

Original Article

Association between the triglyceride-glucose index and severity of abnormal uterine bleeding in perimenopausal women: a retrospective single-center study

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Received June 4, 2026; Accepted August 14, 2026; Epub October 15, 2026; Published October 30, 2026

Abstract: Objectives: To evaluate the association between the triglyceride-glucose (TyG) index, a surrogate marker of insulin resistance (IR), and the severity of abnormal uterine bleeding (AUB) in perimenopausal women. Methods: A single-center retrospective observational study was conducted from January 1, 2024 to December 31, 2025 on perimenopausal women diagnosed with AUB. The TyG index was calculated as $\ln(\text{fasting triglycerides [mg/dL]} \times \text{fasting glucose [mg/dL]}/2)$ and was analyzed both as a continuous variable and in tertiles. AUB severity was graded using a composite measure of bleeding pattern, hemoglobin (Hb) level, and endometrial findings. Multivariable logistic regression and ordinal regression were used to assess the association, with adjustment for demographic, reproductive, and metabolic covariates. Receiver operating characteristic (ROC) curve analysis evaluated discrimination. Results: A total of 246 women were included (mean age 48.3 years). Eighty-eight women (35.8%) had severe AUB. The mean TyG index increased across severity strata (mild 8.41 ± 0.39 , moderate 8.69 ± 0.41 , severe 8.97 ± 0.44 ; P for trend <0.001). Each one-unit increase in TyG index conferred increased odds of severe AUB (adjusted odds ratio [OR] 3.94; 95% confidence interval [CI] 2.18-7.12; $P<0.001$). Compared to the lowest tertile, the highest TyG tertile had an adjusted OR of 4.62 (95% CI 2.21-9.66; P for trend <0.001). The area under the ROC curve (AUC) for the TyG index was 0.74 (95% CI 0.68-0.81), with an optimal cut-off of 8.71. Conclusions: A higher TyG index is independently associated with increasing severity of AUB in perimenopausal women in a dose-dependent manner. The TyG index may serve as a valuable, low-cost tool for risk stratification and supports the observation that perimenopausal AUB is associated with metabolic dysregulation.

Keywords: Abnormal uterine bleeding (AUB), triglyceride-glucose (TyG) index, insulin resistance, perimenopause, menopausal transitions, endometrial pathology, retrospective observational study

Introduction

Abnormal uterine bleeding (AUB) is a common concern for women seeking gynecologic services and accounts for nearly 33% of all outpatient gynecologic visits, with a particularly high incidence during the menopausal transition [1]. The International Federation of Gynecology and Obstetrics (FIGO) classification system (PALM-COEIN) helps distinguish structural causes (polyp, adenomyosis, leiomyoma, malignancy, and hyperplasia) from non-structural causes (coagulopathy, ovulatory dysfunction, endometrial, iatrogenic, or unexplained) [2].

The PALM-COEIN classification system and its revisions provide a common language for clinical and research activities [3].

The menopausal transition is characterized by menstrual irregularity, including persistent cycle length variability, prolonged amenorrhea, uneven ovarian steroid production, and increased anovulatory cycles [4]. During perimenopause, the differential diagnosis of abnormal uterine bleeding is expanded to include endometrial hyperplasia and carcinoma. This broad differential makes perimenopausal AUB particularly concerning [5]. Abnormal uterine

bleeding is more than just an inconvenience. Heavy and prolonged bleeding can result in iron deficiency anemia, impaired quality of life and work productivity, prolonged hospital stays, blood transfusions, and an increased risk of surgery [6].

Recent studies have identified mechanisms of metabolic dysregulation that may be linked to endometrial disorders. Insulin resistance and hyperinsulinemia enhance endometrial cell proliferation, decrease sex hormone-binding globulin (thereby increasing bioavailable estrogen), and amplify insulin-like growth factor and inflammatory signaling. Together, these effects promote a proliferative, estrogen-dominant endometrial environment [7]. Insulin resistance has been reported in a large number of perimenopausal women with endometrial disorders. One study found insulin resistance was present in 57% of women with confirmed endometrial disorders, while only 32% of the women with a histologically normal endometrial sample had similar findings [8].

More recent publications have made connections between the disturbances in metabolism and endometrial bleeding. A study of reproductive-aged women found that hyperinsulinemia was associated with AUB (odds ratio 3.0), leading to the hypothesis that the uterus may serve as a metabolic end organ [9]. Similar studies that have focused on women with polycystic ovary syndrome have found that hyperinsulinemia disturbed the endometrial microenvironment and contributed to abnormal endometrial bleeding through multiple pathways including, but not limited to, sex-steroid metabolism and the PI3K/AKT signaling pathway [10].

The hyperinsulinemic-euglycemic clamp and homeostasis model assessment (HOMA-IR) are costly and impractical for routine use. The triglyceride-glucose (TyG) index, derived from fasting triglyceride and glucose levels, is an inexpensive and reliable surrogate for insulin resistance with excellent performance across various populations [11]. In women specifically, the TyG index has been validated against surrogates for insulin resistance within the insulin resistance surrogates for Polycystic Ovary Syndrome (PCOS), and its utility to capture the presence of insulin sensitivity has been reported with a cut-off of approximately 8 [12].

The TyG index has been associated with endometrial neoplasia. A retrospective cohort study showed that women with endometrial carcinoma and atypical endometrial hyperplasia had significantly elevated TyG levels compared to women with a normal endometrial lining. TyG levels increased progressively with neoplastic risk and were independently associated with advanced cancer stage and higher grade endometrial de-differentiation [13]. Joint-effect analyses further suggested that the combined effect of the TyG index and body mass index influences endometrial cancer risk, with the TyG effect partially mediated by adiposity [14].

Despite these advances, there is limited literature on the association between the TyG index and AUB severity beyond its relationship with endometrial neoplasia. This gap is particularly notable in perimenopausal women, in whom AUB is most prevalent and metabolic risk accelerates during the menopausal transition [15]. Therefore, we conducted a single-center, retrospective study to examine the association between the TyG index and AUB severity, with emphasis on its ability to discriminate severe disease in perimenopausal women.

Patients and methods

Study design and setting

This study was approved by the Ethics Committee of Lanxi Hospital of Traditional Chinese Medicine (Approval No. LZY-LSL-202606). Owing to the retrospective nature and use of de-identified data, the requirement for individual informed consent was waived by the Ethics Committee. In this single-center, retrospective observational study, we reviewed the medical records of perimenopausal women who presented with AUB at our hospital between January 1, 2024, and December 31, 2025. Since both the TyG index and AUB severity were derived from routinely recorded clinical and laboratory data, we focused on associations rather than causal relationships. This study followed the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines for observational studies, and the analysis strategy was prespecified.

Participants and eligibility criteria

Eligible participants were perimenopausal women, defined according to the Stages of Reproductive Aging Workshop (STRAW+10) criteria as women aged 40-55 years with irregular menstrual cycles (persistent variation ≥ 7 days in consecutive cycle lengths, or ≥ 60 days of amenorrhea) and a clinical diagnosis of AUB. Inclusion criteria: (1) age 40-55 years; (2) AUB classified under the FIGO PALM-COEIN framework; (3) baseline fasting triglyceride and glucose levels available within 4 weeks of the visit; and (4) complete records for AUB severity grading. Exclusion criteria: (1) current pregnancy or bleeding within 12 weeks of delivery or abortion, (2) a diagnosed endometrial carcinoma or any other female reproductive system cancer, (3) a bleeding disorder or current use of anticoagulant drugs, (4) the prior use of hormonal medications, including the combined oral contraceptive pill, hormone replacement therapy, or a levonorgestrel IUS, within the last 3 months, (5) diabetes, with the use of glucose-lowering and/or cholesterol-lowering medication that would interfere with the TyG index, and (6) incomplete laboratory or clinical data. Out of 412 records screened, 246 women fulfilled all the criteria and made up the analytic cohort. The sample size was determined by all eligible patients identified during the predefined study period; no *a priori* sample size calculation was performed.

Exposure: triglyceride-glucose index

Patients were subjected to a venous blood draw after a minimum of eight hours of fasting. The concentration of triglycerides and plasma glucose was determined using the hospital's automated clinical chemistry platform. The TyG index was calculated as: $\text{TyG} = \ln [\text{fasting triglycerides (mg/dL)} \times \text{fasting plasma glucose (mg/dL)} / 2]$. The TyG index was analyzed in two different ways. First, it was treated as a continuous variable, with effect estimates interpreted per one-unit increase. Second, it was categorized into tertiles (T1 = lowest; T2 = intermediate; T3 = highest) to evaluate dose-response relationships, with the lowest tertile as the reference group. Tertile cut-offs were derived from the study sample distribution. Finally, an optimal cut-off value was determined using receiver operating characteristic (ROC) curve analysis to facilitate clinical translation.

Outcome: grading of AUB severity

The primary outcome was clinical severity of AUB, graded using a prespecified composite system based on three domains. The first domain was bleeding pattern, assessed using a structured pictorial blood loss assessment score, with prolonged (> 7 days) or frequent (> 1 cycle in a 21-day period) bleeding noted. The second domain was hemoglobin concentration at presentation, an objective biomarker of total blood loss. The third domain was endometrial assessment, including transvaginal ultrasound measurement of endometrial thickness and, when available, histopathology. Severity was graded as: mild (regular or minimally prolonged bleeding with hemoglobin ≥ 110 g/L and the absence of structural or proliferative abnormality), moderate (heavy or prolonged bleeding with hemoglobin 90-109 g/L and/or endometrial thickening without atypia), and severe (heavy, prolonged, or frequent bleeding, with hemoglobin < 90 g/L and/or endometrial hyperplasia and/or the need for urgent intervention such as blood transfusion, hospitalization, or surgery). For the binary analyses, severe AUB was compared to the combined mild and moderate AUB.

Covariates

Covariates were selected *a priori* based on biological plausibility and literature evidence, including: (1) age, (2) body-mass index (BMI), (3) parity, (4) age at menarche, (5) hypertension, (6) uterine structural lesions (leiomyoma or polyp) on imaging, (7) systemic inflammatory burden, (neutrophil-to-lymphocyte ratio [NLR]), and (8) total cholesterol and high cholesterol high-density lipoprotein. Because BMI is a determinant of the TyG index and an independent correlate of endometrial pathology, we constructed sequential models to assess the impact of BMI adjustment on the TyG-severity association.

Statistical analysis

All analyses were performed using SPSS 26.0 (IBM Corp., Armonk, NY, USA) and R 4.3.1 (R Foundation for Statistical Computing, Vienna, Austria). Continuous variables were summarized as means $\pm$ standard deviations (SD) or medians with interquartile ranges. Categorical

variables were summarized as frequencies with percentages. Continuous variables were compared across AUB severity strata using one-way analysis of variance (ANOVA) or the Kruskal-Wallis test. Categorical variables were compared by chi-square or Fisher exact test, with trend tested across ordered severity. The primary analysis used multivariable logistic regression to derive odds ratios (ORs) and 95% confidence intervals (CIs) for severe AUB, with the TyG index as both as a continuous variable and categorized by tertiles; trend was tested using the likelihood-ratio test. Three nested models were constructed: Model 1 was unadjusted; Model 2 was adjusted for age, parity, and age at menarche; and Model 3 was further adjusted for BMI, hypertension, structural lesions, the NLR, and lipid covariates. Ordinal logistic regression was used to assess the association with the three-level severity outcome, and the proportional odds assumption was formally tested.

The discriminative ability of the TyG index for severe AUB was evaluated using ROC analysis. The area under the curve (AUC) and its 95% CI were reported. The Youden index was used to identify the optimal cut-off, with sensitivity, specificity, and predictive values reported. Pre-specified subgroup analyses examined effect modification by BMI category (<25 vs ≥ 25 kg/m²) and structural lesion status. Interaction was assessed using the likelihood-ratio test. Several sensitivity analyses were performed: (1) excluding women with any structural PALM lesions to isolate the metabolic-endometrial axis; (2) excluding women with endometrial hyperplasia to assess whether the association was neoplasia-driven; and (3) using HOMA-IR as an alternative exposure when insulin data were available. A two-tailed $P < 0.05$ was considered significant.

The Cochran-Armitage test was used to assess linear trends across ordered severity. Multivariable logistic regression models were fitted using the *glm* function in R, and ordinal logistic regression used the *polr* function from the MASS package. ROC analysis was conducted using the pROC package, with the Youden index method applied to determine optimal cut-off values.

Results

Baseline characteristics

During the two-year study period, 246 perimenopausal women with AUB met all eligibility criteria and were included. Their mean age was 48.3 ± 4.1 years, mean BMI was 25.6 ± 3.8 kg/m² and mean TyG index was 8.69 ± 0.46 . Among them, 71 women (28.9%) were classified as mild AUB, 87 (35.4%) as moderate AUB, and 88 (35.8%) as severe AUB. **Table 1** presents the baseline demographic, reproductive, and metabolic data of the analytic sample, categorized by AUB severity. Age, BMI, fasting triglycerides and glucose, TyG index, and hypertension prevalence all increased with AUB severity. In contrast, hemoglobin concentration decreased progressively. This was consistent with cumulative blood losses in loss in more severe disease.

TyG index across AUB severity

TyG index increased progressively with AUB severity. **Table 2** displays how the mean TyG index increased from 8.41 with mild disease to 8.69 with moderate disease, and 8.97 with severe disease (P for trend < 0.001). The percentage of women with severe AUB who were classified in the highest TyG tertile also increased, from 16.9% to 56.8%. This pattern was also observed for mean fasting triglycerides and glucose. These findings provide initial evidence of a robust relationship between the TyG index and clinical bleeding severity.

Association between TyG index and severe AUB

In multivariable logistic regression analysis, an increased TyG index was identified as a significant independent predictor of severe AUB (**Table 3**). In the unadjusted model, a one-unit increase in the TyG index was associated with a >4 -fold increase in the odds of severe AUB (OR 5.31, 95% CI 3.10-9.10). Although the estimate was attenuated, the association remained significant after adjustment for age, parity, and age at menarche (model 2: OR 4.58, 95% CI 2.59-8.10), and further for BMI, hypertension, structural lesions, NLR, and lipids (model 3: OR 3.94, 95% CI 2.18-7.12). Adjustment for BMI partially attenuated the association, sug-

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Table 1. Baseline characteristics of perimenopausal women with AUB by severity stratum

Characteristic	Mild (n=71)	Moderate (n=87)	Severe (n=88)	p-value
Age, mean (SD), y	46.9 (3.9)	48.2 (4.0)	49.6 (3.9)	<0.001
BMI, mean (SD), kg/m ²	24.1 (3.3)	25.5 (3.6)	27.1 (3.8)	<0.001
Parity, median (IQR)	1 (1-2)	2 (1-2)	2 (1-2)	0.12
Age at menarche, mean, y	13.6 (1.4)	13.4 (1.5)	13.2 (1.5)	0.18
Fasting triglycerides, mean (SD), mg/dL	118 (41)	139 (48)	168 (57)	<0.001
Fasting glucose, mean (SD), mg/dL	92 (9)	96 (11)	101 (13)	<0.001
TyG index, mean (SD)	8.41 (0.39)	8.69 (0.41)	8.97 (0.44)	<0.001
Hemoglobin, mean (SD), g/L	122 (11)	101 (9)	82 (12)	<0.001
Hypertension, n (%)	11 (15.5)	21 (24.1)	31 (35.2)	0.01
Structural lesion (P/L), n (%)	19 (26.8)	28 (32.2)	33 (37.5)	0.36

SD, standard deviation; IQR, interquartile range; BMI, body-mass index (body mass index); TyG, triglyceride-glucose; P/L, polyp or leiomyoma; ANOVA, analysis of variance. *p*-values are for trend across severity strata. Continuous variables with normal distribution were compared using one-way ANOVA (F-statistic: Age F=8.74, BMI F=13.21, Fasting triglycerides F=19.58, Fasting glucose F=14.36, TyG index F=38.92, Hemoglobin F=282.65). Parity was compared using the Kruskal-Wallis test (H=4.23). Age at menarche was compared using one-way ANOVA (F=1.72). Categorical variables were compared using the chi-square test (Hypertension $\chi^2=9.18$; Structural lesion $\chi^2=2.05$).

Table 2. Distribution of the TyG index and its components across AUB severity strata

Measurement	Mild (n=71)	Moderate (n=87)	Severe (n=88)	p-trend
TyG index, mean (SD)	8.41 (0.39)	8.69 (0.41)	8.97 (0.44)	<0.001
Triglycerides, mean (SD), mg/dL	118 (41)	139 (48)	168 (57)	<0.001
Glucose, mean (SD), mg/dL	92 (9)	96 (11)	101 (13)	<0.001
In TyG tertile 1, n (%)	34 (47.9)	35 (40.2)	13 (14.8)	<0.001
In TyG tertile 2, n (%)	25 (35.2)	31 (35.6)	25 (28.4)	
In TyG tertile 3, n (%)	12 (16.9)	21 (24.1)	50 (56.8)	

TyG, triglyceride-glucose; SD, standard deviation. Sample sizes: Mild n=71, Moderate n=87, Severe n=88. Tertile cut-points derived from the study-sample distribution: T1 <8.49, T2 8.49-8.89, T3 >8.89. Continuous variables are presented as mean (SD). The TyG index SD values by stratum are: Mild 0.39, Moderate 0.41, Severe 0.44. Triglyceride SD values: Mild 41, Moderate 48, Severe 57 mg/dL. Glucose SD values: Mild 9, Moderate 11, Severe 13 mg/dL. P-trend was assessed using the Cochran-Armitage test for proportions (tertile distribution, $\chi^2=31.47$) and one-way ANOVA for continuous variables (TyG index F=38.92, Triglycerides F=19.58, Glucose F=14.36).

Table 3. Multivariable logistic regression for severe AUB per one-unit increase in TyG index

Model	OR (95% CI)	p-value	Adjustment set
Model 1 (unadjusted)	5.31 (3.10-9.10)	<0.001	None
Model 2	4.58 (2.59-8.10)	<0.001	+ age, parity, menarche
Model 3 (fully adjusted)	3.94 (2.18-7.12)	<0.001	+ BMI, HTN, lesion, NLR, lipids

OR, odds ratio; CI, confidence interval; BMI, body-mass index; HTN, hypertension; NLR, neutrophil-to-lymphocyte ratio. Outcome is severe versus mild-to-moderate AUB.

gesting that the TyG-AUB relationship may be partly mediated by adiposity.

Dose-response across TyG tertiles

The TyG index was assessed in tertiles to observe a dose-response relationship (**Table 4**). Using the lowest tertile as the reference, the odds of severe AUB in the middle and the

highest tertile were 2.18 (95% CI 1.02-4.66) and 4.62 (95% CI 2.21-9.66), respectively (P for trend <0.001). By ordinal logistic regression, the common odds ratio for the highest versus lowest tertile was 2.96 (95% CI 1.88-4.66), and the proportional odds assumption was satisfied. This ordered increase in risk across tertiles supports a dose-dependent relationship.

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Table 4. Adjusted association between TyG tertiles and AUB severity (logistic and ordinal models)

TyG tertile	Severe, n/N	Severe AUB OR (95% CI)*	Ordinal OR (95% CI)†
T1 (<8.49)	13/82	1.00 (reference)	1.00 (reference)
T2 (8.49-8.89)	25/81	2.18 (1.02-4.66)	1.74 (1.10-2.75)
T3 (>8.89)	50/83	4.62 (2.21-9.66)	2.96 (1.88-4.66)
P for trend	-	<0.001	<0.001

*Fully adjusted (model 3) odds of severe versus mild-to-moderate AUB. †Fully adjusted common odds ratio from proportional-odds ordinal regression across all three severity levels. OR, odds ratio; CI, confidence interval.

Table 5. ROC analysis of the TyG index and metabolic models for identifying severe AUB

Predictor	AUC (95% CI)	Cut-off	Sens. %	Spec. %
TyG index alone	0.74 (0.68-0.81)	8.71	72.7	67.7
BMI alone	0.69 (0.62-0.76)	26.3	64.8	66.5
TyG + BMI	0.79 (0.73-0.85)	-	77.3	71.5
TyG + BMI + HTN	0.82 (0.76-0.87)	-	79.5	73.4

AUC, area under the curve; CI, confidence interval; Sens., sensitivity; Spec., specificity; BMI, body-mass index; HTN, hypertension. Cut-off for BMI in kg/m².

Table 6. Subgroup analysis of the association between TyG index and severe AUB

Subgroup	n	Adjusted OR per unit (95% CI)	P-interaction
BMI <25 kg/m ²	118	3.28 (1.31-8.22)	0.34
BMI ≥25 kg/m ²	128	4.41 (2.05-9.49)	-
No structural lesion	166	4.12 (1.98-8.58)	0.71
Structural lesion present	80	3.67 (1.49-9.04)	-
Age 40-49 y	139	3.71 (1.66-8.29)	0.58
Age 50-55 y	107	4.28 (1.84-9.95)	-

OR, odds ratio; CI, confidence interval; BMI, body-mass index. Estimates are fully adjusted (model 3) and expressed per one-unit increase in TyG index within each subgroup.

Diagnostic performance of the TyG index

Table 5 summarizes the discriminative performance of the TyG Index for severe AUB. When assessed alone, the TyG index yielded an AUC of 0.74 (95% CI 0.68-0.81), with 72.7% sensitivity and 67.7% specificity at the optimal cut-off of 8.71. When combined with BMI, the AUC improved to 0.79 (95% CI 0.73-0.85). The highest AUC of 0.82 (95% CI 0.76-0.87) was achieved with the combined model of TyG index, BMI, and hypertension. BMI alone yielded an AUC of 0.69. These findings suggest that the TyG index provides discriminative information beyond adiposity.

Subgroup analyses

Table 6 shows that higher TyG index was consistently associated with severe AUB across all subgroups. The effect estimate was greater in

women with BMI ≥25 kg/m² (adjusted OR per unit 4.41, 95% CI 2.05-9.49) than in leaner women (adjusted OR=3.28, 95% CI 1.31-8.22). However, this interaction was not significant (P for interaction =0.34). Regardless of structural PALM lesions status, the TyG index was associated with severe AUB. The effect estimates were: No lesions (adjusted OR=4.12, 95% CI 1.98-8.58) and with lesions (adjusted OR 3.67, 95% CI 1.49-9.04).

Sensitivity analyses

Most prespecified sensitivity analyses confirmed the robustness of the primary findings (**Table 7**). In women without structural PALM lesions, the association remained robust (adjusted OR 4.12, 95% CI 1.98-8.58). After excluding cases of endometrial hyperplasia, the adjusted OR was 3.86 (95% CI 2.06-7.23), indicating that the association was not driven

Table 7. Sensitivity analyses for the association between TyG index and severe AUB

Analysis	n	Adjusted OR per unit (95% CI)
Primary analysis (full cohort)	246	3.94 (2.18-7.12)
Exclude structural PALM lesions	166	4.12 (1.98-8.58)
Exclude endometrial hyperplasia	229	3.86 (2.06-7.23)
Hemoglobin-based severity outcome	246	3.71 (2.01-6.85)
HOMA-IR as alternative exposure*	154	2.88 (1.52-5.46)

*Among women with available fasting insulin; OR expressed per one-unit increase in HOMA-IR. OR, odds ratio; CI, confidence interval.

solely by proliferative neoplasia. The association was similar when severity was defined by hemoglobin-based anemia (adjusted OR 3.71, 95% CI 2.01-6.85). Similar results were obtained when the analysis was limited to women with available insulin data and HOMA-IR was used as the exposure variable.

Discussion

This single-center, retrospective study of 246 perimenopausal women with AUB found that a higher TyG index was independently associated with increased bleeding severity in a dose-response manner. The TyG index increased incrementally across mild, moderate, and severe disease, with a nearly fourfold adjusted odds ratio for severe AUB. Women in the highest TyG tertile had severe AUB > four times more when compared to those in the lowest TyG tertile. For discriminating AUB severity, the TyG index had an AUC of 0.74 and provided information beyond BMI. This study was the first to link the TyG index to AUB severity in a perimenopausal population.

The evidence linking insulin resistance to endometrial disease continues to accumulate [16]. Insulin resistance has been reported in a high proportion of perimenopausal women with endometrial pathology (57%) compared to those without (32%) [17]. Furthermore, hyperinsulinemia was an independent risk factor for AUB (OR=3.0), supporting the concept of the uterus as a metabolic end organ [18]. Our results provide the evidence that lipids and glucose serve as simple metabolic indicators for the assessment of bleeding severity.

The choice of the TyG index as the exposure variable is substantiated by numerous validation studies. The TyG index shows strong correlation with gold-standard and commonly

used surrogate measures of insulin resistance. Moreover, it outperforms many alternatives across different populations and requires only routinely measured fasting laboratory values [19]. In women, the TyG index has been validated as a surrogate for insulin resistance in polycystic ovary syndrome. These studies report cut-offs in the low-8 range for identifying poor insulin sensitivity [20]. The optimal cut-off of 8.71 for severe AUB is higher than insulin-sensitivity thresholds, likely because our outcome represented an advanced clinical phenotype rather than merely insulin resistance, and because perimenopausal women experience metabolic shifts that elevate the TyG index distribution [21].

A key strength of our analysis was the dose-response relationship we observed. Risk increased progressively from the middle to the upper TyG tertile, with a graded relationship confirmed by ordinal regression across all three severity levels. A biological gradient—a classical criterion for causality—was present and robust to extensive adjustments and sensitivity analyses, suggesting that the relationship was not an artefact of confounding by adiposity or structural disease. The association persisted after excluding women with structural PALM lesions or endometrial hyperplasia, supporting a metabolic-bleeding axis independent of overt neoplasia.

Several interrelated mechanisms may explain this association. Compensatory hyperinsulinemia, driven by insulin resistance, promotes endometrial epithelial and stromal cell proliferation through insulin and insulin-like growth factor signaling, inhibits apoptosis, and leads to endometrial hyperplasia—a fragile tissue prone to irregular shedding and heavy bleeding. This irregular shedding is associated with heavy menstrual bleeding. Hyperinsulinemia

also reduces hepatic sex-hormone-binding globulin production, increasing bioavailable estradiol and promoting estrogen-dominant endometrial cell proliferation, which is exacerbated by perimenopausal anovulation [22]. Cellular disturbances, including PI3K/AKT and MAPK pathway activation and dysregulation of sex steroid metabolic enzymes, link the TyG index to pathologic endometrial bleeding [23].

Notably, baseline data show that fasting glucose, fasting triglycerides, and hypertension prevalence all increased significantly across AUB severity strata. Elevated fasting glucose in the severe AUB group (101 ± 13 mg/dL) compared to the mild group (92 ± 9 mg/dL) suggests that subclinical hyperglycemia, even within the non-diabetic range, may contribute to endometrial pathology through chronic glycototoxicity and advanced glycation end-product accumulation, impairing decidualization and promoting aberrant angiogenesis. Similarly, the progressive increase in fasting triglycerides from 118 ± 41 mg/dL in the mild group to 168 ± 57 mg/dL in the severe group reflects worsening dyslipidemia, which may independently disrupt the endometrial microenvironment through altered prostaglandin metabolism and chronic low-grade inflammation. Hypertension (15.5% in mild vs. 35.2% in severe cases) may further exacerbate endometrial bleeding through microvascular endothelial dysfunction, impaired hemostasis, and shared upstream metabolic drivers including insulin resistance and sympathetic overactivation. These findings suggest that the TyG index captures a constellation of metabolic derangements, including hyperglycemia, hyperlipidemia, and hypertension, that collectively influence AUB severity. Dyslipidemia, reflected by the lipid component of the TyG index, may independently contribute. Triglyceride-rich or low-HDL cholesterol profiles are metabolic disorder signals and have been connected to endometrial and other reproductive disorders. Chronic low-grade inflammation and altered adipokine signaling are thought to disrupt the endometrial microenvironment [21, 24]. The partial attenuation of the TyG-AUB association after BMI adjustment is consistent with previous joint-effect analyses showing that BMI mediates part of the TyG-endometrial outcome relationship, while the TyG index retains an independent effect [24].

The established connection between the TyG index and endometrial neoplasia further supports the clinical relevance of our findings. A retrospective cohort study reported that women with endometrial carcinoma or atypical hyperplasia had significantly higher TyG levels than those with normal endometrium. That study also found a stepwise increase in endometrial carcinoma incidence across TyG tertiles, with advanced grade and poor differentiation independently associated with higher TyG tertiles [25]. Within this continuum, our findings suggest that the TyG index may identify perimenopausal women with more clinically significant AUB and higher risk of proliferative endometrial neoplasia. This identifies a group who may benefit from earlier assessments or metabolic intervention, given the latent period preceding endometrial hyperplasia or carcinoma.

Using the TyG index for risk stratification makes metabolic management a more plausible approach. Adding the TyG index to BMI and blood pressure yielded a higher AUC of 0.82 for severe AUB, suggesting that metabolic assessment should be integrated into clinical evaluation of perimenopausal women with AUB [19]. This population is at heightened metabolic risk, so metabolic screening offers benefits beyond gynecologic care [21].

Subgroup analyses provided further insight into the interplay between metabolic status and AUB severity. The numerically stronger association in overweight/obese women (BMI ≥ 25 kg/m²; adjusted OR 4.41) versus lean women (BMI < 25 kg/m²; adjusted OR 3.28), though not reaching interaction significance ($P=0.34$), is biologically plausible because adiposity amplifies insulin resistance and endometrial effects through increased aromatase-mediated estrogen synthesis and adipokine-driven inflammation. The non-significant interaction also indicates that the TyG index retains predictive value across BMI categories, supporting its utility as an independent metabolic marker. This finding aligns with the ROC analysis, where TyG plus BMI yielded a higher AUC (0.79) than either marker alone, suggesting that the TyG index captures metabolic information beyond adiposity. These findings have therapeutic implications. If insulin resistance is modifiable and correlates with AUB severity, then weight management, dietary strategies,

and possibly insulin-sensitizing agents could be employed. This could reduce bleeding severity and the need for hormonal or surgical intervention. It may be time to expand the scope of peri-menopausal AUB management to address cardiometabolic risk factors. However, further studies are needed before recommending such an approach.

There were still several limitations to this study. The sample size of this study was modest and from a single center, which may have limited the generalizability. Unmeasured factors, such as the dietary or exercise habits, may have confounded the results. In addition, severity grading was based on clinical standards, and histopathology was not available for all participants. The modest sample size may have underpowered some analyses. Lastly, individuals on lipid-lowering or glucose-lowering therapy were excluded. This was necessary to ensure TyG index interpretability, but may have introduced selection bias, as excluded individuals likely had the highest metabolic risk.

This study had several strengths. It used a well-defined perimenopausal sample, standardized FIGO classification, and a prespecified severity grading system incorporating bleeding pattern, hemoglobin, and endometrial assessment. The study also benefited from sensitivity analyses excluding structural and hyperplastic disease, corroborative HOMA-IR analysis, nested models, ordinal regression, ROC analysis, and multiple sensitivity analyses. The use of a low-cost, readily accessible exposure marker may enhance the applicability of our findings.

Future work should prospectively validate this association in multi-center settings with serial metabolic and bleeding measurements. It will also be important to define and validate TyG cut-offs for perimenopausal AUB and to determine whether lowering TyG reduces bleeding severity and proliferative endometrial disease. Integrating the TyG index with imaging, histopathology, and inflammatory and adipokine biomarkers may further enhance risk stratification. In the absence of such evidence, we suggest that TyG index assessment, along with fasting lipids and glucose, can be considered in the evaluation of perimenopausal women with AUB.

In summary, a higher TyG index is independently and dose-dependently associated with increased AUB severity in perimenopausal women. It identifies severe disease with moderate accuracy, which improves when coupled with adiposity and blood pressure measures. Insulin resistance appears central to perimenopausal AUB, and the TyG index proves a cost effective and easily implemented candidate for risk stratification. This provides a rationale for future studies of metabolically focused prevention and treatment approaches.

Acknowledgements

The authors thank all the staff of the Department of Gynecology at Lanxi Hospital of Traditional Chinese Medicine for their support in data collection and patient care.

Disclosure of conflict of interest

None.

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