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ORIGINAL

Relationship between heart age and cardiometabolic risk scales in 139634 Spanish workers

Relación entre la edad del corazón y escalas de riesgo cardiometabólico en 139634 trabajadores españoles

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Abstract

Introduction: Cardiometabolic diseases are highly prevalent worldwide and are responsible for high morbidity and mortality. Cardiovascular risk (CVR) is usually determined from scales that assess the probability of occurrence in a given period. Currently, other CVR scales have been developed that assess the aging of both the heart and blood vessels. The aim of this study is to assess the association between some cardiometabolic risk scales and heart age.
Methods: Descriptive study in 139634 Spanish workers in which CVR was determined by applying the age of the heart and also different cardiometabolic risk scales such as atherogenic dyslipidemia, lipid triad, metabolic syndrome, diabesity, hypertriglyceridemic waist circumference, and risk of type 2 diabetes.
Results: Heart age values are higher in people with high cardiometabolic risk applying all scales. The risk of presenting moderate or high values of heart age is higher among people with high cardiometabolic risk, especially in case of lipid triad and high values of the Findrisk test. The value of the Findrisk test for predicting moderate vascular age is low, whereas for high heart age the value of this test is high.
Conclusions: There is a good association between heart age and the cardiometabolic risk scales analyzed. The predictive value of the Findrisk test is low for moderate heart age and high for high heart age.

Key words: Heart age, atherogenic dyslipidemia, metabolic syndrome, Findrisk test, diabesity, hypertriglyceridemic waist circumference.

Resumen

Introducción: Las enfermedades cardiometabólicas tienen una elevada prevalencia en el mundo y son responsables de una elevada morbimortalidad. El riesgo cardiovascular (RCV) se determina habitualmente a partir de escalas que valoran la probabilidad de aparición en un periodo determinado. Actualmente se han desarrollado otras escalas de RCV que valoran el envejecimiento tanto del corazón como de los vasos sanguíneos. El objetivo de este estudio es valorar la asociación entre algunas escalas de riesgo cardiometabólico y la edad del corazón.
Material y métodos: Estudio descriptivo en 139634 trabajadores españoles en los que se determina el RCV aplicando la edad del corazón y también diferentes escalas de riesgo cardiometabólico como dislipemia aterogénica, triada lipídica, síndrome metabólico, diabesidad, cintura hipertrigliceridémica y riesgo de diabetes tipo 2.
Resultados: Los valores de edad del corazón son más elevados en las personas con alto riesgo cardiometabólico aplicando todas las escalas. El riesgo de presentar valores moderados o altos de edad del corazón es mayor entre las personas con alto riesgo cardiometabólico, especialmente en caso de triada lipídica y valores altos del test de Findrisk. El valor del test de Findrisk para predecir edad vascular moderada es bajo, mientras que para edad del corazón alta el valor de este test es elevado.
Conclusiones: Existe buena asociación entre edad del corazón y las escalas de riesgo cardiometabólico analizadas. El valor predictivo del test de Findrisk es bajo para edad del corazón moderada y alto para edad del corazón alta.

Palabras clave: Edad del corazón, dislipemia aterogénica, síndrome metabólico, test de Findrisk, diabesidad, cintura hipertrigliceridémica.

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Introduction

Cardiometabolic pathologies are a group of diseases that affect the heart[1] and blood vessels[2] and are fundamentally caused by unhealthy lifestyles of individuals[3]. It is a process generally due to atherosclerosis[4], which is caused by the accumulation of cholesterol and other substances and results in hardening of the arterial wall.

According to data published by the World Health Organization (WHO), more people die each year worldwide from this cause than from any other cause[5]. The same organization states that 8 out of every 10 myocardial infarctions or cerebrovascular accidents could be prevented[6] if early detection[7] and healthy lifestyles[8] were established or if risk factors were effectively controlled[9].

Cardiometabolic diseases (CMD) include such prevalent pathologies as heart failure, arterial hypertension, dyslipidemia and diabetes mellitus.

The risk of presenting SCD has traditionally been defined as a percentage of risk in a given period of time, which is usually 10 years[10]. This percentage assessment can give a false sense of security, so other tools have been developed that establish, in absolute values, the estimated age of both the heart and the blood vessels, known as heart age[11] and vascular age[12]. These tools, according to some authors, facilitate understanding of the level of risk to which individuals are subjected[13].

The aim of this study is to assess the relationship between one of these tools, heart age, and different scales that assess cardiometabolic risk, such as atherogenic dyslipidemia, the lipid triad, metabolic syndrome, hypertriglyceridemic waist circumference, diabesity, and the risk of type 2 diabetes.

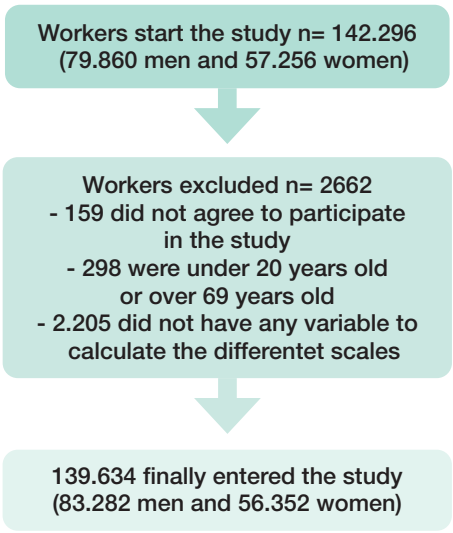
Methods

An observational, descriptive and cross-sectional study was carried out in a group of 139634 workers from different Spanish regions between January 2019 and June 2020. The workers were selected among those who had attended the health examinations carried out in the different participating companies.

In order to be included in the study, a series of inclusion criteria were established, among which we highlight the following:
- To be between 18 and 69 years of age.
- To be part of the staff of one of the participating companies.
- Acceptance to participate in the study by consenting to the use of the data for epidemiological purposes.

The flow chart of the participants in the study is shown in **figure 1**.

Figure 1: Flow chart of the participants.



Determination of variables

All the health professionals belonging to the different participating companies were responsible for obtaining the precise analytical, clinical and anthropometric parameters to determine the cardiometabolic risk scales and the age of the heart. In order to avoid possible biases in the measurements, all the measurement techniques were previously standardized.

Waist circumference was obtained with the person standing upright, with the abdomen as relaxed as possible and placing the tape measure parallel to the floor and at the level of the last floating rib.

Blood pressure was determined after a rest period of no less than 10 minutes. The person was placed in a seated position and three determinations were made at one-minute intervals, establishing the mean of the three as the final result.

The blood tests were performed after a fasting period of not less than twelve hours. Enzymatic techniques were used to determine triglycerides, cholesterol and glycemia. HDL values were obtained by precipitation techniques, LDL values were obtained from the Friedewald formula provided that triglycerides were not higher than 400 mg/dL, otherwise a direct determination was made.

Heart age (CE) is a novel scale that is determined on the basis of the classic Framingham Scale[14]. Unlike the traditional cardiovascular risk scales that estimate the probability of a cardiovascular event occurring in the next decade, the CE estimates how our heart has aged.

Its calculation requires a series of variables such as gender, age, height and weight, abdominal waist circumference, presence of family members with cardiovascular problems, smoking, diabetes, lipid profile,

systolic blood pressure, and antihypertensive treatment. All these data can be used to access a calculator (www.heartage.me.). The calculation of CE can be performed in the interval between 20-80 years.

A concept called ALLY[15] (avoidable years of life lost) has been developed, which is obtained by subtracting CAD from chronological age. In a previous article, our group[16] determined the cut-off points for moderate ALLY (11 years) and high ALLY (17 years).

Blood glucose levels were stratified according to the criteria of the American Diabetes Association[17], according to which a person is considered diabetic when blood glucose levels are above 125 mg/dL in two different measurements, or when HbA1c values ≥ 6.5% or if he or she is on hypoglycemic treatment.

As estimators of cardiometabolic risk, the following were calculated:

- Atherogenic dyslipidemia (AD) and lipid triad (LT).
Atherogenic dyslipidemia[18] was considered AD when high triglyceride values coexisted with low HDL values in the same person. If high LDL values were also associated, it was considered LT[19].

- Metabolic syndrome (MS).
MS was determined on the basis of two criteria[20]:

a) The presence of at least three of these parameters, blood pressure greater than 130/85 mmHg; triglycerides above 150 mg/dL or under treatment to lower it; low HDL, glycemia above 100 mg/dL or specific treatment for it and waist circumference above 88 cm in women and 102 cm in men corresponds to SM NCEP ATP III.

b) The International Diabetes Federation (IDF) establishes SM if: in addition to presenting at least two of the parameters mentioned above (triglycerides, HDL, blood pressure and glycemia), a waist circumference greater than 94 cm in men and 80 cm in women appears.

- Risk of type 2 diabetes with the Findrisk[21] test.
To determine the risk of presenting type 2 diabetes we will use the Findrisk test. This questionnaire includes 8 items: age, waist circumference, body mass index, physical activity, family history of diabetes, consumption of fruits and vegetables, consumption of antihypertensive drugs and personal history of hyperglycemia. Values above 14 will indicate a high risk[22].

- Diabesity.
Diabesity is considered to exist when the same person has obesity determined by a body mass index of 30 kg/m^2 or more and diabetes[23].

- Hypertriglyceridemic waist.
We speak of a hypertriglyceridemic waist when we find in the same person high triglyceride values (greater than 150 mg/dL) and high abdominal waist circumference values (greater than 102 cm in men and greater than 88 cm in women)[24].

A smoker is an individual who in the last month has consumed at least 1 cigarette per day (or a similar amount in other consumption modalities) or who has quit smoking less than 1 year ago.

When we applied the questionnaire on adherence to the Mediterranean diet (14 questions rated between 0 and 1 point), we considered adherence to be high at values of 925 or higher.

Physical activity was assessed with the International Physical Activity Questionnaire (IPAQ)[26].

Alcohol consumption was quantified using alcohol units (AU). Considering that 1 AU is equivalent to 10 grams of pure ethanol. We consider high consumption as from 14 AU in women and 21 in men per week[27].

Social class was determined based on the 2011 National Classification of Occupations (CNO-11)28 and applying the criteria of the Spanish Society of Epidemiology. We stratified it into: Social class I. Includes management personnel, university professionals, athletes and artists. Social class I. Includes intermediate occupations and skilled self-employed workers. Social class III. Includes low-skilled workers.

Ethical considerations and aspects

The ethical standards of the Institutional Research Council and the 2013 Declaration of Helsinki are always followed, and anonymity and confidentiality are guaranteed. The study was approved by the Research Ethics Committee of the Balearic Islands (CEI-IB): IB 4383/20. The data of each employee included in the study were coded, and only those responsible for the study knew the identity of each individual.

The researchers undertook to strictly comply with the provisions of Organic Law 3/2018, of December 5, on the protection of personal data and guarantee of digital rights, which guarantees the right of participants to access, rectify, cancel, and oppose the data collected.

Statistical analysis

For quantitative variables, Student's t test was used to calculate the mean and standard deviation. When the variables were qualitative, the chi-square test was used to calculate prevalence. For ROC curves, the areas under the curve were determined. Multivariate analysis was performed by applying multinomial logistic regression. SPSS 28.0 was used for statistical analysis. The accepted level of statistical significance was $p<0.05$.

Results

Table I shows the values of the analytical, clinical, anthropometric, sociodemographic and healthy habits variables of the 139634 (83282 men 59.6% and 56352 women 40.4%) workers who participated in this study. The mean age of the sample was slightly over 40 years, with the largest group being 30-49 years. In all cases, the variables were less favorable in males. Most of the workers were of social class III and with primary education. The prevalence of sedentary lifestyle was higher in men, as was low adherence to the Mediterranean diet. Tobacco consumption, and especially alcohol consumption, was also higher in men.

Table II shows that the ALLY values for heart age were higher in both men and women when the cardiometabolic risk scales showed higher values. In all cases, these mean ALLY values were higher in men. The differences observed between both sexes were always statistically significant.

The prevalence of elevated ALLY heart age values also shows higher values when the cardiometabolic risk scales show higher values. As we have seen with the mean values, in the case of prevalences we also observed higher figures in men. The differences by sex are statistically significant in all cases. The complete data can be seen in **table III**.

Table IV shows the results of the multivariate analysis using multinomial logistic regression. In all cases, the risk of moderate or high ALLY increases as the values of the different cardiometabolic risk scales increase. The highest odss ratios appear for Findrisk and lipid triad.

Figure 2 shows the areas under the Findrisk curve for predicting the occurrence of moderate and high ALLY. In women the areas are larger than in men. In both sexes the predictive value of Findrisk is higher for ALLY high heart age.

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 ALLY heart age according different cardiometabolic risk scales by sex.

ALLY heart age	n	Men Mean (SD)	p-value	n	Women Mean (SD)	p-value
No AD	77846	6.1 (7,8)	<0.0001	53852	1.2 (9.5)	<0.0001
Yes AD	5436	16.1 (5.7)		2500	11.7 (8.4)	
No LT	80918	6.4 (8.0)	<0.0001	55268	1.4 (9.6)	<0.0001
Yes LT	2364	17.1 (4.7)		1084	14.0 (7.3)	
No MS NCEP ATPIII	69256	5.2 (7.5)	<0.0001	51860	0.6 (9.1)	<0.0001
Yes MS NCEP ATPIII	14026	14.2 (6.6)		4492	13.5 (7.9)	
NO MS IDF	66966	5.3 (7.6)	<0.0001	53152	1.0 (9.3)	<0.0001
Yes MS IDF	16316	12.8 (7.0)		3200	12.7 (8.1)	
Finrisk low	44928	4.2 (7.2)	<0.0001	38258	-0.9 (8.4)	<0.0001
Finrisk slightly elevated	22418	7.1 (7.5)		9894	4.6 (9.6)	
Finrisk moderate	6490	11.1 (7.6)		3724	7.1 (9.7)	
Finrisk high	3780	13.0 (7.3)		2566	10.0 (9.3)	
Finrisk very high	486	16.4 (5.8)		62	19.8 (0.4)	
No diabesity	80826	6.4 (7.9)	<0.0001	55478	1.4 (9.5)	<0.0001
Yes diabesity	2456	17.4 (4.8)		874	17.2 (5.4)	
No HTGW	71340	5.9 (7.9)	<0.0001	54806	1.4 (9.5)	<0.0001
Yes HTGW	11942	11.5 (7.6)		1546	12.2 (8.5)	

ALLY HA Avoidable lost life life years

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

ALLY heart age	Men					Women				
	n	Normal %	Moderate %	High %	p-value	n	Normal %	Moderate %	High %	p-value
No AD	77846	74.5	10.9	14.6	<0.0001	53852	83.0	6.3	10.7	<0.0001
Yes AD	5436	20.1	15.5	64.4		2500	43.5	13.7	42.8	
No LT	80918	72.6	11.1	16.3	<0.0001	55268	82.2	6.4	11.4	<0.0001
Yes LT	2364	14.1	15.1	70.8		1084	31.9	14.6	53.5	
No MS NCEP ATPIII	69256	78.9	10.0	11.1	<0.0001	51860	85.4	5.9	8.7	<0.0001
Yes MS NCEP ATPIII	14026	31.6	17.2	51.2		4492	33.6	14.3	52.1	
NO MS IDF	66966	78.3	9.7	12.0	<0.0001	53152	83.8	6.1	10.1	<0.0001
Yes MS IDF	16316	40.7	17.5	41.8		3200	38.2	15.3	46.6	
Finrisk low	44928	83.0	8.8	8.2	<0.0001	38258	90.1	4.4	5.5	<0.0001
Finrisk slightly elevated	22418	71.9	12.2	15.6		9894	73.2	9.8	17.0	
Finrisk moderate	6490	49.5	17.7	32.8		3724	62.5	12.5	25.0	
Finrisk high	3780	37.7	17.7	44.6		2566	50.0	14.8	35.2	
Finrisk very high	486	17.7	17.3	65.0		62	0.0	0.0	100.0	
No diabesity	80826	72.8	11.1	16.1	<0.0001	55478	82.3	6.6	11.2	<0.0001
Yes diabesity	2456	11.6	13.4	75.0		874	15.6	8.5	75.9	
No HTGW	71340	74.9	10.4	14.7	<0.0001	54806	82.4	6.4	11.2	<0.0001
Yes HTGW	11942	47.4	15.7	36.9		1546	40.4	13.2	46.4	

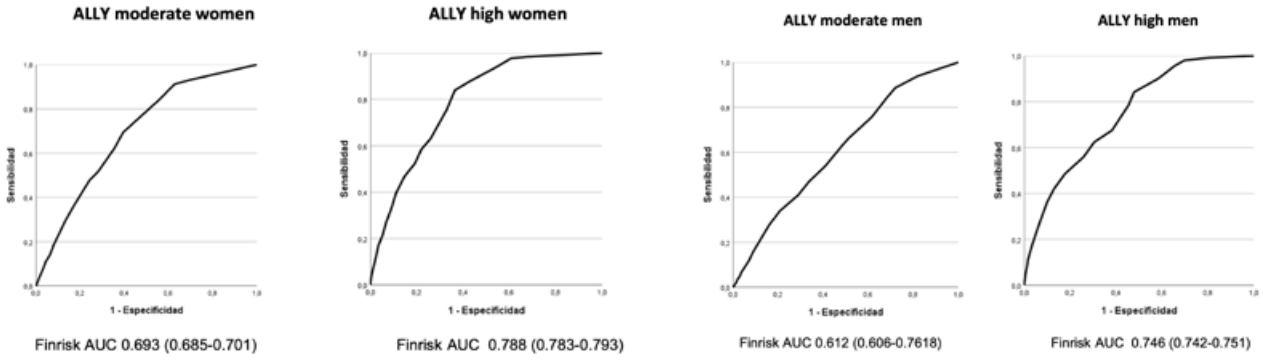
ALLY HA Avoidable lost life life years heart age. AD Atherogenic dyslipidemia. LT Lipid triad MS Metabolic syndrome NCEP ATPIII National Cholesterol Education Program Adult Treatment Panel III IDF International Diabetes Federation HTGW Hypertriglyceridemic waist phenotype

Table IV: Multinomial logistic regression.

	ALLY HA moderate	ALLY HA high
	OR (95% CI)	OR (95% CI)
No AD	1	1
Yes AD	2.15 (2.00-2.30)	2.24 (2.09-2.40)
No LT	1	1
Yes LT	4.37 (3.94-4.84)	3.63 (3.31-3.98)
No MS NCEP ATPIII	1	1
Yes MS NCEP ATPIII	2.59 (2.46-2.73)	2.68 (2.53-2.83)
NO MS IDF	1	1
Yes MS IDF	1.39 (1.32-1.47)	1.13 (1.07-1.20)
Finrisk low	1	1
Finrisk slightly elevated	2.40 (1.86-3.08)	2.14 (1.74-2.63)
Finrisk moderate	2.73 (2.13-3.51)	2.57 (2.09-3.15)
Finrisk high	4.75 (3.70-6.09)	4.47 (3.65-5.47)
Finrisk very high	8.94 (6.97-11.47)	9.05 (7.38-11.10)
No diabesity	1	1
Yes diabesity	2.17 (1.92-2.45)	2.00 (1.81-2.21)
No HTGW	1	1
Yes HTGW	1.33 (1.26-1.41)	1.38 (1.30-46)

ALLY HA Avoidable lost life life years heart age. AD Atherogenic dyslipidemia. LT Lipid triad
MS Metabolic syndrome NCEP ATPIII National Cholesterol Education Program Adult Treatment Panel III
IDF International Diabetes Federation HTGW Hypertriglyceridemic waist phenotype

Figure 2: ROC curves.



Discussion

The mean values and the prevalence of high values of ALLY heart age increase in parallel with the increase in the values of the different cardiometabolic risk scales analyzed in this study.

High values of all the cardiometabolic risk scales considered in this study increase the risk of moderate and high ALLY heart age, especially Findrisk and lipid triad.

The value of the Findrisk test for predicting the occurrence of ALLY moderate heart age is low, whereas for predicting ALLY high heart age it can be considered high. In both cases the values are higher in women.

Due to the absence of studies assessing the relationship between heart age and cardiometabolic risk scales, we cannot compare our results with those obtained by other authors. To try to compensate for this deficit, we will compare the cardiometabolic risk scales with other scales that assess cardiovascular risk.

The EVA study[29] carried out in 501 Spaniards with an average age of 55.9 years assessed the relationship between vascular and cardiac aging, lifestyle and the components of the metabolic syndrome. The results showed that those with metabolic syndrome had higher values for heart age and vascular age.

In the 18,490 participants of the global MARE[30] consortium assessing, among other things, healthy vascular aging, the prevalence of metabolic syndrome was found to be lower in those with healthy vascular aging.

A Spanish study using Bayesian networks[31] also found an association between cardiac age and metabolic syndrome.

A descriptive study of 59,041 Spanish workers[32] in the Mediterranean area found that those with prediabetes had higher values for the classic cardiovascular risk scales and also for heart age and vascular age.

Another Spanish study in a large sample assessed the relationship between the values of the Findrisk test and different cardiovascular risk scales[33], including heart age. It found, as we did, that the ALLY heart age values increased as the values of the Findrisk test increased.

An Iranian study[34] concluded that diabesity was a predictor of the incidence of cardiovascular disease and stroke.

Another Spanish study carried out in more than 418000 workers[35] assessed the relationship between atherogenic dyslipidemia and lipid triad with the values of different classic cardiovascular risk scales and with vascular age determined with the Framingham and SCORE criteria, observing that the ALLY values with both criteria were higher in persons with atherogenic dyslipidemia and lipid triad.

Strengths and weaknesses

The main strengths of this study are the enormous sample size, the large number of cardiometabolic risk scales analyzed, and the fact that it is one of the first articles to assess the relationship between heart age and other cardiometabolic risk scales, so that it can become a reference for subsequent studies on this subject.

The main weakness is that some of the scales, such as Findrisk, assess risk and do not start from an objective value.

Conclusions

There is a good relationship between the ALLY heart age values and the values of the different cardiometabolic risk scales analyzed (atherogenic dyslipidemia, lipid triad, metabolic syndrome with the NCEP ATPIII and IDF criteria, Findrisk test, diabesity and hypertriglyceridemic waist).

The risk scales that most increase the possibility of moderate or high ALLY heart age values are Findrisk and lipid triad.

The predictive value of the Findrisk test is low for moderate ALLY heart age in both sexes and high, also for both sexes in the case of high ALLY heart age.

Conflict of Interest

The authors declare that there is no conflict of interest.

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