Original Research


# Assessment of triglyceride glucose index and triglyceride to HDL cholesterol ratio as markers of insulin resistance defined by the Homeostatic Model Assessment 2 in Middle Eastern adults with excess adiposity

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## Abstract

**Background.** Insulin resistance (IR) drives early cardiometabolic risk in populations with high adiposity. Simple fasting markers, such as the triglyceride-glucose (TyG) index and the triglyceride-to-HDL cholesterol ratio (TG/HDL-C), may be helpful. Still, their performance against the updated, non-linear Homeostatic Model Assessment 2 (HOMA2) model in Middle Eastern adults remains unclear.

**Objectives.** Compare TyG versus TG/HDL-C for HOMA2-defined IR; test modification by Body Mass Index (BMI) (overweight vs. obesity); and evaluate discrimination, calibration, and clinical utility.

**Methods.** Cross-sectional study of 140 adults without diabetes with overweight/obesity. Fasting triglycerides, HDL-C, glucose, and insulin were assayed under quality control; HOMA2-IR, %S, and %B were derived. Multivariable linear models (per-SD predictors) adjusted for age, sex, and BMI; multiplicative interactions probed effect modification. Higher IR was defined as the sex-specific top quartile of HOMA2-IR. Discrimination (Area Under the Curve AUC; DeLong test), calibration (intercept, slope, Brier), decision-curve analysis (DCA), multiple imputation (20 datasets), and prespecified sensitivity checks were performed.

**Results.** TyG independently tracked higher HOMA2-IR (β=0.127 per SD; 95% CI 0.033-0.220; p=0.0078), whereas TG/HDL-C was null. TyG×BMI interaction was significant (p=0.0011): negligible in overweight (β≈0.01; p=0.85) but strong in obesity (β=0.29; p<0.001). Discrimination was similar (AUC TyG 0.714 vs TG/HDL-C 0.707; ΔAUC=0.007; p=0.801). DCA showed a higher net benefit for TyG, especially TyG+BMI, across thresholds of 0.20-0.60. Calibration was acceptable; bootstrap-validated metrics and extensive sensitivity analyses were consistent.

**Conclusions.** In adults without diabetes with excess adiposity, TyG captures HOMA2-defined IR more consistently than TG/HDL-C, with the greatest incremental value in obesity. As a low-cost fasting metric, TyG, particularly when combined with BMI, may refine triage for further evaluation; external validation in regional cohorts is warranted.

**Keywords:** insulin resistance, triglycerides, glucose, high-density lipoproteins, obesity

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## Introduction

Insulin resistance (IR) links excess adiposity to type 2 diabetes and cardiovascular disease, a relationship first articulated by Reaven's "Syndrome X" concept [1]. In IR, impaired suppression of adipose lipolysis increases free-fatty-acid flux to the liver, promoting very-low-density lipoprotein (VLDL) overproduction; together with cholesteryl ester transfer protein (CETP) and hepatic lipase activity, this yields hypertriglyceridemia and reduced HDL-C, the classic atherogenic pattern that often precedes dysglycemia [2,3]. Because the hyperinsulinemic-euglycemic clamp is impractical for screening, simple fasting markers are widely used.

Two commonly used fasting indices for assessing insulin resistance are the triglyceride-to-HDL cholesterol ratio (TG/HDL-C) and the triglyceride-glucose (TyG) index. TG/HDL-C helps differentiate insulin-sensitive from insulin-resistant phenotypes in multiple cohorts [4], while TyG correlates with clamp measures and predicts metabolic and cardiovascular outcomes [5-7]. The updated HOMA2 model improves upon legacy HOMA-IR by accounting for non-linear insulin-glucose relations and hepatic/peripheral components [8]. In Jordan, overweight (BMI ≥ 25 kg/m²) affects ~60.7% of adults and obesity (BMI ≥ 30 kg/m²) ~32.3%; the prevalence of impaired fasting glycaemia is ~6.1% and raised fasting glucose/medication is ~8.2% in adults aged 18-69 years [9]. These burdens highlight the urgent need for accessible, low-cost, and physiology-informed markers that can refine early risk assessment in resource-limited clinical settings.

Although TG/HDL-C and TyG are both fasting, low-cost indices, they capture partially distinct metabolic signals. TG/HDL-C reflects the atherogenic dyslipidemia pattern (high triglycerides and low HDL-C), and its performance as an insulin resistance surrogate has been reported to vary by sex and ethnicity [10]. Meanwhile, TyG integrates triglycerides and fasting glucose and has been summarized in recent umbrella review evidence as being associated with a broad range of cardiometabolic outcomes, although the certainty of evidence varies across outcomes [11]. These differences support a direct, head-to-head comparison of TyG and TG/HDL-C against a common reference standard (HOMA2) within a Middle Eastern cohort with excess adiposity.

Although TG/HDL-C and TyG have been widely studied, few investigations have focused on Middle Eastern adults without diabetes and with excess adiposity, or applied the updated non-linear HOMA2 model as the reference standard. Their relative performance in this high-risk group has not been directly compared, and key aspects of clinical validity, such as calibration and decision-curve analysis, remain unexplored. This study addresses these gaps by evaluating TyG and TG/HDL-C against HOMA2-defined insulin resistance within an overweight or obese Middle Eastern cohort.

We prespecified three hypotheses. H1, primary: both TG/HDL-C and TyG would be positively and independently associated with continuous HOMA2-IR; H2, secondary: TyG would demonstrate superior discrimination compared with TG/HDL-C for top-quartile HOMA2-IR, with a clinically meaningful AUC margin (≥0.03); and H3, effect modification: associations would be stronger in participants with obesity than overweight ones, with sex interaction examined exploratorily.

## Objective

To compare TyG and TG/HDL-C against HOMA2-IR (continuous and top-quartile definitions), evaluate discrimination, calibration, and decision-curve utility (thresholds 0.20-0.60), and test effect modification by BMI (overweight vs. obesity) and sex in adults without diabetes with overweight/obesity.

## Methods

### Study design and setting

We conducted a cross-sectional study of 140 adults with overweight or obesity and without diabetes, recruited from outpatient clinics and the community (February-May 2025). Reporting followed STROBE guidelines; analyses were prespecified before examining exposure outcome associations [12]. Ethical approval was obtained, and all participants provided written informed consent. Diagnostic definitions followed American Diabetes Association (ADA) thresholds [13].

### Participants

Eligibility: age 18–60 years, BMI ≥25 kg/m², and fasting plasma glucose (FPG) <126 mg/dL (adults without diabetes per ADA) [13].

Exclusions: known diabetes, HbA1c ≥6.5%, lipid-lowering or insulin-sensitizing agents within 3 months, pregnancy, chronic kidney/liver disease, untreated thyroid disorder, acute illness within 2 weeks, fasting <10 h, hemolysis, or >1 freeze–thaw cycle.

Although the ADA also recognizes a 2 h plasma glucose ≥200 mg/dL during an oral glucose tolerance test (OGTT) and a random plasma glucose ≥200 mg/dL with classic symptoms as diagnostic criteria, these measures were not assessed in this study; therefore, diabetes status was determined using available fasting plasma glucose and HbA1c values, along with known diagnosis/medication history.

Recruitment was consecutive via clinic lists and community postings; trained staff obtained consent and recorded screening outcomes to assess selection bias.

### Measurements and laboratory procedures

Visits occurred after a 10–12 h overnight fast. Pre-analytical controls included standardized morning phlebotomy (07:30–10:30), seated rest ≥5 min, and tourniquet time <1 min. Anthropometric measurements were obtained using calibrated devices (weight and

height), and BMI was calculated as weight (kg) divided by height squared (m²). Venous blood (plain tubes) was transported on ice, centrifuged within 2 h, and aliquoted at −80 °C.

Assays: glucose by enzymatic hexokinase (International Federation of Clinical Chemistry and Laboratory Medicine IFCC-traceable) on the A25 BioSystems analyzer; lipids by enzymatic colorimetry (HDL-C by direct assay) on the same platform; insulin by chemiluminescent immunoassay (Cobas e411; inter-assay CV <8%). Quality assurance included lot-to-lot verification, two-level internal controls per shift, blind duplicates (10%), and Westgard-rule acceptance. Inter-assay CVs were glucose <2.5%, total cholesterol <3.0%, triglycerides <3.5%, HDL-C <3.5% and insulin <8.0%.

**Variables and derived indices**

• Primary outcome: HOMA2-IR (HOMA2 Calculator v2.2.4, Oxford Diabetes Trials Unit), which models the nonlinear insulin-glucose relationship and reports %S and %B in a normal-reference scale [8].

• Secondary outcomes: HOMA2-%S and HOMA2-%B.

• Exposures: TG/HDL-C = triglycerides ÷ HDL-C [4]; while TyG was calculated as ln([triglycerides × glucose]/2) with both analytes in mg/dL, as originally described.

• Prespecified covariates: age, sex, and BMI (continuous). To avoid over-adjustment, Low-Density Lipoprotein Cholesterol (LDL-C) and total cholesterol were reserved for sensitivity analyses. Waist-to-height ratio (waist ÷ height) was evaluated as an alternative adiposity metric. (Waist-to-height ratio was included as a sensitivity analysis to reflect central adiposity; hip circumference and body composition measures (e.g., percent body fat) were not routinely available, so BMI was retained as the primary adiposity measure in the main analyses.)

• Effect modifiers: BMI category (overweight 25.0-29.9 vs. obesity ≥30.0) and sex (multiplicative interaction terms with stratum-specific estimates if indicated).

**Sample size**

With 140 participants, the study had 80% power (α = 0.05, two-tailed) to detect correlations as small as r ≈ 0.24 between triglyceride-derived indices and HOMA2-IR, corresponding to an AUC difference of about 0.08-0.10. Accordingly, the study was not powered to detect small discrimination differences, such as ΔAUC = 0.03, prespecified as clinically meaningful.

**Statistical analysis**

Analyses were prespecified, two-sided (α=0.05), and run in R with a fixed seed; continuous predictors were z-scored (per-SD effects). Missing data: MICE (m=20; PMM k=5) on raw triglycerides, HDL-C, glucose, insulin, and covariates; within each imputed set, TG/HDL-C, TyG, and HOMA2-IR were passively recalculated (algebraic ties), planned interactions included, and estimates pooled by Rubin's rules [14,15].

Primary models used log (HOMA2-IR) regressed on TG/HDL-C and TyG (separately/jointly), adjusted for age, sex, BMI; LDL-C and total cholesterol entered only in sensitivity analyses. Joint models were retained if VIF<5; otherwise, separate models were compared by Akaike Information Criterion (AIC) and Akaike weights. Reported β (per-SD), 95% CI, partial $R^2$, Akaike weight.

Heteroskedasticity HC3; checks untransformed outcome and rank-based regression. Effect modification (BMI overweight 25.0-29.9 vs obesity ≥30.0; sex) was tested via multiplicative interactions; when p_interaction<0.10, stratum-specific slopes and marginal effects (95% CIs) were shown. Secondary outcomes (HOMA2%S, %B) used the same models with sign alignment and inverse transforms.

Discrimination/calibration/utility logistic models classified "higher IR" as the sex-specific top quartile of HOMA2-IR (no validated regional cut points). ROC/AUCs compared by DeLong's test [16]; calibration intercept, slope. Internal validation using 200 bootstraps for optimism-corrected AUC, Brier, and calibration [17]. Decision-curve analysis compared TyG, TG/HDL-C, BMI, and TyG+BMI across thresholds 0.20–0.60 vs treat-all/none. Thresholds of 0.20–0.60 were chosen because they represent the range where preventive actions such as counseling, retesting, or lifestyle advice are most clinically relevant; risks below 0.20 are seldom acted on, and those above 0.60 typically trigger evaluation regardless of the marker [17,18].

Youden's J (bootstrap CIs) was summarized descriptively only [19]. Robustness was also examined across alternative definitions (sex-specific 75th/80th/90th percentiles).

Multiplicity Benjamini-Hochberg FDR (q=0.10) within prespecified families (primary associations; exploratory interaction/discrimination) [20]; primary inferences from the primary family.

Diagnostics linearity (restricted cubic splines; component-plus-residual plots; if indicated, 3-4 knot, AIC-selected splines), multicollinearity (VIF), heteroskedasticity (Breusch–Pagan; HC3 retained), and influence (Cook's D>4/n with leave-one-out).

Sensitivity analyses excluding fasting <12 h; winsorizing TG/glucose at 1st/99th percentiles; adding LDL-C and total cholesterol; BMI- and sex-stratified models; excluding ADA-defined IFG (100–125 mg/dL); refitting with untransformed HOMA2-IR and rank-based regression; substituting waist-to-height ratio for BMI.

**Ethics**

The protocol was approved by the BAU Review Board, Approval No. 44/4/2024/2025, and all participants provided written informed consent. Analyses followed a prespecified statistical analysis plan archived before unblinding exposure outcome associations.

## Results

We enrolled 140 adults without diabetes with excess adiposity; 69 were overweight (49.3%), and 71 were participants with obesity (50.7%). Compared with the overweight group, participants with obesity had higher triglycerides and lower HDL-C, yielding higher TG/HDL-C ratios and TyG values, and they showed higher HOMA2-IR [2.40 (1.77–3.76) vs 1.62 (1.20–2.74)]. Age and sex distributions were broadly similar between groups (Table I).

In multivariable linear models of HOMA2-IR (continuous), a 1-SD higher TyG was associated with a 0.127 SD higher HOMA2-IR (95% CI 0.033–0.220; p=0.0078), whereas TG/HDL-C showed no meaningful association (β=0.027; 95% CI −0.110–0.164; p=0.701). Model fit favored TyG ($R^2$ 0.254; AIC 203.73) over TG/HDL-C ($R^2$ 0.214; AIC 210.96), yielding Akaike weights 0.974 vs 0.026, respectively (Table II).

Effect modification by adiposity status was evident for TyG, with a p for interaction of 0.0011. The association was negligible in overweight participants (β = 0.01; 95% CI −0.12 to 0.14; p = 0.85) but strong in those with obesity (β = 0.29; 95% CI 0.17 to 0.40; p < 0.0001). TG/HDL-C showed no evidence of BMI interaction (p = 0.391). Exploratory sex-stratified analyses suggested steeper slopes in men than women, though statistical support was weaker (TyG×sex p = 0.240; TG/HDL-C×sex p = 0.160) (Figure 1).

Physiological exploration showed that TG/HDL-C was not associated with HOMA2-%S or HOMA2-%B (%S: β = −0.05; p = 0.42; %B: β = 0.08; p = 0.19). In contrast, TyG was inversely associated with insulin sensitivity (%S: β = −0.21; 95% CI −0.32 to −0.10; p < 0.001) and positively related to β-cell function (%B: β = 0.15; 95% CI 0.04-0.26; p = 0.008), consistent with reduced sensitivity accompanied by compensatory β-cell activity.

Calibration performance was acceptable for both models. The TyG model showed an apparent intercept of 0.000 and a slope of 1.00, with optimism-corrected bootstrap intercept of 0.038 (95% CI −0.305 to 0.477) and a slope of 0.726 (0.386-1.374). The TG/HDL-C model showed an apparent interception of 0.000 and a slope of 1.00, with bootstrap intercept 0.023 (−0.450 to 0.424) and slope 0.691 (0.380-1.267). Apparent and validated AUCs were similar (0.714 vs 0.707; optimism-corrected ≈ 0.687 for both), and Brier scores were ≈0.177, indicating stable overall accuracy. Findings were robust across prespecified sensitivity analyses (see statistical analysis).

In ROC analyses, both indices showed modest discrimination for higher insulin resistance (top sex-specific quartile of HOMA2-IR), with AUCs of 0.714 for TyG and 0.707 for TG/HDL-C; the between-model difference was minimal (ΔAUC = 0.007) and not statistically significant (DeLong p = 0.801) (Figure 2A). Decision-curve analysis, however, revealed clearer clinical distinctions: TG/HDL-C provided little incremental net benefit compared with BMI, whereas TyG consistently outperformed both TG/HDL-C and BMI across common probability thresholds. A composite TyG+BMI model achieved the greatest net benefit across the clinically relevant range (0.2-0.6), supporting its utility for risk stratification (Figure 2 B). Exploratory thresholding with Youden's J suggested approximate cut-points of ~3.2 for TG/HDL-C and ~8.7 for TyG [19]. TG/HDL-C demonstrated a weaker sensitivity specificity balance, while TyG performed more consistently; bootstrap resampling confirmed the stability of these estimates, although they remain sample-dependent and are not proposed as clinical cut-offs.

**Table I.** Baseline characteristics of participants by BMI category.

| Group | no | Age (years) | Female (%) | BMI (kg/m²) | Triglycerides (mg/dL) | HDL-C (mg/dL) | TG/HDL-C Ratio | TyG Index | HOMA2-IR |
|---|---|---|---|---|---|---|---|---|---|
| Overweight | 69 | 32.4 ± 13.1 | 78.3% | 27.6 ± 1.4 | 119.0 ± 52.2 | 37.5 ± 12.0 | 3.70 ± 2.38 | 8.51 ± 0.52 | 1.62 (1.20–2.74) |
| Participants with obesity | 71 | 34.6 ± 13.2 | 71.8% | 35.3 ± 4.8 | 143.2 ± 68.8 | 29.5 ± 10.0 | 5.85 ± 4.32 | 8.72 ± 0.47 | 2.40 (1.77–3.76) |

Abbreviations: BMI, body mass index; HDLC, high-density lipoprotein cholesterol; TG, triglycerides; TG/HDLC, triglyceridetoHDL cholesterol ratio; TyG, triglyceride glucose index; HOMA2IR, Homeostatic Model Assessment 2 insulin resistance. Data are in mean ± SD or median (IQR).

**Table II.** Associations of TG/HDL-C and TyG with HOMA2-IR in multivariable models (per 1-SD).

| Model (predictor entered) | β/SD (95% CI) | p-value | Model $R^2$ | AIC | Akaike weight |
|---|---|---|---|---|---|
| TyG (per 1-SD) | 0.127 (0.033-0.220) | 0.0078 | 0.254 | 203.730 | 0.974 |
| TG/HDL-C (per 1-SD) | 0.027 (−0.110-0.164) | 0.701 | 0.214 | 210.960 | 0.026 |

Abbreviations: TyG, triglyceride-glucose index; TG/HDLC, triglyceridetoHDL cholesterol ratio; CI, confidence interval; AIC, Akaike information criterion.

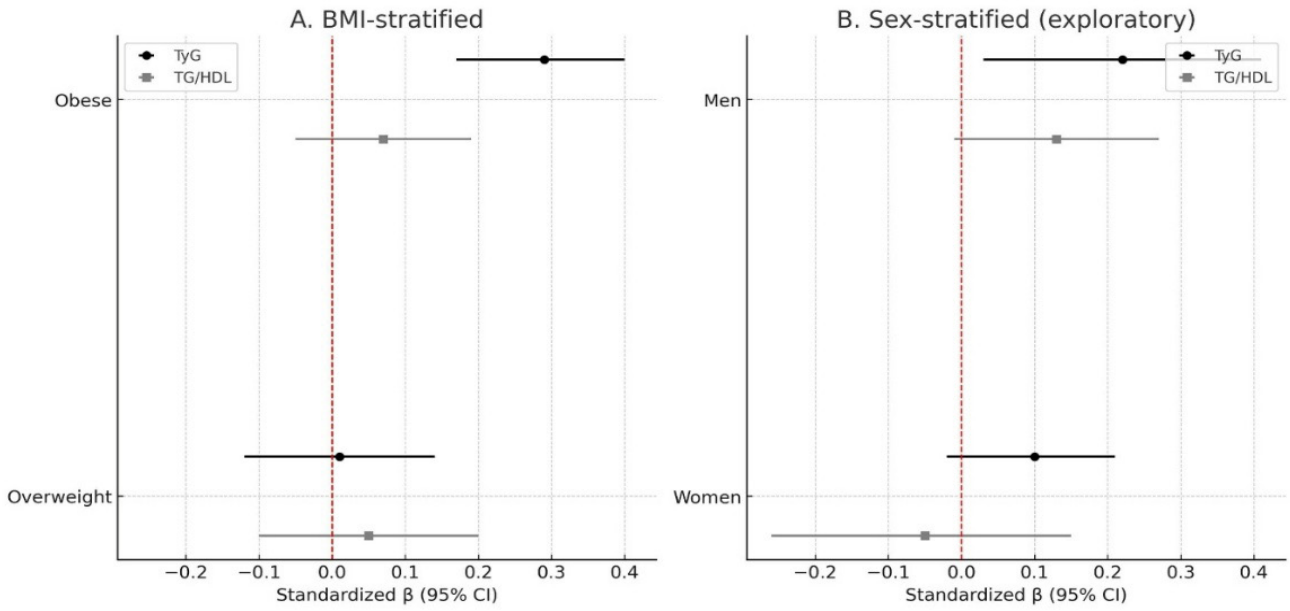


**Figure 1.** Adjusted associations of TyG and TG/HDL with HOMA2-IR by **(A)** BMI and **(B)** sex, Standardized β (95% CI) from linear models with per-SD predictor scaling; adjusted for age, sex, and BMI, except within the stratifier (BMI strata: age+sex; sex strata: age+BMI).

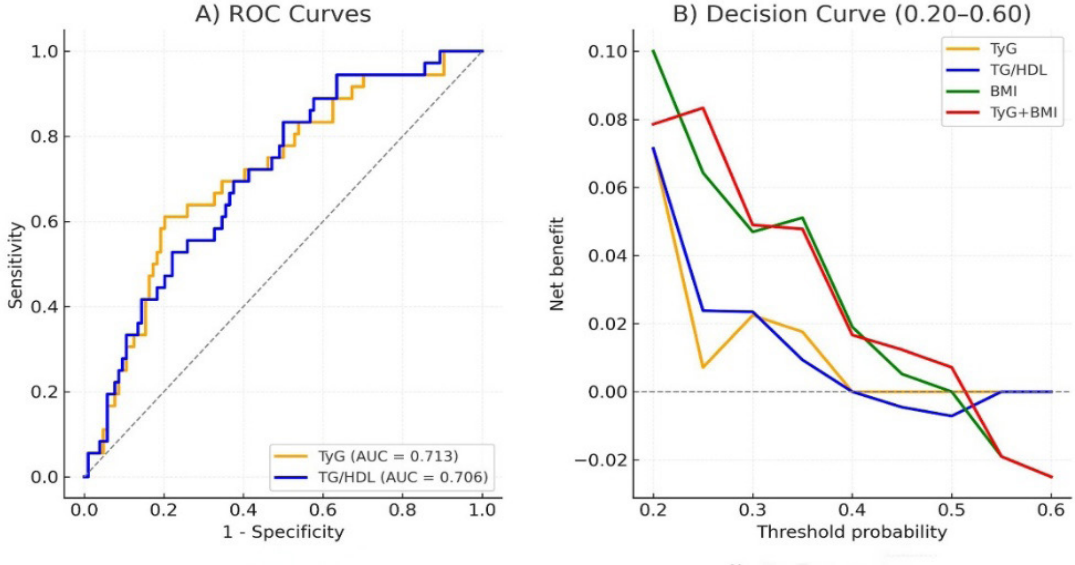


**Figure 2.** Discrimination and clinical utility of lipid indices for higher HOMA2-IR.
**(A)** ROC curves comparing TyG and TG/HDL-C for classifying higher HOMA2-IR (sex-specific top quartile).
**(B)** Decision-curve analysis (thresholds 0.20–0.60) comparing net benefit for TyG, TG/HDL-C, BMI, and a combined TyG+BMI model, against treat-all and treat-none strategies.

Flexible spline diagnostics showed no material nonlinearity for TyG (LRT $p \approx 0.060$) and only mild curvature for TG/HDL-C (LRT $p \approx 0.007$), supporting an approximately linear association for TyG.

## Discussion

Under a prespecified analysis plan, we found that adults with obesity had a distinctly more adverse lipid-glycemic profile than those who were overweight, with higher triglycerides, lower HDL-C, higher TG/HDL-C and TyG, and markedly higher HOMA2-IR; age and sex distributions were similar between groups. This baseline contrast sets the stage for the core associations observed in adjusted models. Consistent with our prespecified primary association hypothesis, we hypothesized that both TG/HDL-C and TyG would be positively and independently associated with continuous HOMA2-IR. In the observed data, however, only TyG met this criterion after adjustment, whereas TG/HDL-C did not [4–7,8,21].

In multivariable analyses, TyG emerged as a clear, independent correlate of insulin resistance, whereas TG/HDL-C did not. Model comparisons consistently favored TyG, underscoring its stronger explanatory value in this cohort. These findings align with prior work that validates TyG against clamp-derived insulin sensitivity and links TyG to future metabolic and cardiovascular events [5–7,21]. At the same time, the variable performance of TG/HDL-C reported across settings likely reflects its dependence on HDL metabolism and its modifiers (sex hormones, inflammation, lifestyle). By using HOMA2 rather than legacy HOMA-IR, we anchored these comparisons to a framework that accounts for non-linear insulin-glucose relations, an advantage in ranges without diabetes [4,8,21].

Comparability with prior studies should be interpreted cautiously because many validations of TyG and TG/HDL cholesterol used clamp-derived indices, OGTT-based indices, or legacy HOMA IR. HOMA2 is an updated non-linear model, and its values are not numerically interchangeable with HOMA IR; therefore, cut-offs and effect sizes across studies may differ depending on the reference method. Nonetheless, HOMA2 is commonly used in contemporary datasets and has been applied in recent regional biobank analyses, supporting its relevance as a reference framework in non-diabetic populations [8,15,22].

Adiposity materially amplified the TyG signal, as evidenced by a strong TyG×BMI interaction (p_interaction = 0.0011), with TyG essentially flat in the overweight group (β≈0.01) but steep in obesity (β≈0.29), whereas TG/HDL-C showed no evidence of BMI interaction (Figure 1). Exploratory sex analyses suggested steeper slopes in men than women, though statistical support was weaker and did not reach conventional significance. Biologically, these gradients are expected because as adipose tissue becomes insulin-resistant, lipolysis increases free-fatty-acid flux to the liver, driving VLDL overproduction and hepatic insulin resistance, the dyslipidemia-dysglycemia loop that TyG compresses into a single fasting metric. Evidence that Middle Eastern populations face high burdens of adiposity and dysglycemia underscores the practical value of a fasting index that still adds information beyond BMI. This directly addresses our effect-modification hypothesis, as the association between TyG and HOMA2-IR was stronger in obesity than in overweight, whereas the exploratory sex interaction did not achieve statistical significance [1–3,9].

In the Middle Eastern setting, lifestyle and socioeconomic factors can influence lipid-glucose indices, including dietary patterns, physical activity, smoking, and broader social determinants. National surveillance data indicate a high burden of cardiometabolic risk factors in Jordanian adults, consistent with a regional transition toward more sedentary behavior and energy-dense diets. Because our dataset did not include detailed measures of diet, physical activity, smoking, or socioeconomic status, residual confounding is possible and should be addressed in future regional studies that integrate these characteristics [9].

Central adiposity may relate more closely to visceral fat and insulin resistance than BMI alone. In our sensitivity analysis using the waist-to-height ratio, conclusions were unchanged, supporting robustness; however, future work should evaluate whether the waist-to-hip ratio or body composition measures improve risk stratification in regional populations.

When the outcome was framed dichotomously (top sex-specific quartile of HOMA2-IR), TyG and TG/HDL-C showed very similar discrimination (AUC 0.714 vs 0.707; ΔAUC ~0.007; DeLong p = 0.801) (Figure 2A) and comparable overall accuracy by Brier score. Yet decision-curve analysis told a more decision-relevant story, showing that across clinically plausible threshold probabilities (≈0.20–0.60), TyG outperformed both TG/HDL-C and BMI, and the TyG+BMI combination delivered the highest net benefit (Figure 2B). Clinically, this means that even with closely matched AUCs, TyG helps identify more people who would benefit from further evaluation without a commensurate increase in false positives, an advantage the AUC can average away. Calibration performance was also acceptable for both models, with apparent slopes were ~1 with intercepts of ~0, and optimism-corrected bootstrap slopes remained acceptable (TyG slope 0.726; TG/HDL-C slope 0.691), supporting reliable predicted risk estimates. Accordingly, our prespecified discrimination hypothesis expecting a clinically meaningful AUC margin (≥0.03) in favor of TyG was not met; however, decision-curve analysis still favored TyG (particularly TyG+BMI) across relevant thresholds, underscoring decision-focused gains despite similar AUCs [16–18].

Beyond HOMA2-IR, secondary physiological readouts reinforced these distinctions. TG/HDL-C was not associated with insulin sensitivity (HOMA2-%S) or β-cell function (HOMA2-%B), whereas TyG was inversely related to %S and positively related to %B. This pattern is physiologically coherent, reflecting compensatory β-cell hypersecretion in the face of reduced insulin sensitivity. Also, it is consistent with expected metabolic changes

in early insulin resistance (reduced sensitivity with compensatory β-cell response), supporting the biological plausibility of TyG as a practical surrogate marker [5–7,21].

Flexible spline diagnostics confirmed that TyG showed near-linearity (LRT p ≈ 0.060) while TG/HDL-C showed only mild curvature (LRT p ≈ 0.007), further supporting the stability of the TyG–HOMA2-IR relationship. Robustness checks strengthen confidence in these inferences. After Benjamini–Hochberg correction, both the main TyG effect and its BMI-specific amplification remained significant, while other associations did not. Influential-point, multicollinearity, and heteroskedasticity diagnostics did not flag concerns, and results were consistent across prespecified sensitivity analyses (see Statistical Analysis). Exploratory Youden thresholds (~8.7 for TyG; ~3.2 for TG/HDL-C) were stable in bootstrap resampling but are sample and utility dependent; they are therefore offered as descriptive markers rather than clinical cut-offs [17–19].

Finally, we extend prior work by evaluating these lipid-derived indices against HOMA2, prespecifying adiposity-based effect modification, and assessing clinical utility in a Middle Eastern cohort. From a practical standpoint, combining a simple fasting index with BMI may help prioritize individuals for further assessment (e.g., lifestyle counseling, repeat testing, or formal metabolic evaluation). External validation and prospective studies linking these markers to outcomes remain essential before routine implementation [5,6,8,18,21].

## Limitations

These findings reflect cross-sectional associations and motivate prospective evaluation. HOMA2 offered a practical approach for population-level assessment of insulin resistance, and diabetes status was defined using available criteria. We adjusted for key covariates; future studies incorporating detailed lifestyle measures and independent Middle Eastern cohorts can further refine interaction estimates and validate decision-curve and cut-point performance.

## Conclusions

In adults without diabetes and with excess adiposity, the triglyceride-glucose (TyG) index was more consistently associated with HOMA2-defined insulin resistance than the triglyceride/HDL cholesterol ratio, with stronger associations among participants with obesity. Discrimination was similar, but decision-curve analysis suggested greater net clinical benefit for TyG, especially when combined with BMI, across clinically plausible thresholds. Together, these findings support TyG as a pragmatic marker for risk stratification in this setting, while external validation in independent Middle Eastern cohorts and prospective outcome studies remains essential.

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