



## RESEARCH ARTICLE

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# Surrogate indices as tools for investigating the dynamics of insulin resistance in different body mass index categories

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## ABSTRACT

**Introduction:** Insulin resistance (IR) is a complex pathophysiological condition multifactorial etiology characterized by diminished responsiveness of insulin target tissues. Today, various diagnostic approaches involving different laboratory parameters are available, but simple and non-invasive indices based on mathematical models are increasingly used in practice. This study aims to assess the effectiveness of various clinical surrogate indices in predicting IR across a population with varying body weights.

**Methods:** The matched case-control study was conducted between January 2021 and December 2022. Secondary data extracted from the medical records of 129 subjects was analyzed, including demographic characteristics (age and gender), anthropometric measures (height and weight), and biochemical laboratory test results. y further divided into two subgroups based on body mass index (BMI): overweight (BMI between 25 and 29.9 kg/m<sup>2</sup>) and obese (BMI of 30 kg/m<sup>2</sup> or higher). Using laboratory data values for six widely used clinical surrogate markers were calculated: Homeostatic model assessment for IR (HOMA-IR), quantitative insulin sensitivity check index (QUICKI), Mcauley index (MCAi), metabolic score for IR (METS-IR), Triglyceride to Glucose Index (TyG), and TyG to BMI (TyG-BMI).

**Results:** Significant differences in HOMA-IR levels were observed between the groups ( $p < 0.001$ ). A similar pattern was found for the TyG-BMI, with notable differences ( $p < 0.001$ ). The obese participants had the highest mean levels for METS-IR and the TyG index while the control group had the highest mean values for the QUICKI and MCAi indices ( $p < 0.001$ ). According to the analysis, three indices showed statistical significance in predicting IR independent of BMI ( $p < 0.05$ ). Sensitivity and specificity were higher in the obese group (0.704 and 0.891) than in the overweight group (0.631 and 0.721).

**Conclusion:** Given that IR is a multifactorial disease, using derived indices based on a combination of biochemical parameters and anthropometric indicators can significantly aid in predicting and mitigating numerous complications.

**Keywords:** Insulin resistance; homeostatic model assessment for insulin resistance, triglyceride to glucose index; triglyceride to glucose index-body mass index

## INTRODUCTION

Insulin resistance (IR) is a complex pathophysiological condition characterized by diminished responsiveness of insulin (INS) target tissues, notably the liver, skeletal muscle, and adipose tissue, to the metabolic actions of INS (1). The pathogenesis of IR is multifactorial, involving an intricate interplay of genetic predispositions, metabolic disruptions, and a range of environmental factors. Notably, oxidative

stress, mitochondrial dysfunction, chronic inflammation, and genetic mutations, are included in the disruption of INS signal transduction pathways. In addition, lifestyle factors, including poor dietary choices, obesity, and physical inactivity, significantly contribute to the development and exacerbation of IR (2-4). The resultant metabolic disturbances from IR encompass hyperinsulinemia, impaired suppression of hepatic gluconeogenesis, enhanced lipolysis in adipocytes, and reduced glucose (GLU) uptake in muscle tissues, leading to systemic metabolic dysregulation (1-5). Moreover, IR is intricately associated with a spectrum of adverse health conditions, including but not limited to, visceral obesity, dyslipidemia, endothelial dysfunction, cardiovascular diseases, oncogenic processes, polycystic ovary syndrome (PCOS), and non-alcoholic fatty liver

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disease (3,6). However, the most important complication of IR is type 2 diabetes mellitus (DM2), a condition that significantly contributes to the global burden of disease (7).

While IR has traditionally been associated with an elderly population, recent trends indicate a notable increase in its prevalence among middle-aged individuals, a shift attributed primarily to rising obesity rates and sedentary lifestyle practices (6). Epidemiological studies reveal that approximately 46.5% of the global adult population is affected by IR, with the incidence rate in the United States surpassing that observed in European countries (8,9). The influence of gender on IR prevalence is also significant, with data showing that younger males are more frequently affected than females (10). The variability in IR prevalence across populations can be attributed to variations in adipose tissue distribution and the biological effects of sex hormones, such as estrogen and testosterone. These elements are important for understanding the pathophysiological mechanisms behind IR and for its clinical evaluation and management (4,11). Notably, the condition is profoundly prevalent in women with PCOS and obesity, affecting around 80% of this subgroup, and remains a concern for 30-40% of women with PCOS who maintain a normal body weight (12). Emerging research further highlights a concerning trend of IR incidence among adolescents, including those with normal body weight, underscoring the need for heightened awareness and early intervention strategies (10,13).

It is important to acknowledge that the observed disparities in IR prevalence may stem from globally inconsistent diagnostic criteria, demographic variations in the studied populations, and thresholds for the diagnostic parameters (1,9). The hyperinsulinemic clamp technique, despite being the gold standard for diagnosing IR, is seldom utilized in routine clinical praxis due to its extensive duration, cost, and procedural complexity (14). Today, various diagnostic approaches involving different laboratory parameters are available, but simple and non-invasive indices based on mathematical models are increasingly used in practice (14,15). Among these, the Homeostasis Model Assessment of IR (HOMA-IR) and the Triglyceride/Glucose Index (TyG) are commonly used indices for IR diagnosis, incorporating fasting glucose levels into calculations (15). HOMA-IR considers fasting INS levels, while the TyG index, bypasses the direct measurement of INS, and therefore is widely used in clinical practice, mainly for primary care screening purposes. The TyG index is particularly valuable in evaluating lipid metabolism disorders that play a role in IR development (16). Other indices, the Metabolic Score for IR (METS-IR), the TyG to body mass index (BMI) ratio, and measures of INS sensitivity, such as the validated Quantitative Insulin Sensitivity Check Index (QUICKI) and the McAuley index (MCAi), have been utilized in numerous research studies to assess IR. When interpreting these indices, threshold values should be considered with the understanding that age, gender, and ethnicity may affect the results (14,17,18). Therefore, this study aims to evaluate the efficacy of various clinical surrogate indices in predicting IR across a population with a range of body weights.

## METHODS

This matched case-control study was conducted between January 2021 and December 2022. Ethical approval was obtained from the Ethics Committee of the Faculty of Health Studies at the University of Sarajevo (number 04-7-17-6/23). In our study, secondary data extracted from medical records were used, and patients' informed consent was not required. Personal data were protected and treated confidentially following the principles of the Declaration of Helsinki.

We analyzed data from 129 subjects, and they included demographic characteristics (age and gender), anthropometric measures (height and weight), and biochemical laboratory test results. Among the included subjects, 91 had confirmed diagnoses of IR and body mass index (BMI) exceeding 25 kg/m<sup>2</sup> and they were selected for the primary study group. This group was subsequently stratified based on BMI score into two subgroups: Overweight (BMI ranging from 25 to 29.9 kg/m<sup>2</sup>) and obese (BMI of 30 kg/m<sup>2</sup> or higher). Data from 38 healthy subjects with a BMI <25 kg/m<sup>2</sup> were matched with the study group based on age and gender and were selected as a control group. In addition, the average age of the subjects rounded to the closest 5 was used for further analysis. The study's exclusion criteria were age under 18, those with a confirmed diagnosis of diabetes mellitus or PCOS, subjects receiving treatments that might influence the laboratory test results, and subjects with incomplete data records.

Blood specimens were obtained from participants following a 12-hour overnight fast, adhering to the protocols of good laboratory practice. The analytical procedure for GLU quantification employed the GLU oxidase spectrophotometry method, whereas INS concentrations were assessed using a chemiluminescence immunoassay technique. The established reference intervals for GLU and INS adhered to the manufacturer's guidelines, set at 3.9-6.2 mmol/L for GLU and 2.2-25.0 µIU/mL for INS, respectively. For the determination of total cholesterol (TC), high-density lipoproteins (HDL), and triglycerides (TGL), enzymatic methods were utilized, specifically leveraging the enzymatic activities of cholesterol oxidase-peroxidase, catalase, and glycerol kinase-peroxidase, with measurements conducted photometrically. The reference ranges for TC, TGL and HDL were 3.9-5.2 mmol/L, 0.1-1.7 mmol/L, and 1.15-2.2 mmol/L, respectively. The calculation of low-density lipoprotein (LDL) levels was performed using the Friedewald formula [LDL = (TC) - (HDL) - (TGL/5)], with reference range 2.6-4.1 mmol/L. The analytical processes were conducted utilizing Mindray CL-900i and Mindray BS-480 analyzers, products of Shenzhen Mindray Bio-Medical Electronics Co., China. To ensure the accuracy and precision of the measurements, commercial control samples provided by RANDOX Controls, at two different concentration levels, were incorporated into the analysis.

Utilizing laboratory data, we calculated values for six widely used clinical surrogate markers, employing the following calculations from the study Romo-Romo et al.:

1. Homeostatic model assessment for IR - HOMA-IR = [Fasting Glucose (mmol/L) × Fasting Insulin (mU/L)]/22.5,

- Quantitative insulin sensitivity check index - QUICKI =  $1/[\text{Log}(\text{Fasting Insulin (mU/L)}) + \text{Log}(\text{Fasting Glucose (mg/dL)})]$ ,
- McAuley index -  $\text{MCAi} = \text{Exp}\{2.63 - [0.28 \times \text{Ln}(\text{Fasting Insulin (mU/L)})] - [0.31 \times \text{Ln}(\text{Fasting Triglycerides (mg/dL)})]\}$ ,
- Metabolic score for IR -  $\text{METS-IR} = [\text{Log}((2 \times \text{Fasting Glucose (mg/dL)}) + \text{Fasting Triglycerides (mg/dL)}) \times \text{BMI (kg/m}^2)] / [\text{Log}(\text{HDL Cholesterol (mg/dL)})]$ ,
- Triglyceride to glucose index -  $\text{TyG} = \text{Ln}[\text{Fasting Triglycerides (mg/dL)} \times \text{Fasting Glucose (mg/dL)} / 2]$ ,
- TyG to body mass index =  $\text{TyG index} \times \text{BMI (kg/m}^2)$ .

Statistical analysis in this study was conducted using SPSS software (version 27.0, IBM Corp., Armonk, NY, USA). Continuous variables were presented as mean (M) and standard deviation (SD), and categorical variables were summarized by their frequency (N) and percentage (%). The normality of data distribution was evaluated using the Kolmogorov-Smirnov test, and for data not adhering to a normal distribution, non-parametric tests were employed. For comparing categorical variables across different groups, Pearson's Chi-square test was utilized, whereas the Kruskal-Wallis (KW) test was applied for continuous variables. The associations between categorical variables and the various indices were explored through multivariate regression analysis, reporting odds ratios (OR), and 95% confidence intervals (95% CI). To assess the diagnostic accuracy of the clinical surrogate markers in overweight and obese individuals, receiver operating characteristic (ROC) curves were plotted, and the diagnostic performance was quantified using the area under the curve (AUC). A  $p \leq 0.05$  was considered statistically significant, setting the threshold for statistical significance at 5%. The data sets used and/or analyzed in this study are available on request from the corresponding author

## RESULTS

The baseline characteristics of the study population are presented in Table 1. A total of 129 subjects with a mean age of  $34.43 \pm 6.71$  years and females in the majority ( $n = 103$ ; 79.8%) were included in the study. The largest proportion of study participants was in the overweight group ( $n = 54$ ; 41.9%), followed by the control group ( $n = 38$ ; 29.5%) and the obese group ( $n = 37$ ; 28.7%). Statistically significant differences were not found between the groups in terms of gender ( $\chi^2 = 1.699$ ;  $p = 0.428$ ) and age ( $\chi^2 = 5.333$ ;  $p = 0.069$ ).

In Table 2, the levels of the biochemical parameters in the study groups are presented. Both subgroups with IR

had statistically higher mean GLU levels ( $5.334 \pm 0.578$ ,  $5.422 \pm 0.480$  mmol/L;  $p < 0.001$ ), TC levels ( $5.358 \pm 0.731$ ,  $5.690 \pm 0.678$  mmol/L;  $p < 0.001$ ), LDL ( $3.409 \pm 0.743$ ,  $3.620 \pm 0.630$  mmol/L;  $p < 0.001$ ), and TGL ( $1.690 \pm 0.525$ ,  $1.975 \pm 0.650$  mmol/L;  $p < 0.001$ ) than the control group. INS concentrations were significantly higher ( $p < 0.001$ ), being twice as high in overweight subjects ( $14.722 \pm 5.098$   $\mu\text{IU/mL}$ ) and threefold higher in obese subjects ( $19.311 \pm 6.426$   $\mu\text{IU/mL}$ ), compared to the control group ( $6.679 \pm 3.053$   $\mu\text{IU/mL}$ ). The mean HDL levels did not differ significantly between the groups ( $p = 0.903$ ).

Significant differences in HOMA-IR levels were observed between the groups ( $p < 0.001$ ). In the overweight group, levels were twice as high ( $3.526 \pm 1.423$ ), and in the obese group threefold higher ( $4.670 \pm 1.637$ ) compared to the control group ( $1.505 \pm 0.736$ ). A similar pattern was found for the TyG-BMI, with notable differences ( $p < 0.001$ ). The obese participants had the highest mean levels for METS-IR and the TyG index ( $50.73 \pm 13.12$  and  $5.382 \pm 1.881$ , respectively), while the control group had the highest mean values for the QUICKI ( $0.369 \pm 0.030$ ) and MCAi ( $8.013 \pm 1.212$ ) indices ( $p < 0.001$ ) (Table 3).

The AUC and ROC analyses for six indices associated with IR and sensitivity stratified by BMI are presented in (Table 4, Figure 1A and B). According to the analysis, three indices showed statistical significance in predicting IR independent of BMI ( $p < 0.05$ ). In the obese group, TyG-BMI had good predictive power for discriminating IR with the highest AUC (0.820), along with the highest sensitivity and specificity (0.841 and 0.877, respectively). In contrast, it had limited discriminatory power in the overweight group, with an AUC of 0.602 and lower sensitivity (0.631) and specificity (0.721). Ty-G showed moderate predictive power in the obese group with an AUC of 0.734, a sensitivity of 0.769, and a specificity of 0.707, while the predictive power was limited in the overweight group. HOMA-IR showed moderate predictive power in the obese group (AUC = 0.720) and limited in the overweight group (AUC = 0.602). Sensitivity and specificity were higher in the obese group (0.704 and 0.891) than in the overweight group (0.631 and 0.721).

## DISCUSSION

In the evaluation of IR, various indices are currently in use. However, according to literature data, their applicability can be limited in certain scenarios, necessitating cautious interpretation of results (17). Our research focused on the utility of the six most frequently used derived indices for

**TABLE 1.** Baseline characteristics of study participants

Variable	IR group				Control		Total		$\chi^2$	p-value
	Overweight		Obese		n	%	n	%		
	n	%	n	%						
Gender										
Male	12	22.2	9	24.3	5	13.2	26	20.2	1.699	0.428
Female	42	77.8	28	75.7	33	86.8	103	79.8		
Age (years)										
<35	25	46.3	17	45.9	26	68.4	68	52.7	5.333	0.069
≥35	29	53.7	20	54.1	12	31.6	61	47.3		

**TABLE 2.** Biochemical parameters according to the body mass index categories

Variable	IR group		Control	Kruskal–Wallis test	p-value
	Overweight	Obese			
	Mean±SD (Min-Max)	Mean±SD (Min-Max)	Mean±SD (Min-Max)		
GLU (mmol/L)	5.334±0.578 (4.190-8.010)	5.422±0.480 (4.550-6.360)	4.961±0.249 (4.240-5.430)	22.605	<0.001
INS (μIU/mL)	14.722±5.098 (7.200-34.490)	19.311±6.426 (7.620-31.200)	6.679±3.053 (3.200-17.330)	74.997	<0.001
TC (mmol/L)	5.358±0.731 (3.890-6.830)	5.690±0.678 (4.650-7.310)	4.330±0.952 (3.710-8.190)	44.522	<0.001
HDL (mmol/L)	1.168±0.211 (0.760-1.640)	1.159±0.201 (0.760-1.650)	1.207±0.268 (0.930-1.880)	0.205	0.903
LDL (mmol/L)	3.409±0.743 (1.700-5.700)	3.620±0.630 (2.300-5.000)	2.555±0.830 (1.700-6.000)	34.498	<0.001
TGL (mmol/L)	1.690±0.525 (0.660-3.450)	1.975±0.650 (0.790-3.640)	1.253±0.375 (0.720-2.830)	36.439	<0.001

GLU: Glucose; INS: Insulin; TC: Total cholesterol; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; TGL: Triglycerides; SD: Standard deviation

**TABLE 3.** Clinical surrogate biomarkers according to the body mass index category

Variable	IR group		Control	Kruskal–Wallis test	p-value
	Overweight	Obese			
	Mean±SD (Min-Max)	Mean±SD (Min-Max)	Mean±SD (Min-Max)		
Homeostatic model assessment for insulin resistance	3.526±1.423 (1.600-8.900)	4.670±1.637 (1.800-7.700)	1.505±0.736 (0.700-4.100)	38.702	<0.001
Metabolic score for insulin resistance	46.90±9.44 (30.73-78.12)	50.73±13.12 (30.73-85.80)	44.55±6.94 (34.30-68.27)	27.524	<0.001
Triglyceride to glucose index	4.531±1.594 (1.756-9.612)	5.382±1.881 (2.046-10.265)	3.114±1.014 (1.778-7.514)	38.281	<0.001
Triglyceride to glucose index - body mass index	124.060±46.366 (49.859-275.890)	172.981±63.144 (65.066-342.844)	73.680±24.044 (41.615-177.322)	57.680	<0.001
Quantitative insulin sensitivity check index	0.321±0.015 (0.281-0.354)	0.309±0.016 (0.286-0.349)	0.369±0.030 (0.311-0.408)	76.360	<0.001
McAuley index	5.794±0.955 (3.507-8.084)	5.146±0.931 (3.567-7.596)	8.013±1.212 (4.521-9.467)	67.030	<0.001

**TABLE 4.** Receiver operating characteristics curve analysis of surrogate clinical indices in the detection of insulin resistance in obese and overweight individuals

Group	Variable	area under the curve (95% confidence intervals)	Sensitivity	Specificity	Cut off	p-value
Overweight	HOMA-IR	0.602 (0.505-0.699)	0.631	0.721	2.620490	0.047
	METS	0.396 (0.299-0.493)	0.341	0.491	38.6561	0.428
	TyG-BMI	0.562 (0.461-0.633)	0.611	0.581	77.83518	0.050
	Ty-G	0.584 (0.484-0.684)	0.597	0.594	3.16850	0.049
	QUICKI	0.378 (2.81-0.476)	0.211	0.472	0.30419	0.491
	MCAi	0.384 (0.285-0.482)	0.384	0.612	4.86249	0.474
Obese	HOMA-IR	0.720 (0.633-0.808)	0.704	0.891	2.99510	0.024
	METS	0.330 (0.233-0.428)	0.361	0.451	32.6472	0.472
	TyG-BMI	0.820 (0.737-0.903)	0.841	0.877	123.44868	<0.001
	Ty-G	0.734 (0.636-0.833)	0.769	0.707	3.67293	0.019
	QUICKI	0.172 (0.100-0.244)	0.138	0.197	0.28489	0.681
	MCAi	0.194 (0.144-0.274)	0.241	0.184	3.53703	0.512

HOMA-IR: Homeostatic model assessment for insulin resistance; TyG: Triglyceride to glucose; BMI: Body mass index; METS: Metabolic score; QUICKI: Quantitative insulin sensitivity check index; MCAi: McAuley index

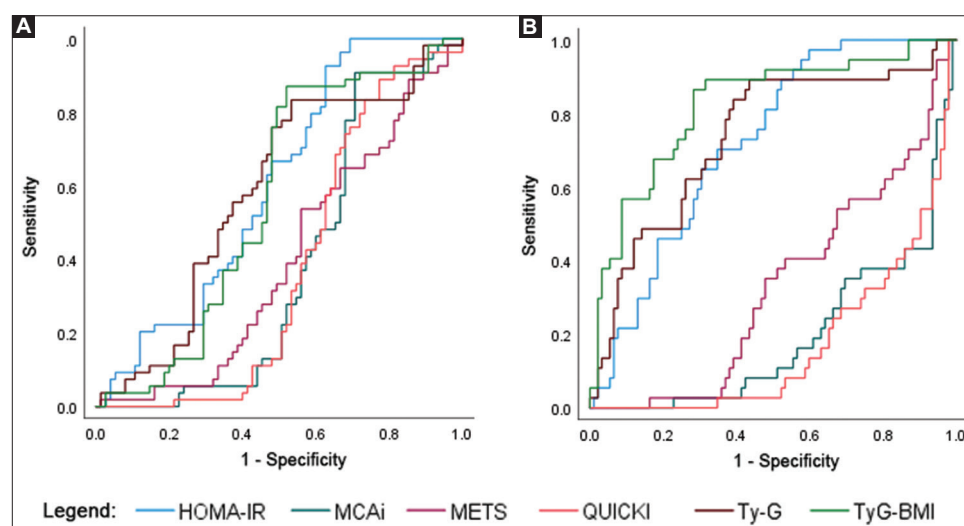
assessing IR and insulin sensitivity (IS) across different BMI categories, given the significant role obesity plays in IR development. Among the utilized indices, Quicki, MCAi, and METS demonstrated no predictive value in assessing IR across different BMI categories. Observed mean values were higher among individuals with normal BMI, compared to overweight and obese individuals, and this finding supports the index's role in IS assessment.

For accurate interpretation of derived indices values, it's crucial to consider various factors, including age, gender, and mentioned BMI. Notably, our study observed a predominance of the female gender with IR, aligning with previously conducted studies by Yilmaz et al. (19) and Benites-Zapata (20). The correlation between BMI and IR is further highlighted in Horáková's et al. study (21),

suggesting that the risk of developing IR significantly increases with BMI, regardless of age.

We observed statistically significant differences in lipid parameters among overweight and obese subjects, except for HDL cholesterol levels. Our findings align with a study by Agius et al. (22) and contrast with Yilmaz et al. (19). However, incorporating these parameters in the assessment of IR could be highly advantageous. Dyslipidemia, when combined with IR, results in a decrease in HDL cholesterol levels and an increase in triglyceride and LDL cholesterol levels. This combination impedes the pancreas's ability to adequately respond to INS secretion when blood GLU levels are elevated. It is known that dyslipidemia and IR pose a high risk for the development of cardiovascular disease, and the application of derived indices could potentially assist





**FIGURE 1.** ROC analysis of surrogate clinical indices in the detection of insulin resistance in obese and overweight individuals. (A) - ROC analysis of the indices for the overweight group, (B) - ROC analysis of the indices for the obese group. ROC: Receiver operating characteristic.

in preventing numerous complications. In this context, the use of effective and precise indices is of immense benefit, as they aid in reducing health complications stemming from the associated metabolic disorders.

In recent years, the HOMA-IR index has shown considerable potential for assessing IR in clinical practice. These indices could offer valuable insights into the management and prevention of conditions associated with IR. In an Iranian cross-sectional study conducted by Mohammadabadi et al. (23), the mean value of the HOMA-IR was  $1.9 \pm 0.21$  among 61 obese women with IR. In contrast, Yilmaz et al. (19) reported a mean HOMA-IR value of  $4.52 \pm 4.6$  in the obese group, with a slightly lower cut-off value of  $>2.24$ . Interestingly, a Chinese study with a higher cut-off value of 3.39 reported significantly higher HOMA-IR values of  $8.05 \pm 7.98$  in subjects with DM2 and BMI values below  $35 \text{ kg/m}^2$  (24). In our study, which predominantly included obese women, a mean HOMA index value of  $4.670 \pm 1.637$  was reported. Although previous studies have reported a significant advantage of the TyG index in the assessment of IR compared to HOMA-IR (23-25), slightly different results were observed in our study with moderate and limited discriminatory power of HOMA-IR in both groups. The variability of the research results is due to the use of non-standardized cut-off values of the HOMA-IR index for the assessment of IR as well as for the values of the TyG index. Furthermore, the observed differences might be the result of different sample sizes, metabolic disorders, and the impact of the menstrual cycle on GLU concentration. Although most studies indicate that age has no direct influence on the value of the HOMA-IR index, it is assumed that the frequent occurrence of obesity and unregulated GLU levels in older people could be one of the reasons for this (25,26).

The data from the literature show a significant benefit of the TyG-derived index in practice and the potential for application at the primary care level, which is extremely important to avoid additional testing. Moreover, this index is useful in screening the population and helpful in the prevention of complications and the modification of lifestyle habits that contribute to the worsening of IR (25). The mean

value of the TyG index in our study was higher in obese subjects than in overweight subjects  $5.382 \pm 1.881$  versus  $4.531 \pm 1.594$ . Considering that in our study the group studied was predominantly women, similar results were obtained in the study by Guerrero-Romero (16), where the mean value of the TyG index was higher in women than in men in both categories of obesity. The study by Mohammadabadi et al. (23), which included only obese women of childbearing age, had a mean TyG index value of  $4.7 \pm 0.02$ , while the study by Luo et al. (24) showed a slightly higher TyG index value of  $8.11 \pm 0.83$  in subjects with DM2. The authors noted that the use of this index is important due to the possibility of assessing dyslipidemia in conjunction with the HOMA-IR index.

The use of effective and accurate indices is of great benefit in this case, as they reduce health complications resulting from the associated metabolic disorders. One such example is the TyG-BMI index. The mean value of this index was similar to the values obtained in Romo-Romo's et al. study (18)  $172.981 \pm 63.144$  versus  $175.43 \pm 18.43$ , although the included subjects in both categories had lower BMI index values compared to our results. However, the Taiwanese authors Er et al. (27), point out that the application of this index needs to be adjusted to a specific population due to ethnic characteristics and the influence of the BMI index. The influence of the variability of anthropometric parameters on the results of the derived indices was also shown by METS-IR. The mean value of METS-IR in the study by Widjaja et al. (28) in adolescents with IR was  $51.39 \pm 9.02$ , while the values in our study were slightly lower and amounted to  $50.73 \pm 13.12$  in obese subjects. Nevertheless, it is important to point out that this index showed better results in subjects at risk of developing IR, such as healthy and non-obese subjects, especially those with normal BMI values (18,28). With the aim of applicability in practice and validation of the results, including the indices for the assessment of IR that use anthropometric values for calculation, it is necessary to take into account population characteristics such as the prevalence of obesity, the distribution of muscle and body fat and dietary habits (22).

In the ROC analysis, TyG-BMI, TyG, and HOMA-IR showed the potential of the derived indices as indicators of IR in obese individuals, while HOMA-IR showed the greatest potential in the overweight group. The Er et al. (27) study showed that the TyG-BMI surrogate index with an AUC value of 0.801 had significant utility in the assessment of IR in non-diabetic individuals. Compared to the current study, a slightly higher AUC value of 0.820 (0.737-0.903) was found in the obese group and this index showed the highest sensitivity of 84.1%. A slightly lower sensitivity of 77.8% was found in the study by Mirr et al. (29), while a higher sensitivity of this index was found in the group of overweight subjects. In this study, the TyG index showed the highest sensitivity compared to other derived indices in obese subjects, indicating the importance of assessing disorders of fat and carbohydrate metabolism in people with IR. The study by Mirr et al. (29) recorded a slightly higher AUC value of 0.877 (0.819-0.922), while the study by Luo et al. (24) in a group of subjects with DM2 showed an AUC value of 0.785 (0.691-0.879). In the current study, the TyG index showed a slightly lower AUC value of 0.734 (0.636-0.833) in the obese group with high sensitivity and specificity. Compared to the previous parameters, the HOMA-IR showed high sensitivity and specificity in both groups of subjects, justifying the reason for its wide application in clinical practice. The study showed that the AUC value in the obese subjects group was 0.720 (0.633-0.808), slightly higher results were recorded in the study by Luo et al. (24) with AUC of 0.73 (0.588-0.873). In addition to the assessment of IR, the study by Vladu et al. (30) showed that HOMA-IR may be a predictor of CVD in subjects with DM2. The reported cut-off value was 2.926 with a sensitivity and specificity of 82.4% and 75%, respectively. Interestingly, our study found a sensitivity and specificity of 70% and 89%, respectively, in the obese subject group with a slightly higher cut-off value of 2.99. This suggests that our subjects have a higher risk of developing CVD compared to obese subjects based on HOMA-IR values, but more extensive studies are needed to confirm this.

## CONCLUSION

Given the complexity of IR and its far-reaching impact on public health, a comprehensive and multidisciplinary approach to its understanding, prevention and management is essential. Although in our study the indices examined for the assessment of IR gave different results in both categories, we believe that they have recently become an important aspect in the assessment of these patients. Especially considering that IR is a multifactorial disease, we believe that using other derived indices based on a combination of lipid parameters and anthropometric indicators such as BMI can significantly contribute to the prediction and reduction of numerous complications. This has been demonstrated by the TyG-BMI in this study. In the near future, we need to investigate and adapt the potential of other anthropometric indicators in combination with derived indices to a larger population.

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## DECLARATION OF INTERESTS

Authors declare no conflicts of interest.

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