity < 0.001) and phenotypic age (*P* for non-linearity = 0.005), with a turning point at 8.66(Table S1, S2). For values below 8.66, each 1-unit increase in the TyG index was associated with a linear increase in biological aging, while for values above 8.66, the rate of increase in biological aging accelerated significantly. A linear relationship was observed for KDM biological age acceleration (*P* for linearity = 0.54), while a nonlinear relationship was found for phenotypic age (*P* for non-linearity = 0.002) (Fig. 2).

Subgroup analysis of TyG index and biological aging

In subgroup analyses, significant interactions ($P < .05$) were observed between the TyG index and factors such as age, gender, BMI, hypertension, and diabetes mellitus (Fig. 3, S1, S2). Despite these interactions, the TyG index consistently showed a significant positive association with biological aging across all subgroups.

Discussion

This study is the first to demonstrate a positive correlation between the TyG index and biological aging (BA) as well as advanced aging, even after adjusting for covariates. In this cross-sectional analysis of a nationally representative sample, we observed that a higher TyG index is consistently associated with increased biological aging, regardless of the specific definition of BA used. The robustness of these findings was confirmed through trend tests and stratified analyses, which showed that the positive association between the TyG index and biological aging persisted across all subgroups, despite significant interactions. Additionally, smooth curve fitting revealed a non-linear relationship between the TyG index and both BA and advanced aging, particularly for KDM biological age (*P* for non-linearity < 0.001) and phenotypic age (*P* for non-linearity = 0.005), with a turning point at a TyG index of 8.66.

The TyG index, derived from triglycerides and fasting glucose levels, has emerged as a useful surrogate for insulin resistance, a key driver of various metabolic and aging-related conditions [11, 24–27]. Elevated TyG levels have been associated with a heightened risk of cardiovascular diseases, stroke, and mortality, particularly in

Table 1 Population characteristics by categories of TyG index

Characteristics	Total	T1(≤ 8.34)	T2(8.34–8.89)	T3(>8.89)	*p*
	N **= 178899911.30**	***n*** **= 63542361.03**	***n*** **= 59626928.22**	***n*** **= 55,730,622**	
age, years	46.907(16.64)	42.152(16.22)	47.765(16.82)	51.412(15.47)	< 0.0001
Gender, (%)	88994810.93(49.75)	25861915.85(40.70)	31212817.32(52.35)	31920077.76(57.28)	< 0.0001
Male	88994810.93 (49.75)	25861915.85 (40.70)	31212817.32 (52.35)	31920077.76 (57.28)	
Female	89905100.32 (50.25)	37680445.18 (59.30)	28414110.91 (47.65)	23810544.24 (42.72)	
Race, (%)					
Non-Hispanic White	127646429.84 (71.35)	43414601.52 (68.32)	43199052.35 (72.45)	41032775.97 (73.63)	< 0.0001
Non-Hispanic Black	17930179.14 (10.02)	9467239.64 (14.90)	5152005.41 (8.64)	3310934.09 (5.94)	
Mexican American	14018724.31 (7.84)	3909188.95 (6.15)	4982746.39 (8.36)	5126788.96 (9.20)	
Other Race	19304577.96 (10.79)	6751330.91 (10.62)	6293124.07 (10.55)	6260122.98 (11.23)	
Education level, (%)					
< 9	9412232.39 (5.26)	2369266.68 (3.73)	2969169.04 (4.98)	4073796.67 (7.31)	< 0.0001
9–12	63496058.38 (35.49)	19076852.85 (30.02)	22393635.17 (37.56)	22025570.37 (39.52)	
> 12	105991620.48 (59.25)	42096241.50 (66.25)	34264124.02 (57.46)	29631254.96 (53.17)	
Marital status, (%)					
Married or living with a partner	117075232.60 (65.44)	39629476.26 (62.37)	39049848.02 (65.49)	38395908.32 (68.90)	< 0.0001
Living alone	61824678.65 (34.56)	23912884.76 (37.63)	20577080.20 (34.51)	17334713.68 (31.10)	
PIR, (%)					
≤ 1.3	33598843.30 (18.78)	11124305.44 (17.51)	11331389.65 (19.00)	11143148.21 (19.99)	0.042
1.31–3.50	67030049.19 (37.47)	23645094.56 (37.21)	21944811.47 (36.80)	21440143.16 (38.47)	
>3.50	78271018.76 (43.75)	28772961.02 (45.28)	26350727.10 (44.19)	23147330.64 (41.53)	
Smoking status, (%)					
Current	93524384.59 (52.28)	37266686.97 (58.65)	30574991.33 (51.28)	25682706.29 (46.08)	< 0.0001
Former	46904597.17 (26.22)	13933302.90 (21.93)	15714478.83 (26.35)	17256815.44 (30.96)	
Never	38470929.49 (21.50)	12342371.16 (19.42)	13337458.06 (22.37)	12791100.27 (22.95)	
Drinking status, (%)					
No	38871275.98 (21.73)	13387225.86 (21.07)	12127172.02 (20.34)	13356878.11 (23.97)	0.0047
Yes	140028635.27 (78.27)	50155135.17 (78.93)	47499756.20 (79.66)	42373743.89 (76.03)	
Physical activity, MET-min/week	683.919 [75.13,2600.00]	960.000 [169.14,3360.00]	570.733 [50.40,2471.27]	504.000 [15.80,1920.00]	< 0.0001
BMI, (%)					
≤ 25	55614538.96 (31.09)	30656536.12 (48.25)	17181732.87 (28.82)	7776269.97 (13.95)	< 0.0001
25.1–30	60071568.25 (33.58)	18778195.18 (29.55)	21132844.42 (35.44)	20160528.66 (36.17)	
> 30	63213804.03 (35.33)	14107629.73 (22.20)	21312350.93 (35.74)	27793823.38 (49.87)	
hypertension (%)	44795433.50 (25.04)	9435124.61 (14.85)	15357669.53 (25.76)	20002639.36 (35.89)	< 0.0001
diabetes mellitus (%)	24067066.84 (13.45)	2732559.13 (4.30)	5669553.99 (9.51)	15664953.72 (28.11)	< 0.0001
CVD (%)	55508482.94 (31.03)	19541095.58 (30.75)	17262114.76 (28.95)	18705272.61 (33.56)	0.004
cancer (%)	16232889.02 (9.07)	4509831.68 (7.10)	5490994.65 (9.21)	6232062.69 (11.18)	0.0001
KDM biological age, years	46.762 (16.21)	40.936 (15.61)	47.506 (15.90)	52.609 (14.90)	< 0.0001
Phenotypic age, years	43.350 (17.86)	37.581 (17.19)	44.180 (17.68)	49.039 (16.79)	< 0.0001
KDM biological age acceleration, (%)					
No	93764070.65 (52.41)	40147428.46 (63.18)	31316291.11 (52.52)	22300351.08 (40.01)	< 0.0001
Yes	85135840.60 (47.59)	23394932.57 (36.82)	28310637.12 (47.48)	33430270.92 (59.99)	
Phenotypic age acceleration, (%)					
No	143679437.91 (80.31)	54403575.97 (85.62)	48725002.04 (81.72)	40550859.89 (72.76)	< 0.0001
Yes	35220473.35 (19.69)	9138785.05 (14.38)	10901926.18 (18.28)	15179762.11 (27.24)	

Data were presented as weighted percentages or means (95% confidence intervals)

TyG, triglyceride glucose. PIR, Poverty–income ratio. BMI, body mass index. MET, metabolic equivalent. CVD, cardiovascular disease. KDM, Klemera–Doubal method

individuals with metabolic syndrome and diabetes [12, 20, 21, 28–33]. This biomarker's significance extends to predicting adverse health outcomes in various populations, underscoring its relevance in metabolic research and clinical practice.

Biological aging, characterized by the gradual decline in physiological function and increased susceptibility to age-related diseases, is influenced by a complex interplay of genetic, environmental, and lifestyle factors [34]. Researchers have utilized biomarkers such as telomere

Table 2 Association between TyG index and KDM biological age/phenotypic age

	Crude model		Model I		Model II		Model III	
	β(95%CI)	*P*-value	β(95%CI)	*P*-value	β(95%CI)	*P*-value	β(95%CI)	*P*-value
KDM biological age								
TyG	7.70(7.14,8.25)	< 0.001	2.25(2.09,2.42)	< 0.001	2.35(2.19,2.52)	< 0.001	1.64(1.46,1.82)	< 0.001
TyG tertiles								
T1	Reference		Reference		Reference		Reference	
T2	6.57(5.73,7.41)	< 0.001	1.29(1.09,1.50)	< 0.001	1.37(1.18,1.57)	< 0.001	0.92(0.73,1.10)	< 0.001
T3	11.67(10.79,12.56)	< 0.001	2.98(2.73,3.24)	< 0.001	3.10(2.86,3.34)	< 0.001	1.93(1.69,2.17)	< 0.001
P for trend	< 0.001		< 0.001		< 0.001		< 0.001	
Phenotypic age								
TyG	7.45(6.78,8.11)	< 0.001	1.34(1.11,1.57)	< 0.001	1.36(1.14,1.59)	< 0.001	0.40(0.21,0.59)	< 0.001
TyG tertiles								
T1	Reference		Reference		Reference		Reference	
T2	6.60(5.65,7.54)	< 0.001	0.70(0.45,0.94)	< 0.001	0.71(0.47,0.95)	< 0.001	0.26(0.05,0.47)	0.016
T3	11.46(10.44,12.47)	< 0.001	1.75(1.45,2.06)	< 0.001	1.77(1.47,2.08)	< 0.001	0.36(0.10,0.62)	0.008
P for trend	< 0.001		< 0.001		< 0.001		0.007	

Crude model: no other covariates were adjusted

Model I: Adjust for age, gender

Model II: Adjust for age, gender, race, education, marital status, PIR

Model III: Adjust for age, gender, race, education, marital status, PIR, smoke, drinking status, physical activity, BMI, hypertension, diabetes mellitus, CVD history, cancer

TyG, triglyceride glucose. KDM, Klemera–Doubal method. CI, Confidence Interval. Ref, reference. PIR, Poverty–income ratio. BMI, body mass index. CVD, cardiovascular disease

Table 3 Association between TyG index and KDM biological age/phenotypic age acceleration

	Crude model		Model I		Model II		Model III	
	OR (95%CI)	*P*-value	OR (95%CI)	*P*-value	OR (95%CI)	*P*-value	OR (95%CI)	*P*-value
KDM biological age acceleration								
TyG	2.06 (1.89,2.25)	< 0.001	2.70(2.45,2.96)	< 0.001	2.88(2.62,3.17)	< 0.001	2.17(1.95,2.42)	< 0.001
TyG tertiles								
T1	Reference		Reference		Reference		Reference	
T2	1.55(1.39,1.74)	< 0.001	1.91(1.70,2.13)	< 0.001	2.01(1.79,2.25)	< 0.001	1.67(1.48,1.87)	< 0.001
T3	2.57(2.26,2.93)	< 0.001	3.74(3.27,4.28)	< 0.001	4.03(3.52,4.62)	< 0.001	2.59(2.24,3.00)	< 0.001
P for trend	< 0.001		< 0.001		< 0.001		< 0.001	
Phenotypic age acceleration								
TyG	1.85(1.68,2.04)	< 0.001	1.69(1.53,1.87)	< 0.001	1.75(1.58,1.94)	< 0.001	1.15(1.04,1.27)	0.006
TyG tertiles								
T1	Reference		Reference		Reference		Reference	
T2	1.33(1.14,1.56)	< 0.001	1.19(1.01,1.41)	0.033	1.22(1.03,1.45)	0.023	0.99(0.83,1.18)	0.88
T3	2.23(1.90,2.61)	< 0.001	1.89(1.61,2.21)	< 0.001	1.97(1.66,2.34)	< 0.001	1.10(0.92,1.32)	0.289
P for trend	< 0.001		< 0.001		< 0.001		0.264	

Crude model: no other covariates were adjusted

Model I: Adjust for age, gender

Model II: Adjust for age, gender, race, education, marital status, PIR

Model III: Adjust for age, gender, race, education, marital status, PIR, smoke, drinking status, physical activity, BMI, hypertension, diabetes mellitus, CVD history, cancer

TyG, triglyceride glucose. KDM, Klemera–Doubal method. OR, Odds Ratio. CI, Confidence Interval. Ref, reference. PIR, Poverty–income ratio. BMI, body mass index. CVD, cardiovascular disease

length, oxidative stress indicators, and systemic inflammation to assess biological aging [6, 7, 23]. In addition to these biomarkers, various methods, including the KDM and PhenoAge, have been employed in numerous studies to assess biological aging and its associations with chronic diseases such as cardiovascular disease, metabolic disorders, and cognitive decline. KDM, which utilizes chronological age along with several biomarkers, has gained recognition for its ability to more accurately reflect the physiological state and age-related diseases compared to chronological age alone. On the other hand, PhenoAge, which integrates a set of clinical variables, has

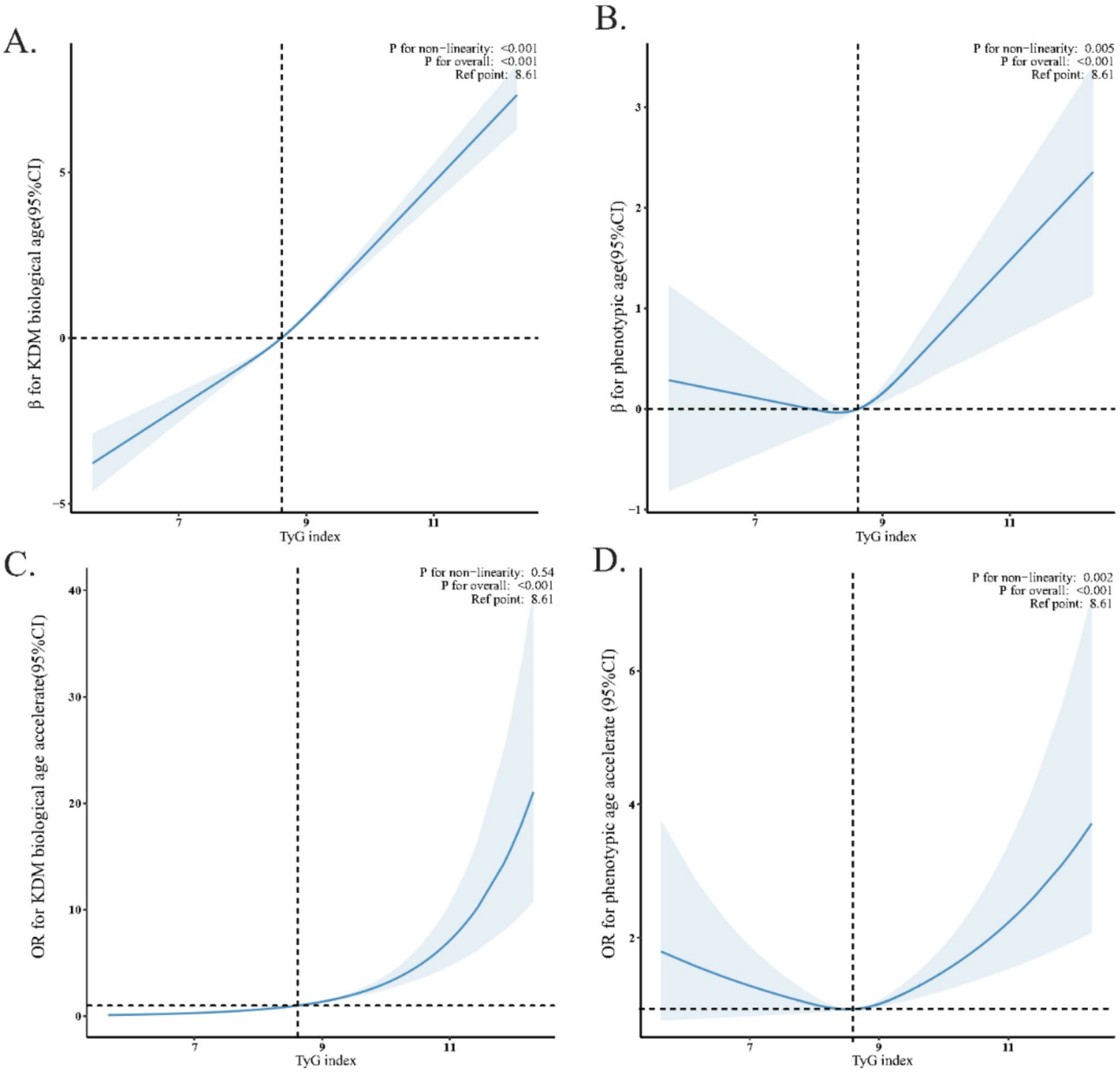

Fig. 2 Association of TyG index with KDM biological age/phenotypic age (**A**, **B**) and KDM biological age/phenotypic age acceleration (**C**, **D**) data were fitted by a survey-weighted multivariable linear / logistic regression model based on restricted cubic splines. Solid and dashed lines represent the predicted value and 95% confidence intervals. They were adjusted for age, gender, race, education, marital status, PIR, smoke, drinking status, physical activity, BMI, hypertension, diabetes mellitus, cardiovascular disease history, cancer. KDM, Klemera–Doubal method. TyG, triglyceride glucose. PIR, Poverty–income ratio. BMI, body mass index. OR, Odds Ratio. CI, Confidence Interval

shown strong correlations with aging-related diseases and mortality in diverse populations. These tools, validated in various cohorts, provide a more comprehensive understanding of aging beyond chronological age [3, 35].

The link between TyG and biological aging is particularly noteworthy. Elevated TyG levels reflect insulin resistance, which contributes to increased oxidative stress and systemic inflammation—both of which accelerate the aging process. High TyG levels are associated with elevated markers of inflammation, such as C-reactive protein, and oxidative damage [36, 37], which further drive biological aging. Research also highlights the relationship between TyG and age-related conditions. Higher TyG levels are connected to greater risks of cardiovascular events, metabolic syndrome, and type 2 diabetes, with a growing body of evidence indicating that TyG plays a role in the development of age-related conditions, such as sarcopenia and cognitive decline in older adults [38, 39], emphasizing its potential role in monitoring age-related health issues.

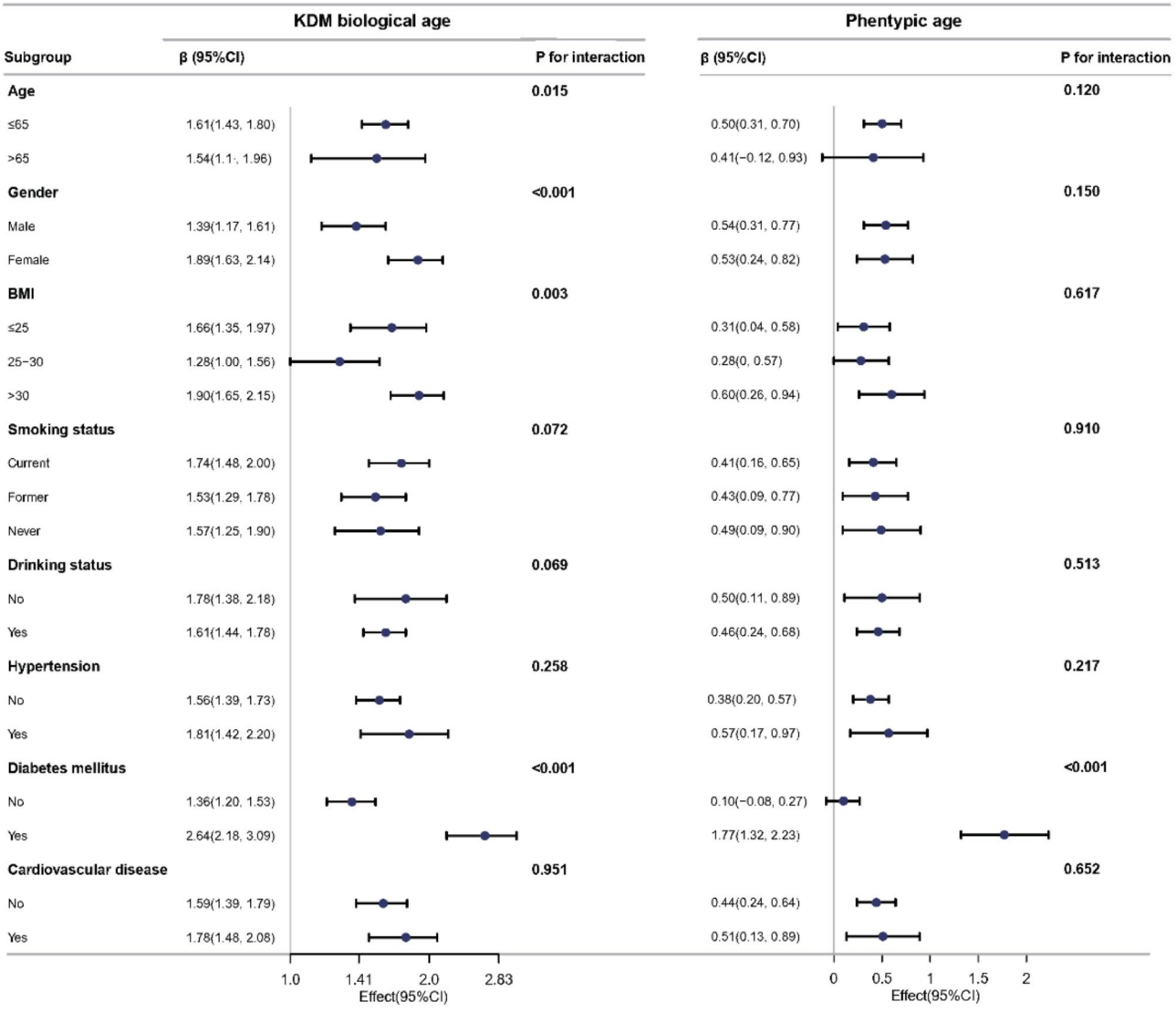

Fig. 3 Subgroup analyses of the association between TyG index and phenotypic age and KDM biological age. Adjusted for age, gender, race, education, marital status, PIR, smoke, drinking status, physical activity, BMI, hypertension, diabetes mellitus, cardiovascular disease history, cancer. TyG, triglyceride glucose. KDM, Klemera–Doubal method. PIR, Poverty–income ratio. BMI, body mass index. CI, Confidence Interval

Building on this, the positive correlation between the TyG index and biological aging can be explained through several interrelated mechanisms. TyG serves as a proxy for insulin resistance, a condition that disrupts glucose and lipid metabolism. This disruption can lead to metabolic syndrome, characterized by obesity, dyslipidemia, and hypertension [40]—all of which are associated with accelerated biological aging. Chronic insulin resistance promotes systemic inflammation and oxidative stress, both of which contribute significantly to the aging process [9]. Elevated TyG levels are linked to increased oxidative stress, resulting from an imbalance between free radicals and antioxidants, leading to cellular damage and accelerated aging at the cellular level [36]. Additionally, high TyG levels correlate with increased markers of chronic inflammation, such as C-reactive protein [37], which can damage tissues and organs, exacerbating age-related diseases and functional decline. Insulin resistance, as indicated by TyG, also impairs endothelial function [41], which can lead to cardiovascular diseases and further accelerate aging. Moreover, TyG is often elevated in individuals with metabolic syndrome—a cluster of conditions like abdominal obesity, high blood pressure, and dyslipidemia—that are strongly associated with accelerated biological aging.

Finally, the threshold of 8.66 emerges as a pivotal point in this relationship, suggesting that TyG levels above this value are associated with a significantly higher risk of accelerated biological aging. Elevated TyG levels reflect advanced metabolic disturbances, which may accelerate

aging and increase morbidity and mortality. Biologically, this threshold likely represents a stage where insulin resistance drives accelerated aging through mechanisms such as oxidative stress, chronic inflammation, and mitochondrial dysfunction. These processes contribute to cellular damage, impaired vascular health, and reduced energy production, all of which exacerbate aging.

This study is the first to explore the link between the triglyceride glucose index and biological aging. The use of NHANES, which employs a complex sampling design, ensures reliable extrapolation to the broader U.S. population. The research perspective of this study is both innovative and therapeutically valuable, offering new insights into the connection between metabolic indicators and aging. However, being cross-sectional, it cannot establish causality and may be affected by unmeasured variables. The study focused on clinical markers of biological aging rather than molecular or cellular levels, though using two methods for biological age calculation enhances result robustness. Future research should include diverse populations, such as children and those from different regions and health conditions, to further understand this relationship.

Conclusions

Higher TyG levels are linked to greater biological age and a higher risk of age acceleration. This underscores the potential of the TyG index as a simple and effective marker for assessing the risk of accelerated aging, which could be crucial for identifying individuals at higher risk for age-related diseases and for targeting interventions to promote healthy aging.

Abbreviations

IR	Insulin resistance
BA	Biological age
TyG	Triglyceride–glucose
NHANES	National Health and Nutrition Examination Survey
HD	Homeostatic dysregulation
KDM	Klemera–Doubal method
PA	Phenotypic age
AL	Allostatic load
NCHS	National Center for Health Statistics
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology
CRP	C-reactive protein
CA	Chronological age
PIR	Poverty-to-income ratio
BMI	Body mass index
MET	Metabolic Equivalent of Task
CVD	Cardiovascular disease
OR	Odds ratios
CI	Confidence interval
PhenoAgeAccel	Phenotypic age acceleration

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12933-025-02631-w .

Supplementary file 1.

Acknowledgements

We thank the Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University for supporting our work. We express our appreciation to the NHANES administration for facilitating access to the pertinent data on the NHANES website.

Author contributions

L.Y.P designed the study, conducted the data collection and analysis, wrote the manuscript and reviewed the manuscript. L.J conducted data analysis and reviewed the manuscript. All authors read and approved the final manuscript.

Funding

This study was supported by The Youth Project of National Natural Science Foundation of China (grant number 81900362).

Data availability

These survey data are free and publicly available, and can be downloaded directly from the NHANES website (http://www.cdc.gov/nchs/nhanes.htm) by users and researchers worldwide.

Received: 11 October 2024 / Accepted: 5 February 2025
Published online: 28 February 2025

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