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Association between triglyceride-glucose index and its correlation indexes and stress urinary incontinence in postmenopausal women: evidence from NHANES 2005–2018

Xueping Huang^{1*}, Wen Hu¹ and Limei Li^{1*}

Abstract

Background Postmenopausal women are more susceptible to stress urinary incontinence (SUI), and insulin resistance (IR) is closely related to SUI. The triglyceride-glucose (TyG) index is an efficient metric for assessing IR. Investigating whether TyG index and its correlation indexes were correlated with SUI in postmenopausal women was the aim of this research.

Methods Data from 2,132 postmenopausal women from the National Health and Nutrition Examination Survey (NHANES) were included in the study for analysis. Weighted multiple logistic regression was used to evaluate the correlation between the TyG index and its correlation indexes and SUI. The nonlinear correlation between the TyG correlation indexes and SUI, as well as the diagnostic efficacy for SUI, was investigated using the smooth curve approach and receiver operating characteristics. Through detailed subgroup analysis, the stability and generalization of the results are confirmed.

Results Of the 26.87 million, 13.63 million, or 50.73%, suffered from SUI. The prevalence of SUI was significantly higher in the fourth quartile of TyG-BMI (OR = 1.93, 95% CI 1.13–2.84), TyG-WC (OR = 1.76, 95% CI 1.23–2.51), and TyG-WHtR (OR = 1.81, 95% CI 1.28–2.55) compared to the first quartile. Among the three models, TyG-WHtR always maintained a more significant correlation with SUI (Model 1:OR = 1.30; Model 2:OR = 1.33; Model 3:OR = 1.24). Smooth curve fitting results showed that TyG correlation indexes were not linearly correlated with SUI ($P > 0.05$). Subgroup analysis further confirmed the reliability and applicability of the results. TyG-BMI had the greatest diagnostic performance for SUI out of the four markers.

Conclusions In comparison to TyG, TyG correlation indexes showed a more significant correlation with SUI among postmenopausal women in US, with TyG-BMI showing the best diagnostic effectiveness.

Keywords Triglyceride-glucose index, Triglyceride glucose-body mass index, Triglyceride glucose-waist circumference, Triglyceride glucose-waist height ratio, Stress urinary incontinence, Insulin resistance, NHANES

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Introduction

Stress urinary incontinence (SUI) is one of the health killers of women, which is characterized by uncontrolled leakage of urine when there is pressure added to the abdomen. SUI rises in frequency with age, from 51.3% in women between the ages of 40 and 59 to 53.1% in women over 60 [1]. SUI can reduce a woman's overall quality of life and harm a woman's physical, social, financial, and emotional health [2]. The feelings of uncertainty and humiliation that women with SUI experience may cause them to alter their routines and way of life (such as engaging in fewer social or physical activities) and possibly develop mental health conditions including anxiety and depression [3, 4]. As society ages and the need for enhanced quality of life increases, the health risks associated with SUI in women, particularly postmenopausal women, will intensify.

Due to its excellent performance in describing insulin resistance (IR), the triglyceride-glucose (TyG) index is increasingly trusted [5]. Although it might be challenging to determine a person's potential risk of diabetes when their fasting blood sugar is normal, the TyG index seems to do the job [6, 7]. TyG may be a very good indicator of poor cardiovascular outcomes and is directly linked to cardiovascular disease (CVD) [8, 9]. Furthermore, the TyG index predicted non-obstructive heart disease more prominently than the plasma atherogenic index (AIP) [10, 11]. According to recent studies, the prevalence of SUI is positively correlated with a higher TyG [12]. Nevertheless, studies mostly focused on American adult females over the age of 20 and did not examine the link between postmenopausal women's SUI and the TyG index.

Obesity is the killer of human health, and it has an inseparable relationship with hypertension, diabetes and CVD [13–15]. Among the many risk factors affecting SUI, obesity plays a very important role [16, 17]. According to the research, IR was better assessed using TyG in conjunction with obesity indices than using TyG alone [18]. Simultaneously, the obesity index and TyG together may more accurately predict CVD mortality and identify those at risk for early CVD [8]. Research has shown that TyG-body mass index (BMI) levels in Americans were associated with various forms of UI, including SUI [19], nonetheless, its association with postmenopausal individuals has not been shown in the literature. Because they are embarrassed and uncomfortable about “leaking urine,” women with SUI seldom report and seek treatment, which may lead to their missing the ideal window for therapy. This cross-sectional research was predicated on the hypothesis that TyG index paired with obesity indexes had a greater correlation with SUI. Different from earlier investigations, its study participants were confined to postmenopausal women. The outcomes of

this research may bring fresh ideas for the early identification and treatment of SUI.

Methods

Study population

Gathering health data on Americans via questionnaires, physical examinations, interviews, and other means is the main purpose of the National Health and Nutrition Examination Survey (NHANES), which provided the data utilized in this research. Research in epidemiology and health sciences makes extensive use of the results. Cross-sectional research benefit greatly from the extensive, free, publicly available NHANES database.

Seven cycles (2005–2018) data were retrieved, with a total of 70,190 people completing the survey. Initially, Male participants ($n=34,709$), premenopausal women ($n=28,182$), cancer patients ($n=1147$), and participants with renal failure ($n=262$) were excluded. Subsequently, omitted were those lacking TyG-related index data ($n=3224$) and those without SUI diagnostic data ($n=37$). In addition, individuals lacking covariate data were excluded ($n=497$). Lastly, 2132 people were enrolled (Fig. 1).

Menopause judgment

Whether the participants were postmenopausal was determined through a self-reported reproductive health questionnaire. They were asked a set of two questions: (1) Whether they had experienced menstruation at least once within the past year, and (2) The reason for not having had menstruation during that time. Respondents were categorized as postmenopausal if they selected “menopause/hysterectomy” for the second question and “no” for the first.

Assessment of SUI

Each participant was asked questions about urinary incontinence in a Mobile Screening Center (MEC) interview room. Respondents were asked, “Have you ever had minor pee leaks while exercising, weightlifting, or coughing in the last 12 months?” People who said “yes” were assessed SUI.

Calculation of TyG correlation indexes

According to earlier research, the TyG index and its correlation indexes are calculated as follows: (1) $TyG = \ln [\text{triglycerides (mg/dl)} \times \text{glucose (mg/dl)} / 2]$; (2) $TyG\text{-}BMI = TyG \times BMI$; (3) $TyG\text{-}waist \text{ circumference (WC)} = TyG \times WC$; (4) $TyG\text{-}waist\text{-}to\text{-}height \text{ ratio (WHtR)} = TyG \times WHtR$ [8].

Assessment of covariates

The research further assessed the impact of age, race, educational attainment, marital status, vitamin D

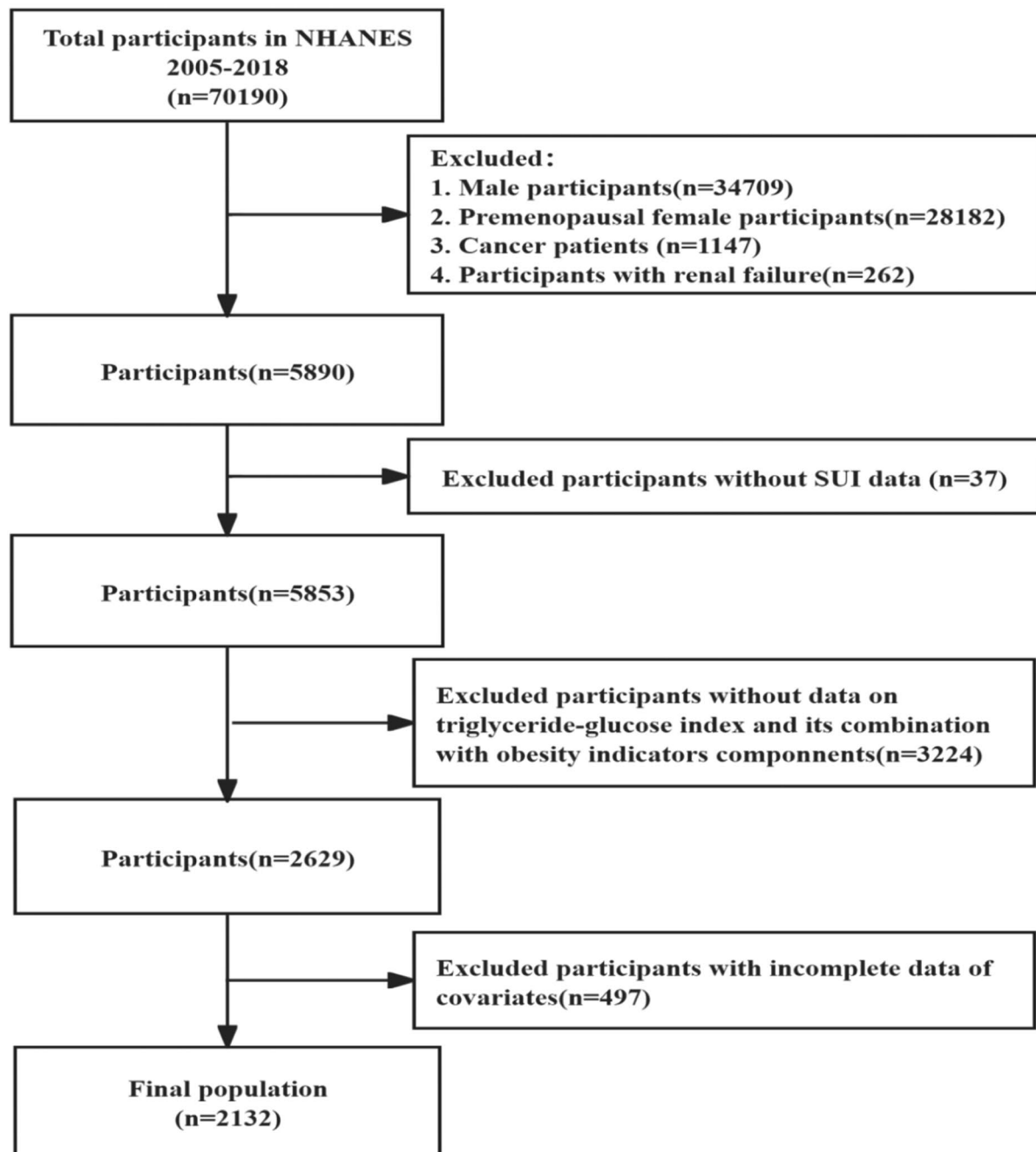


Fig. 1 Research sample screening flow chart

levels, smoking, vaginal deliveries, hysterectomy, poverty-to-income ratio (PIR), menopausal hormone therapy (MHT), hypertension, diabetes, and chronic pulmonary illness, in accordance with other studies' results. A person is deemed to be smoking if their serum cotinine level is more than 3ng/mL [20]. MHT was classified as women who self-reported taking any kind of progesterone or estrogen preparation. Hypertension and diabetes are diagnosed through self-reported forms. Individuals who have been diagnosed with emphysema, chronic

bronchitis, or asthma by a physician or other health care provider are considered to have chronic lung disease.

Statistical analysis

Complex sample design and sample weights that meet NHANES analytic standards are taken into consideration in this research. Categorical data are given as frequency (%), whereas continuous variables are expressed as mean (standard deviation [SD]) or median (interquartile distance [IQR]). Postmenopausal women were grouped

according to whether they had SUI, and differences between groups were compared using univariate analysis of variance, Kruskal-Wallis H test, or Chi-square test.

In this study, TyG and its related indexes (TyG-BMI, TyG-WC, and TyG-WHtR) were used as continuous variables and quartiles (Q1, Q2, Q3, Q4), and a multivariate weighted logistic regression model was used to explore the correlation between the four indicators and SUI. This study converted TyG-BMI (every 10 units) and TyG-WC (every 10 units) in the analysis because of the high value, but this did not alter the data's initial trend. The results were expressed as odds ratios (OR) and 95% confidence intervals (CI). Based on previous research, three models were developed: Model 1 is a preliminary model that does not change any variables. Model 2 was modified to account for PIR, age, race, educational attainment, marital status. Chronic lung disease, diabetes, hypertension, hysterectomy, MHT, smoking, vitamin D, and the number of vaginal births were adjusted in model 3, which is built on the basis of Model 2. The nonlinear relationship between TyG and its correlation indexes with SUI was verified by smooth curve fitting technique. Area under the curve (AUC) was calculated by receiver operating characteristic curve (ROC) analysis to evaluate the sensitivity and specificity of TyG correlation indexes in predicting SUI. Subgroup analysis was performed according to age (<65, ≥65), race, vaginal deliveries (<3, ≥3), hysterectomy, MHT, hypertension, and diabetes.

R Statistical Software (version 4.2.2, <http://www.R-project.org>, The R Foundation) and the Free Statistics analytical platform (version 1.9.2), located in Beijing, China, were used for all studies.

Results

Baseline attributes

Our study included a statistical analysis of 26.87 million Americans with a weighted mean age of 61.40 years (SD, 10.39), of whom 13.63 million, or 53%, had SUI, as shown in Table 1. Clearly, TyG, TyG-BMI, TyG-WC, and TyG-WHtR were higher in people with SUI.

Association of TyG and its correlation indexes with SUI

In Table 2, of the three models, TyG-BMI (every 10 points) (OR=1.04, 95% CI 1.02–1.06), TyG-WC (every 10 points) (OR=1.01, 95% CI 1.00–1.02) and TyG-WHtR (OR=1.24, 95% CI 1.09–1.40) were positively correlated with SUI. TyG-WHtR always maintained the most significant correlation with SUI. Interestingly, no correlation was observed between TyG and SUI (OR=1.1, 95% CI 0.88–1.39). In addition, in the fourth quartile of TyG-BMI (OR=1.93, 95% CI 1.13–2.84), TyG-WC (OR=1.76, 95% CI 1.23–2.51) and TyG-WHtR (OR=1.81, 95% CI 1.28–2.55), the prevalence of SUI was higher than the top four quartiles.

Smooth curve fitting results were shown in Fig. 2. In addition to TyG, there was a significant linear relationship between TyG correlation indexes and SUI (P for non-linearity > 0.05).

In Fig. 3, TyG-BMI had showed the strongest diagnostic impact on SUI (AUC: 0.582, 95% CI 0.558–0.606), followed by TyG-WC (AUC: 0.578, 95% CI 0.554–0.603) and TyG-WHtR (AUC: 0.578, 95% CI 0.554–0.602).

Subgroup analyses

Subgroup analysis performed by age, race, vaginal deliveries, hysterectomy, MHT, hypertension, and diabetes was carried out after the variables had been controlled. Since the subgroup analysis of various categories did not substantially alter the positive link between TyG correlation parameters with SUI, the findings remained consistent. Interestingly, no correlation was seen between SUI and TyG correlation parameters in postmenopausal women receiving MHT (Fig. 4).

Discussion

After controlling for factors including demographics, chronic illnesses, vaginal birth, and MHT, this comprehensive cross-sectional investigation discovered that the incidence of SUI in postmenopausal women rose linearly as the TyG-related indexes rose. It's interesting to see that the TyG index and SUI did not correlate. Furthermore, TyG-related characteristics were more successful in predicting SUI than TyG itself. The TyG correlation index consistently maintained a positive connection with SUI across several subgroups, demonstrating the stability and generalizability of the study's findings. Interestingly, in postmenopausal women using MHT, the link between SUI and TyG correlation indexes disappeared.

TyG has been shown to perform very well in identifying IR, and when compared to more conventional indicators, it has the benefit of being more simple and cost-effective [5, 21, 22]. At present, studies on the link between TyG and its correlation measures with SUI are still immature, especially those on postmenopausal people. According to previous research results, IR is an important factor in UI, because women with diabetes have a significantly higher chance of developing UI [23]. There was a significant link between the insulin resistance metabolic score (METS-IR) index and different kinds of UI, notably SUI (OR=1.023), and this relationship was more prominent in American women [24]. Zhao et al. were interested in the connection between TyG and SUI. The findings of their study shown that when TyG levels rose, so did the likelihood of SUI in adult women [12]. According to this study results, TyG in postmenopausal women is not associated with SUI; this may be because risk factors for SUI may increase with age, such as reduced estrogen and atrophy of pelvic floor muscle function, which leads to

Table 1 Features of the NHANES 2005–2018 study participants

Characteristic	Participants			P-value
	Total	Without SUI	With SUI	
Weighted population, n[in millions]	26.87	13.24	13.63	
Age, mean(SD), years	61.40 (10.39)	61.74 (10.87)	61.08 (9.89)	0.225
Race, n[in millions](%)				
Mexican American	1.44(5.36)	0.68(5.14)	0.75(5.56)	< 0.001
Non-Hispanic White	19.89(74.03)	9.40(70.95)	10.50(77.02)	
Non-Hispanic Black	2.90(10.79)	1.82(13.77)	1.08(7.89)	
Other Race	2.64(9.83)	1.34(10.14)	1.30(9.52)	
Education level, n[in millions](%)				
Less than high school	5.00(18.52)	2.35(17.71)	2.63(19.31)	0.768
High school or GED	7.70(28.57)	3.84(28.99)	3.84(28.16)	
Above high school	14.23(52.91)	7.10(53.30)	7.16(52.53)	
Marital status, n[in millions](%)				
Married or living with partner	16.60(61.78)	7.92(59.83)	8.68(63.67)	0.145
Never married	7.95(2.96)	0.47(3.54)	0.33(2.40)	
Others	9.48(35.26)	4.85(36.64)	4.62(33.93)	
PIR, median[IQR]	2.98 [1.58, 5.00]	2.95 [1.58, 5.00]	3.05 [1.59, 5.00]	0.76
VitaminD, mean(SD)	74.16 (31.18)	75.32 (31.40)	73.03 (30.94)	0.248
Smoking, n[in millions](%)				
No	21.76(80.97)	10.92(82.47)	10.84(79.50)	0.214
Yes	5.11(19.03)	2.32(17.53)	2.79(20.50)	
Vaginal deliveries, mean(SD)	2.39 (1.77)	2.34 (1.79)	2.43 (1.76)	0.397
Hysterectomy, n[in millions](%)				
No	18.57(69.12)	9.24(69.74)	9.34(68.51)	0.626
Yes	8.30(30.88)	4.01(30.26)	4.29(31.49)	
MHT, n[in millions](%)				
No	16.98(63.20)	8.69(65.59)	8.30(60.87)	0.135
Yes	9.89(36.80)	4.56(34.41)	5.33(39.13)	
Hypertension, n[in millions](%)				
No	13.32(49.57)	7.044(53.19)	6.28(46.06)	0.009
Yes	13.55(50.43)	6.20(46.81)	7.35(53.94)	
Diabetes, n[in millions](%)				
No	23.02(85.67)	11.70(88.37)	11.32(83.05)	0.004
Yes	3.85(14.33)	1.54(11.63)	2.31(16.95)	
Chronic lung disease, n[in millions](%)				
No	21.68(80.69)	11.15(84.18)	10.54(77.30)	0.003
Yes	5.19(19.31)	2.09(15.82)	3.09(22.70)	
TyG, mean(SD)	8.69 (0.59)	8.64 (0.57)	8.74 (0.60)	0.007
TyG-BMI, mean(SD)	258.17 (64.46)	248.90 (60.10)	267.19 (67.25)	< 0.001
TyG-WC, mean(SD)	866.32 (159.88)	844.80 (154.71)	887.22 (162.11)	< 0.001
TyG-WHtR, mean(SD)	5.39 (1.01)	5.26 (0.96)	5.52 (1.04)	< 0.001

a lower predictive value of TyG in postmenopausal individuals [25].

It has been progressively acknowledged that TyG in conjunction with obesity indices is a handy and surrogate indicator of IR [18, 21]. According to recent research, TyG and obesity markers work well together to predict death from cardiovascular disease, all causes, and metabolic syndrome [8, 26, 27]. Moreover, TyG and its related indexes are also closely related to diabetes [28], high blood pressure [29], liver damage [30], and cholelithiasis [31]. When women enter menopause, the risk of

metabolic syndrome, high blood pressure, central obesity and dyslipidemia is significantly increased [32]. Postmenopausal women have a heightened susceptibility to centripetal obesity attributable to decreased estrogen levels, atypical body fat distribution, and abdominal fat buildup [33]. Consequently, it is reasonable to conjecture that the TyG index, in conjunction with obesity metrics, may provide enhanced efficacy in evaluating SUI in postmenopausal women. This investigation shown that, in comparison to TyG, TyG correlation indexes exhibited a more significant correlation with SUI in postmenopausal

Table 2 Relationship between TyG index and its correlation indexes and SUI

Parameters	OR (95% CI)					
	Model 1	P-value	Model 2	P-value	Model 3	P-value
TyG						
Continuous	1.32(1.07,1.61)	0.008	1.28(1.04,1.58)	0.02	1.1(0.88,1.39)	0.392
Q1(6.70–8.30)	1(Ref)		1(Ref)		1(Ref)	
Q2 (8.31–8.68)	1.03(0.72,1.46)	0.874	1.03(0.71,1.49)	0.869	0.98(0.67,1.42)	0.906
Q3(8.69–9.09)	1.44(1.01,2.06)	0.044	1.41(0.98,2.01)	0.062	1.31(0.90,1.90)	0.16
Q4(≥ 9.10)	1.56(1.13,2.15)	0.007	1.51(1.08,2.12)	0.017	1.23(0.86,1.76)	0.26
TyG-BMI						
Continuous	1.05(1.03,1.07)	< 0.001	1.05(1.03,1.07)	< 0.001	1.04(1.02,1.06)	< 0.001
Q1(11.72–21.38)	1(Ref)		1(Ref)		1(Ref)	
Q2(21.39–25.18)	1.08(0.75,1.54)	0.673	1.13(0.79,1.60)	0.502	1.11(0.78,1.57)	0.562
Q3(25.19–29.67)	1.4(0.96,2.03)	0.076	1.48(1.02,2.14)	0.041	1.39(0.96,2.02)	0.084
Q4(≥ 29.68)	2.11(1.49,3.00)	< 0.001	2.25(1.58,3.21)	< 0.001	1.93(1.13,2.84)	0.001
TyG-WC						
Continuous	1.02(1.01,1.02)	< 0.001	1.02(1.01,1.03)	< 0.001	1.01(1.00,1.02)	0.002
Q1(47.64–75.59)	1(Ref)		1(Ref)		1(Ref)	
Q2(75.60–85.82)	1.07(0.74,1.57)	0.708	1.13(0.77,1.65)	0.523	1.07(0.74,1.56)	0.706
Q3(85.83–97.20)	1.51(1.08,2.11)	0.017	1.58(1.12,2.22)	0.01	1.45(1.03,2.04)	0.032
Q4(≥ 97.21)	2.02(1.46,2.79)	< 0.001	2.13(1.53,2.95)	< 0.001	1.76(1.23,2.51)	0.002
TyG-WHtR						
Continuous	1.3(1.16,1.45)	< 0.001	1.33(1.19,1.49)	< 0.001	1.24(1.09,1.40)	0.001
Q1(2.94–4.57)	1(Ref)		1(Ref)		1(Ref)	
Q2(4.76–5.42)	1.34(0.95,1.89)	0.09	1.42(1.01,2.00)	0.045	1.35(0.96,1.91)	0.085
Q3(5.43–6.10)	1.34(0.94,1.91)	0.1	1.41(0.99,2.02)	0.058	1.28(0.89,1.83)	0.181
Q4(≥ 6.11)	2.09(1.51,2.88)	< 0.001	2.2(1.59,3.05)	< 0.001	1.81(1.28,2.55)	< 0.001

Model 1: No adjustments were made. Model 2: Corrected for RIR, age, marital status, race, and education. Age, race, education, diabetes, hysterectomy, hypertension, marital status, PIR, MHT, smoking, vitamin D, and vaginal births were all taken into account in Model 3

women, with TyG-BMI showing the best diagnostic effectiveness. Notably, in postmenopausal women receiving MHT, TyG in conjunction with obesity markers did not correlate with SUI. This may be because estrogen treatment may strengthen the pelvic floor muscles, prevent urine incontinence, and alleviate the clinical symptoms of SUI [34, 35].

The most prevalent metabolic diseases in postmenopausal women are IR and obesity (particularly central obesity), which may be brought on by aging and estrogen depletion [36]. There is still uncertainty about the precise pathophysiological process behind IR and SUI. It is believed that insulin is a nutrient that regulates neuronal development and proliferation. The peripheral nervous system regulates the discharge and storage of urine; the urethral sphincter and the bladder's detrusor muscle cooperate to carry out this function; IR may harm these peripheral nerves and muscles, resulting in incontinence [37, 38]. Insulin, on the other hand, modulates oxidative capacity and mitochondrial metabolism via PI3K/Akt signaling [39, 40]. IR stimulates mitochondrial malfunction of neurons, resulting to increased oxidative stress, oxidative damage in the urethral sphincter, and aging of urinary tract epithelial cells, which adversely impacts the bladder's efficient contraction capacity and

produces lower urinary tract symptoms [41, 42]. At the same time, the decrease of estrogen in postmenopausal women is also an important factor promoting oxidative stress response [43]. On the other hand, compared to the normal control group, the pelvic floor muscles in the IR group exhibited reduced electrical activity and strength, indicating that greater levels of IR are associated with worse pelvic floor muscular strength. In female rats, the external urethral sphincter atrophied after diabetes induction [44]. In postmenopausal women, the buildup of abdominal fat raises internal abdominal pressure, compresses the pelvic floor's neuromuscular tissue over time, and causes chronic strain, which is a major contributor to urine leakage [45]. Inflammatory substances released by adipose tissue also cause oxidative stress reactions, which harm the collagen and pelvic floor muscle supporting structures [46]. These results imply that disorder of peripheral neuronal activity, oxidative stress response and pelvic floor muscle damage are key pathogenic causes of SUI in postmenopausal women.

Strengths and limitations

One of the key advantage of this research is its consideration of sample weights, which improves the sample's representativeness and enables the results to be

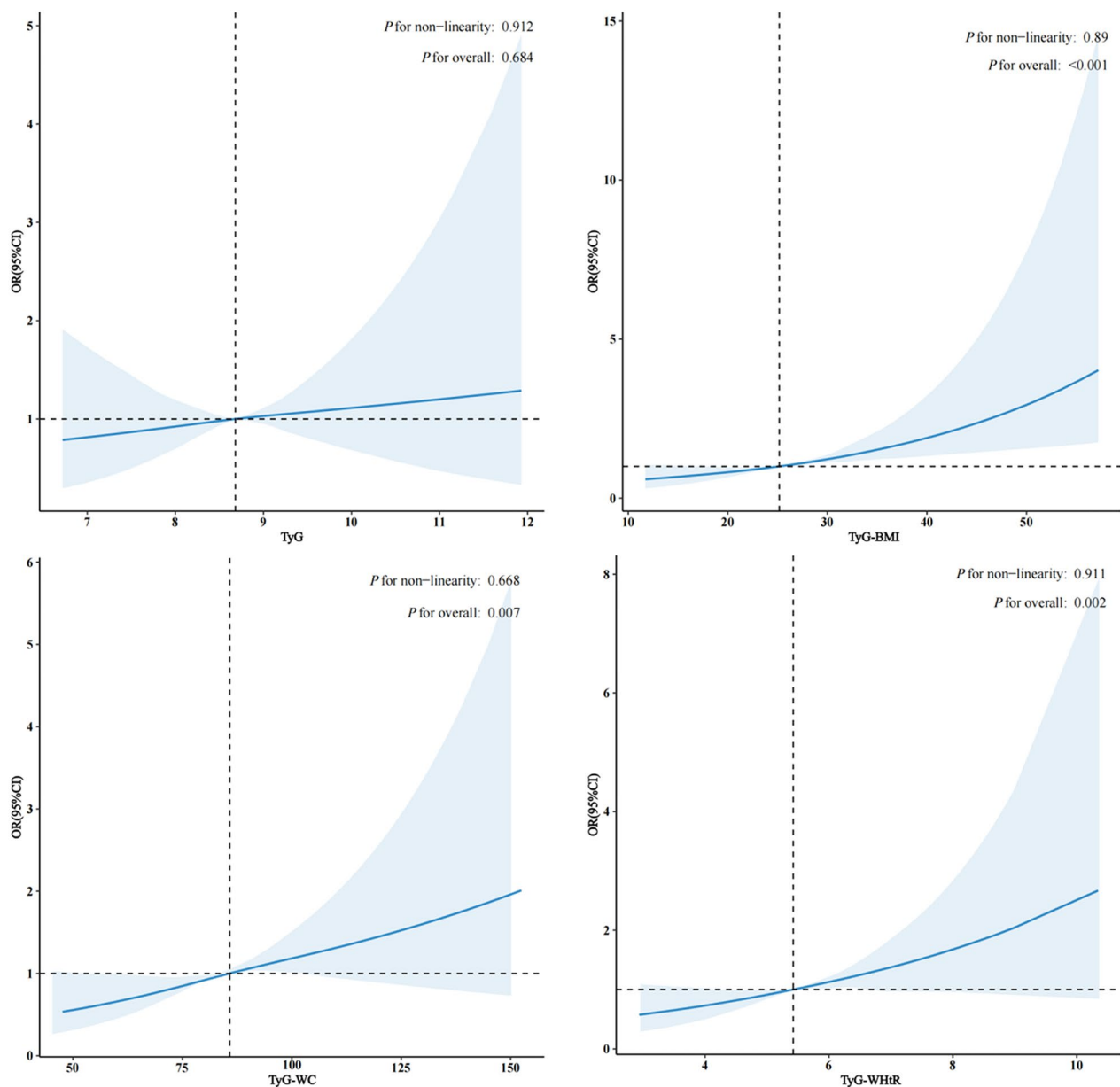


Fig. 2 The TyG index, its correlation indexes, and SUI were shown to have a linear correlation in the smoothed curve fitting plot. Solid blue lines and shadows represent predicted values and 95% confidence intervals

extrapolated to the whole US. In order to increase the trustworthiness of the findings, simultaneously corrected for confounding variables such as the quantity of vaginal births, hysterectomy, and MHT. The research has several drawbacks. First, it was unable to establish a causal link between TyG and its correlation indexes and SUI because of the limitations of cross-sectional investigations. Second, even if do it's best to control for confounding variables, it is impossible to completely ignore the influence of other uncontrollable conditions (such as asphysical work and diet) on the findings. Lastly, the study's results

can't be applied to other demographics since all of the participants were postmenopausal women in the US.

Conclusions

The TyG correlation indexes in postmenopausal women in the United States was positively connected with the prevalence of SUI, suggesting a better diagnostic association than TyG. This results might aid in the early detection and prevention of SUI and direct medical practitioners to create more customized approaches at various phases of SUI treatment.

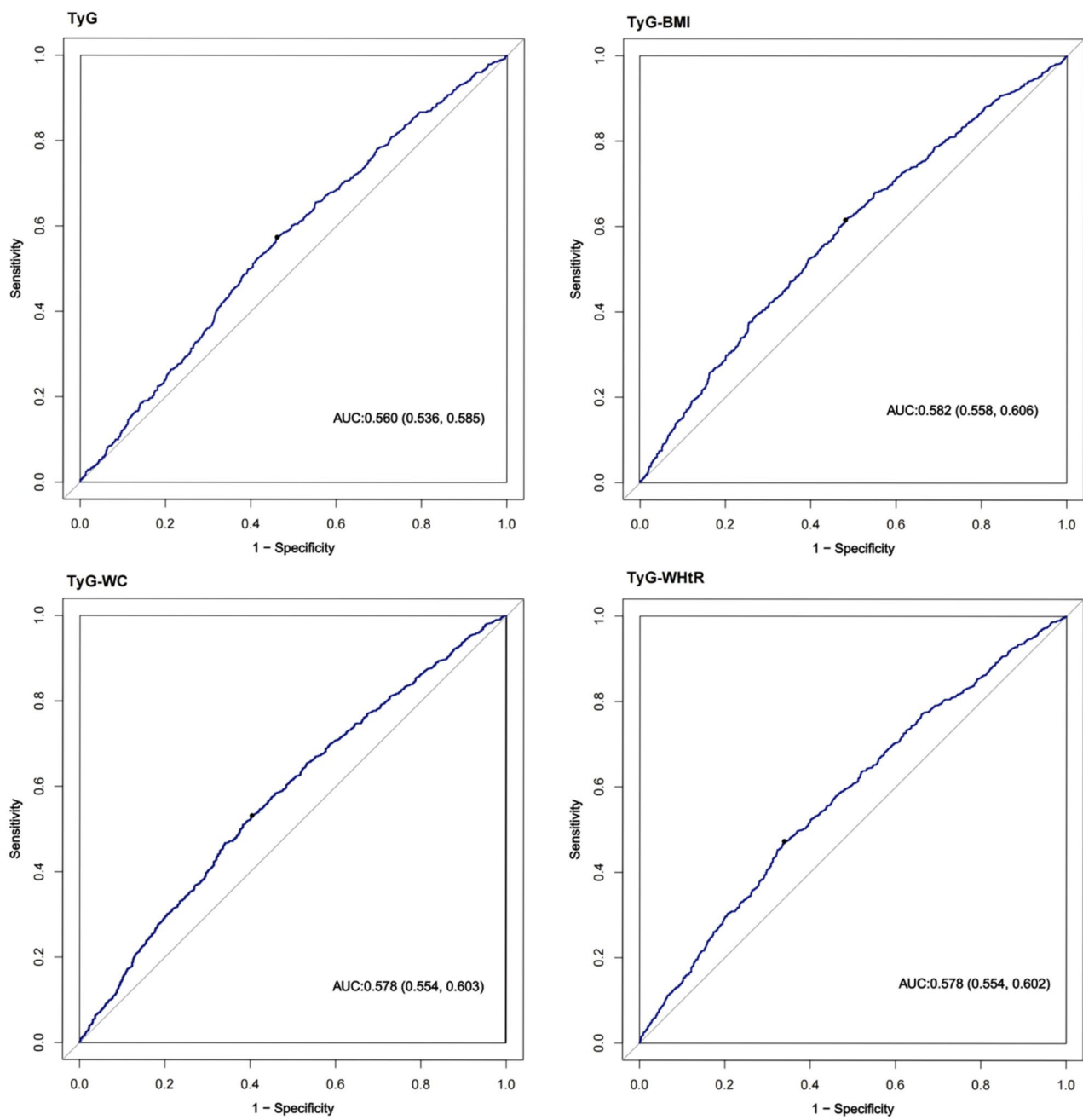


Fig. 3 The receiver operating characteristic (ROC) curve confirmed the diagnostic effectiveness of the TyG index and its correlation indexes for SUI

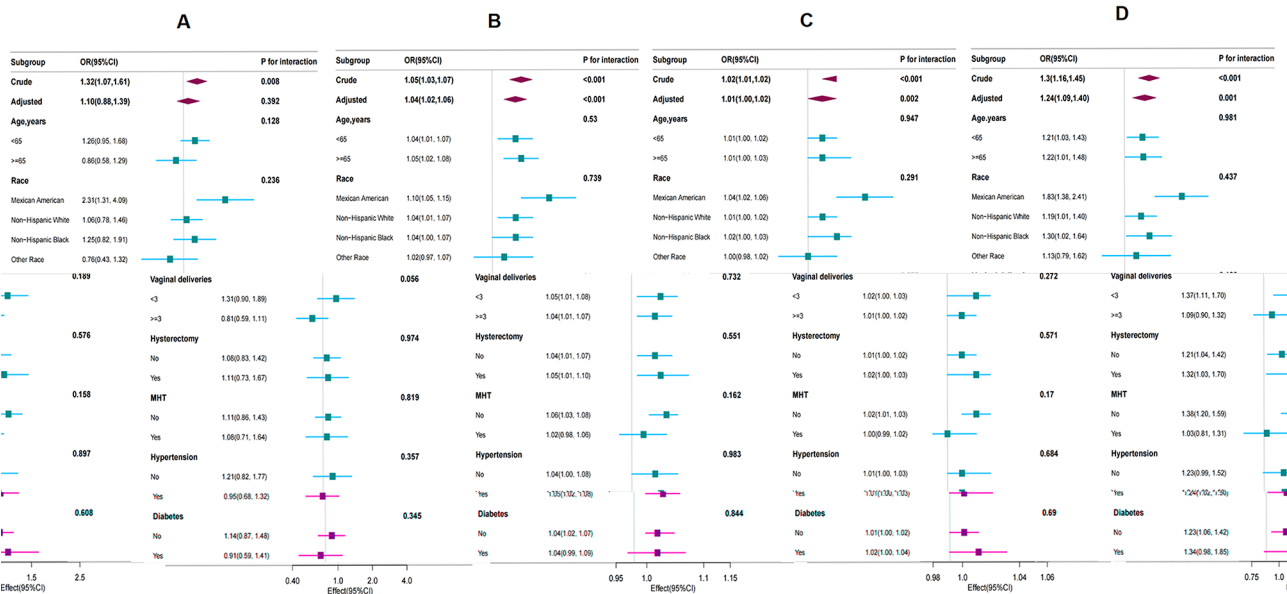


Fig. 4 Subgroup analysis showed the relationship between TyG (A), TyG-BMI (B), TyG-WC (C), TyG-WHtR (D) and SUI in different groups

Abbreviations

SUI	Stress urinary incontinence
IR	Insulin resistance
TyG	Triglyceride-glucose
NHANES	National Health and Nutrition Examination Survey
TyG-BMI	Triglyceride-glucose waist circumference
TyG-WC	Standard Deviation
TyG-WHtR	Triglyceride-glucose waist-height ratio
OR	Odds ratio
CI	Confidential interval
ROC	Receiver operating characteristics
UI	Urine incontinence
CVD	Cardiovascular disease
AIP	Atherogenic index of plasma
PIR	Poverty-to-income ratio
MHT	Menopausal hormone therapy
AUC	Area under the curve
SD	Standard deviation
IQR	Interquartile distanc

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12944-024-02414-4>.

Supplementary Material 1

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Author contributions

XH was responsible for the study design, data extraction, and statistical analysis, as well as writing the manuscript.WH contributed to the study design, statistics, and revisions. LL participated in the study design, revision, and final review. All authors read and approved the final manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

The portions of this study involving human participants, human materials, or human data were conducted in accordance with the Declaration of Helsinki and were approved by the NCHS Ethics Review Board. The patients/ participants provided their written informed consent to participate in this study.

Competing interests

The authors declare no competing interests.

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