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Links Between the Triglyceride-Glucose Index, Combined Metabolic Indices, and Non-Suicidal Self-Injury in Adolescents with Depression: Exploring The Mediating Effect of Sleep Quality

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Abstract

This study aimed to investigate whether the Triglyceride-Glucose (TyG) index and its derived measures—TyG-BMI, TyG-WC, and TyG-WHtR—are linked to non-suicidal self-injury (NSSI) in adolescents diagnosed with Major Depressive Disorder (MDD), and to assess whether sleep quality serves as an intermediary factor in these associations. A total of 157 adolescents aged 12–18 years, all diagnosed with MDD, were enrolled from the Department of Mental Health at the Second Hospital of Lanzhou University between July 2022 and December 2024. Participants were separated into two groups based on DSM-5 criteria: those with NSSI (n = 78) and those without (n = 79). Blood samples collected after fasting were used to calculate the TyG index and its combined indices. Data were analyzed using multivariable logistic regression, restricted cubic spline analysis, mediation modeling, and ROC curve evaluation to examine predictive performance. Adolescents engaging in NSSI exhibited higher median TyG index values (8.23 [7.95–8.45]) compared with their non-NSSI peers (7.73 [7.33–8.21], $P < 0.001$). After adjusting for potential confounders, all TyG-related indices showed significant associations with NSSI, with the strongest effects observed among female participants (e.g., TyG: OR = 3.50, 95 percent CI: 1.82–6.74, $P < 0.001$). Sleep quality partially explained the connection between TyG and NSSI, accounting for 17.1% of the effect ($P = 0.026$). Among the combined indices, TyG-WC demonstrated moderate predictive ability for NSSI (AUC = 0.745, 95% CI: 0.666–0.824).These findings indicate that TyG and its derived indices are positively associated with NSSI behaviors in adolescents with MDD, and that sleep quality partially mediates these associations. These measures may serve as practical, cost-effective tools for early identification of adolescents at elevated risk for self-injurious behavior.

Keywords: Adolescents, Depressive disorder, Non-suicidal self-injury, Sleep quality, Triglyceride-glucose index

Introduction

Major Depressive Disorder (MDD) is a widespread psychiatric condition marked by persistent low mood and related functional impairments, often first appearing during adolescence [1]. Globally, roughly 3–4% of adolescents experience depressive symptoms severe enough to warrant clinical attention [2]. Non-suicidal self-injury (NSSI) refers to deliberate, self-directed harm without suicidal intent, including actions such as cutting, scratching, or burning the skin [3]. While often stigmatized, NSSI is thought to represent a maladaptive coping mechanism, frequently linked to emotional dysregulation, interpersonal difficulties, and heightened risk for further harmful behaviors, including suicidal ideation [4]. Research suggests that approximately half of adolescents with MDD engage in NSSI [5, 6], and those with both depression and NSSI tend to exhibit more severe symptoms and poorer clinical outcomes [7].

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Although traditionally considered a psychological response, evidence increasingly implicates biological factors in NSSI, particularly metabolic and inflammatory dysregulation [8]. The Triglyceride-Glucose (TyG) index, derived from fasting triglyceride and glucose concentrations, has emerged as a reliable marker of insulin resistance (IR) [9]. IR occurs when cells fail to respond effectively to insulin, prompting compensatory hyperinsulinemia to maintain glucose homeostasis [10]. Insulin resistance has been associated with multiple psychiatric conditions, including depression [11], and elevated TyG levels may correlate with symptom severity via inflammation, oxidative stress, and disrupted metabolic pathways [12, 13].

Recent studies highlight the reciprocal relationship between metabolic disturbances and sleep quality. TyG may partly reflect disrupted sleep, while poor sleep itself can exacerbate IR through neuroendocrine and inflammatory mechanisms [14–16]. Sleep patterns are influenced by psychosocial and behavioral factors—such as stress, emotional state, and circadian habits—which in turn affect metabolic regulation. Thus, while the TyG index represents downstream metabolic consequences, sleep represents a modifiable mediator in this pathway. Importantly, poor sleep has been linked to increased impulsivity, emotion regulation difficulties, and greater risk of NSSI in adolescents [17, 18].

Sex differences may further shape these dynamics. Adolescent girls are more susceptible to mood disorders, exhibit higher sensitivity to metabolic changes, and are more likely to engage in NSSI compared with boys [19, 20]. As such, analyses that account for sex differences are crucial for understanding these relationships.

While prior research has examined associations between TyG and depressive symptoms, its relationship with NSSI and predictive capacity in depressed adolescents remains poorly understood. Sleep quality may act as a key mediator, and sex may modulate these associations. This study therefore aimed to: (1) examine the links between TyG indices and NSSI; (2) assess the mediating role of sleep quality; and (3) explore potential sex-specific effects.

The study addressed four questions: (1) Are TyG and its combined indices associated with NSSI and sleep quality? (2) Does sleep quality mediate the TyG–NSSI relationship? (3) Are these associations moderated by sex? (4) Does sex influence the mediating role of sleep quality? We hypothesized that (1) higher TyG levels correlate with NSSI and poorer sleep quality; (2) sleep quality partially mediates the TyG–NSSI association; (3) the TyG–NSSI link differs between sexes; and (4) sex moderates the mediating effect of sleep quality.

Materials and Methods

Study population

This study recruited 157 adolescents aged 12–18 years with MDD from the Department of Mental Health at the Second Hospital of Lanzhou University between July 2022 and December 2024. Eligibility criteria included: (1) diagnosis of a current depressive episode according to DSM-5 criteria; (2) HAMD-17 score ≥17; (3) age between 12 and 18 years; and (4) informed consent from both participants and their legal guardians. Exclusion criteria were: (1) neurological, major physical, or endocrine disorders; (2) history or current diagnosis of schizophrenia, bipolar disorder, substance use, or substance-induced psychiatric disorders; (3) pregnancy or lactation; (4) first-degree family history of bipolar disorder or mania; (5) modified electroconvulsive therapy in the past 6 months; and (6) hearing or color vision impairments.

All participants were treated with selective serotonin reuptake inhibitors (SSRIs) during the study period, and none were receiving lipid-lowering therapy. Based on DSM-5 criteria for NSSI, participants were categorized into NSSI (n = 78) and non-NSSI (n = 79) groups. Ethical approval was obtained from the Ethics Committee of the Second Hospital of Lanzhou University (Approval No. 2020A-134), and written informed consent was obtained from all participants and their guardians. **Figure 1** illustrates participant selection, exclusion criteria, and study design.

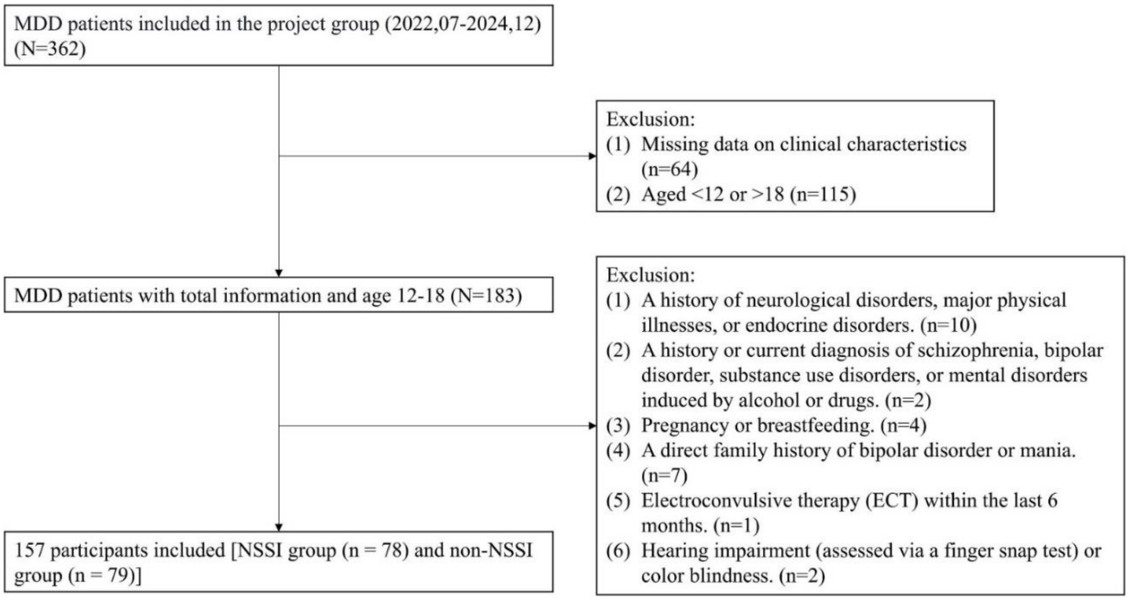


Figure 1. Diagram of participant recruitment and screening.

Key measurements

Demographics and baseline characteristics

Demographic and lifestyle information was collected using a tailored questionnaire, covering participants' age, gender, monthly household income per capita (PCI), body mass index (BMI), waist circumference (WC), and habits such as smoking and alcohol use. Following confirmation of diagnosis by a senior psychiatrist, a trained clinician provided participants and their guardians with a detailed explanation of the study's purpose and procedures. All evaluations and sample collections were performed by trained personnel who had completed reliability training, achieving a Kappa coefficient of 0.85 to ensure assessment consistency.

Evaluation of Non-Suicidal Self-Injury (NSSI)

NSSI was determined according to DSM-5 criteria through structured interviews conducted by qualified psychiatrists or clinical psychologists. To maintain standardization, all assessors underwent a comprehensive training program in the application of DSM-5 criteria for NSSI. A subset of interviews was randomly re-evaluated by a second rater to assess inter-rater reliability, resulting in a high agreement (Kappa = 0.80). The diagnostic requirements were as follows [21]:

- Engagement in deliberate self-harming behaviors (e.g., cutting, burning, scratching, needle-sticking, biting, or hitting) on at least five occasions within the past year, intended to cause mild or moderate injury.
- Behavior motivated by emotional or cognitive relief, resolution of interpersonal conflicts, or the generation of positive feelings.
- The self-injury is associated with at least one of the following: interpersonal difficulties, persistent negative thoughts or emotions, repeated engagement over time, or frequent uncontrollable self-harm thoughts.
- Actions are socially non-normative (excluding behaviors like nail-biting or scab-picking) and are not part of cultural, religious, or cosmetic practices.
- Behaviors or their consequences significantly disrupt academic, social, or other essential functioning.
- Behavior does not occur exclusively during psychotic episodes, delirium, intoxication, withdrawal, or as stereotyped patterns in neurodevelopmental disorders.
- The behavior is not better explained by another psychiatric or medical condition.

Psychological and sleep assessments

- Suicidal Thoughts: Measured using the Chinese adaptation of the Beck Suicidal Ideation Scale (BSSI), where the first five items (scored 0–3) assess severity of suicidal thinking; higher scores indicate greater suicidal ideation. Cronbach's alpha was 0.78 (95% CI: 0.76–0.83) [22].

- Depression Severity: Assessed with the 17-item Hamilton Depression Rating Scale (HAMD-17); higher total scores indicate more severe depressive symptoms. Cronbach's alpha was 0.88 (95% CI: 0.86–0.90) [23].
- Anxiety Level: Evaluated using the Hamilton Anxiety Rating Scale (HAMA), where elevated scores reflect greater anxiety. Cronbach's alpha was 0.92 (95% CI: 0.90–0.93) [24].
- Sleep Quality: Assessed with the Pittsburgh Sleep Quality Index (PSQI), encompassing seven domains: subjective sleep quality, sleep latency, duration, efficiency, disturbances, use of sleep medication, and daytime dysfunction. Total scores range from 0–21, with higher scores representing poorer sleep. Cronbach's alpha in this study was 0.84 (95% CI: 0.82–0.87) [25].

Blood collection and biomarker analysis

Participants provided 6 mL fasting venous blood samples in the morning. Plasma was separated via centrifugation at 3000 rpm for 15 minutes, labeled, and stored at −80°C until analysis. Biochemical markers, including fasting plasma glucose (FPG, mg/dL), triglycerides (TG, mg/dL), total cholesterol (TC, mg/dL), high-density lipoprotein cholesterol (HDL-C, mg/dL), and low-density lipoprotein cholesterol (LDL-C, mg/dL), were quantified using a fully automated analyzer.

Metabolic indices were derived using the following formulas [12]:

- TyG index: ln [TG × FPG / 2]
- TyG-BMI: TyG × BMI
- TyG-WC: TyG × WC
- TyG-WHtR: TyG × (WC/Height)
- METS-IR: ln (2 × FPG + TG) × BMI / ln (HDL-C)
- RC: TC − HDL-C − LDL-C

BMI was calculated as weight (kg) divided by height squared (m^2), and WC was measured in centimeters.

Data quality and follow-up

To ensure data accuracy, participants were followed for at least 1 year after enrollment. Patients unable to attend in-person visits were contacted via phone to update diagnostic status and verify inclusion/exclusion criteria. This approach ensured that only participants meeting the study requirements were included in analyses.

Covariates

Numerical covariates encompassed participant age. Nominal variables, applied for stratification purposes, consisted of gender (male or female), level of education achieved (below secondary school completion, secondary school graduate, beyond secondary school), household income per person on a monthly basis (up to 1250 yuan, 1251 to 2500 yuan, exceeding 2500 yuan), drinking habits (current/former/never), tobacco use (current/former/never), and existence of accompanying health issues (present/absent). Accompanying health issues were identified by the occurrence of one or more of the following participant-reported diagnoses: diabetes mellitus, abnormal blood lipids, renal insufficiency, renal calculi, cardiac insufficiency, cerebrovascular accident, hepatic disorders, rheumatoid joint disease, or malignant neoplasms.

Analytical methods

Every statistical computation was carried out using R programming environment, release 4.5.1 (accessible at https://cran.r-project.org/), incorporating dedicated libraries for examining interactions. Statistical significance was determined at a two-tailed probability value below 0.05. Data for continuous variables following a normal pattern were summarized as average values accompanied by standard deviations, with intergroup differences evaluated through unpaired t-tests. Non-normally distributed continuous measures were summarized using medians along with interquartile ranges, and comparisons across groups employed the Wilcoxon rank-sum procedure. Discrete variables were summarized with counts and proportions [n (%)], while group differences were tested via chi-squared analyses or Fisher's exact procedure in cases where criteria were violated.

Associations between the triglyceride-glucose (TyG) index, related composite measures, sleep characteristics, and non-suicidal self-injury (NSSI) were examined through multiple-variable logistic regression models and generalized linear modeling approaches. To explore possible gender-specific patterns, the entire set of evaluations was performed separately for males and females. Additionally, intermediary effect assessment was undertaken to assess if symptoms of depression acted as a mediating factor in the link connecting the TyG index to NSSI. The intermediary analysis involved 1,000 bootstrapped samples to derive indirect effect estimates, calculate the mediated proportion, and determine statistical relevance. Lastly, receiver operating characteristic (ROC) plots were constructed based on adjusted multiple logistic regression frameworks that accounted for age, gender, body mass index, and additional pertinent factors. Individual metabolic markers (TyG, TyG combined with BMI, TyG combined with waist circumference, TyG combined with waist-to-height ratio) were entered one at a time as the primary independent variable. Values for the area under the curve alongside 95% confidence intervals were derived to evaluate predictive performance.

Results and Discussion

Baseline features of study participants

The study involved 157 young individuals diagnosed with major depressive disorder, among whom 78 (49.68%) indicated engagement in NSSI, whereas 79 (50.32%) did not. In terms of behavioral patterns, those engaging in NSSI displayed greater prevalence of alcohol intake (29.49% compared to 10.13%, P = 0.004) and tobacco usage (20.51% compared to 6.33%, P = 0.015). From a clinical standpoint, participants with NSSI demonstrated heightened severity in depression (HAMD scores: 22.85 ± 5.31 versus 19.32 ± 7.21, P < 0.001), anxiety (HAMA scores: 27.30 ± 7.01 versus 24.19 ± 9.57, P = 0.021), and thoughts of suicide (BSSI scores: 2.37 ± 0.54 versus 1.82 ± 0.79, P < 0.001), together with diminished sleep characteristics (PSQI scores: 14.17 ± 4.13 versus 9.44 ± 5.18, P < 0.001).

Regarding body composition and lipid profiles, the group with NSSI presented elevated waist measurements (69.12 ± 4.42 versus 66.40 ± 4.17, P < 0.001), waist-to-height proportions (41.41 ± 3.06 versus 40.19 ± 3.09, P = 0.014), overall cholesterol concentrations, triglyceride concentrations, and low-density lipoprotein cholesterol concentrations. Furthermore, individuals reporting NSSI showed markedly increased values for the TyG index and its integrated variants (TyG-BMI, TyG-WC, TyG-WHtR; all with P values under 0.01). Comprehensive details are available in **Table 1.**

Table 1. Comparison of variables between adolescents with and without NSSI

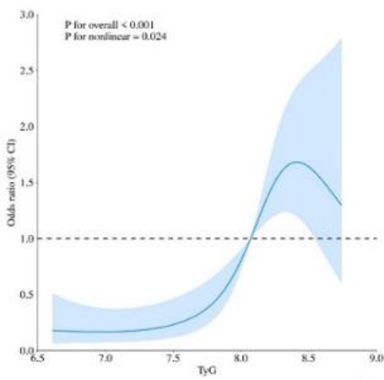
Variable	Total (n = 157)	NSSI (n = 78)	Non-NSSI (n = 79)	P-value	Test Statistic
Age (years), Mean ± SD	15.36 ± 1.77	15.44 ± 1.94	15.29 ± 1.59	0.610	t = -0.51
Sex, n (%)				0.034	χ^2 = 4.48
Male	55 (35.0)	21 (26.9)	34 (43.0)		
Female	102 (65.0)	57 (73.1)	45 (57.0)		
Education level, n (%)				0.813	χ^2 = 0.41
Below high school	67 (42.7)	32 (41.0)	35 (44.3)		
High school	76 (48.4)	38 (48.7)	38 (48.1)		
Above high school	14 (8.9)	8 (10.3)	6 (7.6)		
Monthly household income (PCI, yuan), n (%)				0.950	χ^2 = 0.10
≤1250	46 (29.3)	23 (29.5)	23 (29.1)		
1251–2500	69 (44.0)	35 (44.9)	34 (43.0)		
>2500	42 (26.8)	20 (25.6)	22 (27.9)		
Comorbidities, n (%)				0.140	χ^2 = 2.18
Yes	36 (22.9)	14 (17.9)	22 (27.8)		
No	121 (77.1)	64 (82.1)	57 (72.2)		
Alcohol use, n (%)				0.004	-
Current	31 (19.8)	23 (29.5)	8 (10.1)		
Former	2 (1.3)	1 (1.3)	1 (1.3)		
Never	124 (79.0)	54 (69.2)	70 (88.6)		
Smoking status, n (%)				0.015	-
Current	21 (13.4)	16 (20.5)	5 (6.3)		
Former	4 (2.6)	1 (1.3)	3 (3.8)		
Never	132 (84.1)	61 (78.2)	71 (89.9)		

Frequency of NSSI (per year), Mean ± SD	1.73 ± 2.07	3.47 ± 1.59	0.00 ± 0.00	<0.001	t = -19.36
Frequency of NSSI (per month), Mean ± SD	6.96 ± 7.85	13.12 ± 6.84	0.89 ± 1.38	<0.001	t = -15.48
Self-harm methods, n (%)				<0.001	-
None	47 (29.9)	0 (0.0)	47 (59.5)		
Cutting	83 (52.9)	58 (74.4)	25 (31.7)		
Scratching	6 (3.8)	4 (5.1)	2 (2.5)		
Burning	11 (7.0)	8 (10.3)	3 (3.8)		
Needle-sticking	5 (3.2)	4 (5.1)	1 (1.3)		
Biting	3 (1.9)	2 (2.6)	1 (1.3)		
Hitting	2 (1.3)	2 (2.6)	0 (0.0)		
HAMD score, Mean ± SD	21.07 ± 6.56	22.85 ± 5.31	19.32 ± 7.21	<0.001	t = -3.50
HAMA score, Mean ± SD	25.74 ± 8.51	27.30 ± 7.01	24.19 ± 9.57	0.021	t = -2.33
BSSI score, Mean ± SD	2.10 ± 0.73	2.37 ± 0.54	1.82 ± 0.79	<0.001	t = -5.07
DSST score, Mean ± SD	52.66 ± 12.37	51.76 ± 13.00	53.56 ± 11.74	0.364	t = 0.91
PSQI score, Mean ± SD	11.79 ± 5.24	14.17 ± 4.13	9.44 ± 5.18	<0.001	t = -6.32
Height (m), Mean ± SD	1.66 ± 0.08	1.67 ± 0.08	1.66 ± 0.09	0.245	t = -1.17
Weight (kg), Mean ± SD	55.78 ± 11.21	57.27 ± 11.41	54.32 ± 10.88	0.099	t = -1.66
Waist Circumference (cm), Mean ± SD	67.75 ± 4.49	69.12 ± 4.42	66.40 ± 4.17	<0.001	t = -3.97
BMI (kg/m²), Mean ± SD	20.11 ± 3.67	20.47 ± 3.93	19.75 ± 3.39	0.223	t = -1.22
Waist-to-Height Ratio, Mean ± SD	40.79 ± 3.13	41.41 ± 3.06	40.19 ± 3.09	0.014	t = -2.49
Fasting Plasma Glucose (mg/dL), Median (Q1, Q3)	83.88 (78.84, 88.02)	84.51 (78.97, 88.96)	83.34 (78.93, 87.39)	0.368	Z = -0.90
Total Cholesterol (mg/dL), Median (Q1, Q3)	131.48 (108.28, 150.43)	147.91 (130.03, 169.18)	109.82 (96.67, 131.48)	<0.001	Z = -7.06
Triglycerides (mg/dL), Median (Q1, Q3)	73.51 (46.06, 106.28)	86.80 (65.76, 113.59)	50.48 (38.53, 84.14)	<0.001	Z = -4.34
HDL-C (mg/dL), Median (Q1, Q3)	42.92 (38.67, 49.11)	42.54 (33.74, 49.40)	43.70 (39.25, 48.72)	0.628	Z = -0.48
LDL-C (mg/dL), Median (Q1, Q3)	78.50 (61.49, 97.45)	96.09 (84.40, 110.31)	63.03 (52.78, 75.02)	<0.001	Z = -8.65
TyG index, Median (Q1, Q3)	8.07 (7.53, 8.39)	8.23 (7.95, 8.45)	7.73 (7.33, 8.21)	<0.001	Z = -4.37
TyG-BMI, Median (Q1, Q3)	153.74 (140.42, 176.82)	159.32 (145.55, 182.18)	146.77 (134.39, 166.85)	0.007	Z = -2.68
TyG-WC, Median (Q1, Q3)	536.37 (502.45, 573.84)	559.02 (530.38, 588.22)	509.57 (471.47, 545.10)	<0.001	Z = -5.30
TyG-WHtR, Median (Q1, Q3)	322.18 (296.76, 347.48)	333.51 (317.21, 355.18)	302.70 (284.21, 328.58)	<0.001	Z = -4.78
METS-IR, Median (Q1, Q3)	28.16 (25.63, 32.58)	28.77 (26.04, 32.69)	27.61 (25.32, 32.16)	0.171	Z = -1.37
RC, Median (Q1, Q3)	8.12 (3.87, 13.92)	8.31 (5.12, 15.47)	8.12 (3.29, 13.92)	0.269	Z = -1.11

Links between the TyG index and non-suicidal self-injury

Following adjustment for age, gender, drinking habits, tobacco use, educational level, concomitant illnesses, and per capita income, elevated values of the TyG index along with its composite measures (TyG-BMI, TyG-WC, TyG-WHtR) demonstrated significant connections to heightened likelihood of NSSI and deteriorated sleep characteristics (all with P values below 0.01). Analyses using restricted cubic splines indicated that these relationships were largely nonlinear, displaying patterns that were either J-shaped or steadily rising **(Figure 2**). In particular, the probabilities of experiencing NSSI and impaired sleep rose more steeply once the TyG index and its derived metrics surpassed specific cutoff points.

Across the entire cohort, the TyG index continued to serve as a robust indicator for NSSI (adjusted odds ratio = 3.50, 95% confidence interval: 1.82–6.74, P < 0.001) and sleep characteristics (beta coefficient = 3.56, 95% confidence interval: 2.43–4.68, P < 0.001). When analyses were separated by gender, the relationships appeared more pronounced in female participants, where the adjusted odds ratio for NSSI attained 7.69 (95% confidence interval: 2.67–22.11, P < 0.001), while the corresponding links in male participants were less robust and lacked statistical significance. Likewise, the TyG-based measures showed reliable ties to reduced sleep quality in participants of both genders, although the magnitude of these effects was greater among females.



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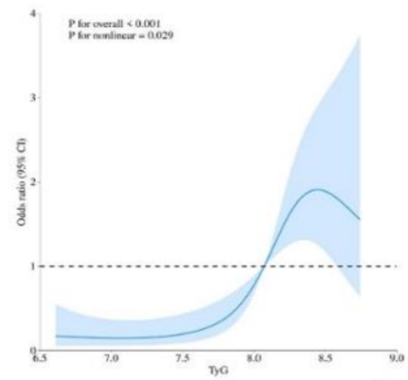

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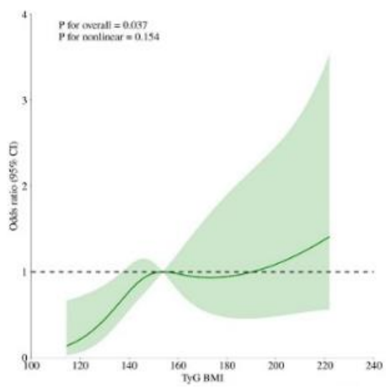

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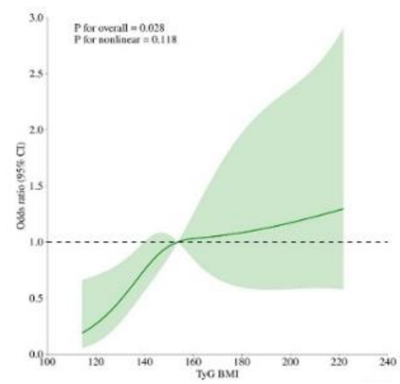

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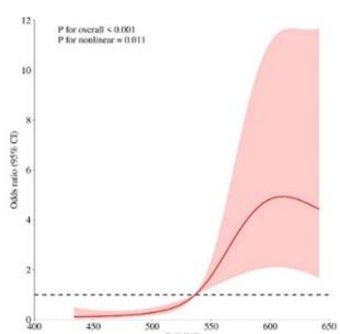

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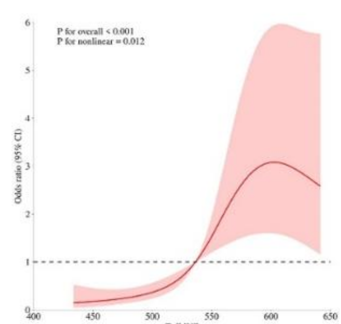

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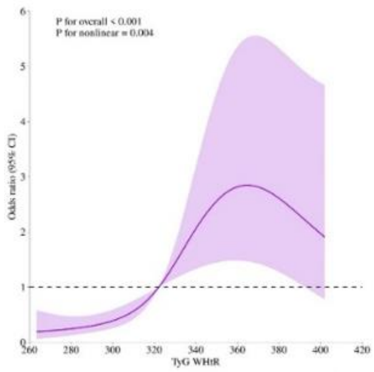

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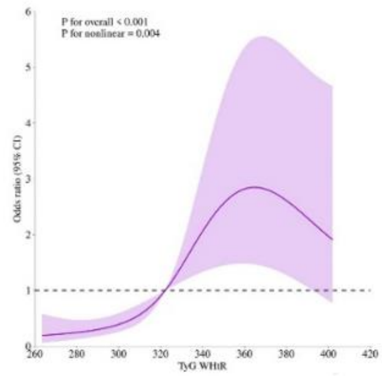


d2)

Figure 2. Relationships of metabolic indices with non-suicidal self-injury (NSSI): (a) TyG index and NSSI; (b) TyG-BMI index and NSSI; (c) TyG-WC index and NSSI; (d) TyG-WHtR index and NSSI.

Model 1 represents the unadjusted (crude) analysis; Model 2 represents the fully adjusted analysis controlling for age, gender, alcohol consumption, smoking status, educational attainment, concomitant illnesses, and per capita income.

Additionally, the presence of NSSI was independently and strongly linked to diminished sleep quality (adjusted odds ratio = 1.27, 95% confidence interval: 1.15–1.40, P < 0.001). Comprehensive findings are displayed in **Table 2** and **Figure 2.**

Table 2. Associations of TyG, TyG-BMI, TyG-WC, and TyG-WHtR indices with NSSI and sleep quality

Variable	Adjusted b/OR (95% CI)	P-value	Crude b/OR (95% CI)	P-value
TyG index vs. NSSI				
Total	3.5007 (1.8175–6.7403)	<0.001	3.1107 (1.7320–5.5800)	<0.001
Male	2.1656 (0.7289–6.4316)	0.1642	1.7490 (0.7262–4.2139)	0.2120
Female	7.6910 (2.6731–22.1110)	<0.001	5.1261 (2.2223–11.8235)	<0.001
TyG index vs. Sleep quality				
Total	3.5554 (2.4335–4.6773)	<0.001	3.5659 (2.4750–4.6568)	<0.001
Male	2.9273 (1.2235–4.6311)	0.0015	2.5228 (0.7892–4.2564)	<0.001
Female	3.9969 (2.5332–5.4606)	<0.001	4.1121 (2.7148–5.5094)	<0.001
TyG-BMI vs. NSSI				
Total	1.0135 (1.0026–1.0246)	<0.001	1.0125 (1.0025–1.0227)	<0.001
Male	1.0026 (1.0015–1.0038)	<0.001	0.9978 (0.9809–1.0150)	0.8000
Female	1.0246 (1.0076–1.0420)	0.0043	1.0225 (1.0069–1.0384)	0.0046
TyG-BMI vs. Sleep quality				
Total	0.0412 (0.0184–0.0641)	<0.001	0.0378 (0.0155–0.0600)	0.0011
Male	0.0334 (−0.0041–0.0708)	0.087	0.0286 (−0.0092–0.0664)	0.144
Female	0.0440 (0.0142–0.0738)	0.0047	0.0419 (0.0142–0.0690)	0.0038
TyG-WC vs. NSSI				
Total	1.0180 (1.0101–1.0259)	<0.001	1.0143 (1.0078–1.0208)	<0.001
Male	1.0087 (0.9976–1.0200)	0.1270	1.0078 (0.9983–1.0173)	0.1074
Female	1.0320 (1.0169–1.0473)	<0.001	1.0255 (1.0140–1.0371)	<0.001
TyG-WC vs. Sleep quality				
Total	0.0348 (0.0232–0.0464)	<0.001	0.0336 (0.0224–0.0447)	<0.001
Male	0.0294 (0.0113–0.0475)	0.0026	0.0263 (0.0077–0.0449)	0.0076
Female	0.0381 (0.0229–0.0532)	<0.001	0.0371 (0.0230–0.0513)	<0.001
TyG-WHtR vs. NSSI				
Total	1.0194 (1.0092–1.0296)	<0.001	1.0182 (1.0088–1.0278)	<0.001

Male	1.0069 (0.9913–1.0227)	0.3887	1.0039 (0.9912–1.0168)	0.5460
Female	1.0367 (1.0182–1.0555)	<0.001	1.0305 (1.0153–1.0460)	<0.001
TyG-WHtR vs. Sleep quality				
Total	0.0486 (0.0303–0.0669)	<0.001	0.0471 (0.0291–0.0651)	<0.001
Male	0.0391 (0.0113–0.0669)	0.0083	0.0360 (0.0085–0.0634)	0.0131
Female	0.0558 (0.0311–0.0804)	<0.001	0.0549 (0.0313–0.0786)	<0.001
NSSI vs. Sleep quality				
Total	1.2713 (1.1528–1.4027)	<0.001	1.2519 (1.1456–1.3663)	<0.001
Male	1.4305 (1.1049–1.8520)	0.0065	1.2907 (1.0779–1.5441)	0.0053
Female	1.2874 (1.1399–1.4540)	<0.001	1.2513 (1.1303–1.3846)	<0.001

Role of sleep characteristics as an intermediary between TyG index and non-suicidal self-injury

Assessment of intermediary pathways demonstrated that sleep quality substantially influenced the connection from the TyG index to non-suicidal self-injury in youth affected by major depressive disorder. The term ACME refers to the average causal mediation effect (reflecting the indirect component), ADE denotes the average direct effect, and PM represents the share of the overall effect explained through mediation by sleep quality.

For the combined group of participants, the adjusted ACME value was 0.0027 (95% confidence interval ranging from 0.00014 to 0.00942, P = 0.026), which corresponded to 17.1 percent of the full effect (overall effect: β = 0.0156, 95 percent confidence interval from 0.0040 to 0.0225). The remaining direct component (ADE) retained significance (β = 0.0130, 95 percent confidence interval from 0.0034 to 0.0187, P < 0.001), consistent with partial mediation.

Analyses conducted separately for each gender revealed a clear intermediary effect in females (adjusted ACME = 0.0040, 95 percent confidence interval from 0.0002 to 0.0136, P = 0.004; proportion explained by mediation = 29.3 percent), while no noteworthy mediation emerged among males. Complete data are shown in **Table 3** and **Figure 3.**

Table 3. Sleep quality as a mediator in the association between TyG index and NSSI

Variable	Crude b	P-value	95% CI (Lower, Upper)	Adjusted b	P-value	95% CI (Lower, Upper)
ACME (Indirect Effect)						
Total	0.0021	0.048	0.0001, 0.0079	0.0027	0.026	0.00014, 0.00942
Male	0.0002	0.770	-0.0011, 0.0056	0.0002	0.598	-0.0026, 0.0069
Female	0.0055	0.004	0.0004, 0.0165	0.0040	0.004	0.0002, 0.0136
ADE (Direct Effect)						
Total	0.0118	<0.001	0.0027, 0.0182	0.0130	<0.001	0.0034, 0.0187
Male	0.0063	0.006	0.0001, 0.0156	0.0048	0.048	0.0001, 0.0166
Female	0.0152	0.008	0.0029, 0.0211	0.0098	0.008	0.0009, 0.0159
Total Effect						
Total	0.0139	<0.001	0.0030, 0.0220	0.0156	<0.001	0.0040, 0.0225
Male	0.0065	<0.001	0.0001, 0.0168	0.0050	0.024	0.0001, 0.0176
Female	0.0206	<0.001	0.0041, 0.0287	0.0139	<0.001	0.0013, 0.0230
Proportion Mediated (PM)						
Total	0.1520	0.048	0.0017, 0.4244	0.1710	0.026	0.0201, 0.4771
Male	0.0255	0.770	-0.1503, 0.4555	0.0466	0.980	-0.6406, 0.7022
Female	0.2660	0.004	0.0625, 0.7293	0.2927	0.004	0.0839, 0.7832

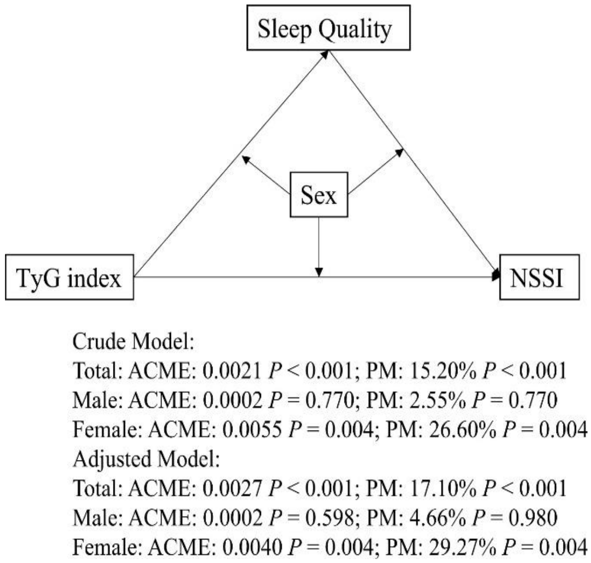
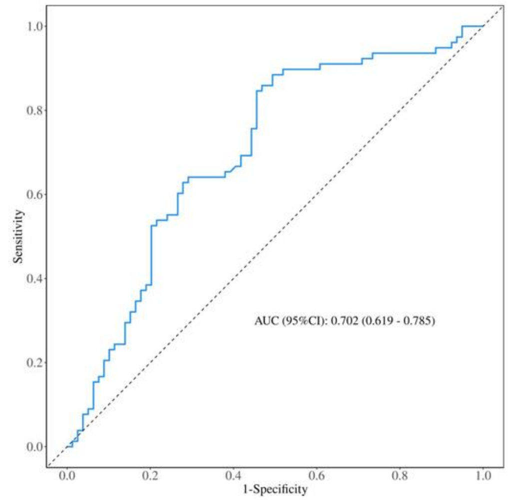


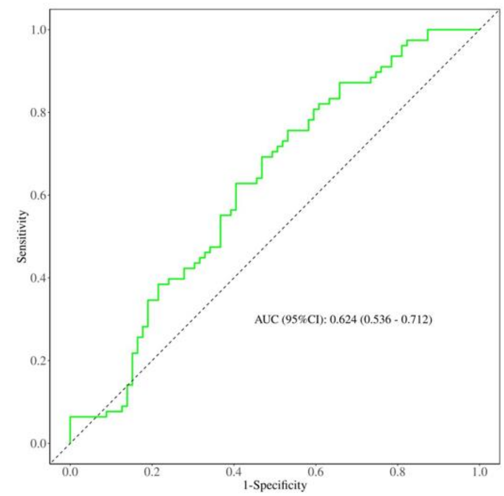
Figure 3. Intermediary Models. This figure depicts the mediation frameworks where the TyG index serves as the predictor variable, sleep quality acts as the intermediary factor, and non-suicidal self-injury (NSSI) functions as the outcome variable. ACME indicates average causal mediation effects; ADE indicates average direct effect; PM indicates proportion mediated.

Analysis of receiver operating characteristic curves

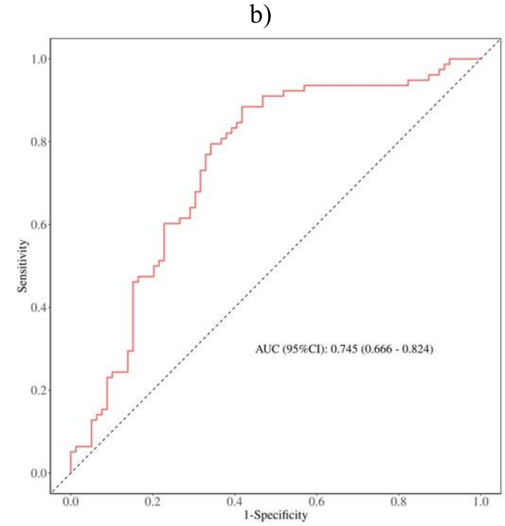
Receiver operating characteristic curves, constructed from logistic regression models adjusted for relevant confounders, showed that each of the four metabolic markers possessed reasonable capability to distinguish adolescents engaging in NSSI. These curves display the trade-off between false positive rates (FPR) and true positive rates (TPR), while the area under the curve (AUC) quantifies overall classification accuracy. The AUC values along with their 95% confidence intervals were: TyG index, 0.702 (0.619–0.785); TyG-BMI, 0.624 (0.536–0.712); TyG-WC, 0.745 (0.666–0.824); and TyG-WHtR, 0.721 (0.639–0.803). Comprehensive findings are illustrated in **Figure 4.**



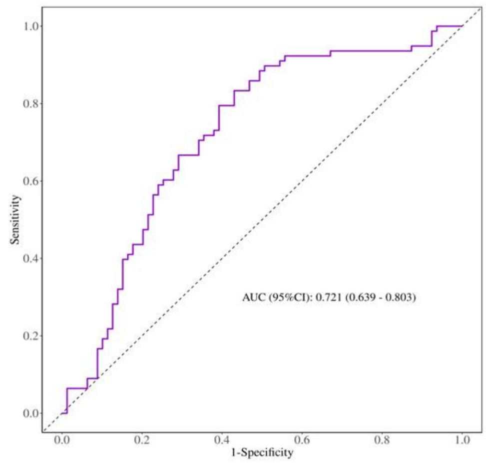
a)



b)



c)



d)

Figure 4. ROC curve analysis of diagnostic performance. (a) TyG, (b) TyG-BMI, (c) TyG-WC, and (d) TyG-WHtR for predicting NSSI.

This research explored the relationships between the TyG index, its derived measures, sleep quality, and nonsuicidal self-injury (NSSI) in a cohort of 157 adolescents diagnosed with depressive disorder, recruited from the Department of Mental Health at the Second Hospital of Lanzhou University between July 2022 and December 2024. The study revealed notable associations, often nonlinear (J-shaped), between TyG-related metrics and the likelihood of NSSI and poor sleep, with these associations being particularly pronounced in female participants. Sleep quality emerged as a significant mediator in the link between TyG and NSSI. Given that the TyG index is a cost-effective and practical surrogate marker of insulin resistance (IR), overcoming the limitations of more complex assessments such as HEC and HOMA-IR [26–28], it may serve as a useful tool for identifying adolescents with depression at elevated risk for self-injury.

The strong correlation between TyG index and NSSI underscores the potential role of IR as a biological mechanism contributing to self-injurious behaviors. Although the precise pathways remain to be fully defined, IR may influence NSSI risk through several interconnected mechanisms. IR is known to alter brain neurochemistry, including dopamine dysfunction and increased monoamine oxidase activity, which can promote emotional dysregulation and depressive behaviors central to NSSI [29–32]. Moreover, IR-related chronic inflammation [33] can affect neural circuits involved in emotion regulation and impulse control [34], potentially lowering the threshold for maladaptive coping strategies like self-harm. The observed J-shaped pattern suggests a critical threshold beyond which metabolic dysregulation significantly elevates neuropsychiatric risk, highlighting the need for targeted intervention in high-risk adolescents.

Mediation analyses indicated that sleep quality partially explained the association between the TyG index and NSSI. Elevated TyG values were linked to poorer sleep, which in turn was associated with higher NSSI risk. Mechanistically, insulin resistance and elevated triglycerides may disrupt circadian rhythms and the secretion of hormones regulating sleep, such as melatonin and cortisol [35, 36]. Sleep disturbances can further impair prefrontal-limbic circuits responsible for emotional regulation, increasing impulsivity, intensifying negative emotions, and reducing coping capacity [37]. In adolescents, these effects may increase vulnerability to self-harm as a maladaptive strategy for managing emotional distress. These results align with prior research demonstrating that poor sleep exacerbates emotional dysregulation, impulsivity, and negative mood—well-established risk factors for NSSI. Identifying sleep as a mediating factor suggests that interventions targeting sleep could mitigate the impact of metabolic disturbances on self-injury risk in adolescents with elevated TyG indices.

Sex-specific analyses revealed stronger associations in females, with higher TyG levels correlating with poorer sleep and increased NSSI risk compared to males. This supports prior evidence that adolescent girls may be more susceptible to the psychological consequences of metabolic dysfunction [38, 39]. Our findings extend this understanding by demonstrating that sleep quality serves as a key mediating pathway in females, but not in males. Potential mechanisms include hormonal fluctuations (e.g., estrogen, progesterone) affecting both insulin sensitivity and emotional regulation [40], as well as sex differences in stress response systems and neural circuits governing impulse control [41]. These results highlight the importance of considering sex-specific pathways, particularly sleep disturbances, when assessing metabolic risk for self-injurious behaviors and designing targeted preventive strategies.

This is the first study to investigate the link between the TyG index and NSSI in adolescents with depression. Among the indices examined, TyG-WC demonstrated the highest predictive accuracy, suggesting that integrating markers of insulin resistance and central obesity provides better risk stratification than measuring IR alone. This emphasizes the clinical relevance of assessing central adiposity in the metabolic evaluation of adolescents with depressive disorders.

Nevertheless, several limitations must be acknowledged. The cross-sectional design prevents causal inference, leaving uncertainty regarding the temporal direction of the associations between TyG, sleep, and NSSI. The sample size was modest, particularly for sex-stratified analyses, which may reduce statistical power and increase the likelihood of chance findings. All participants were hospitalized, limiting generalizability to broader adolescent populations, and the absence of healthy controls constrains comparative analyses. Genetic predispositions and early life experiences, such as childhood trauma or socioeconomic disadvantage, may also influence both metabolic and mental health outcomes, complicating interpretation [42, 43]. Future longitudinal studies in more diverse populations are warranted to clarify causal pathways and explore the contributions of genetic and psychosocial factors.

Conclusion

This study demonstrates significant associations between the TyG index, its derived measures, sleep quality, and NSSI among adolescents with depressive disorder. The relationships were nonlinear, with higher TyG-related values corresponding to increased NSSI risk, particularly in females. Sleep quality partially mediated this relationship, highlighting its potential as an intervention target. Of the indices examined, TyG-WC showed the strongest predictive capacity for identifying adolescents at elevated NSSI risk. These findings suggest that the TyG index and its derivatives could serve as practical, low-cost tools for early identification and targeted prevention of self-injurious behaviors in clinical settings.

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