

Surrogate Insulin Resistance Indices as Markers of Lifetime Cardiovascular Disease Risk Across Obesity Phenotypes in Bangladeshi Adults: A Cross-sectional Study

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Abstract

Background

Obesity is a major independent risk factor for insulin resistance and cardiovascular disease (CVD). Combining BMI with waist circumference identifies distinct obesity phenotypes that may differ in insulin resistance and cardiovascular risk. The triglyceride-glucose (TyG) index and triglyceride-to-high-density lipoprotein cholesterol ratio (TG/HDL-C) are inexpensive surrogate markers of insulin resistance. However, their ability to identify lifetime CVD risk across obesity phenotypes has not been evaluated in Bangladeshi adults.

Methods

This cross-sectional study included 400 eligible adults from the outpatient department of Bangladesh Medical University between August 2022 and February 2023. Participants were initially classified as non-obese or obese. Then 301 obese participants were further categorized into phenotype A (obese BMI, non-obese WC), phenotype B (non-obese BMI, obese WC) and phenotype C (obese BMI and obese WC). The TyG index and TG/HDL-C ratio were calculated from fasting glucose and lipid profiles. Lifetime CVD risk was estimated using the QRISK lifetime CVD risk calculator. Group comparisons were performed using the Kruskal–Wallis test followed by Dunn–Bonferroni post hoc analysis. Multivariable logistic regression was used to determine the associations of the TyG index and TG/HDL-C ratio with lifetime CVD risk. Diagnostic performance was evaluated using ROC curve analysis.

Results

Surrogate insulin resistance indices and lifetime CVD risk were significantly higher in phenotype C compared with phenotype A. The TyG index [aOR 16.64, 95% CI 8.56–32.35] and TG/HDL-C ratio [aOR 1.72, 95% CI 1.52–1.94] were associated with elevated lifetime CVD risk. Phenotype-specific optimal cutoff values of TyG index to detect CVD risk were 8.81 (AUC = 0.773) for phenotype A, 9.04 (AUC = 0.789) for phenotype B and 9.15 (AUC = 0.819) for phenotype C. Correspondingly, optimal cutoff values of TG/HDL-C were 3.93 (AUC = 0.901), 4.72 (AUC = 0.830) and 4.94 (AUC = 0.877) for phenotype A, B and C respectively.

Conclusions

The TyG index and TG/HDL-C ratio demonstrated good discriminatory performance for identifying individuals at elevated lifetime CVD risk. Phenotype-specific cutoff values may improve individualized cardiovascular risk stratification after external validation, particularly in resource-limited settings such as Bangladesh.

Clinical trial registration

Not applicable.

Background

Non-communicable diseases (NCDs) are the leading cause of morbidity and mortality worldwide, accounting for 43 million deaths annually, representing almost 75% of all global deaths. Among all NCDs, CVD alone caused an estimated 19 million deaths in 2021, most from heart attacks and stroke [1]. It poses a substantial public health challenge, particularly in low- and middle-income countries such as Bangladesh, where the burden of non-communicable diseases continues to rise [2]. Obesity is a well-established independent risk factor for CVD and all-cause mortality [3]. However, body mass index (BMI), the most widely used measure of obesity, has some limitations in assessing adiposity in South Asian populations because individuals with a normal BMI may still have excess abdominal adiposity and an increased risk of cardiometabolic disease [4–6]. Therefore, relying solely on BMI may underestimate cardiovascular risk.

Combining BMI with waist circumference (WC) provides a more comprehensive assessment of adiposity and allows individuals to be classified into distinct obesity phenotypes: phenotype A (obese BMI, non-obese WC), phenotype B (non-obese BMI, obese WC) and phenotype C (obese BMI, obese WC) [7]. These phenotypes may better reflect differences in metabolic abnormalities and cardiovascular risk than BMI alone.

Insulin resistance is considered the primary mechanism linking obesity to CVD [8, 9]. Excess adipose tissue promotes the release of free fatty acids, inflammatory cytokines and reactive oxygen species, leading to insulin resistance, dyslipidemia, endothelial dysfunction, oxidative stress and accelerated atherosclerosis [10–13]. Consequently, biomarkers of insulin resistance may help to identify individuals at increased cardiovascular risk.

The hyperinsulinaemic–euglycaemic clamp is the gold standard method for measuring insulin resistance, which is costly, invasive and impractical for large-scale clinical use [14]. Similarly, the homeostatic model assessment of insulin resistance (HOMA-IR) requires plasma insulin measurement, which is not readily available in many resource-limited settings [15]. In contrast, the triglyceride–glucose (TyG) index and the triglyceride-to-high-density lipoprotein cholesterol (TG/HDL-C) ratio are inexpensive, easily calculated surrogate markers of insulin resistance derived from routine laboratory tests such as fasting blood glucose levels and fasting lipid profile [16, 17]. Both have been associated with insulin resistance, type 2 diabetes, metabolic syndrome, non-alcoholic fatty liver disease and cardiovascular disease [18, 19].

Several validated risk prediction tools are available for estimating cardiovascular risk, including the Framingham Risk Score, QRISK2 and the ASCVD risk calculator [20]. However, most estimate only a 10-

year risk. The QRISK lifetime model provides a more comprehensive assessment of cardiovascular risk over the life course [21].

Because different obesity phenotypes have distinct influences on insulin resistance and cardiometabolic risk, the diagnostic performance of surrogate insulin resistance indices may also differ across obesity phenotypes [7, 22]. However, there is a lack of studies on lifetime CVD risk across different obesity phenotypes in Bangladeshi adults, especially using TyG index and TG/HDL-C ratio. Therefore, the study aimed to evaluate the diagnostic performance of TyG index and TG/HDL-C ratio for identifying elevated lifetime CVD risk across different obesity phenotypes in Bangladeshi adults.

Methods

Study design and setting

This observational cross-sectional study was conducted at Bangladesh Medical University (BMU) from August 2022 to February 2023. A non-probability convenience sampling technique was used to enroll 400 eligible participants according to predefined inclusion and exclusion criteria. The study protocol was approved by the Institutional Review Board of BMU and written informed consent was obtained from all participants before enrollment.

Sample size:

The sample size was calculated based on expected sensitivity of TG/HDL-C ratio for identifying high lifetime CVD risk from a previous study [22], using the formula: $n = Z^2 P(100-P)/d^2$, where Z was 1.96 for a 95% confidence level, P was the expected sensitivity of the TG/HDL-C ratio (86%) [22], and d was the allowable error (8.5%). Considering a reported prevalence of high lifetime CVD risk of 23% [22], the total required sample size was: $N = 377$. Ultimately, A total of 400 participants were included in the study.

Study population

Initially 582 accompanying attendants were assessed for eligibility. A total 400 Participants were enrolled according to the eligibility criteria. Adults of either sex were eligible for inclusion. Individuals with a history of cardiovascular disease (myocardial infarction or angina), diabetes or prediabetes (fasting plasma glucose ≥ 6.1 mmol/L and/or 2-hour plasma glucose ≥ 7.8 mmol/L after a 75-g oral glucose load), cerebrovascular disease, chronic liver disease, malignancy, pregnancy, or current use of lipid-lowering agents or corticosteroids were excluded because these conditions and medications may influence glucose metabolism, lipid metabolism, insulin resistance and cardiovascular risk.

Study variables

Sociodemographic characteristics (age, sex, smoking status, family history of cardiovascular disease and treatment history for hypertension), anthropometric measurements (height, weight, body mass index [BMI] and waist circumference [WC]), blood pressure, fasting plasma glucose, 2-hour plasma glucose

and fasting lipid profile (total cholesterol, triglycerides, HDL-cholesterol and LDL-cholesterol) were recorded. The triglyceride–glucose (TyG) index was calculated as $\ln [\text{fasting triglycerides (mg/dL)} \times \text{fasting blood glucose (mg/dL)} / 2]$ [22] and the triglyceride-to-HDL-cholesterol (TG/HDL-C) ratio was calculated as $\text{fasting triglycerides (mg/dL)} / \text{fasting HDL-cholesterol (mg/dL)}$ [23]. Lifetime cardiovascular disease (CVD) risk was estimated using the QRISK Lifetime 2011 software, based on the original lifetime-risk model developed by Hippisley et al. A lifetime CVD risk score $\geq 50\%$ was considered indicative of high lifetime CVD risk [21].

Classification of obesity phenotypes

Participants were initially classified as non-obese or obese based on Asian-specific BMI and WC criteria [Obese BMI ($\geq 25.00 \text{ kg/m}^2$); Obese WC ($\geq 90.00 \text{ cm}$ in men and $\geq 80.00 \text{ cm}$ in women)] [7]. Non-obese participants had both a non-obese BMI and WC. Obese participants were defined as having an obese BMI and/or WC. Obese subjects were subsequently classified into three obesity phenotypes; phenotype A (obese BMI, non-obese WC), phenotype B (non-obese BMI, obese WC) and phenotype C (obese BMI, obese WC). This classification enabled assessment of the independent and combined effects of general and central obesity on insulin resistance and lifetime cardiovascular risk.

Data sources and measurements

Sociodemographic and clinical information were collected by interview using a predesigned questionnaire and data collection sheet (Supplementary file-1). Blood pressure was measured with the participant in a seated position using a standard sphygmomanometer. Anthropometric measurements included height, weight, body mass index (BMI), and waist circumference (WC). Height was measured with participants barefooted and standing upright. Body weight was measured in kilograms using a portable digital weighing scale while participants wore light clothing and no shoes. BMI was calculated as weight in kilograms divided by height in meters squared (kg/m^2). Waist circumference was measured in centimeters using a non-stretchable measuring tape positioned immediately above the iliac crest. Under aseptic conditions, fasting venous blood was for measurement of fasting plasma glucose, lipid profile, SGPT, S. creatinine. Another venous blood sample was collected 2 h after a 75-g oral glucose load for measurement of 2-h post-load plasma glucose. All biochemical analyses were performed at the Department of Biochemistry and Molecular Biology, Bangladesh Medical University. Serum total cholesterol, serum triglycerides, serum high-density lipoprotein cholesterol, SGPT, serum creatinine was measured in enzymatic method. Low-density lipoprotein cholesterol (LDL-C) was calculated using the Friedewald equation. LDL-C was not calculated when serum triglyceride concentrations exceeded 400 mg/dL. Individuals with high FPG, high 2hPG, high SGPT and high S. creatinine were excluded. TyG and TG/HDL-C were calculated using standard formulas and lifetime cardiovascular risk was estimated using the QRISK lifetime 2011 software. All the sociodemographic, clinical, anthropometric, laboratory information and calculated data were recorded in the questionnaire and data collection sheet (Supplementary file -1).

Bias

Several measures were undertaken to minimize potential bias. Standardized protocols were used for anthropometric measurements and laboratory analyses. published definitions were applied for obesity phenotypes and surrogate insulin resistance indices. Exclusion criteria were applied to reduce the effect of confounding variables. However, selection bias due to convenience sampling from a single tertiary-care center, information bias from self-reported variables and residual confounding variables from unmeasured lifestyle and socioeconomic factors cannot be completely excluded.

Statistical analysis

Data were entered and analyzed using IBM SPSS Statistics version 26. Continuous variables are presented as mean $\pm$ standard deviation (SD) for normally distributed data or median (interquartile range [IQR]) for non-normally distributed data. Differences among obesity phenotypes were assessed using the Kruskal–Wallis test followed by Dunn–Bonferroni post hoc comparisons. Multivariable logistic regression analysis was performed to examine the independent associations of TyG and TG/HDL-C with lifetime CVD risk after adjustment for WC in separate models. Model fit was evaluated using the McFadden R^2 and the Hosmer–Lemeshow goodness-of-fit test. Multicollinearity was assessed using variance inflation factors (VIFs), with VIF <5 indicating the absence of problematic multicollinearity. Receiver operating characteristic (ROC) curve analysis was performed to evaluate the diagnostic performance of TyG index and TG/HDL-C ratio for identifying high lifetime CVD risk across obesity phenotypes. Optimal cutoff values were determined using the Youden index. P value <0.05 was considered statistically significant.

Missing data

LDL-C was calculated using the Friedewald formula. LDL-C could not be calculated for 19 participants (4.75%) because their triglyceride concentrations exceeded 400 mg/dL, a level at which the Friedewald equation is not considered appropriate. Consequently, analyses involving LDL-C were performed with available LDL-C values from 381 participants.

Use of artificial intelligence

During the preparation of this manuscript, the authors used ChatGPT (5.6) to assist with English-language editing and to improve the clarity and readability of selected passages. ChatGPT was not used for data collection, statistical analysis or generation of the study results. All AI-assisted content were critically reviewed and verified by the authors, who take full responsibility for the final content of the manuscript.

Results

A total 582 participants were assessed for eligibility. Eligible 400 participants were enrolled in the study and remaining 182 participants were excluded. From enrolled participants, 99 were classified as non-

obese, while the remaining 301 were classified as obese. The obese participants were further categorized into three obesity phenotypes: phenotype A (n = 36), phenotype B (n = 69) and phenotype C (n = 196). The flow of participants and obesity phenotype is presented in figure 1.

Baseline characteristics of the obese participants

Among the three obesity phenotypes, phenotype C exhibited the greatest anthropometric and metabolic burden. Body mass index and body weight increased progressively from phenotype B to phenotype A and were highest in phenotype C, whereas waist circumference was lowest in phenotype A and highest in phenotype C (all $P < 0.001$; Table 2). Similarly, serum triglyceride levels, the TyG index, the TG/HDL-C ratio and lifetime cardiovascular disease (CVD) risk were lowest in phenotype A and highest in phenotype C ($P = 0.014$, $P = 0.015$, $P = 0.018$ and $P = 0.018$, respectively). In contrast, age, total cholesterol, HDL-cholesterol and LDL-cholesterol did not differ significantly across the three obesity phenotypes (Table 1).

Table 1. Baseline characteristics of participants across obesity phenotypes

Variable	Phenotype A	Phenotype B	Phenotype C	p value
BMI (kg/m²)	25.8 (25.4-27.1) ^a	23.5 (22.6-24.0) ^b	27.5 (26.2-29.9) ^c	<0.001
Age (years)	37.5 (33.8-45.0) ^a	36.0 (33.0-43.0) ^a	38.0 (33.0-45.8) ^a	0.698
WC (cm)	81.0 (78.8-88.0) ^a	91.0 (87.0-94.0) ^b	96.0 (91.0-100.0) ^c	<0.001
Weight (kg)	67.5 (62.8-72.5) ^a	61.0 (57.0-68.0) ^b	72.0 (67.0-80.0) ^c	<0.001
TG (mg/dL)	127 (107-181) ^a	164 (112-241) ^{ab}	175 (122-254) ^b	0.014
TC (mg/dL)	167 (155-193) ^a	170 (150-193) ^a	176 (158-206) ^a	0.153
HDL-C (mg/dL)	40.0 (30.3-46.0) ^a	36.0 (30.0-43.0) ^a	35.7 (31.0-45.0) ^a	0.247
LDL-C (mg/dL)	101 (76.9-121.0) ^a	99.5 (74.8-118) ^a	104 (86-122) ^a	0.279
TyG index	8.74 (8.49-9.08) ^a	9.04 (8.58-9.23) ^{ab}	9.05 (8.64-9.43) ^b	0.015
TG/HDL-C	3.30 (2.43-5.34) ^a	4.27 (3.00-6.65) ^b	4.61 (2.87-7.81) ^b	0.018
Lifetime CVD risk (%)	39.8 (35.4-49.1) ^a	40.8 (37.7-51.0) ^{ab}	44.5 (38.9-52.5) ^b	0.018

BMI, body mass index; WC, waist circumference; TG, triglycerides; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TyG index, triglyceride–glucose index. Data are presented as median (interquartile range [IQR]). Group differences were assessed using the Kruskal–Wallis test, followed by Dunn's post hoc test with Bonferroni correction for pairwise comparisons. Values with different superscript letters within a row differ significantly ($P < 0.05$).

Association of surrogate insulin resistance indices and lifetime CVD risk

Binomial logistic regression analysis was performed to examine the associations between surrogate insulin resistance indices and high lifetime cardiovascular disease (CVD) risk (Table 2). In the unadjusted models, both the triglyceride–glucose (TyG) index and the triglyceride-to-high-density lipoprotein cholesterol (TG/HDL-C) ratio were significantly associated with high lifetime CVD risk (TyG index: OR 18.90, 95% CI 9.83–36.40; TG/HDL-C ratio: OR 1.75, 95% CI 1.55-1.98; both $P < 0.001$). These associations remained statistically significant after adjustment for WC. In the adjusted model, a one unit rise in TyG index was associated with a 16.64-fold higher odds of high CVD burden (95% CI 8.56-32.35), whereas each unit increase in the TG/HDL-C ratio was associated with a 72% increase in the odds of high lifetime CVD risk (OR 1.72, 95% CI 1.52–1.94; both $P < 0.001$).

Table 2. Association between surrogate insulin resistance indices and high lifetime CVD risk

Biomarker	Model	OR	95% CI	P value
TyG index	Unadjusted	18.90	9.83–36.40	<0.001
	Adjusted*	16.64	8.56-32.35	<0.001
TG/HDL-C ratio	Unadjusted	1.75	1.55-1.98	<0.001
	Adjusted*	1.72	1.52–1.94	<0.001

OR, odds ratio; CI, confidence interval; TyG index, triglyceride–glucose index; TG/HDL-C ratio, triglyceride-to-high-density lipoprotein cholesterol ratio.

*Adjusted for WC

Model performance: For the TyG index, McFadden’s pseudo- R^2 was 0.280 and the Hosmer–Lemeshow test indicated acceptable calibration [$\chi^2(8) = 9.83, p = 0.277$]. For the TG/HDL-C ratio, McFadden’s pseudo- R^2 was 0.360 and the Hosmer–Lemeshow test likewise indicated acceptable calibration [$\chi^2(8) = 8.33, p = 0.402$]. Variance inflation factors were <5 .

Diagnostic performance of TyG index

The TyG index demonstrated good discriminatory ability to identify individuals with high lifetime cardiovascular disease (CVD) risk, with an area under the receiver operating characteristic (ROC) curve (AUC) of 0.835 (95% CI 0.795–0.875; $P < 0.001$) in overall study participants. The optimal cut-off value was 9.03, yielding a sensitivity of 81.45% and a specificity of 71.01%. The TyG index also showed good diagnostic performance across all obesity phenotypes. The optimal cut-off values were 8.81 for phenotype A (sensitivity 85.71%, specificity 65.52%), 9.04 for phenotype B (sensitivity 90.00%, specificity 69.39%) and 9.15 for phenotype C (sensitivity 74.32%, specificity 77.05%) (Table 3).

Table 3. Diagnostic performance of the TyG index as marker of lifetime CVD risk across obesity phenotype.

Performance	Overall	Phenotype A	Phenotype B	Phenotype C
AUC (95% CI)	0.835 (0.795-0.875)	0.773 (0.600-0.947)	0.789 (0.677-0.901)	0.819 (0.757-0.877)
p value	<.001	0.002	<.001	<.001
Optimal cut-off	9.03	8.81	9.04	9.15
Sensitivity	81.45% (73.48-87.86)	85.71% (42.13-99.64)	90.00% (68.30-98.77)	74.32% (62.38-83.78)
Specificity	71.01% (65.27-76.30)	65.52% (45.67-82.06)	69.39% (54.58-81.75)	77.05% (68.57-84.10)
PPV	55.80% (50.76-60.73)	37.50% (25.04-51.87)	54.55% (43.44-65.21)	66.27% (58.02-73.63)
NPV	89.50% (85.40-92.55)	95% (73.23-99.17)	94.44% (81.84-98.46)	83.19% (76.84-88.06)
Accuracy	74.25% (69.67-78.47)	69.44% (51.89-83.65)	75.36% (63.51-84.95)	76.02% (69.42-81.82)

AUC, area under the receiver operating characteristic curve; PPV, positive predictive value; NPV, negative predictive value. Figures in parentheses are 95% confidence intervals.

Diagnostic performance of TG/HDL-C ratio

The TG/HDL-C ratio also demonstrated good diagnostic performance for identifying high lifetime CVD risk, with an AUC of 0.888 (95% CI 0.856–0.920; $P < 0.001$) in overall study subjects. The optimal cut-off value was 4.92, providing a sensitivity of 85.48% and a specificity of 76.09%. Phenotype-specific AUCs ranged from 0.830 to 0.901, indicating consistently good discriminatory ability across obesity phenotypes. The optimal cut-off values were 3.93 for phenotype A (sensitivity 85.70%, specificity 75.90%), 4.72 for phenotype B (sensitivity 90.00%, specificity 67.35%) and 4.94 for phenotype C (sensitivity 87.84%, specificity 75.41%) (Table 4).

Table 5. Diagnostic performance of the TG/HDL-C ratio as marker of lifetime CVD risk across obesity phenotype.

Parameter	Overall	Phenotype A	Phenotype B	Phenotype C
AUC (95% CI)	0.888 (0.856-0.920)	0.901 (0.796-0.982)	0.830 (0.729-0.932)	0.877 (0.830-0.924)
p value	<.001	<.001	<.001	<.001
Optimal cut-off	4.92	3.93	4.72	4.94
Sensitivity	85.48% (78.03-91.16)	85.70% (62.40-97.03)	90.00% (68.30-98.77)	87.84% (77.16-94.29)
Specificity	76.09% (70.61-81.00)	75.90% (56.46-89.7)	67.35% (52.00-80.05)	75.41% (66.73-82.75)
PPV	61.63% (56.25-66.74)	50.00% (34.41-65.59)	52.94% (42.31-63.31)	68.42% (61.09-74.94)
NPV	92.11% (88.33-94.73)	97.00% (75.23-99.72)	94.29% (81.37-98.42)	91.09% (84.60-95.00)
Accuracy	79.00% (74.68-82.89)	80.56% (63.98-91.81)	73.91% (61.94-91.21)	80.10% (73.82-85.45)

AUC, area under the receiver operating characteristic curve; PPV, positive predictive value; NPV, negative predictive value. Figures in parentheses are 95% confidence intervals.

Discussion

Obesity is a major independent risk factor for cardiovascular disease and different obesity phenotypes characterized by general and central adiposity confer varying degrees of cardiometabolic risk. In this cross-sectional study, we evaluated the surrogate markers of insulin resistance, the TyG) index and the TG/HDL-C ratio for identifying elevated lifetime CVD risk across obesity phenotypes in Bangladeshi adults.

Among the 301 obese participants classified as obese, 65.12% belonged to phenotype C (combined general and central obesity), indicating that it was the predominant obesity pattern in our obese subjects. This observation agrees with a previous report that South Asians tend to accumulate both overall and visceral adiposity, predisposing them to adverse cardiometabolic outcomes [24].

Phenotype C exhibited the greatest metabolic burden, with significantly higher triglyceride levels, TyG index, TG/HDL-C ratio and lifetime CVD risk than phenotype A, whereas age and conventional cholesterol parameters were similar across phenotypes. Visceral adipose tissue is metabolically more active than subcutaneous fat, releasing excess free fatty acids and pro-inflammatory cytokines that promote insulin resistance, dyslipidemia and endothelial dysfunction [25–27]. The absence of significant differences between phenotypes B and C for TyG and TG/HDL-C further emphasizes the dominant contribution of central obesity to metabolic impairment. These findings are consistent with previous studies in Bangladeshi and other South Asian populations [28].

The present study demonstrated a significant difference in lifetime cardiovascular disease (CVD) risk across obesity phenotypes, with phenotype C exhibiting a significantly higher risk than phenotype A, whereas no significant differences were observed between the adjacent phenotypes (A vs. B and B vs. C). This pattern suggests a progressive increase in cardiovascular risk across obesity phenotypes rather than an abrupt transition, with phenotype B likely representing an intermediate cardiometabolic state. These findings highlight the importance of incorporating waist circumference in addition to body mass index (BMI) when assessing obesity-related cardiometabolic risk. Reliance on BMI alone may fail to identify individuals with excess abdominal adiposity who remain at increased cardiovascular risk despite having normal BMI values. Previous studies have consistently demonstrated that central obesity is more strongly associated with insulin resistance, type 2 diabetes mellitus, metabolic syndrome and cardiovascular disease than general obesity alone. Adipose tissue in abdominal region is metabolically more active and promotes chronic low-grade inflammation, dyslipidemia, endothelial dysfunction and insulin resistance, thereby accelerating atherosclerotic processes [29, 30]. Consequently, waist circumference provides complementary information beyond BMI for cardiovascular risk stratification. The coexistence of general and central obesity, as observed in phenotype C, may therefore represent the highest-risk adiposity phenotype because it reflects both increased overall fat mass and excess visceral fat accumulation, resulting in a cumulative adverse effect on cardiometabolic health [29–31].

Multivariable logistic regression demonstrated that both TyG and TG/HDL-C were independently associated with high estimated lifetime CVD risk after adjustment for WC. The TyG index remained strongly associated (adjusted OR 16.64, 95% CI 8.56–32.35), while TG/HDL-C also showed an independent association (adjusted OR 1.72, 95% CI 1.52–1.94) with CVD risk. Although the effect size for TyG was greater than that reported previously. Methodological differences like the inclusion of only non-diabetic individuals, the relatively narrow TyG range and the use of estimated lifetime CVD risk rather than true cardiovascular events, may explain this observation [22, 32, 33].

Both TyG and TG/HDL-C demonstrated good discriminatory performance across all obesity phenotypes, with AUC values ranging from 0.77 to 0.90. These findings are consistent with previous studies reporting good discriminatory ability of these indices for cardiometabolic outcomes [22, 32–34].

The phenotype-specific optimal cut-off values observed in this study suggest that obesity phenotype-specific thresholds may improve individualized cardiovascular risk stratification compared with a single universal cut-off.

From a clinical perspective, these findings are particularly relevant for Bangladesh and other resource-limited settings, because TyG and TG/HDL-C can be derived from routine fasting blood glucose and lipid measurements, they represent inexpensive and readily available tools for cardiovascular risk assessment and primary prevention. Incorporating these indices into routine clinical practice may facilitate earlier identification of high-risk individuals where advanced investigations are unavailable. Several limitations should be acknowledged. First, the cross-sectional design does not permit determination of temporal or causal relationships between the surrogate insulin resistance indices and

lifetime CVD risk. Second, obesity phenotypes were defined using anthropometric measurements rather than imaging-based assessments of body fat distribution. Third, recruitment from a single tertiary-care center using non-probability sampling may limit the generalizability of the findings. Furthermore, the exclusion of individuals with diabetes or prediabetes may also limit the generalizability of the results to these populations. Finally, lifetime CVD risk was estimated using the QRISK model rather than determined from observed cardiovascular events and residual confounding cannot be excluded despite multivariable adjustment.

Despite these limitations, this is the first study to evaluate TyG index and TG/HDL-C ratio across obesity phenotypes for detecting lifetime cardiovascular risk in Bangladeshi adults. Our findings support the potential role of these inexpensive surrogate markers in improving cardiovascular risk assessment and emphasize the importance of considering obesity phenotype when stratifying cardiovascular risk.

Conclusion

Combined general and central obesity was associated with the highest lifetime cardiovascular disease (CVD) risk and the highest values of insulin resistance indices among Bangladeshi adults. Individuals with central obesity despite a normal BMI also demonstrated an unfavorable cardiovascular risk profile, highlighting the importance of measuring waist circumference alongside BMI for more accurate cardiovascular risk assessment. The TyG index and TG/HDL-C ratio were independently associated with high lifetime CVD risk and showed good discriminatory performance across different obesity phenotypes. Because both indices can be derived from routine fasting blood glucose and lipid measurements, they represent inexpensive and readily available tools for cardiovascular risk stratification, particularly in resource-limited settings such as Bangladesh. The phenotype-specific cut-off values identified in this study may further improve individualized risk assessment. However, these findings should be validated in larger, prospective, multicenter studies before implementation in routine clinical practice.

Abbreviations

AUC, Area Under the Curve

BMI, Body mass index

CI, Confidence Interval

CVD, Cardiovascular disease

HDL-C, High-density lipoprotein cholesterol

HOMA-IR, Homeostatic model assessment of insulin resistance

LDL-C, Low-density lipoprotein cholesterol

NCD, Non-communicable disease

NPV, Negative Predictive Value

OR, Odds Ratio

PPV, Positive Predictive Value

ROC, Receiver operating characteristic

SD, Standard Deviation

SPSS, Statistical Package for the Social Sciences

TC, Total Cholesterol

TG, Triglyceride

TG/HDL-C, Triglyceride-to-high-density lipoprotein cholesterol ratio

TyG, Triglyceride-glucose index

WC, Waist circumference

Declarations

Ethics approval and consent to participate

All methods were performed in accordance with the relevant guidelines and regulations of the Declaration of Helsinki. Ethical approval was obtained from Institutional Review Board (IRB) of Bangladesh Medical University (former Bangabandhu Sheikh Mujib Medical University) [Approval No. BSMMU/2022/7248; Registration no: 3987; approved on 16 July 2022]. Written informed consent was obtained from all participants before enrolment using an informed consent form. A copy of the consent form is available from the corresponding author upon reasonable request.

Consent for publication

Not applicable.

Clinical trial registration

Not applicable.

Availability of data and materials

The datasets generated and/or analysed during the current study are available from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

AS and MMH conceptualized and designed the study. AS, TNS, CMMR, SNR, REB and MMH contributed to data acquisition, analysis and interpretation. AS, TC, MEM and REB drafted the manuscript. All authors revised and approved the final manuscript and agreed to be accountable for all aspects of the work.

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Figures

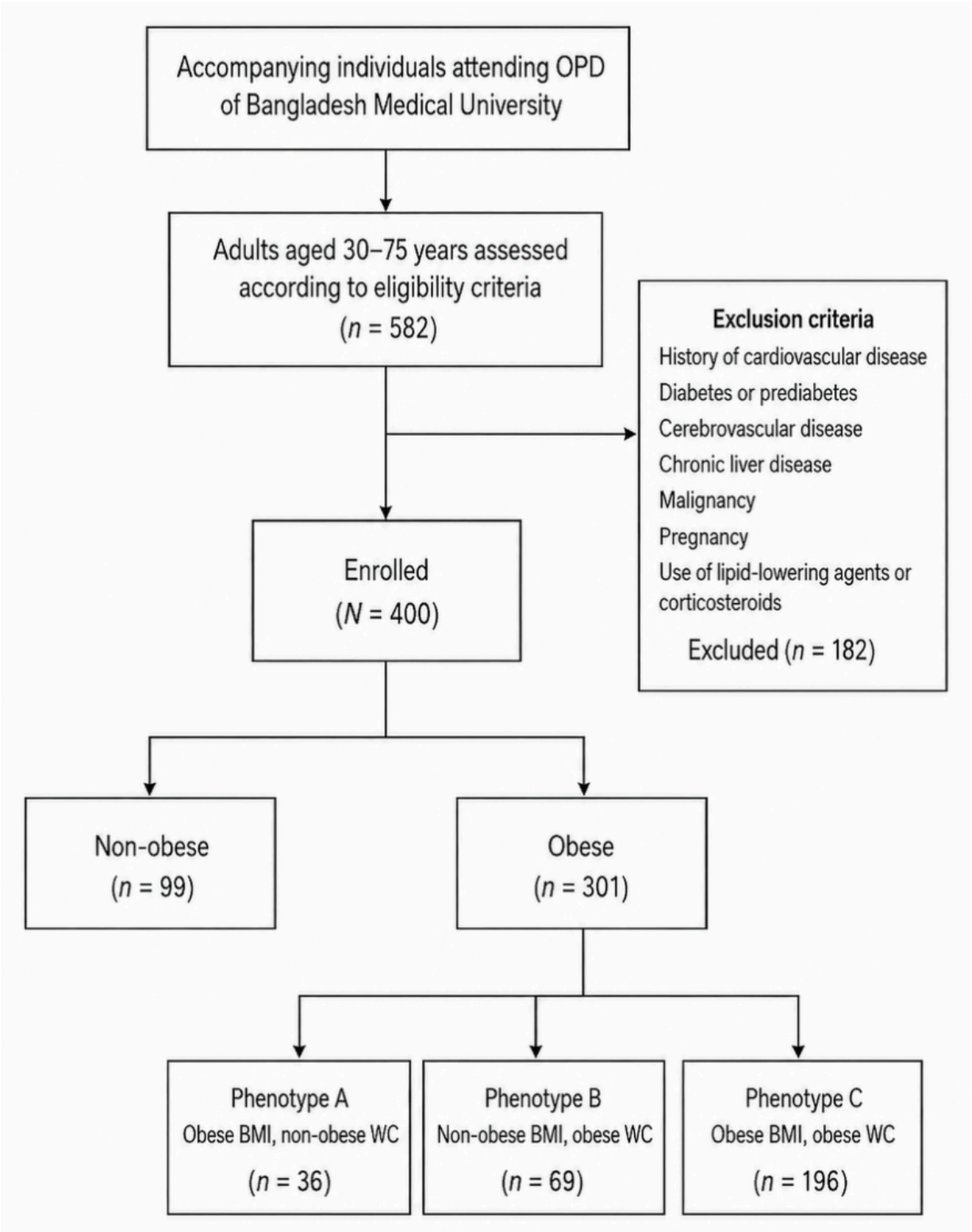


Figure 1

Participant flow

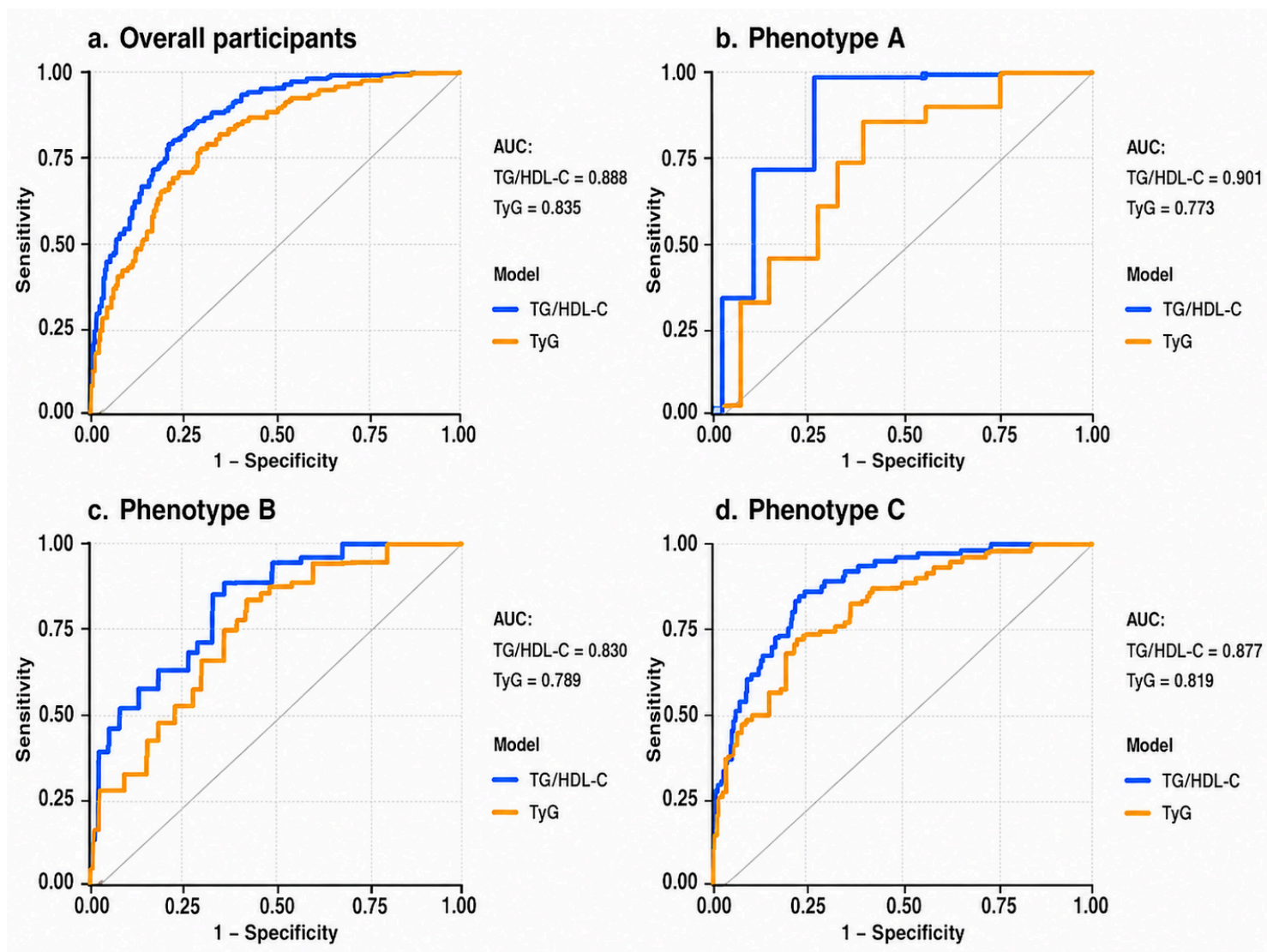


Figure 2

ROC curves of surrogate insulin resistance indices for identifying elevated lifetime CVD risk. Receiver operating characteristic curves show the discriminatory performance of the triglyceride-to-high-density lipoprotein cholesterol ratio (TG/HDL-C) and triglyceride–glucose (TyG) index among (a) overall study participants, (b) obesity phenotype A, (c) obesity phenotype B and (d) obesity phenotype C. The areas under the curve for TyG index and TG/HDL-C ratio were 0.835 and 0.888 in the overall study population, 0.773 and 0.901 in phenotype A, 0.789 and 0.830 in phenotype B and 0.819 and 0.877 in phenotype C, respectively. The diagonal line represents discrimination no better than chance.

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