

## ORIGINAL

# Association between atherogenic dyslipidemia and lipid triad with cardiovascular risk scales in 418.343 Spanish workers

*Asociación entre dislipemia aterogénica y tríada lipídica con escalas de riesgo cardiovascular en 418.343 trabajadores españoles*

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## Abstract

**Introduction and objectives:** Cardiovascular diseases in their genesis generally present an anatomopathological process such as atherosclerosis. Atherogenic dyslipidemia (AD) and lipid triad (TL) are parameters that can predict the appearance of atherosclerosis. The aim of this study is to assess the relationship between AD and LT with different cardiovascular risk (CVR) scales.

**Material and methods:** A descriptive, cross-sectional study was carried out in a large sample of Spanish workers, specifically 418343, in which the presence or absence of AD and TL was assessed. Different CVR scales such as REGICOR, SCORE 2, ERICE and vascular age were also determined using the Framingham and SCORE criteria.

**Results:** The mean values of all CVR scales and the prevalence of elevated values of these scales are higher in both AD and TL. The scale that most increases the risk of presenting both AD and TL is ALLY of Framingham vascular age. The CVR scales, in general, have a low predictive power for both AD and TL.

**Conclusions:** There is a good association between the CVR scales analyzed and AD and TL. The value of these CVR scales for predicting AD and TL is low, with the exception of ALLY with the Framingham criteria.

**Key words:** Atherogenic dyslipidemia, cardiovascular disease, cardiovascular risk, atherosclerosis.

## Resumen

**Introducción y objetivos:** Las enfermedades cardiovasculares en su genesis presentan generalmente un proceso anatomopatológico como es la aterosclerosis. La dislipemia aterogénica (DA) y la tríada lipídica (TL) son parámetros que pueden predecir la aparición de aterosclerosis. El objetivo de este estudio es valorar la relación que existe entre la DA y TL con diferentes escalas de riesgo cardiovascular (RCV).

**Material y métodos:** Estudio descriptivo y transversal realizado en una amplia muestra de trabajadores españoles, concretamente 418343, en los que se valora la presencia o no de DA y TL. También se determinan diferentes escalas de RCV como REGICOR, SCORE 2, ERICE y edad vascular con los criterios de Framingham y SCORE.

**Resultados:** Los valores medios de todas las escalas de RCV y la prevalencia de valores elevados de estas escalas son superiores tanto en la DA como en la TL. La escala que más incrementa el riesgo de presentar tanto DA como TL es ALLY de edad vascular Framingham. Las escalas de RCV, en general, tienen un bajo poder de predicción tanto de DA como de TL.

**Conclusiones:** Existe una buena asociación entre las escalas de RCV analizadas y la DA y TL. El valor de estas escalas de RCV para predecir DA y TL es bajo, a excepción de ALLY con los criterios de Framingham.

**Palabras clave:** Dislipidemia aterogénica, enfermedad cardiovascular, riesgo cardiovascular, aterosclerosis.

## Introduction

Cardiovascular diseases (CVD) are currently responsible for a high morbidity and mortality rate in the vast majority of countries<sup>1</sup> and are considered by all to be the leading cause of death worldwide. There are many diseases that can be included in this concept, from diseases of the heart itself such as coronary heart disease to conditions of the vascular tree such as arterial hypertension<sup>2</sup>.

There are direct methods for evaluating CVD<sup>3,4</sup> (analytical, imaging, etc.) and indirect methods based mainly on the determination, using scales<sup>5</sup>, of the risk of presenting a cerebrovascular event in a given period, which is generally established as ten years.

In the vast majority of these health problems, one element that is always present is atherosclerosis<sup>6</sup>. This condition occurs when fatty elements build up on the walls of the blood vessel (artery). This accumulation of fat gives rise to what is called plaque<sup>7</sup>. This causes problems in different organs of our body. If an artery becomes clogged, it can lead to the occurrence of different cerebrovascular events.

Atherogenic dyslipidemia and lipid triad<sup>8</sup> are two clinical entities characterized by the coexistence of pathological values of different lipid parameters such as triglycerides

and HDL, in the case of dyslipidemia, and these two and LDL in the case of the triad. These two parameters are early predictors of atherosclerosis, hence their clinical importance.

Based on the above, the aim of this study is to determine the relationship of atherogenic dyslipidemia and the lipid triad with different scales that determine cardiovascular risk in a group of Spanish workers from different regions and work groups.

## Methods

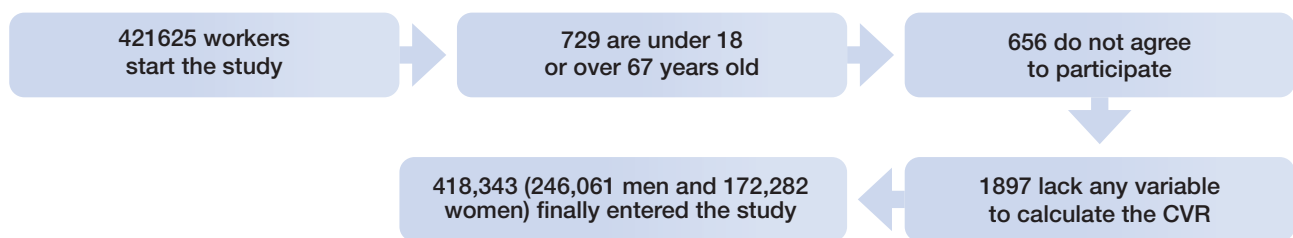
In a group of 418,343 Spanish workers (172,282 women and 246,061 men), a cross-sectional descriptive study was carried out using data from occupational medical examinations performed between January 2019 and June 2020. The workers belonged to the primary, secondary and tertiary sectors.

Inclusion criteria were established as follows:

- Age between 18 and 69 years.
- Working in one of the companies included in the study.
- Agreeing to participate in the study.

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

**Figure 1:** Flowchart of participants.



### Determination of variables

The responsibility for identifying the clinical, analytical, and anthropometric variables required to calculate the various scales included in the study fell on the health workers of the participating companies. The measurements were standardized to reduce interobserver bias.

Using the subject upright and the abdomen relaxed, the waist circumference was measured using a tape measure at the level of the last rib.

With the patient seated and after at least 10 minutes of rest, blood pressure was measured using an OMRON M3 sphygmomanometer. The mean blood pressure was calculated from three measurements.

After fasting for at least 12 hours, the analytical parameters were collected using precipitation methods for HDL cholesterol and enzymatic methods for glucose, triglycerides, and cholesterol. Using the Friedewald formula (valid only for triglyceride amounts under 400), LDL-cholesterol was calculated. In mg/dL, all analytical parameters were presented.

Different cardiovascular risk scales were calculated:

- Registro Gironí del Cor (REGICOR)<sup>9,10</sup>.

The likelihood of having a fatal or non-fatal cerebrovascular incident over the following ten years is determined by this scale. It can be computed for ages between 35 and 74. It is divided into four categories: low less than 5%,

moderate, high between 10% and 14% high, and very high more than 15%.

- Systematic Coronary Risk Evaluation 2 (SCORE2)<sup>11</sup>

Assesses the probability of a cerebrovascular event occurring in the next decade. It can be calculated between 40 and 69 years of age. Its classification varies according to age group (under 50 years and over 50 years) so that in the first group we will consider low or moderate risk if it is less than 2.5%, high between 2.5-7.5% and very high above 7.5%, while in the second group it will be low or moderate risk if it is less than 5%, high between 5-10% and very high above 10%.

- Framingham and SCORE vascular age<sup>12</sup>.

Both vascular age scales are based on cardiovascular risk scales with the same name and both are calculated from tables. In both cases, the concept of ALLY<sup>13</sup> (avoidable lost life years) can be applied, which is calculated by subtracting the vascular age from the chronological age. Our group established 10 years as moderate ALLY values and 18 years as high values<sup>14</sup>.

- ERICE score<sup>15</sup>.

The Spanish Cardiovascular Risk Equation (ERICA) is based on data from several epidemiological studies in different regions of Spain. It assesses the probability of a fatal cerebrovascular event occurring in the next ten years and can be calculated between the ages of thirty and eighty. Total cholesterol, age, smoking, diabetes, sex, systolic blood pressure and the presence or absence of antihypertensive drug treatment are the factors used to calculate it.

Low (less than 5%), mild (5-9%), moderate (10-14%), moderate-high (15-19%), high (20-29%), and extremely high (greater than 30%) are the five categories.

If the combination of high triglyceride levels, low HDL cholesterol levels (less than 50 mg/dL for women and less than 40 mg/dL for males), and normal LDL cholesterol levels was present, atherogenic dyslipidemia<sup>16</sup> was evaluated. A lipid triad<sup>17</sup> was deemed to exist if LDL cholesterol also surpassed 160 mg/dL.

Diabetes was defined as having fasting blood glucose levels greater than 125 mg/dL or using hypoglycemic medications.

A smoker was defined as someone who had smoked one or more cigarettes per day for the previous 30 days, or the equivalent in another mode of consumption, or someone who had quit smoking within the previous 12 months.

The workers were divided into three social groups using the 2011 National Classification of Occupations (CNO-11) and the Spanish Society of Epidemiology standards<sup>18</sup>. I. Managers, college employees, athletes, and creatives. Unskilled employees, part two.

## Ethical considerations and aspects

The study adhered to the 2013 Declaration of Helsinki as well as the institutional research committee's ethical requirements. The obtained data's confidentiality and anonymity could always be maintained. The Research Ethics Committee of the Balearic Islands (CEI-IB) gave the study their blessing with IB 4383/20. Only the person in charge of the study was able to decode the data used to identify each of the workers who were participating in the study. The research team committed to carefully upholding Organic Law 3/2018, of December 5, on the protection of personal data and guarantee of digital rights, ensuring that each participant in this study could exercise their right to access, rectification, erasure, and opposition to the use of their data for any purpose.

## Statistical analysis

For quantitative data, the t-student test was used to calculate the mean and standard deviation. The chi-square test was used to calculate prevalence for qualitative variables. ROC curves were used to evaluate how well the cardiovascular risk scales predicted the presence of atherogenic and triadic dyslipidemia. Calculations were made for the area under the curve (AUC), the cut-off points' sensitivity, specificity, and Youden index. Multinomial logistic regression was used to do the multivariate analysis. To conduct the statistical analysis, SPSS 28.0 was employed. p0.05 was the accepted cutoff for statistical significance.

## Results

The characteristics of the study participants are shown in **table I**. Men made up more than 58%. The majority group was between the ages of 30 and 49, with a mean age of 40. Over 75% were from socioeconomic class III, and over 33% smoked. In women, all variables had more favorable values.

**Table II** demonstrates that people of both sexes with atherogenic dyslipidemia and lipid triad have higher mean values on all evaluated cardiovascular risk scales.

When the prevalence of elevated values for each of the cardiovascular risk measures included in the study is evaluated, **table III** exhibits the similar tendency.

The outcomes of the multinomial logistic regression analysis are displayed in **table IV**. As the scores on the cardiovascular risk scales rise, so does the risk of atherogenic dyslipidemia and the lipid triad. The ALLY Framingham vascular age was shown to have the greatest OR values.

The areas under the curve of the various cardiovascular risk measures for predicting atherogenic dyslipidemia and the lipid triad are shown in **table V** and **figure 2**. The results for ALLY Framingham vascular age show the highest values.

Table I: Characteristics of the population.

	Women n=172,282 Mean (SD)	Men n=246,061 Mean (SD)	Total n=418,343 Mean (SD)	p-value
Age (years)	39.6 (10.8)	40.6 (11.1)	40.2 (11.0)	<0.0001
Height (cm)	161.8 (6.5)	174.6 (7.0)	169.4 (9.3)	<0.0001
Weight (kg)	66.2 (14.0)	81.4 (14.7)	75.1 (16.2)	<0.0001
Waist circumference (cm)	74.8 (10.6)	86.2 (11.1)	81.5 (12.2)	<0.0001
SBP (mmHg)	117.4 (15.7)	128.2 (15.5)	123.7 (16.5)	<0.0001
DBP (mmHg)	72.6 (10.4)	77.8 (11.0)	75.6 (11.0)	<0.0001
Total cholesterol (mg/dL)	190.6 (35.8)	192.6 (38.9)	191.8 (37.7)	<0.0001
HDL-c (mg/dL)	56.8 (8.7)	50.3 (8.5)	53.0 (9.1)	<0.0001
LDL-c (mg/dL)	116.1 (34.8)	118.0 (36.7)	117.2 (35.9)	<0.0001
Triglycerides (mg/dL)	89.1 (46.2)	123.7 (86.4)	109.5 (74.6)	<0.0001
Glycaemia	87.8 (15.1)	93.3 (21.3)	91.0 (19.2)	<0.0001
ALT (U/L)	20.2 (13.6)	31.0 (20.2)	26.6 (18.6)	<0.0001
AST (U/L)	18.2 (7.9)	24.4 (13.3)	21.7 (11.7)	<0.0001
GGT (U/L)	20.4 (19.7)	35.8 (39.3)	29.6 (33.6)	<0.0001
	%	%	%	p
18-29 years	20.7	18.8	19.6	
30-39 years	29.7	27.6	28.4	
40-49 years	29.6	30.1	29.9	
50-70 years	20.0	23.6	22.2	
Social class I	6.9	4.9	5.7	
Social class II	23.4	14.9	18.4	
Social class III	69.7	80.3	75.9	
Non-smokers	67.2	66.6	66.9	
Smokers	32.8	33.4	33.2	

SBP systolic blood pressure. DBP diastolic blood pressure. HDL-c high density lipoprotein-cholesterol. LDL-c low density lipoprotein-cholesterol. ALT aspartate transaminase. ALT alanine transaminase GGT gammaglutamyl transferase.

Table II: Mean values of cardiovascular risk scales according presence or absence of atherogenic dyslipidemia and lipid triad by sex.

	Women					Men				
	Non AD		Yes AD		p-value	Non AD		Yes AD		p-value
	n	Mean (SD)	n	Mean (SD)		n	Mean (SD)	n	Mean (SD)	
ALLY VA SCORE2	80164	4.1 (5.1)	5132	6.5 (5.4)	<0.0001	116929	7.4 (6.8)	14611	10.0 (7.2)	<0.0001
SCORE	80164	0.4 (0.9)	5132	1.0 (1.4)	<0.0001	116929	1.7 (2.2)	14611	2.2 (2.7)	<0.0001
ALLY VA Framingham	130226	0.2 (11.5)	6395	14.0 (13.8)	<0.0001	181651	5.7 (10.0)	18178	16.5 (10.8)	<0.0001
REGICOR	126345	2.9 (2.2)	6318	3.5 (2.3)	<0.0001	177759	3.3 (2.2)	18168	3.8 (2.7)	<0.0001
ERICE	130226	2.6 (3.2)	6395	4.4 (4.6)	<0.0001	181644	4.4 (5.1)	18178	6.8 (6.7)	<0.0001
	n	Non LT	n	Non LT	p-value	n	Non LT	n	Non LT	p-value
ALLY VA SCORE2	83852	4.1 (5.2)	1444	8.0 (5.6)	<0.0001	127158	7.5 (6.9)	4382	11.7 (7.4)	<0.0001
SCORE	83852	0.5 (1.0)	1444	1.3 (1.6)	<0.0001	127158	1.7 (2.2)	4382	2.4 (2.9)	<0.0001
ALLY VA Framingham	134969	0.6 (11.7)	1652	19.3 (12.9)	<0.0001	194562	6.3 (10.3)	5267	19.9 (10.4)	<0.0001
REGICOR	131035	2.9 (2.2)	1628	3.8 (2.6)	<0.0001	190723	3.3 (2.2)	5204	4.4 (3.2)	<0.0001
ERICE	134969	2.6 (3.3)	1652	5.1 (4.5)	<0.0001	194555	4.6 (5.2)	5267	6.7 (6.3)	<0.0001

ALLY VA Avoidable lost life years vascular age. SCORE Systematic Coronary Risk Evaluation. REGICOR Registro Gironi del Corazón. ERICE Ecuación de riesgo cardiovascular española. AD atherogenic dyslipidemia. LT lipid triad.

Table III: Prevalence of high values of cardiovascular risk scales according presence or absence of atherogenic dyslipidemia and lipid triad by sex.

	Women					Men				
	Non AD		Yes AD		p-value	Non AD		Yes AD		p-value
	n	%	n	%		n	%	n	%	
ALLY VA SCORE >10	80164	15.0	5132	28.1	<0.0001	116929	33.5	14611	48.6	<0.0001
SCORE high-very high	80164	1.1	5132	3.0	<0.0001	116929	10.5	14611	17.8	<0.0001
ALLY VA Framingham >10	130226	17.8	6395	57.3	<0.0001	181651	29.4	18178	69.4	<0.0001
REGICOR high-very high	126345	1.5	6318	2.3	<0.0001	177759	1.9	18168	3.5	<0.0001
ERICE high-very high	130226	0.2	6395	3.1	<0.0001	181644	2.2	18178	5.2	<0.0001
	n	%	n	%	p-value	n	%	n	%	p-value
ALLY VA SCORE >10	83852	15.4	1444	37.5	<0.0001	127158	34.5	4382	57.7	<0.0001
SCORE2 high-very high	83852	1.1	1444	4.8	<0.0001	127158	10.9	4382	22.1	<0.0001
ALLY VA Framingham >10	134969	19.0	1652	74.8	<0.0001	194562	31.7	5267	82.1	<0.0001
REGICOR high-very high	131035	1.6	1628	3.0	<0.0001	190723	2.0	5204	6.0	<0.0001
ERICE high-very high	134969	0.2	1652	0.7	<0.0001	194555	2.4	5267	4.4	<0.0001

ALLY VA Avoidable lost life years vascular age. SCORE Systematic Coronary Risk Evaluation. REGICOR Registro Gironi del Corazón. ERICE Ecuación de riesgo cardiovascular española. AD atherogenic dyslipidemia. LT lipid triad.

**Table IV:** Multinomial logistic regression.

	Atherogenic dyslipidemia	Lipid triad
	OR (95% CI)	OR (95% CI)
ALLY VA SCORE <10	1	1
ALLY VA SCORE ≥10	2.17 (2.11-2.24)	3.03 (2.87-3.19)
ALLY VA Framingham <10	1	1
ALLY VA Framingham ≥10	6.01 (5.85-6.18)	11.34 (10.68-12.04)
SCORE2 low	1	1
SCORE2 moderate	1.29 (1.22-1.36)	1.48 (1.35-1.62)
SCORE high-very high	2.51 (2.40-2.63)	3.26 (3.04-3.50)
REGICOR low	1	1
REGICOR moderate	1.25 (1.15-1.36)	1.61 (1.42-1.82)
REGICOR high-very high	1.97 (1.82-2.14)	3.26 (2.88-3.68)
ERICE low	1	1
ERICE moderate	1.21 (1.12-1.31)	1.19 (1.14-1.24)
ERICE high-very high	3.41 (3.18-3.66)	2.65 (2.33-3.02)

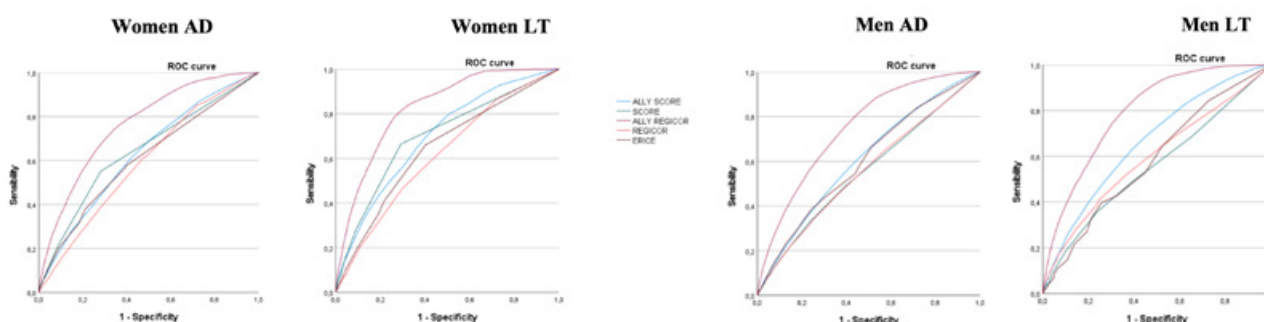
ALLY VA Avoidable lost life years vascular age. SCORE Systematic Coronary Risk Evaluation. REGICOR Registro Gironi del Corazón. ERICE Ecuación de riesgo cardiovascular española. AD atherogenic dyslipidemia. LT lipid triad.

**Table V:** Areas under the curve and cutoff points of the different cardiovascular risk scales for predicting atherogenic dyslipidemia and lipid triad.

	AD Women	LT Women
	AUC (95% ci)	AUC (95% ci)
ALLY VA SCORE	0.628 (0.620-0.636)	0.698 (0.685-0.711)
SCORE2	0.641 (0.633-0.649)	0.6978 (0.684-0.713)
ALLY VA Framingham	0.762 (0.756-0.769)	0.826 (0.817-0.835)
REGICOR	0.592 (0.584-0.599)	0.616 (0.602-0.630)
ERICE	0.607 (0.598-0.615)	0.641 (0.627-0.656)
	AD Men	LT Men
ALLY VA SCORE	0.609 (0.604-0.614)	0.663 (0.655-0.671)
SCORE	0.555 (0.550-0.560)	0.558 (0.548-0.567)
ALLY VA Framingham	0.748 (0.744-0.752)	0.795 (0.789-0.801)
REGICOR	0.556 (0.551-0.562)	0.594 (0.585-0.603)
ERICE	0.601 (0.596-0.606)	0.584 (0.575-0.592)

ALLY VA Avoidable lost life years vascular age. SCORE Systematic Coronary Risk Evaluation. REGICOR Registro Gironi del Corazón. ERICE Ecuación de riesgo cardiovascular española. AD atherogenic dyslipidemia. LT lipid triad.

**Figure 2:** ROC curve.



## Discussion

The prevalence of elevated values and the mean values of all the cardiovascular risk scales used in this investigation are higher in persons with lipid triad and atherogenic dyslipidemia.

With the exception of the ALLY Framingham, the ROC curves have moderate values for the areas under the

curve, making them ineffective as predictors of AD and LT.

We have not been able to find studies that relate either atherogenic dyslipidemia or the lipid triad to any scale that assesses cardiovascular risk, so we will focus this discussion on the relationship of cardiovascular disease

to atherosclerosis and on the relationship of dyslipidemia to scales that predict cardiovascular risk.

Alterations in the plasma lipid profile that are often associated with clinical conditions are known as dyslipidemias. Dyslipidemias, particularly elevated plasma levels of LDL cholesterol, are important risk factors for cardiovascular disease, but some forms, such as hypertriglyceridemia, are associated with serious diseases in other organ systems, such as nonalcoholic fatty liver disease and acute pancreatitis.

An investigation carried out by our group in 610 Spanish veterinarians<sup>19</sup> concluded that the level of cardiovascular risk determined with different scales, most of which were included in this study, correlated very well with the values of the different lipid parameters and was much higher in those veterinarians who had dyslipidemia. Similar results were obtained in a Bolivian study<sup>20</sup> carried out in 1094 miners and in another by the same group in 5370 farmers<sup>21</sup>. Another study carried out in more than 59000 workers<sup>22</sup> also found this association.

As indicated above, although atherosclerosis is a physiological process, in certain situations it will accelerate and can cause certain cardiovascular diseases<sup>23</sup>. Atherogenic dyslipidemia and the lipid triad are parameters that predict the appearance of atherosclerosis.

Lipoprotein a is a complex circulating lipoprotein, and there is ample scientific evidence of its important role as a risk factor for atherosclerotic cardiovascular disease<sup>24</sup>. Lipoprotein a has many similarities with low-density lipoprotein (LDL), but differs from LDL in that it has an additional apolipoprotein called apo(a)<sup>25</sup>.

### **Strengths and limitations**

The study's biggest advantages are its massive sample size—more than 418 000 workers—and the extensive use of cardiovascular risk assessments.

The primary drawback is that results may not be extrapolated to other groups because the cardiovascular risk measures utilized were designed for the Spanish population.

### **Conclusions**

For all of the assessed cardiovascular risk scales, atherogenic dyslipidemia and the lipid triad are associated with greater mean values and higher prevalence of elevated values.

In the multivariate analysis, ALLY Framingham is the scale that significantly raises the risk of presenting AD and LT.

With the exception of ALLY Framingham, we noticed in the ROC curves that the cardiovascular risk scales do not accurately classify the existence of atherogenic dyslipidemia and lipid triad.

### **Conflict of Interest**

The authors declare that there is no conflict of interest.



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