eISSN 2255-0569

ORIGINAL

Relationship between heart age and insulin resistance risk scales in 139634 Spanish workers

Relación entre la edad del corazón y escalas de riesgo de resistencia a la insulina en 139634 trabajadores españoles

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Received: 21 - VIII - 2023
Accepted: 21 - IX - 2023

doi: 10.3306/AJHS.2024.39.01.16

Abstract

Introduction: Insulin resistance is a key factor in the development of type 2 diabetes, which is one of the most prevalent cardiometabolic disorders. Heart age is a new tool for assessing cardiovascular risk. The aim of this study is to assess the association between heart age and different insulin resistance risk scales.
Material and methods: Descriptive and cross-sectional study in 139634 Spanish workers in which both heart age and different insulin resistance risk scales such as TyG index, METS-IR and triglycerides/HDL were determined.
Results: Heart age values increase as do the values of the insulin resistance risk scales. The risk of presenting elevated heart age values increases in those with high values of the insulin resistance scales, with the highest odds ratios being found for TyG index. The value of the insulin resistance risk scales for predicting the occurrence of moderate or high ALLY heart age values is not high.
Conclusions: There is a good relationship between heart age values and the values of the insulin resistance risk scales, however the predictive value of these insulin resistance scales for predicting elevated ALLY heart age values is low.

Key words: heart age, insulin resistance, risk scales.

Resumen

Introducción: La resistencia a la insulina es un factor clave para que aparezca diabetes tipo 2 que es una de las alteraciones cardiometabólicas más prevalentes. La edad del corazón es una nueva herramienta para valorar el riesgo cardiovascular. El objetivo de este estudio es valorar la asociación que existe entre la edad del corazón y diferentes escalas de riesgo de resistencia v la insulina.
Material y métodos: Estudio descriptivo y transversal en 139634 trabajadores españoles en los que se determinan tanto la edad del corazón como distintas escalas de riesgo de resistencia a la insulina como TyG index, METS-IR y triglicéridos/HDL.
Resultados: Los valores de edad del corazón se incrementan a medida que lo hacen los valores de las escalas de riesgo de resistencia a la insulina. El riesgo de presentar valores elevados de edad del corazón se incrementa en aquellas personas con valores altos de las escalas de resistencia a la insulina, siendo las odds ratio más elevadas las encontradas para TyG index. El valor de las escalas de riesgo de resistencia a la insulina para predecir la aparición de valores moderados o altos de edad cardiaca ALLY no es elevado.
Conclusiones: Existe buena relación entre los valores de edad del corazón y los valores de las escalas de riesgo de resistencia a la insulina, sin embargo el valor predictivo de estas escalas de resistencia a la insulina para predecir valores elevados de ALLY edad del corazón es bajo.

Palabras clave: edad del corazón, resistencia a la insulina, escalas de riesgo.

Cite as: Sastre-Alzamora T, Tomás-Gil P, Paublini H, Pallarés L, Ramírez-Manent JI, López-González AA. Relationship between heart age and insulin resistance risk scales in 139634 Spanish workers. *Academic Journal of Health Sciences 2024*; 39 (1):16-22 doi: 10.3306/AJHS.2024.39.01.16

Introduction

Cardiovascular diseases are currently considered to be one of the main public health problems in practically all countries of the world, due to their high prevalence and high morbidity and mortality[1].

Many cardiovascular disease risk scales have been developed in recent decades, most of them assessing the probability of presenting a cerebrovascular event, fatal or non-fatal, in a given period of time, generally established as ten years[2]. For some, these scales give a false sense of security, since the values obtained are in most cases low despite the coexistence of different risk factors. To resolve this situation, scales have appeared in recent years that assess the aging of the heart or vascular tree and that are also expressed as an absolute number and not as a percentage, a situation that for some authors makes it easier to understand the level of risk to which the person is exposed[3].

Insulin resistance appears when different cells (muscle cells, adipocytes or hepatocytes) do not respond adequately to the action of insulin, so that blood glucose absorption cannot take place. To compensate for this situation, there is an increase in insulin production to allow glucose to enter the cells[4]. As long as the pancreas is able to produce sufficient insulin, blood glucose levels will remain normal, but as insulin production decreases, blood glucose levels will rise, which can lead to the onset of prediabetes[5] and later diabetes[6].

The aim of this study is to determine the relationship between the values of different insulin resistance risk scales and the values of the heart age scale.

Methods

A cross-sectional descriptive study was carried out on 139634 workers attending medical check-ups, and belonging to different work sectors and different Spanish regions. The study was carried out between January 2019 and June 2020.

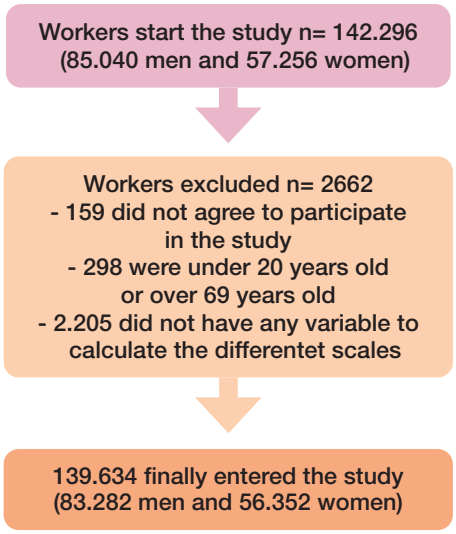
Inclusion criteria were: age between 18 and 69 years.
- Working in the companies included in the study.
- Accepting participation in the study and the transfer of data.

The flow chart is presented in **figure 1**.

Determination of variables

The health professionals from the different companies that participated in the study were responsible for carrying out the analytical determinations and the anthropometric and clinical measurements necessary to obtain the variables included in this study. To avoid possible interobserver bias, all measurements were standardized.

Figure 1: Flow chart of the participants.



To obtain the waist circumference, a tape measure was placed parallel to the floor and at the level of the last floating rib while the patient was in a standing position and with the abdomen relaxed.

To obtain blood pressure, the patient had to rest for at least 10 minutes beforehand. The person was seated and three measurements were taken, calculating the mean value of the three.

Blood tests were obtained after a minimum fasting period of 12 hours using enzymatic processes for blood glucose, cholesterol and triglycerides and precipitation for HDL-cholesterol. LDL-cholesterol was obtained using the Friedewald formula. All the results of all the variables were expressed in mg/dL.

Cardiac age is a new instrument that is calculated on the basis of the classic Framingham cardiovascular risk scale. While the classic cardiovascular risk scales assess the probability of a cerebrovascular event in the next decade, whether fatal or non-fatal, Heart Age assesses the aging of the heart.

Different variables are used to calculate heart age, such as age, sex, height, weight, abdominal circumference, family history of cardiovascular disease, diabetes, tobacco use, lipid profile, systolic blood pressure and consumption of antihypertensive drugs[7]. A calculator is used to obtain the age of the heart, which is available at: www.heartage.me. This calculator can be applied to people between 20 and 80 years of age. The range of values varies between minus 20 and plus 20 years, the limits being 18 and 80 years.

An important concept is the so-called ALLY[8] (avoidable years of life lost), which is the result of subtracting the age of the heart from the chronological age. A publication by our group established the cut-off points, with moderate

ALLY being considered moderate from 11 years of age and high ALLY from 17 years of age onwards[9].

Blood glucose was classified according to the indications of the American Diabetes Association10, which establishes that a person is diabetic if: blood glucose values exceed 125 mg/dL in two different determinations, or if the HbA1c ≥ 6.5% or when the person consumes hypoglycemic agents.

Determination of the percentage of the body's insulin resistance was analysed with the following scales:

Different scales are calculated to assess the risk of insulin resistance:

- Metabolic Insulin Resistance Score (METS-IR)[11]. METS-IR = Ln [(2FPG) + TG] BMI)/(Ln[HDLc]). High values are considered from 50
- The triglyceride and glucose index (TyG index) and some of its variants:
  - TyG = Ln [fasting TG (mg/dL) FPG (mg/dL)/2][12]. High values are considered from 8.8
  - The triglyceride glucose-body mass index (TyG-BMI)[13]
  - TyG - waist circumference (TyG-WC)[13]
- Triglycerides/HDL[14] High values are considered from 2.4

A smoker is a person who has consumed at least one cigarette a day (or the equivalent in other tobacco modalities) in the last 30 days or who has quit smoking less than 1 year ago.

Heart-healthy eating habits were determined by means of the questionnaire on adherence to the Mediterranean diet[15]. This questionnaire consists of 14 questions that are scored with 0 or 1 point, with adherence being considered high if the final score is 9 or higher.

Physical activity was assessed by applying the IPAQ[16] (International Physical Activity Questionnaire). Alcohol intake was quantified in alcohol units (AU). In Spain, one AU is equivalent to 10 grams of pure ethanol. High consumption was considered to be higher if it exceeded 14 AU in women and 21 in men.

The determination of social class is obtained from the National Classification of Occupations 2011[17] and following the criteria established by the Spanish Society of Epidemiology. According to the CNO-11, workers were classified into three social classes: I. Managers, university professionals, athletes and artists. II. Intermediate occupations and skilled self-employed workers. III. Unskilled workers.

Ethical considerations and aspects

In our research, the ethical norms and the Declaration of Helsinki of the year 2013 have been respected at all times. The anonymity and confidentiality of all people is guaranteed. The research received the approval of the Research Ethics Committee of the Balearic Islands (CEI-IB): IB 4383/20. The information of each participant was coded and only the person responsible for the study could know their identity. All researchers complied with Organic Law 3/2018, of December 5, on the protection of personal data and guarantee of digital rights, which guarantees the right of access, rectification, cancellation and opposition of the data collected at all times.

Statistical analysis

Student's t test was used to analyze the quantitative variables, calculating the means and standard deviations. The chi-square test was applied for the qualitative variables, calculating the prevalence. ROC curves were calculated by determining the areas under the curve (AUC). A multinomial logistic regression analysis was performed, calculating the odds ratio. Statistical analysis was performed with the SPSS 28.0 program. The accepted level of statistical significance was $p<0.05$.

Results

Table I shows the anthropometric, clinical, analytical, sociodemographic and healthy habits characteristics of the 139,634 workers who entered the study (83,282 men 59.6% and 56,352 women 40.4%). The mean age of the sample was slightly over 40 years, with the majority of people between the ages of 30 and 49. All the variables showed more favorable values in women. Most of the workers belonged to social class III and their educational level was elementary. The prevalence of high physical activity and high adherence to the Mediterranean diet were lower in men. Approximately one in three people included in the study were a smoker. One third of the people smoked.

The mean values of ALLY heart age according to the values of the different risk scales for insulin resistance are presented in **table II**. The mean values of ALLY increase at the same time as the values of the risk scales of insulin resistance. In all cases the differences observed are statistically significant.

The prevalence of elevated values increases as do the values of the different insulin resistance risk scales. In all cases the observed differences are also statistically significant. The complete data is presented in **table III**.

Table IV presents the results of the multinomial logistic regression analysis. The risk of presenting either moderate or high values of ALLY heart age increases in parallel with the increase in the values of the insulin resistance risk scales. The highest OR values were those found for the TyG index.

Figure 2 and **table V** present the results of the ROC curves. The areas under the curve of all the insulin resistance risk scales to predict the presence of moderate values of ALLY heart age are low, while for ALLY high heart age it is considered moderate.

Table I: Characteristics of the population.

	Men n=83,282 Mean (SD)	Women n=56,352 Mean (SD)	p-value
Age (years)	41.4 (10.7)	40.1 (10.4)	<0.0001
Height (cm)	173.8 (7.1)	161.2 (6.5)	<0.0001
Weight (kg)	83.2 (14.6)	66.3 (13.9)	<0.0001
Body mass index (kg/m²)	27.5 (4.5)	25.5 (5.3)	<0.0001
Waist circumference (cm)	90.2 (10.3)	76.3 (10.5)	<0.0001
Waist to height ratio	0.52 (0.06)	0.47 (0.07)	<0.0001
Systolic blood pressure (mmHg)	126.2 (15.9)	115.6 (15.7)	<0.0001
Diastolic blood pressure (mmHg)	76.6 (10.9)	71.1 (10.7)	<0.0001
Total cholesterol (mg/dl)	199.6 (38.6)	194.6 (36.9)	<0.0001
HDL-cholesterol (mg/dl)	50.0 (7.7)	54.7 (9.2)	<0.0001
LDL-cholesterol (mg/dl)	122.6 (37.4)	121.5 (37.1)	<0.0001
Triglycerides (mg/dl)	133.8 (95.6)	90.8 (49.7)	<0.0001
Glycaemia (mg/dl)	93.0 (25.4)	86.8 (18.1)	<0.0001
n (%)	n (%)	p-value	
18-29 years	12558 (15.1)	10110 (18.0)	<0.0001
30-39 years	24648 (29.6)	17460 (31.0)	
40-49 years	25178 (30.2)	17094 (30.3)	
50-59 years	17370 (20.9)	9984 (17.7)	
60-70 years	3528 (4.2)	1704 (3.0)	
Social class I	6234 (7.5)	7632 (13.6)	<0.0001
Social class II	19856 (23.8)	18112 (32.1)	
Social class III	57192 (68.7)	30608 (54.3)	
Primary school	55306 (66.4)	27086 (48.1)	
Secondary school	22408 (26.9)	22574 (40.0)	
University	5568 (6.7)	6692 (11.9)	
Non-smokers	55618 (66.8)	38252 (67.9)	<0.0001
Smokers	27664 (33.2)	18100 (32.1)	
Non physical activity	51984 (62.4)	28962 (51.4)	<0.0001
Yes physical activity	31298 (37.6)	27390 (48.6)	
Non healthy food	54792 (65.8)	29764 (52.8)	<0.0001
Yes healthy food	28490 (34.2)	26588 (47.2)	
Non alcohol consumption	56022 (67.3)	47536 (84.4)	<0.0001
Yes alcohol consumption	27260 (32.7)	8816 (15.6)	

HDL high density lipoprotein. LDL Low density lipoprotein

Table II: Mean values of heart age according different insulin resistance risk scales by sex.

ALLY HA	n	Men Mean (SD)	p-value	n	Women Mean (SD)	p-value
METS-IR normal	72302	5.9 (7.8)	<0.0001	52206	1.0 (9.4)	<0.0001
METS-IR high	10980	12.6 (7.4)		4146	10.3 (9.0)	
TyG index normal	52484	4.4 (7.3)	<0.0001	48696	0.4 (9.1)	<0.0001
TyG index high	30798	10.7 (7.7)		7656	9.7 (9.5)	
TyG-BMI normal	57476	5.1 (7.6)	<0.0001	47070	0.3 (9.1)	<0.0001
TyG-BMI high	25806	10.4 (7.8)		9282	8.4 (9.5)	
TyG-waist normal	59594	5.3 (7.7)	<0.0001	53166	1.2 (9.4)	<0.0001
TyG-waist high	23688	10.4 (7.9)		3186	10.2 (9.3)	
TG/HDL normal	60208	5.0 (7.6)	<0.0001	44594	-0,1 (8.9)	<0.0001
TG/HDL high	23074	11.4 (7.5)		11758	8.4 (9.3)	

METS-IR Metabolic score for insulin resistance. TyG Triglyceride glucosa index BMI Body mass index
WtHR Waist to heigh ratio. TG Triglyceride HDL High density Lipoprotein. ALLY HA Avoidable lost life life years heart age

Table III: Prevalence of high values of heart age according different insulin resistance risk scales by sex.

ALLY HA	Men					Women				
	n	Normal %	Moderate %	High %	p-value	n	Normal %	Moderate %	High %	p-value
METS-IR normal	72302	75,6	10,5	14,0	<0.0001	52206	83,6	10,2	10,2	<0.0001
METS-IR high	10980	40,8	16,2	43,1		4146	51,2	37,7	37,7	
TyG index normal	52484	82,1	8,9	9,1	<0.0001	48696	86,0	8,3	8,3	<0.0001
TyG index high	30798	52,0	15,2	32,8		7656	51,1	36,9	36,9	
TyG-BMI normal	57476	78,8	9,7	11,6	<0.0001	47070	85,8	8,6	8,6	<0.0001
TyG-BMI high	25806	53,6	14,6	31,8		9282	58,2	30,2	30,2	
TyG-waist normal	59594	77,8	9,9	12,3	<0.0001	53166	83,1	10,7	10,7	<0.0001
TyG-waist high	23688	53,7	14,5	31,8		3186	49,6	37,6	37,6	
TG/HDL normal	60208	79,3	9,5	11,1	<0.0001	44594	87,3	7,6	7,6	<0.0001
TG/HDL high	23074	49,2	15,6	35,2		11758	58,3	29,7	29,7	

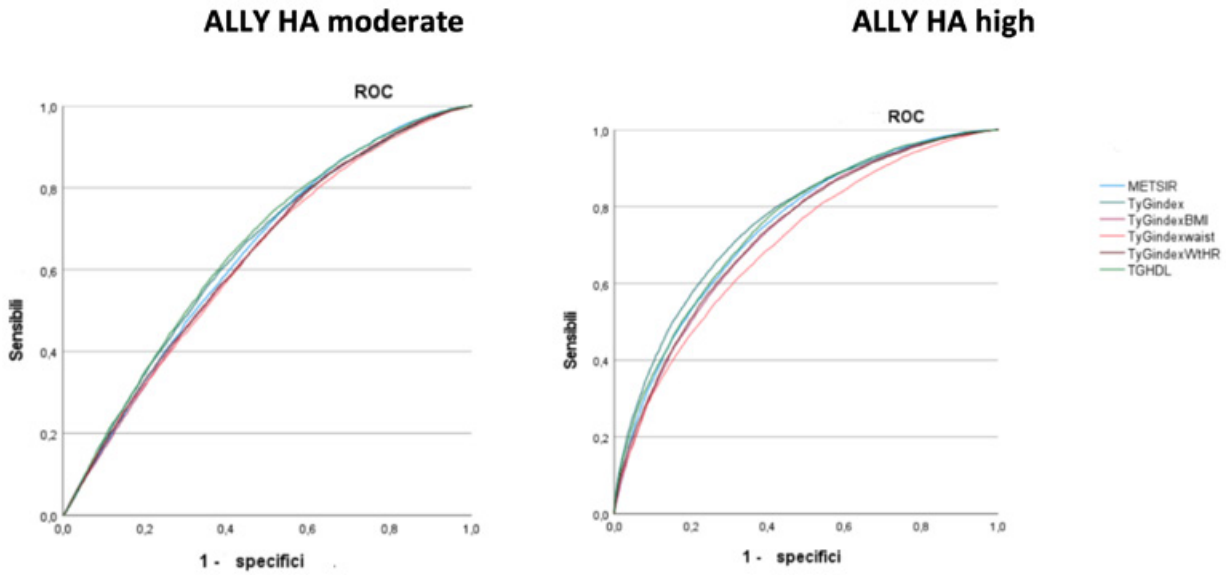
METS-IR Metabolic score for insulin resistance. TyG Triglyceride glucosa index BMI Body mass index
WtHR Waist to heigh ratio. TG Triglyceride HDL High density Lipoprotein. ALLY HA Avoidable lost life life years heart age

Table IV: Binomial logistic regression.

	ALLY HA moderate		ALLY HA high	
	OR (95% CI)	p-value	OR (95% CI)	p-value
METS-IR normal	1		1	
METS-IR high	1.91 (1.82-2.00)	<0.0001	1.99 (1.89-2.09)	<0.0001
TyG index normal	1		1	
TyG index high	2.42 (2.33-2.52)	<0.0001	2.59 (2.47-2.71)	<0.0001
TyG-BMI normal	1		1	
TyG-BMI high	1.49 (1.43-1.55)	0.005	1.49 (1.42-1.55)	<0.0001
TyG-waist normal	1		1	
TyG-waist high	1.06 (1.02-1.10)	<0.0001	1.09 (1.05-1.13)	<0.0001
TG/HDL normal	1		1	
TG/HDL high	1.71 (1.65-1.78)	<0.0001	1.73 (1.66-1.81)	<0.0001

METS-IR Metabolic score for insulin resistance. TyG Triglyceride glucosa index BMI Body mass index WtHR Waist to heigh ratio. TG Triglyceride HDL High density Lipoprotein. ALLY HA Avoidable lost life life years heart age.

Figure 2: ROC curve.



ALLY HA Avoidable lost life life years heart age

Table V: Area under the curve (ROC curve).

	ALLY HA moderate AUC (95% CI)	ALLY HA high AUC (95% CI)
METS-IR	0.637 (0.632-0.642)	0.746 (0.743-0.750)
TyG index	0.640 (0.635-0.645)	0.763 (0.759-0.766)
TyG-BMI	0.627 (0.622-0.632)	0.731 (0.728-0.734)
TyG-waist	0.623 (0.618-0.627)	0.705 (0.701-0.709)
TyG-WtHR	0.629 (0.624-0.633)	0.733 (0.730-0.737)
TG/HDL	0.649 (0.644-0.654)	0.752 (0.749-0.756)

METS-IR Metabolic score for insulin resistance. TyG Triglyceride glucosa index BMI Body mass index WtHR Waist to heigh ratio. TG Triglyceride HDL High density Lipoprotein. AUC Area under the curve

Discussion

The mean value and the prevalence of moderate or high values of ALLY cardiac age increase parallel to the values of the different insulin resistance risk scales used in this study. The results of the multinomial logistic regression analysis show that the insulin resistance risk scale with the highest odds ratio is the TyG index.

An exhaustive review of the literature, in different databases, has only allowed us to find a few articles that relate, albeit tangentially, the age of the heart with insulin resistance, for this reason it will not be possible to compare our results with those obtained by other authors.

A study carried out in 501 individuals without cardiovascular disease, with a mean age of 55.9 years, aimed at assessing the relationship between healthy vascular aging, lifestyle and the components of the metabolic syndrome found that vascular age was associated with

smoking, blood pressure, waist circumference and altered basal glycemia[18]. 18 This same group, in another study[19] found that healthy vascular aging was closely related to insulin resistance.

In an investigation carried out in 18,490 participants of the MARE[20] global consortium, without cardiovascular pathologies, in which healthy vascular aging was assessed, it was observed that the prevalence of metabolic syndrome, the genesis of which is insulin resistance, was lower in this group.

A Taiwanese study[21] of 4881 persons found that the risk of atherosclerotic cardiovascular disease, which is related to vascular aging, was higher in persons with metabolic syndrome, persons with elevated glycemia or glycosylated hemoglobin, that is, in persons with possible insulin resistance.

A Russian study[22] conducted in 750 patients with metabolic syndrome aged 35 to 80 years concluded that the presence of type 2 diabetes and insulin resistance was associated with an increased risk of early vascular aging.

Strengths and limitations

The strengths of the study include the large sample size, which exceeds 139,000 participants, the wide variety of insulin resistance risk scales used, and the fact that we can consider this study as a benchmark with which to compare the results found in subsequent studies.

The main limitation is that insulin resistance has been determined using risk scales and not objective methods.

Conclusions

Both the means and the prevalence of moderate and high values of ALLY heart age increase in parallel with the increase in the values of the different insulin resistance risk scales included in this study. The value of the insulin resistance risk scales to predict the appearance of moderate or high values of ALLY heart age is low in the first case and moderate in the second.

Conflict of Interest

The authors declare that there is no conflict of interest.

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