







ORIGINAL

Association between sociodemographic variables, healthy habits and stress with insulin resistance risk scales

Asociación entre variables sociodemográficas, hábitos saludables y estrés con escalas de riesgo de resistencia a la insulina

José Ignacio Ramírez-Manent^{1,2,3} , Ángel Arturo López-González^{1,2,4} ,
Emilio Martínez-Almoyna Rifá^{1,4} , Hernán Paublini Oliveira^{1,4} ,
Cristina Martorell Sánchez^{1,4} , Pedro Juan Tárraga López⁵ 

1. Grupo ADEMA-Salud del Instituto Universitario de Ciencias de la Salud (IUNICS) de Baleares. España

2. Servicio de Salud de las Islas Baleares. España

3. Facultad de Medicina. Universidad de las Islas Baleares. España

4. Facultad de Odontología. Escuela Universitaria ADEMA-UIB. España

5. Facultad de Medicina. Universidad de Castilla la Mancha. España

Corresponding author

Ángel Arturo López-González

E-mail: angarturo@gmail.com

Received: 23 - XI - 2024

Accepted: 22 - XII - 2024

doi: 10.3306/AJHS.2025.40.02.107

Abstract

Introduction: Insulin resistance (IR) is a multifactorial clinical condition that contributes to the development of various pathological processes. This study aims to assess the associations between different sociodemographic variables, healthy habits, and stress with the values of three IR risk scales.

Materials and Methods: A descriptive cross-sectional study was conducted with 24,224 Spanish workers, evaluating how sociodemographic variables (age, gender, and socioeconomic status), healthy habits (smoking, alcohol consumption, physical activity, and adherence to the Mediterranean diet), and stress correlate with IR risk scales such as the triglyceride-glucose index (TyG), the metabolic IR scale (METS-IR), and the single-point insulin sensitivity estimator (SPISE-IR).

Results: All the variables studied showed associations with the values of the three IR risk scales, with the highest odds ratios observed for age and gender.

Conclusions: According to our results, the IR risk profile would be characterized by an older male, from a lower socioeconomic status, who smokes, consumes significant amounts of alcohol, is sedentary, has low adherence to the Mediterranean diet, and experiences stress.

Key words: Insulin resistance, sociodemographic variables, alcohol consumption, stress, TyG index, METS-IR, SPISE-IR.

Resumen

Introducción: La resistencia a la insulina (RI) es una entidad clínica multifactorial que está en la génesis de diversos procesos patológicos. El objetivo de este estudio es valorar como se asocian diferentes variables sociodemográficas, hábitos saludables y estrés con los valores de tres escalas de riesgo de RI.

Material y métodos: Se realiza un estudio descriptivo y transversal en 24224 trabajadores españoles en los que se valora como se asocian variables sociodemográficas (edad, género y estatus socioeconómico), hábitos saludables (tabaco, alcohol, ejercicio físico y dieta mediterránea) y estrés con escalas de riesgo de RI como el índice triglicéridos glucosa, la escala metabólica de RI (METS-IR) y el estimador de sensibilidad a la insulina de un solo punto (SPISE-IR).

Resultados: Todas las variables estudiadas muestran asociación con los valores de las tres escalas de RI, las odds ratio más altas se observan para edad y género.

Conclusiones: Según nuestros resultados el perfil de riesgo de RI sería un varón, de edad avanzada, perteneciente al estatus socioeconómico más desfavorecido, fumador, consumidor importante de alcohol, sedentario, con baja adherencia a la dieta mediterránea y con estrés.

Palabras clave: Resistencia a la insulina, variables sociodemográficas, consumo de alcohol, estrés, TyG index, METS-IR, SPISE-IR.

Cite as: Ramírez-Manent JI, López-González ÁA, Martínez-Almoyna Rifá E, Paublini Oliveira H, Martorell Sánchez C, Tárraga López PJ. Association between sociodemographic variables, healthy habits and stress with insulin resistance risk scales. *Academic Journal of Health Sciences* 2025;40 (2): 107-116 doi: 10.3306/AJHS.2025.40.02.107

Introduction

Insulin resistance (IR) is a metabolic disorder in which peripheral tissues, particularly skeletal muscle, the liver, and adipose tissue, lose their ability to respond efficiently to insulin¹. This condition has gained significant attention over the past decade due to its central role in the development of various metabolic diseases and its substantial contribution to the global burden of chronic non-communicable diseases². Clinically, IR is closely associated with type 2 diabetes mellitus (T2DM), obesity, metabolic syndrome, and a range of cardiovascular diseases, underscoring the importance of understanding its mechanisms, risk factors, and diagnostic methods³.

Insulin is a peptide hormone produced by the β -cells of the pancreatic islets of Langerhans, essential for regulating blood glucose homeostasis. It facilitates glucose uptake in peripheral tissues, promotes glycogen storage in the liver and skeletal muscle, and regulates lipolysis in adipose tissue⁴. IR occurs when, despite normal or elevated insulin levels, cells cannot adequately respond to the insulin signal. This inefficiency forces the pancreas to produce additional insulin in a compensatory attempt to maintain normoglycemia. However, this overproduction is unsustainable, and many individuals ultimately develop hyperglycemia, which over time contributes to the onset of type 2 diabetes⁵.

IR has a significant and rising prevalence worldwide, a trend closely linked to the global increase in obesity and sedentary lifestyles⁶. In the United States and Europe, it is estimated that up to one-third of adults have some degree of IR. This prevalence is higher among individuals with obesity, and the risk increases proportionally with the accumulation of adipose tissue, particularly abdominal or visceral obesity, which is identified as a high-risk factor for IR development. Globally, IR rates are also rising in developing countries such as China, Brazil, and Mexico, where dietary transitions toward high-calorie foods and reduced physical activity have led to increased obesity rates and, consequently, IR⁷.

The impact of IR is not limited to adults. Recent studies have shown a considerable increase in IR prevalence among children and adolescents, largely correlating with rising rates of overweight and childhood obesity. This shift in the epidemiology of IR in younger populations is concerning not only for child health but also for its long-term effects, as young people with IR are at much higher risk of developing T2DM, cardiovascular disease, and other metabolic comorbidities in adulthood⁸.

The pathophysiology of IR is complex and multifactorial, involving a series of dynamic molecular and cellular mechanisms. At the cellular level, insulin signaling begins when the hormone binds to its specific receptor on the plasma membrane of target cells. This event triggers

a signaling cascade, including the phosphorylation of several intracellular mediators, notably the phosphoinositide 3-kinase (PI3K)⁹ pathway and protein kinase B (AKT)¹⁰, both essential for the translocation of glucose transporters like GLUT4 to the cell surface, facilitating glucose uptake¹¹.

In IR conditions, this signaling process is disrupted by several factors, including chronic low-grade inflammation, elevated circulating free fatty acids, and lipid accumulation in peripheral tissues¹². Chronic inflammation is exacerbated by the release of pro-inflammatory cytokines, such as tumor necrosis factor- α (TNF- α)¹³ and interleukin-6 (IL-6)¹⁴, which interfere with insulin signaling mechanisms. Additionally, the accumulation of free fatty acids and lipids in muscle and liver disrupts insulin signaling through lipotoxicity and oxidative stress¹⁵.

Insulin resistance is also frequently accompanied by mitochondrial dysfunction and endoplasmic reticulum stress, further exacerbating insulin signaling alterations. These interconnected pathophysiological mechanisms create a vicious cycle that contributes to the progression of IR and its metabolic complications, highlighting IR's complexity as a multifactorial disorder involving both genetic and environmental factors¹⁶.

Diagnosis of IR in clinical practice and research faces several challenges, largely due to the lack of a universally accepted method and the complexity of assessing insulin sensitivity. However, several direct and indirect methods are used to evaluate IR. The euglycemic-hyperinsulinemic clamp is considered the reference or "gold standard" for measuring insulin sensitivity. This procedure involves the continuous infusion of insulin and glucose at controlled rates, allowing for the evaluation of the amount of glucose needed to maintain normoglycemia under constant hyperinsulinemia. While this technique provides an accurate measure of insulin sensitivity, its use is limited outside research settings due to its complexity, high cost, and resource requirements¹⁷.

In clinical practice, less complex indirect methods are commonly used to estimate IR, with the Homeostatic Model Assessment for Insulin Resistance (HOMA-IR), calculated from fasting glucose and insulin levels, being one of the most widely applied¹⁸. Other indices, such as the Matsuda insulin sensitivity index¹⁹ and the Quantitative Insulin Sensitivity Check Index (QUICKI)²⁰, are also employed and validated across different populations. These methods are practical and accessible for monitoring IR in clinical settings, though they are less precise than the euglycemic-hyperinsulinemic clamp. Indices like the triglyceride-glucose (TyG) index²¹, the metabolic score for IR (METS-IR)²², and the single-point insulin sensitivity estimator (SPISE-IR)²³ have gained popularity due to their simplicity and good correlation with reference methods.

The clinical implications of IR are broad and significant, as it is a major risk factor for various chronic diseases. The relationship between IR and type 2 diabetes mellitus is particularly relevant, given that nearly 90% of individuals with T2DM have some degree of IR. This disorder is one of the main pathophysiological pathways contributing to diabetes progression in predisposed individuals, and once chronic hyperglycemia is established, the risk of microvascular and macrovascular complications increases considerably²⁴.

IR also plays a central role in the development of metabolic syndrome, a constellation of risk factors including central obesity, dyslipidemia, hypertension, and hyperglycemia²⁵. This syndrome is associated with a significantly higher risk of cardiovascular disease and mortality, highlighting the relevance of IR in the pathogenesis of atherosclerotic disease and other cardiovascular complications. In patients with IR, an atherogenic lipid profile is commonly observed, characterized by elevated triglycerides and low-density lipoproteins (LDL), along with reduced high-density lipoproteins (HDL). Moreover, endothelial dysfunction and arterial stiffness, both consequences of IR, contribute to the development of hypertension and other cardiovascular disorders²⁶.

The objective of this study is to understand how certain sociodemographic variables, health habits, and stress are associated with the risk of insulin resistance as determined by the TyG index, METS-IR, and SPISE-IR.

Material and methods

Our research utilized an observational, cross-sectional, and descriptive study design, involving 24,224 workers from various labor sectors across different regions of Spain. The sample included 12,536 men and 11,688 women, selected from among those who participated in their companies' mandatory annual medical exams, which were conducted as part of the study. Data collection occurred between January 2019 and June 2020.

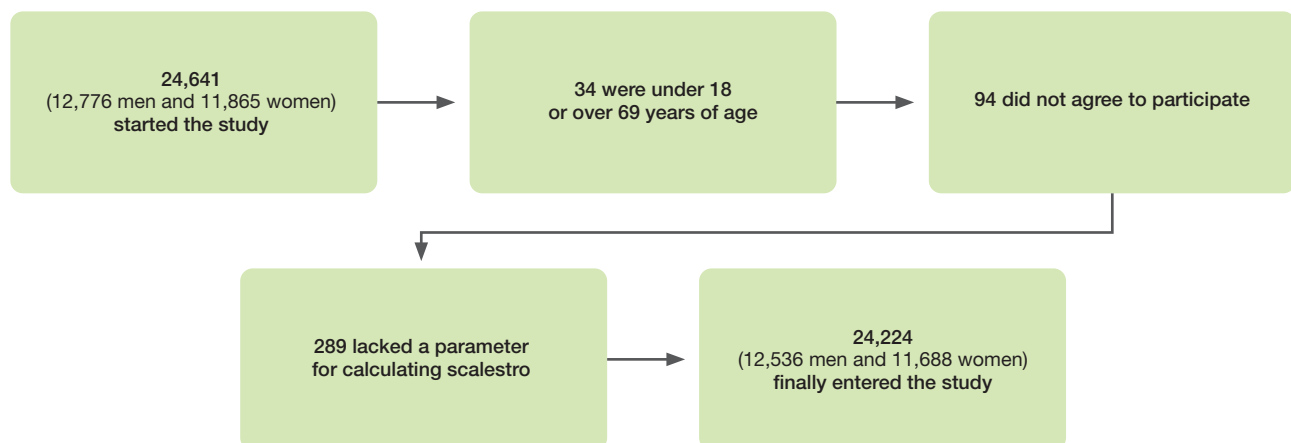
All analytical, anthropometric, and clinical variables were collected by health professionals from the participating companies, with protocols standardized to minimize inter-observer bias.

The following inclusion criteria were applied:

- Age between 18 and 69 years (working age).
- Employment in one of the participating companies, without temporary incapacity at the time of data collection.
- Availability of all variables required to calculate different cardiovascular risk scores.
- Agreement to participate in the study and consent to data use for epidemiological research.

Participant selection for both studies is shown in the flow chart (**Figure 1**).

Figure 1: Flow chart of the participants.



Determination of variables

The occupational health staff of the companies participating in the study was responsible for collecting the necessary data through:

- Medical History: A detailed record was gathered that included sociodemographic data (age, gender, type of occupation) and health-related factors, such

as tobacco use, physical activity, adherence to the Mediterranean diet, and stress levels.

- Physical and Clinical Measurements: Measurements of height, weight, waist and hip circumference, as well as systolic and diastolic blood pressure, were recorded.
- Laboratory Analysis: Tests were conducted to obtain lipid profiles and blood glucose levels.

To avoid bias, measurement techniques were standardized. Height and weight were measured using a SECA 700 scale and a SECA 220 stadiometer, with participants in their underwear, following international ISAK standards. Values were recorded in centimeters and kilograms.

Waist circumference was measured with a SECA measuring tape, positioned between the last rib and the iliac crest, with participants standing and relaxed. Hip circumference was measured similarly, placing the tape at the widest part of the buttocks.

Blood pressure was measured using an OMRON-M3 sphygmomanometer. Participants were seated, rested for 10 minutes, with their arm at heart level, legs uncrossed, and without having consumed food, tobacco, alcohol, or tea in the past hour. Three measurements were taken at one-minute intervals, and the average was recorded as the final value.

Blood samples were obtained by venipuncture after a 12-hour fast, processed, and refrigerated for a maximum of 48 to 72 hours. Analyses were performed in reference laboratories using standardized methods: triglycerides, total cholesterol, and glucose were measured enzymatically, while HDL was assessed through precipitation methods. LDL was calculated using

the Friedewald formula when triglycerides were below 400 mg/dL; if higher, it was measured directly. Analytical variables were expressed in mg/dL.

The insulin resistance risk scales listed below were applied:

- TyG index²⁷. TyG= LN (triglycerides x glycaemia/2) is considered high risk at 8.5
- Metabolic score for insulin resistance (METS-IR)²⁸. METS-IR = $\ln(2 \times \text{glucose}) + \text{triglycerides} \times \text{BMI} / (\ln(\text{HDL-c}))$. High values are defined as 50 and above.
- Single-Point insulin Sensitivity estimator (SPISE-IR). SPISE = $(=600 \times \text{HDL}^{0.185} / \text{triglycerides}^{0.2} \times \text{BMI}^{1.338})$. SPISE-IR²⁹ = 10/SPISE is considered high risk at 1.51

The job category was determined based on the recommendation of the Spanish Society of Epidemiology, using the 2011 National Classification of Occupations: non-manual workers include executives and university professionals, while the rest are classified as manual workers³⁰.

To determine smoking habits, individuals were classified as smokers if they had consumed at least one cigarette daily (or its equivalent) in the past thirty days or had quit smoking less than a year ago.

Table I: Characteristics of the population.

	Men n=12536	Women n=11688	p-value
	Mean (SD)	Mean (SD)	
Age (years)	45.8 (8.6)	44.0 (8.7)	<0.001
Height (cm)	173.5 (6.7)	161.7 (6.1)	<0.001
Weight (kg)	82.3 (13.5)	66.1 (12.7)	<0.001
Waist circumference (cm)	96.0 (10.7)	88.5 (15.0)	<0.001
Hip circumference (cm)	105.7 (10.3)	103.6 (12.2)	<0.001
Systolic blood pressure (mmHg)	134.5 (18.5)	122.0 (16.9)	<0.001
Diastolic blood pressure (mmHg)	81.2 (11.7)	75.4 (10.9)	<0.001
Total cholesterol (mg/dL)	201.9 (38.9)	196.2 (35.2)	<0.001
HDL-cholesterol (mg/dL)	50.7 (11.3)	60.0 (12.8)	<0.001
LDL-cholesterol (mg/dL)	125.8 (44.6)	118.5 (31.2)	<0.001
Triglycerides (mg/dL)	129.9 (89.0)	88.6 (51.8)	<0.001
Glucose (mg/dL)	94.8 (21.7)	89.3 (16.6)	<0.001
	%	%	p-value
< 30 years	3.8	6.7	<0.001
30-39 years	19.8	21.5	
40-49 years	39.3	45.5	
50-69 years	37.1	26.3	
White collar	6.8	80.7	<0.001
Blue collar	93.2	19.3	
Non smokers	71.5	73.9	<0.001
Smokers	28.5	26.1	
Non physical activity	47.5	49.9	<0.001
Yes physical activity	52.5	50.1	
Non Mediterranean diet	49.5	43.1	<0.001
Yes Mediterranean diet	50.5	56.9	
Non alcohol consumption	60.3	78.3	<0.001
Yes alcohol consumption	39.7	21.7	
Non stress	76.2	83.8	<0.001
Yes stress	23.8	16.2	

HDL High density lipoprotein. LDL Low density lipoprotein. SD Standard deviation.

Alcohol consumption was quantified using standard drink units, the reference method at all levels of care. This system allows for a quick measurement of alcohol intake, converting it to grams of pure alcohol. In Spain, one standard drink unit equals 10 grams of alcohol, equivalent to a glass of wine (100 ml), champagne (100 ml), or beer (200 ml), and half a measure of spirits or cocktails (25 ml). Exceeding 35 standard units per week for men and 20 for women poses a significant long-term health risk³¹.

Adherence to the Mediterranean diet was assessed using the PREDIMED questionnaire, consisting of 14 questions with scores of 0 or 1. A score of nine or higher indicated high adherence³².

Physical activity was evaluated with the International Physical Activity Questionnaire (IPAQ), which examines the frequency, duration, and intensity of physical activity in the last seven days, including time spent walking and sitting³³.

Stress levels were assessed using Cohen's Perceived Stress Scale (PSS), a widely used 10-item tool for measuring daily stress across various cultural contexts³⁴.

Statistical Analysis

A descriptive analysis of categorical variables was conducted using frequencies and distributions. Normality of the sample was tested, and the mean and standard deviation were calculated for quantitative variables. Bivariate associations were analyzed with Student's t-test and the chi-square test for proportions. Variables associated with atherogenic risk were analyzed using multinomial logistic regression and the Hosmer-Lemeshow goodness-of-fit test. SPSS software version 29.0 was used for all statistical analyses, with a significance level of 0.05.

Ethical Considerations

The study adhered to the ethical guidelines of the Declaration of Helsinki. Approval was obtained from the Ethics and Research Committee of the Balearic Islands (CEI-IB), under identifier IB 4383/20. Participants provided written and verbal consent after receiving detailed information on the study's objectives.

To protect confidentiality, data were stored with unique codes known only to the project coordinator, ensuring participant anonymity in reports. The team guaranteed

Table II: Mean values of insulin resistance risk scales According sociodemographic variables, healthy habits and stress by gender.

		TyG index		METS-IR		SPISE-IR	
Men	n	Mean (SD)	p-value	Mean (SD)	p-value	Mean (SD)	p-value
< 30 years	472	8.09 (0.40)	<0.001	34.05 (5.77)	<0.001	1.37 (0.32)	<0.001
30-39 years	2484	8.36 (0.56)		38.14 (7.17)		1.63 (0.44)	
40-49 years	4924	8.56 (0.61)		40.60 (8.19)		1.79 (0.51)	
50-69 years	4656	8.69 (0.58)		42.17 (7.66)		1.87 (0.47)	
White collar	848	8.40 (0.56)	<0.001	38.87 (7.99)	<0.001	1.64 (0.48)	<0.001
Blue collar	11688	8.56 (0.60)		40.56 (7.94)		1.78 (0.49)	
Non smokers	8960	8.50 (0.59)		40.18 (7.79)		1.75 (0.48)	
Smokers	3576	8.68 (0.60)		41.12 (8.31)		1.83 (0.51)	
Non physical activity	5952	8.67 (0.61)	<0.001	42.31 (8.21)	<0.001	1.89 (0.51)	<0.001
Yes physical activity	6584	8.45 (0.57)		38.76 (7.32)		1.67 (0.44)	
Non Mediterranean diet	6205	8.63 (0.61)	<0.001	42.23 (8.20)	<0.001	1.84 (0.50)	<0.001
Yes Mediterranean diet	6331	8.49 (0.56)		38.95 (7.36)		1.71 (0.52)	
Non alcohol consumption	7556	8.51 (0.61)	<0.001	39.83 (7.99)	<0.001	1.74 (0.50)	<0.001
Yes alcohol consumption	4980	8.60 (0.58)		41.38 (7.80)		1.83 (0.47)	
Non stress	9552	8.52 (0.60)	<0.001	39.62 (7.67)	<0.001	1.73 (0.48)	<0.001
Yes stress	2984	8.64 (0.59)		43.10 (8.26)		1.92 (0.50)	
Women	n	Media (dt)	p-value	Media (dt)	p-value	Media (dt)	p-value
< 30 years	776	7.98 (0.41)	<0.001	30.49 (5.88)	<0.001	1.20 (0.31)	<0.001
30-39 years	2516	8.03 (0.43)		33.20 (7.55)		1.35 (0.45)	
40-49 years	5320	8.13 (0.48)		35.11 (7.77)		1.46 (0.46)	
50-69 years	3076	8.39 (0.50)		36.67 (8.16)		1.58 (0.48)	
White collar	2260	7.98 (0.42)	<0.001	31.25 (6.61)	<0.001	1.23 (0.37)	<0.001
Blue collar	9428	8.21 (0.50)		35.65 (7.94)		1.50 (0.47)	
Non smokers	8640	8.14 (0.50)	<0.001	34.63 (8.08)		1.44 (0.48)	<0.001
Smokers	3048	8.23 (0.47)		35.28 (7.32)		1.47 (0.42)	
Non physical activity	5840	8.23 (0.51)	<0.001	36.54 (8.39)	<0.001	1.55 (0.50)	<0.001
Yes physical activity	5848	8.10 (0.46)		33.07 (6.94)		1.35 (0.40)	
Non Mediterranean diet	5038	8.20 (0.50)	<0.001	36.40 (8.37)	<0.001	1.50 (0.51)	<0.001
Yes Mediterranean diet	6650	8.12 (0.47)		33.16 (6.95)		1.38 (0.40)	
Non alcohol consumption	9152	8.12 (0.48)	<0.001	37.61 (8.75)	<0.001	1.62 (0.52)	<0.001
Yes alcohol consumption	2536	8.31 (0.49)		34.02 (7.45)		1.40 (0.44)	
Non stress	9800	8.15 (0.49)	<0.001	37.36 (7.46)	<0.001	1.42 (0.44)	<0.001
Yes stress	1888	8.25 (0.48)		37.07 (9.50)		1.59 (0.56)	

TyG Triglyceride Glucose index. METS-IR Metabolic score for insulin resistance. SPISE-IR Single-Point insulin Sensitivity estimator. SD Standard deviation.

the rights to access, rectification, cancellation, and opposition of data, in compliance with Organic Law 3/2018 on Data Protection.

Results

Table I provides an overview of the anthropometric and clinical data of the 24,224 workers (12,536 men and 11,688 women) in the study. The average age was 45 years, with most participants between 40 and 69 years old. Men demonstrated less favorable anthropometric, clinical, and analytical indicators. Manual laborers were the largest occupational group, and around 27% of participants were smokers (28.5% of men and 26.1% of women). More than half reported engaging in physical activity and following a Mediterranean diet, while alcohol intake and stress levels were notably higher in men. These differences were statistically significant ($p < 0.001$).

Tables II and **III** show the mean values and the prevalence of elevated values in the insulin resistance

(IR) risk scales according to sociodemographic variables, healthy habits, and stress. In both tables, the same trend is observed: an increase in the values of the IR risk scales as age increases, as socioeconomic status decreases, with the presence of unhealthy habits (smoking, alcohol consumption, sedentary lifestyle, and low adherence to the Mediterranean diet), or in the presence of stress. In all cases, the values are lower in women. The observed differences are statistically highly significant ($p < 0.001$).

The results of the multinomial logistic regression are presented in **table IV**. The dependent variables are the IR risk scales, and the independent variables include age, gender, type of work, smoking, alcohol consumption, physical exercise, Mediterranean diet adherence, and stress. To identify any potential confounding variables, additional analyses were conducted by stratifying the variables included in the model; none were found to act as confounders. All analyzed variables showed an association with the IR risk scales ($p < 0.001$), with the highest odds ratios corresponding to age and gender.

Table III: Prevalence of high values of insulin resistance risk scales According sociodemographic variables, healthy habits and stress by gender.

		TyG index high		METS-IR high		SPISE-IR high	
Men	n	%	p-value	%	p-value	%	p-value
< 30 years	472	4.24	<0.001	0.24	<0.001	0.21	<0.001
30-39 years	2484	21.25		8.37		10.47	
40-49 years	4924	30.95		12.84		18.60	
50-69 years	4656	39.78		15.46		22.51	
White collar	848	21.70	<0.001	12.66	<0.001	13.68	<0.001
Blue collar	11688	32.00		9.91		18.07	
Non smokers	8960	27.81		11.74		16.52	
Smokers	3576	40.04		14.32		20.92	
Non physical activity	5952	38.71	<0.001	17.54	<0.001	24.19	<0.001
Yes physical activity	6584	24.61		7.90		11.97	
Non Mediterranean diet	6205	36.41	<0.001	16.58	<0.001	23.20	<0.001
Yes Mediterranean diet	6331	25.92		8.83		13.89	
Non alcohol consumption	7556	30.44	<0.001	11.81	<0.001	16.89	<0.001
Yes alcohol consumption	4980	32.61		13.49		19.12	
Non stress	9552	29.33	<0.001	10.13	<0.001	15.22	<0.001
Yes stress	2984	37.60		19.97		25.94	
Women	n	%	p-value	%	p-value	%	p-value
< 30 years	776	3.61	<0.001	0.16	<0.001	0.11	<0.001
30-39 years	2516	7.15		3.97		5.09	
40-49 years	5320	11.43		4.89		6.02	
50-69 years	3076	32.59		7.28		10.40	
White collar	2260	6.37	<0.001	5.73	<0.001	3.01	<0.001
Blue collar	9428	15.15		1.95		7.42	
Non smokers	8640	12.87	<0.001	4.30		5.91	<0.001
Smokers	3048	15.09		5.24		6.81	
Non physical activity	5840	16.58	<0.001	7.12	<0.001	8.84	<0.001
Yes physical activity	5848	10.33		2.87		4.31	
Non Mediterranean diet	5038	15.87	<0.001	6.87	<0.001	8.51	<0.001
Yes Mediterranean diet	6650	11.56		3.28		4.89	
Non alcohol consumption	9152	11.23	<0.001	3.76	<0.001	5.03	<0.001
Yes alcohol consumption	2536	21.45		9.46		12.15	
Non stress	9800	12.12	<0.001	4.08	<0.001	5.59	<0.001
Yes stress	1888	20.33		9.75		11.65	

TyG Triglyceride Glucose index. METS-IR Metabolic score for insulin resistance. SPISE-IR Single-Point insulin Sensitivity estimator.

Discussion

In our study, all analyzed variables are associated with IR risk scale values, particularly age and gender.

Age is a determining factor in IR, as insulin sensitivity tends to decline with aging in both men and women. This phenomenon is linked to a progressive decrease in muscle mass and function, an increase in visceral fat, and a tendency toward lower physical activity levels, all of which contribute to IR³⁵. Using TyG and METS-IR indices show that older individuals have elevated index values, indicating higher IR compared to younger adults³⁶. These changes not only affect insulin response but also promote a low-grade inflammatory state that exacerbates metabolic dysfunction. This "metabolic aging" suggests that age should be considered when interpreting IR indices and designing preventive interventions³⁷.

Gender also plays a role in modulating IR in our study, likely influenced by hormonal factors. Premenopausal women generally exhibit greater insulin sensitivity than men, attributed to the protective effects of estrogen. However, this advantage appears to diminish after menopause, with women experiencing increased IR and associated risk factors, such as abdominal fat gain and altered lipid profiles³⁸. Studies using SPISE, an index for insulin sensitivity, find that postmenopausal women have higher IR levels than men of the same age³⁹. These findings suggest that IR indices adjusted for gender, as hormonal changes impact insulin sensitivity and its progression in both sexes.

Socioeconomic status (SES) is inversely associated with IR, where individuals of lower SES have a higher risk of developing IR, likely due to multiple related factors, such as less healthy diets, limited access to exercise resources,

and higher levels of chronic stress. Studies using the TyG and METS-IR indices indicate that populations with low SES have higher IR values, associated with higher obesity prevalence and increased consumption of processed and sugary foods⁴⁰. Limited access to healthcare and information on lifestyles also plays a role in this association, highlighting the need for health policies that address socioeconomic inequalities in IR prevention.

In our study, smoking is a well-established risk factor for IR and metabolic diseases. Nicotine and other tobacco components negatively impact insulin sensitivity by promoting oxidative stress, chronic inflammation, and visceral fat accumulation, all of which contribute to IR⁴¹. Population studies show that smokers have elevated TyG and METS-IR indices compared to non-smokers, indicating higher IR⁴². This implies that smoking should be considered an important factor in the development and progression, and that IR indices can be useful for monitoring the metabolic effects of smoking across population groups.

Alcohol consumption in our study is associated with higher IR risk scale values, although the effects on IR are complex and not consistently reported in the literature. Evidence suggests that moderate alcohol consumption, particularly red wine, may have a protective effect on insulin sensitivity, possibly due to the antioxidants and polyphenols in wine, which improve lipid profiles and reduce inflammation⁴³. However, excessive alcohol consumption has the opposite effect, as it is associated with increased abdominal fat, dyslipidemia, and liver damage, all of which exacerbate IR⁴⁴. Studies using TyG and METS-IR indicate that excessive drinkers have higher IR index values. Moderate consumption does not significantly increase IR⁴⁵. This finding suggests that alcohol consumption should be carefully considered in IR studies and when interpreting IR index results across population subgroups.

Table IV: Multinomial logistic regression.

	TyG index high		METS-IR high		SPISE-IR high	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Women	1		1		1	
Men	2.63 (2.46-2.80)	<0.001	2.45 (2.21-2.69)	<0.001	2.78 (2.54-3.03)	<0.001
< 30 years	1		1		1	
30-39 years	1.71 (1.59-1.83)	<0.001	1.17 (1.13-1.22)	<0.001	1.28 (1.19-1.38)	<0.001
40-49 years	2.59 (2.35-2.84)	<0.001	1.52 (1.38-1.67)	<0.001	1.92 (1.69-2.16)	<0.001
50-69 years	8.58 (6.37-10.79)	<0.001	3.55 (3.05-4.06)	<0.001	9.23 (7.03-11.44)	<0.001
White collar	1		1		1	
Blue collar	1.31 (1.16-1.46)	<0.001	1.15 (1.10-1.21)	<0.001	1.17 (1.14-1.21)	<0.001
Non smokers	1		1		1	
Smokers	1.48 (1.38-1.58)	<0.001	1.19 (1.14-1.24)	<0.001	1.15 (1.11-1.19)	<0.001
Yes physical activity	1		1		1	
Non physical activity	1.63 (1.53-1.73)	<0.001	2.45 (2.22-2.69)	<0.001	2.18 (2.00-2.37)	<0.001
Yes Mediterranean diet	1		1		1	
Non Mediterranean diet	1.29 (1.20-1.39)	<0.001	1.92 (1.75-2.09)	<0.001	1.68 (1.51-1.86)	<0.001
Non alcohol consumption	1		1		1	
Yes alcohol consumption	1.19 (1.11-1.27)	<0.001	1.30 (1.23-1.37)	<0.001	1.28 (1.19-1.38)	<0.001
Non stress	1		1		1	
Yes stress	1.31 (1.21-1.41)	<0.001	2.03 (1.84-2.23)	<0.001	1.75 (1.60-1.91)	<0.001

TyG Triglyceride Glucose index. METS-IR Metabolic score for insulin resistance. SPISE-IR Single-Point insulin Sensitivity estimator. OR Odds ratio.

According to our results, the Mediterranean diet shows positive effects in reducing IR due to its high content of healthy fats (such as olive oil), fiber, antioxidants, and polyphenols found in fruits, vegetables, and whole grains. Several studies have shown that a diet rich in these components can improve insulin sensitivity and reduce inflammation and oxidative stress, both of which contribute to IR⁴⁶. Individuals following a Mediterranean diet exhibit lower TyG and METS-IR index values, suggesting lower IR those following Western dietary patterns⁴⁷. These findings support the use of the Mediterranean diet as a strategy for IR prevention and management and highlight of IR indices for assessing dietary effects across populations.

Our results also suggest that physical exercise is an effective intervention to improve insulin sensitivity. Regular physical activity enhances glucose uptake in skeletal muscle and promotes a healthier body composition by reducing visceral fat, which translates to lower IR⁴⁸. Longitudinal and cross-sectional studies have observed that physically active individuals have significantly lower TyG, METS-IR index values compared to sedentary individuals, supporting the beneficial effect of exercise on IR⁴⁹. Physical exercise should be a central component in intervention programs aimed at reducing IR in high-risk populations, and IR indices can be tools for monitoring its benefits in clinical practice.

Chronic stress is another factor associated with IR in our research, likely due to the sustained activation of the hypothalamic-pituitary-adrenal axis, leading to increased cortisol release. Cortisol induces insulin resistance by raising hepatic glucose production and promoting abdominal fat accumulation⁵⁰. Studies using TyG and METS-IR have found that individuals with high stress levels have elevated IR indices, suggesting that stress significantly affects IR pathophysiology⁵¹. This finding underscores the importance of incorporating stress management into comprehensive strategies for reducing IR and improving metabolic health.

Conclusions

In conclusion, factors such as age, gender, socioeconomic status, tobacco and alcohol consumption, Mediterranean diet adherence, physical exercise, and stress are significantly associated with IR. Risk indices such as TyG, METS-IR, and SPISE provide accessible and objective methods for assessing IR and its relationship with these factors in population studies. These findings suggest that personalized interventions, which consider individual and socio-environmental factors, could be more effective in preventing and managing IR and its associated complications. Furthermore, the use of these risk indices allows for practical, continuous assessment in clinical practice and research, facilitating the implementation of public health strategies and preventive measures.

Key strengths of this study include the large sample size and the extensive range of variables that can be associated with the analyzed IR risk scales.

As limitations, it should be noted that, as a cross-sectional study, causal relationships cannot be established. Another limitation is that insulin resistance was not determined using objective methods but rather through validated risk scales.

Conflict of Interest

The authors declared that there is no conflict of interest

References

1. Targher G, Byrne CD, Tilg H. MASLD: a systemic metabolic disorder with cardiovascular and malignant complications. *Gut*. 2024 Mar 7;73(4):691-702. doi: 10.1136/gutjnl-2023-330595. PMID: 38228377.
2. Hutchison AL, Tavaglione F, Romeo S, Charlton M. Endocrine aspects of metabolic dysfunction-associated steatotic liver disease (MASLD): Beyond insulin resistance. *J Hepatol*. 2023 Dec;79(6):1524-1541. doi: 10.1016/j.jhep.2023.08.030. Epub 2023 Sep 18. PMID: 37730124.
3. Yazıcı D, Demir SÇ, Sezer H. Insulin Resistance, Obesity, and Lipotoxicity. *Adv Exp Med Biol*. 2024;1460:391-430. doi: 10.1007/978-3-031-63657-8_14. PMID: 39287860.
4. Subramanian S, Khan F, Hirsch IB. New advances in type 1 diabetes. *BMJ*. 2024 Jan 26;384:e075681. doi: 10.1136/bmj-2023-075681. Erratum in: *BMJ*. 2024 Jun 3;385:q1224. doi: 10.1136/bmj.q1224. PMID: 38278529.

5. Ghadieh HE, Infante M, Sponton CH. Editorial: Mechanistic and physiological implications of insulin resistance in metabolic diseases. *Front Endocrinol (Lausanne)*. 2024 Jul 3;15:1446492. doi: 10.3389/fendo.2024.1446492. PMID: 39027481; PMCID: PMC11255604.
6. Hill MA, Yang Y, Zhang L, Sun Z, Jia G, Parrish AR, et al. Insulin resistance, cardiovascular stiffening and cardiovascular disease. *Metabolism*. 2021 Jun;119:154766. doi: 10.1016/j.metabol.2021.154766. Epub 2021 Mar 22. PMID: 33766485.
7. Hou XZ, Lv YF, Li YS, Wu Q, Lv QY, Yang YT, et al. Association between different insulin resistance surrogates and all-cause mortality in patients with coronary heart disease and hypertension: NHANES longitudinal cohort study. *Cardiovasc Diabetol*. 2024 Feb 28;23(1):86. doi: 10.1186/s12933-024-02173-7. PMID: 38419039; PMCID: PMC10903030.
8. Polidori N, Mainieri F, Chiarelli F, Mohn A, Giannini C. Early Insulin Resistance, Type 2 Diabetes, and Treatment Options in Childhood. *Horm Res Paediatr*. 2022;95(2):149-166. doi: 10.1159/000521515. Epub 2021 Dec 16. PMID: 34915489.
9. Tong C, Wu Y, Zhang L, Yu Y. Insulin resistance, autophagy and apoptosis in patients with polycystic ovary syndrome: Association with PI3K signaling pathway. *Front Endocrinol (Lausanne)*. 2022 Dec 16;13:1091147. doi: 10.3389/fendo.2022.1091147. PMID: 36589825; PMCID: PMC9800521.
10. Sędzikowska A, Szablewski L. Insulin and Insulin Resistance in Alzheimer's Disease. *Int J Mol Sci*. 2021 Sep 15;22(18):9987. doi: 10.3390/ijms22189987. PMID: 34576151; PMCID: PMC8472298.
11. van Gerwen J, Shun-Shion AS, Fazakerley DJ. Insulin signalling and GLUT4 trafficking in insulin resistance. *Biochem Soc Trans*. 2023 Jun 28;51(3):1057-1069. doi: 10.1042/BST20221066. PMID: 37248992; PMCID: PMC10317183.
12. Li H, Meng Y, He S, Tan X, Zhang Y, Zhang X, et al. Macrophages, Chronic Inflammation, and Insulin Resistance. *Cells*. 2022 Sep 26;11(19):3001. doi: 10.3390/cells11193001. PMID: 36230963; PMCID: PMC9562180.
13. Liu F, Wang X, Zhao M, Zhang K, Li C, Lin H, et al. Ghrelin Alleviates Inflammation, Insulin Resistance, and Reproductive Abnormalities in Mice with Polycystic Ovary Syndrome via the TLR4-NF- κ B Signaling Pathway. *Discov Med*. 2024 May;36(184):946-958. doi: 10.24976/Discov.Med.202436184.88. PMID: 38798254.
14. Savage TM, Fortson KT, de Los Santos-Alexis K, Oliveras-Alsina A, Rouanne M, Rae SS, et al. Amphiregulin from regulatory T cells promotes liver fibrosis and insulin resistance in non-alcoholic steatohepatitis. *Immunity*. 2024 Feb 13;57(2):303-318.e6. doi: 10.1016/j.immuni.2024.01.009. Epub 2024 Feb 2. PMID: 38309273; PMCID: PMC10922825.
15. Jabarpour M, Aleyasin A, Shabani Nashtaei M, Amidi F. Astaxanthin supplementation impact on insulin resistance, lipid profile, blood pressure, and oxidative stress in polycystic ovary syndrome patients: A triple-blind randomized clinical trial. *Phytother Res*. 2024 Jan;38(1):321-330. doi: 10.1002/ptr.8037. Epub 2023 Oct 24. PMID: 37874168.
16. Sun J, Zhang Y, Zhang Q, Hu L, Zhao L, Wang H, et al. Metabolic regulator LKB1 controls adipose tissue ILC2 PD-1 expression and mitochondrial homeostasis to prevent insulin resistance. *Immunity*. 2024 Jun 11;57(6):1289-1305.e9. doi: 10.1016/j.immuni.2024.04.024. Epub 2024 May 20. PMID: 38772366.
17. Rebelos E, Honka MJ. PREDIM index: a useful tool for the application of the euglycemic hyperinsulinemic clamp. *J Endocrinol Invest*. 2021 Mar;44(3):631-634. doi: 10.1007/s40618-020-01352-z. Epub 2020 Jul 10. PMID: 32651893.
18. González-González JG, Violante-Cumpa JR, Zambrano-Lucio M, Burciaga-Jimenez E, Castillo-Morales PL, Garcia-Campa M, et al. HOMA-IR as a predictor of Health Outcomes in Patients with Metabolic Risk Factors: A Systematic Review and Meta-analysis. *High Blood Press Cardiovasc Prev*. 2022 Nov;29(6):547-564. doi: 10.1007/s40292-022-00542-5. Epub 2022 Oct 1. PMID: 36181637.
19. Sharma A, Birkeland KI, Nermoen I, Sommer C, Qvigstad E, Lee-Ødegård S, et al. N-terminal pro-B-type natriuretic peptide levels vary by ethnicity and are associated with insulin sensitivity after gestational diabetes mellitus. *Cardiovasc Diabetol*. 2024 Aug 3;23(1):284. doi: 10.1186/s12933-024-02349-1. PMID: 39097697; PMCID: PMC11298077.
20. Jabarpour M, Aleyasin A, Shabani Nashtaei M, Amidi F. Astaxanthin supplementation impact on insulin resistance, lipid profile, blood pressure, and oxidative stress in polycystic ovary syndrome patients: A triple-blind randomized clinical trial. *Phytother Res*. 2024 Jan;38(1):321-330. doi: 10.1002/ptr.8037. Epub 2023 Oct 24. PMID: 37874168.
21. Dang K, Wang X, Hu J, Zhang Y, Cheng L, Qi X, et al. The association between triglyceride-glucose index and its combination with obesity indicators and cardiovascular disease: NHANES 2003-2018. *Cardiovasc Diabetol*. 2024 Jan 6;23(1):8. doi: 10.1186/s12933-023-02115-9. PMID: 38184598; PMCID: PMC10771672.
22. Duan M, Zhao X, Li S, Miao G, Bai L, Zhang Q, et al. Metabolic score for insulin resistance (METS-IR) predicts all-cause and cardiovascular mortality in the general population: evidence from NHANES 2001-2018. *Cardiovasc Diabetol*. 2024 Jul 10;23(1):243. doi: 10.1186/s12933-024-02334-8. PMID: 38987779; PMCID: PMC11238348.
23. Ramírez Gallegos I, Marina Arroyo M, López-González AA, Vicente-Herrero MT, Vallejos D, Sastre-Alzamora T, et al. The Effect of a Program to Improve Adherence to the Mediterranean Diet on Cardiometabolic Parameters in 7034 Spanish Workers. *Nutrients*. 2024 Apr 7;16(7):1082. doi: 10.3390/nu16071082. PMID: 38613115; PMCID: PMC11013770.
24. Zhao Y, Yue R. Aging adipose tissue, insulin resistance, and type 2 diabetes. *Bio gerontology*. 2024 Feb;25(1):53-69. doi: 10.1007/s10522-023-10067-6. Epub 2023 Sep 19. PMID: 37725294.
25. Alemany M. The Metabolic Syndrome, a Human Disease. *Int J Mol Sci*. 2024 Feb 13;25(4):2251. doi: 10.3390/ijms25042251. PMID: 38396928; PMCID: PMC10888680.
26. Shen J, San W, Zheng Y, Zhang S, Cao D, Chen Y, et al. Different types of cell death in diabetic endothelial dysfunction. *Biomed Pharmacother*. 2023 Dec;168:115802. doi: 10.1016/j.biopha.2023.115802. Epub 2023 Oct 31. PMID: 37918258.
27. Mestre Font M, Busquets-Cortés C, Ramírez-Manent JI, Tomás-Gil P, Paublini H, López-González AA. Influence of Sociodemographic Variables and Healthy Habits on the Values of Insulin Resistance Indicators in 386,924 Spanish Workers. *Nutrients*. 2023 Dec 16;15(24):5122. doi: 10.3390/nu15245122. PMID: 38140381; PMCID: PMC10746000.
28. Paublini H, López González AA, Busquets-Cortés C, Tomas-Gil P, Riutord-Sbert P, Ramírez-Manent JI. Relationship between Atherogenic Dyslipidaemia and Lipid Triad and Scales That Assess Insulin Resistance. *Nutrients*. 2023 Apr 27;15(9):2105. doi: 10.3390/nu15092105. PMID: 37432258; PMCID: PMC10180556.
29. Cederholm J, Zethelius B. SPISE and other fasting indexes of insulin resistance: risks of coronary heart disease or type 2 diabetes. Comparative cross-sectional and longitudinal aspects. *Ups J Med Sci*. 2019 Nov;124(4):265-272. doi: 10.1080/03009734.2019.1680583. Epub 2019 Nov 7. PMID: 31694444; PMCID: PMC6968630.

30. Domingo-Salvany A, Bacigalupe A, Carrasco JM, Espelt A, Ferrando J, Borrell C et al. Propuestas de clase social neoweberiana y neomarxista a partir de la Clasificación Nacional de Ocupaciones 2011 [Proposals for social class classification based on the Spanish National Classification of Occupations 2011 using neo-Weberian and neo-Marxist approaches]. *Gac Sanit*. 2013 May-Jun;27(3):263-72. Spanish. doi: 10.1016/j.gaceta.2012.12.009. Epub 2013 Feb 6. PMID: 23394892.
31. Chung T, Creswell KG, Bachrach R, Clark DB, Martin CS. Adolescent Binge Drinking. *Alcohol Res*. 2018;39(1):5-15. PMID: 30557142; PMCID: PMC6104966.
32. Chen EY, Mahurkar-Joshi S, Liu C, Jaffe N, Labus JS, Dong TS, et al. The Association Between a Mediterranean Diet and Symptoms of Irritable Bowel Syndrome. *Clin Gastroenterol Hepatol*. 2024 Jan;22(1):164-172.e6. doi: 10.1016/j.cgh.2023.07.012. Epub 2023 Jul 29. PMID: 37517631; PMCID: PMC10849937.
33. Crowder SL, Li X, Himbert C, Viskochil R, Hoogland AI, Gudenkauf LM, et al. Relationships Among Physical Activity, Sleep, and Cancer-related Fatigue: Results From the International ColoCare Study. *Ann Behav Med*. 2024 Feb 10;58(3):156-166. doi: 10.1093/abm/kaad068. PMID: 38141201; PMCID: PMC10858307.
34. Vetter VM, Drewelies J, Sommerer Y, Kalies CH, Regitz-Zagrosek V, Bertram L, et al. Epigenetic aging and perceived psychological stress in old age. *Transl Psychiatry*. 2022 Sep 26;12(1):410. doi: 10.1038/s41398-022-02181-9. PMID: 36163242; PMCID: PMC9513097.
35. Guo C, He L, Tu Y, Xu C, Liao C, Lai H, et al. Insulin resistance and sarcopenia: a prognostic longitudinal link to stroke risk in middle-aged and elderly Chinese population. *BMC Public Health*. 2024 Oct 9;24(1):2757. doi: 10.1186/s12889-024-20214-4. PMID: 39385146; PMCID: PMC11465621.
36. Huo RR, Liao Q, Zhai L, You XM, Zuo YL. Interacting and joint effects of triglyceride-glucose index (TyG) and body mass index on stroke risk and the mediating role of TyG in middle-aged and older Chinese adults: a nationwide prospective cohort study. *Cardiovasc Diabetol*. 2024 Jan 13;23(1):30. doi: 10.1186/s12933-024-02122-4. PMID: 38218819; PMCID: PMC10790273.
37. Bo T, Gao L, Yao Z, Shao S, Wang X, Proud CG, et al. Hepatic selective insulin resistance at the intersection of insulin signaling and metabolic dysfunction-associated steatotic liver disease. *Cell Metab*. 2024 May 7;36(5):947-968. doi: 10.1016/j.cmet.2024.04.006. PMID: 38718757.
38. Gado M, Tsaousidou E, Bornstein SR, Perakakis N. Sex-based differences in insulin resistance. *J Endocrinol*. 2024 Feb 12;261(1):e230245. doi: 10.1530/JOE-23-0245. PMID: 38265844.
39. De Paoli M, Zakharia A, Werstuck GH. The Role of Estrogen in Insulin Resistance: A Review of Clinical and Preclinical Data. *Am J Pathol*. 2021 Sep;191(9):1490-1498. doi: 10.1016/j.ajpath.2021.05.011. Epub 2021 Jun 5. PMID: 34102108.
40. Gonçalves FCLDSP, de Lira PIC, Oliveira MS, Vila Nova Filho SL, Eickmann SH, Lima MC. Weight Gain from Birth to Adolescence and TyG Index at Age 18 Years: A Cohort Study in Northeast Brazil. *Matern Child Health J*. 2024 Apr;28(4):729-737. doi: 10.1007/s10995-023-03868-1. Epub 2024 Jan 5. PMID: 38180549.
41. Rehman K, Haider K, Akash MSH. Cigarette smoking and nicotine exposure contributes for aberrant insulin signaling and cardiometabolic disorders. *Eur J Pharmacol*. 2021 Oct 15;909:174410. doi: 10.1016/j.ejphar.2021.174410. Epub 2021 Aug 8. PMID: 34375672.
42. Wei B, Dong Q, Ma J, Zhang A. The association between triglyceride-glucose index and cognitive function in nondiabetic elderly: NHANES 2011-2014. *Lipids Health Dis*. 2023 Nov 6;22(1):188. doi: 10.1186/s12944-023-01959-0. PMID: 37932783; PMCID: PMC10629120.
43. Miyagi S, Takamura T, Nguyen TTT, Tsujiguchi H, Hara A, Nakamura H, et al. Moderate alcohol consumption is associated with impaired insulin secretion and fasting glucose in non-obese non-diabetic men. *J Diabetes Investig*. 2021 May;12(5):869-876. doi: 10.1111/jdi.13402. Epub 2020 Oct 13. PMID: 32910554; PMCID: PMC8089003.
44. Marušić M, Paić M, Knobloch M, Liberati Pršo AM. NAFLD, Insulin Resistance, and Diabetes Mellitus Type 2. *Can J Gastroenterol Hepatol*. 2021 Feb 17;2021:6613827. doi: 10.1155/2021/6613827. PMID: 33681089; PMCID: PMC7904371.
45. Lee YC, Park BJ, Lee JH. Sex Differences in the Relationship Between High-Risk Drinking and the Triglyceride-Glucose (TyG) Index: An Analysis Using 2013 and 2015 Korean National Health and Nutrition Examination Survey Data. *Alcohol Alcohol*. 2021 Jun 29;56(4):393-400. doi: 10.1093/alcal/agaa122. Erratum in: *Alcohol Alcohol*. 2021 Jun 29;56(4):510-511. doi: 10.1093/alcal/agab002. PMID: 33249433.
46. Gómez-Sánchez M, Gómez-Sánchez L, Llamas-Ramos R, Rodríguez-Sánchez E, García-Ortiz L, Martí-Lluch R, et al. Relationship between the Mediterranean Diet and Vascular Function in Subjects with and without Increased Insulin Resistance. *Nutrients*. 2024 Sep 14;16(18):3106. doi: 10.3390/nu16183106. PMID: 39339706; PMCID: PMC11435013.
47. Sánchez-Escudero V, García Lacalle C, González Vergaz A, Mateo LR, Marqués Cabrero A. The triglyceride/glucose index as an insulin resistance marker in the pediatric population and its relation to eating habits and physical activity. *Endocrinol Diabetes Nutr (Engl Ed)*. 2021 May;68(5):296-303. doi: 10.1016/j.endien.2020.08.015. Epub 2021 Sep 6. PMID: 34556259.
48. Whillier S. Exercise and Insulin Resistance. *Adv Exp Med Biol*. 2020;1228:137-150. doi: 10.1007/978-981-15-1792-1_9. PMID: 32342455.
49. Tutunchi H, Naeini F, Mobasseri M, Ostadrahimi A. Triglyceride glucose (TyG) index and the progression of liver fibrosis: A cross-sectional study. *Clin Nutr ESPEN*. 2021 Aug;44:483-487. doi: 10.1016/j.clnesp.2021.04.025. Epub 2021 May 7. PMID: 34330512.
50. Kraemer WJ, Ratamess NA, Hymer WC, Nindl BC, Fragala MS. Growth Hormone(s), Testosterone, Insulin-Like Growth Factors, and Cortisol: Roles and Integration for Cellular Development and Growth With Exercise. *Front Endocrinol (Lausanne)*. 2020 Feb 25;11:33. doi: 10.3389/fendo.2020.00033. PMID: 32158429; PMCID: PMC7052063.
51. Song Y, Cui K, Yang M, Song C, Yin D, Dong Q, et al. High triglyceride-glucose index and stress hyperglycemia ratio as predictors of adverse cardiac events in patients with coronary chronic total occlusion: a large-scale prospective cohort study. *Cardiovasc Diabetol*. 2023 Jul 15;22(1):180. doi: 10.1186/s12933-023-01883-8. PMID: 37454147; PMCID: PMC10350280.