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Relationship between values of 7 NAFLD scales and different RCV scales in 219,477 Spanish workers

Relación entre valores de 7 escalas de NAFLD y diferentes escalas de RCV en 219.477 trabajadores españoles.

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Abstract

Introduction: Cardiometabolic diseases are highly prevalent and constitute the leading cause of morbidity and mortality worldwide. Non-alcoholic fatty liver disease (NAFLD) is also very prevalent. The aim of this study is to assess the relationship between different NAFLD risk scales and cardiovascular risk (CVR) scales.
Material and methods: Descriptive, cross-sectional study in 219477 Spanish workers in which the relationship between NAFLD and liver fibrosis risk scales (FLI, HSI, ZJU, FLD, FSI, LAP and BARD score) and CVR scales (REGICOR, SCORE, DORICA, ERICE and vascular age) was assessed.
Results: In our study there is a direct relationship between the increase in the values of the CVR scales and the increase in the risk values of NAFLD and hepatic fibrosis. The value of the CVR scales for predicting the presence of high risk values of NAFLD and liver fibrosis scales using ROC curves is not very high.
Conclusions: There is a good relationship between the values of both types of scales although the predictive value is not good.

Keywords: NAFLD, liver fibrosis, cardiovascular risk.

Resumen

Introducción: Las enfermedades cardiometabólicas son muy prevalentes y constituyen la primera causa de morbimortalidad en todo el mundo. La enfermedad del hígado graso no alcohólico (NAFLD) también es muy prevalente. El objetivo de este estudio es valorar la relación entre diferentes escalas de riesgo de NAFLD y escalas de riesgo cardiovascular (RCV).
Material y métodos: Estudio descriptivo y transversal en 219477 trabajadores españoles en el que se valora la relación entre escalas de riesgo de NAFLD y fibrosis hepática (FLI, HSI, ZJU, FLD, FSI, LAP y BARD score) con escalas de RCV (REGICOR, SCORE, DORICA, ERICE y edad vascular).
Resultados: En nuestro estudio existe una relación directa entre el incremento de los valores de las escalas de RCV y el incremento de los valores de riesgo de NAFLD y fibrosis hepática. El valor de las escalas de RCV para predecir la presencia de valores de alto riesgo de las escalas de NAFLD y fibrosis hepática empleando las curvas ROC no es muy alto.
Conclusiones: Existe buena relación entre los valores de ambos tipos de escalas aunque el valor predictivo no es bueno.

Palabras clave: NAFLD, fibrosis hepática, riesgo cardiovascular.

Introduction

The term non-alcoholic fatty liver disease (NAFLD) is used to refer to a broad group of liver disorders ranging from an initial phase called simple steatosis to more serious conditions such as steatohepatitis and even cirrhosis. Histologically, the lesions that appear in NAFLD are similar to those caused by alcohol consumption, although by definition NAFLD develops only in people who do not drink alcohol or only drink alcohol sporadically.

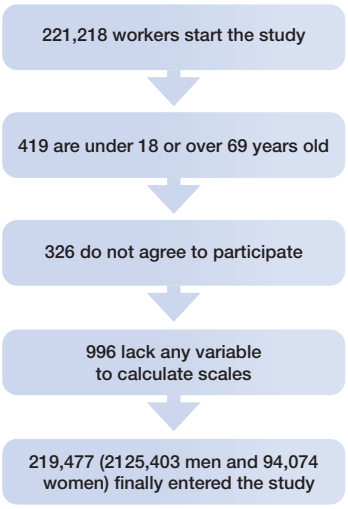
NAFLD was first described in the 1950s by Zelman[1] and was correctly characterized by Ludwig et al2 thirty years later[2]. Thirty years later, it is currently a clinical condition that attracts the attention of healthcare professionals due to its high prevalence, especially in Western countries[3]. Recently, it has been shown that NAFLD can lead to death, not only due to the chronic liver disease[4] it causes, but also as a consequence of alterations in lipid metabolism and increased cardiovascular risk.

The aim of the present study was to assess the relationship between different NAFLD and liver fibrosis risk scales and some cardiovascular risk scales.

Material and methods

A descriptive, cross-sectional study was carried out in 219,477 Spanish workers from different regions and work sectors, mostly in public administration, health, hospitality, construction and commerce. The workers included in the study were selected among those who attended occupational health checkups carried out between January 2017 and December 2019. See flow diagram in **figure 1**.

Figure 1: Flow chart of participants in the study.



Inclusion criteria:

- Age between 18 and 69 years.
- Acceptance to participate in the study.
- Authorization to use the data obtained for epidemiological purposes.
- Belonging to one of the companies included in the study and not being on temporary disability at the time of the study.

The anthropometric (height, weight and waist circumference), analytical and clinical determinations were performed by the different occupational health professionals of the participating companies after standardization of the processes to avoid interobserver bias.

Weight (in kilograms) and height (in centimeters) were determined with a SECA 700 scale-measuring device. Waist circumference was measured with the person in a standing position, upper extremities hanging, feet together and abdomen relaxed. It was placed parallel to the ground at the level of the last floating rib.

Blood pressure was obtained while seated and after a 10-minute rest at rest. Three measurements were obtained one minute apart and the mean was calculated.

Blood analysis was performed after fasting for no less than 12 hours. Cholesterol, triglycerides and glycemia were obtained using enzymatic techniques while HDL was obtained using precipitation techniques. LDL was calculated by applying the Friedewald formula (total cholesterol -HDL-c- triglycerides/5), which is only applicable when triglycerides do not exceed a value of 400.

Seven risk scales were calculated for non-alcoholic fatty liver disease and liver fibrosis:

- Fatty Liver Index (FLI)[6]

$$FLI = (e^{0.953*\log_e(\text{triglycerides}) + 0.139*BMI + 0.718*\log_e(GGT) + 0.053*\text{waist circumference} - 15.745}) / (1 + e^{0.953*\log_e(\text{triglycerides}) + 0.139*BMI + 0.718*\log_e(GGT) + 0.053*\text{waist circumference} - 15.745}) \times 100$$

The cut-off point to consider high risk is 60.

- Hepatic steatosis index (HSI)[7]
HSI = 8 × AST/ALT + BMI + 2 if diabetes, + 2 if female.
The cut-off point to consider high risk is 36.

- Zhejian University index (ZJU index)[8]
ZJU = BMI + Blood glucose (mmol L) + Triglycerides (mmol L) +3 AST/ALT +2 if female.
The cut-off point to consider high risk is 38.

- Fatty liver disease index (FLD)[9]
FLD = BMI+Triglycerides+3 × (AST/ALT) +2 × Hyperglycemia (present=1; absent=0).
The cutoff point to consider high risk is 37.

- Framingham Steatosis Index (FSI)[10]
FSI = -7.981 + 0.011 x age - 0.146 x sex (female =1, male = 0) + 0.173 x BMI + 0.007 x triglycerides + 0.593 x hypertension (yes = 1, no =0) + 0.789 x diabetes (yes = 1, no =0) + 1.1 x AST/ALT ratio ≥1.33 (yes = 1, no =0).

- Lipid accumulation product (LCP)[11]
Men: (waist (cm) - 65) x (triglycerides (mMol)).
Women: (waist (cm) - 58) x (triglycerides (mMol)).
The cut-off point to consider high is 42.7.

- BARD score[12] It is a risk scale for liver fibrosis.

BMI from 28 (1 point), AST/ALT from 0.8 (2 points), diabetes mellitus (2 points). Values between 2-4 points indicate high risk.

Six cardiovascular risk scales are calculated:

- Registro Gironí del Cor (REGICOR)[13].

This is a scale used to determine the possibility of suffering a cerebrovascular event, fatal or otherwise, during the next decade of life. It is applicable between 35 and 74 years of age. Values below 5% are considered low, between 5% and 9% moderate, from 10% to 14% high, and from 15% and above very high.

- Systematic Coronary Risk Evaluation (SCORE)[14]
Estimates the probability of presenting a fatal cerebrovascular event in the next 10 years. It is applicable between 40 and 65 years of age. Values are considered low up to 3%, moderate between 4% and 5%, and high after 5%.

- Dyslipidemia Obesity and Cardiovascular Risk in Spain (DORICA)[15]
Evaluates the risk of presenting a cerebrovascular event in the following decade. It is applicable between 20 and 64 years of age. Risk is considered low if it is less than 5%, slight between 5% and 9%, moderate between 10% and 19%, high between 20% and 39%, and very high above 40%.

- Spanish Cardiovascular Risk Equation (ERICE)[16]
It also calculates the risk of presenting a cerebrovascular event in the following decade. It is applicable between 30 and 80 years of age. It is considered low if it is less than 5%, mild between 5% and 9%, moderate between 10% and 14%, moderate-high between 15%-19%, high between 20%-29% and very high after 30%.

- Framingham vascular age and SCORE[17].
Both are obtained from tables and assess the aging of the vascular tree. A very useful concept is that of ALLY (avoidable lost life years), which is the avoidable years of life lost, corresponding to the difference between the individual's biological age and vascular age[18].

Smoker is any person who has smoked at least one cigarette (or its equivalent in another type of consumption) in the last 30 days or has quit less than 12 months ago.

The social class is determined based on the proposal of the Spanish Society of Epidemiology, which is based on the 2011 National Classification of Occupations[19]. Three groups are established: class I (directors, managers and university professionals), class II (intermediate occupations and self-employed workers) and class III (manual workers).

Results

The mean age of the sample was over 40 years (41.8 years in men and 39.9 years in women), with the majority group being between 30 and 49 years of age. The anthropometric, clinical and analytical variables in all cases show more unfavorable values in men. The social class most represented in the study is class III. Approximately one out of every three workers included in the study was a smoker. All the data can be consulted in **table I**.

Table II shows how all the NAFLD and liver fibrosis risk scales increase their mean values as the values of the different scales that assess cardiovascular risk increase. In all cases, the mean values of the NAFLD and liver fibrosis risk scales are higher in men.

Table III shows that the prevalence of high values of the NAFLD and liver fibrosis risk scales is also higher as the values of the cardiovascular risk scales increase. As with the mean values, higher values are observed in men in all cases.

Table IV shows the results of the multivariate analysis by multinomial logistic regression. The risk of presenting elevated values for all the nonalcoholic fatty liver disease and liver fibrosis risk scales increases as the cardiovascular risk scales increase. The greatest increases are seen with the DORICA scale.

Figure 2 and **table V** show the areas under the curve with their 95% confidence intervals of the cardiovascular risk scales for predicting the presence of high values of the nonalcoholic fatty liver disease and liver fibrosis risk scales. In general, the areas under the curve found are not high and only DORICA and ALLY Framingham vascular age for FLI and BARD score and ERICE for BARD score exceed 70%.

Table I: Characteristics of the population.

	Men n=125,403 Mean (SD)	Women n=94,074 Mean (SD)	p
Age	41.8 (10.5)	39.9 (10.5)	<0.0001
Height	175.2 (6.8)	162.3 (6.3)	<0.0001
Weight	82.6 (15.0)	68.0 (14.7)	<0.0001
SBP	126.1 (15.6)	115.4 (15.5)	<0.0001
DBP	77.3 (11.1)	72.3 (10.5)	<0.0001
Cholesterol	195.6 (37.9)	192.1 (35.5)	<0.001
HDL-c	52.1 (9.8)	57.2 (10.3)	<0.0001
LDL-c	118.4 (35.1)	116.3 (33.5)	<0.001
Tryglicerides	125.7 (76.0)	93.1 (45.6)	<0.0001
Glycaemia	93.4 (21.5)	88.3 (16.0)	<0.0001
AST	29.0 (17.5)	18.7 (11.6)	<0.0001
ALT	24.4 (13.3)	18.2 (7.9)	<0.0001
GGT	32.7 (31.8)	18.8 (16.3)	<0.0001
Creatinine	0.86 (0.17)	0.68 (0.14)	<0.0001
	%	%	p
18-29 years	14.4	19.4	<0.0001
30-39 years	26.6	28.9	
40-49 years	33.6	32.0	
50-59 years	21.5	16.8	
60-69 years	3.9	2.9	
Social class I	6.1	7.5	<0.0001
Social class II	14.5	20.5	
Social class III	79.4	72.0	
Non smokers	67.5	66.7	<0.001
Smokers	32.5	33.3	

SBP systolic blood pressure. DBP diastolic blood pressure. HDL High density lipoprotein. LDL Low density lipoprotein. AST aspartate transaminase. **ALT** alanine transaminase. **GGT** gamma-glutamyl transferase.

Table II: Mean values of NAFLD and liver fibrosis risk scales according to values of cardiovascular risk scales by sex.

		FLI	HSI	ZJU	FLD	FSI	LAP	BARD
Men	**n**	**mean (SD)**	**mean (SD)**	**mean (SD)**	**mean (SD)**	**mean (SD)**	**mean (SD)**	**mean (SD)**
REGICOR low	85617	41.0 (26.6)	37.1 (6.7)	37.4 (5.6)	32.3 (5.3)	0.21 (0.19)	34.5 (29.0)	1.2 (1.1)
REGICOR moderate	21321	43.1 (26.8)	37.5 (6.6)	37.9 (5.7)	32.7 (5.3)	0.23 (0.20)	35.8 (29.7)	1.3 (1.1)
REGICOR high-very high	2103	43.3 (27.6)	37.5 (6.6)	38.0 (5.8)	32.8 (5.4)	0.24 (0.21)	36.5 (31.9)	1.4 (1.1)
SCORE low	56202	42.8 (26.2)	37.3 (6.6)	37.7 (5.5)	32.5 (5.2)	0.22 (0.19)	35.8 (29.6)	1.2 (1.0)
SCORE moderate	10860	47.8 (26.4)	38.1 (6.6)	38.9 (5.8)	33.4 (5.3)	0.29 (0.21)	39.3 (31.0)	2.0 (1.0)
SCORE high	6567	51.5 (25.8)	38.5 (6.4)	39.6 (5.7)	33.9 (5.2)	0.34 (0.21)	41.3 (30.4)	2.2 (0.9)
ERICE low-mild	93513	40.4 (26.4)	36.9 (6.7)	37.2 (5.5)	32.1 (5.3)	0.20 (0.18)	34.4 (29.7)	1.1 (1.0)
ERICE moderate	11280	51.4 (25.9)	39.0 (6.6)	39.8 (5.8)	34.2 (5.3)	0.33 (0.21)	39.8 (26.5)	2.2 (1.0)
ERICE high-very high	2604	52.0 (25.3)	39.3 (6.0)	40.2 (5.5)	34.4 (5.0)	0.36 (0.20)	41.6 (31.1)	2.2 (0.9)
DORICA low-mild	100614	38.3 (26.1)	36.6 (6.7)	36.8 (5.4)	31.8 (5.2)	0.19 (0.17)	32.1 (26.9)	1.0 (1.0)
DORICA moderate	15294	53.3 (26.1)	38.9 (6.6)	39.9 (5.9)	34.4 (5.5)	0.33 (0.21)	45.9 (37.7)	2.0 (1.0)
DORICA high-very high	2187	61.7 (25.0)	39.9 (6.8)	42.0 (6.5)	35.9 (5.5)	0.44 (0.23)	57.4 (41.2)	2.4 (1.0)
ALLY VA Framingham <10 years	74928	36.9 (25.0)	36.2 (6.3)	36.5 (5.1)	31.5 (4.9)	0.18 (0.16)	30.9 (25.1)	1.0 (1.0)
ALLY VA Framingham ≥10 years	32469	53.3 (26.6)	39.4 (7.0)	40.0 (6.0)	34.5 (5.6)	0.32 (0.22)	45.6 (36.7)	1.8 (1.1)
ALLY VA SCORE <10 years	50418	41.7 (25.9)	37.1 (6.4)	37.5 (5.4)	32.3 (5.1)	0.21 (0.18)	34.7 (28.4)	1.2 (1.0)
ALLY VA SCORE ≥10 years	23211	50.0 (26.4)	38.4 (6.9)	39.2 (5.8)	33.7 (5.4)	0.31 (0.21)	41.4 (32.7)	1.8 (1.1)
Women	**n**	**mean (SD)**	**mean (SD)**	**mean (SD)**	**mean (SD)**	**mean (SD)**	**mean (SD)**	**mean (SD)**
REGICOR low	63018	20.0 (22.5)	36.6 (6.9)	37.2 (6.1)	30.3 (5.8)	0.15 (0.16)	19.7 (18.3)	0.7 (0.8)
REGICOR moderate	13551	21.5 (23.5)	37.0 (6.9)	37.6 (6.3)	30.7 (6.0)	0.17 (0.18)	20.6 (17.8)	0.8 (0.9)
REGICOR high-very high	1371	22.0 (23.9)	37.1 (7.0)	37.6 (6.4)	30.7 (6.1)	0.17 (0.17)	20.9 (18.7)	0.8 (0.9)
SCORE low	46626	21.8 (22.8)	37.1 (6.7)	37.7 (5.9)	30.8 (5.7)	0.17 (0.17)	20.9 (18.8)	0.9 (0.9)
SCORE moderate	1479	32.5 (26.3)	39.8 (7.2)	40.5 (6.2)	33.2 (5.9)	0.28 (0.21)	28.4 (23.1)	1.8 (0.8)
SCORE high	414	34.8 (28.9)	39.8 (7.6)	40.7 (6.8)	33.3 (6.6)	0.32 (0.22)	29.9 (24.7)	1.9 (0.8)
ERICE low-mild	73515	20.3 (22.7)	36.6 (6.8)	37.2 (6.1)	30.3 (5.9)	1.15 (0.16)	19.8 (18.4)	0.7 (0.8)
ERICE moderate	2136	32.3 (25.4)	41.4 (6.8)	41.0 (6.2)	33.4 (5.7)	0.28 (0.18)	29.6 (17.3)	1.8 (0.8)
ERICE high-very high	153	34.0 (27.5)	40.7 (7.3(	41.3 (6.8)	33.8 (6.3)	0.29 (0.22)	30.1 (24.7)	1.9 (0.8)
DORICA low-mild	84063	19.3 (22.2)	36.3 (6.8)	36.9 (6.0)	30.1 (5.8)	0.14 (0.16)	19.1 (17.7)	0.6 (0.8)
DORICA moderate	2586	39.7 (28.4)	41.1 (7.4)	42.4 (7.0)	34.8 (6.5)	0.34 (0.24)	35.8 (29.2)	2.0 (0.9)
DORICA high-very high	75	60.3 (29.4)	45.3 (8.4)	49.6 (8.1)	39.9 (7.6)	0.52 (0.28)	58.3 (41.0)	2.6 (0.8)
ALLY VA Framingham <10 years	61797	17.4 (20.3)	35.9 (6.5)	36.5 (5.6)	29.7 (5.5)	0.13 (0.14)	17.6 (15.6)	0.6 (0.7)
ALLY VA Framingham ≥10 years	14007	35.1 (27.7)	40.5 (7.3)	41.2 (6.7)	33.9 (6.4)	0.28 (0.22)	31.2 (25.8)	1.4 (1.0)
ALLY VA SCORE <10 years	42006	20.9 (22.2)	36.9 (6.6)	37.5 (5.8)	30.6 (5.6)	0.16 (0.16)	20.2 (18.0)	0.8 (0.9)
ALLY VA SCORE ≥10 years	6513	30.3 (26.8)	39.2 (7.2)	39.9 (6.5)	32.7 (6.2)	0.26 (0.22)	27.5 (24.1)	1.5 (1.0)

FLI Fatty liver index. HSI Hepatic steatosis index. ZJU Zhejiang University index. FLD Fatty liver disease. FSI Framingham Steatosis index. LAP Lipid accumulation product. REGICOR (Registro Gironi del corazón). SCORE Systematic Coronary Risk Evaluation. DORICA Dislipemia Obesidad y Riesgo Cardiovascular en España ERICE Ecuación de Riesgo Cardiovascular Española. ALLY VA Avoidable lost life años vascular age. Statistically significant differences (p<0.001) in all cases.

Table III: Prevalence of high values of NAFLD and liver fibrosis risk scales according to values of cardiovascular risk scales by sex.

		FLI high	HSI high	ZJU high	FLD high	LAP high	BARD high
Men	**n**	**%**	**%**	**%**	**%**	**%**	**%**
REGICOR low	85617	26.6	51.2	39.7	59.8	43.1	35.5
REGICOR moderate	21321	28.8	53.5	43.4	63.3	45.5	41.1
REGICOR high-very high	2103	31.0	54.5	44.3	63.7	46.2	41.2
SCORE low	56202	27.9	53.0	42.0	65.1	45.3	37.2
SCORE moderate	10860	34.6	60.4	52.3	63.4	51.1	64.3
SCORE high	6567	41.0	62.9	58.1	64.8	56.5	72.9
ERICE low-mild	93513	25.6	50.0	38.4	63.5	42.3	31.9
ERICE moderate	11280	39.7	65.7	57.7	62.6	56.0	71.8
ERICE high-very high	2604	40.6	70.2	64.2	65.4	56.9	74.8
DORICA low-mild	100614	23.1	48.2	35.7	62.4	39.1	29.3
DORICA moderate	15294	42.2	64.7	59.4	62.5	60.5	65.9
DORICA high-very high	2187	56.4	69.8	72.0	56.0	72.8	82.6
ALLY VA Framingham <10 years	74928	20.6	45.7	33.1	64.1	37.4	28.1
ALLY VA Framingham ≥10 years	32469	43.1	67.0	59.2	61.7	59.7	58.2
ALLY VA SCORE <10 years	50418	26.5	52.1	40.6	65.7	43.8	37.5
ALLY VA SCORE ≥10 years	23211	38.0	61.2	54.3	63.2	54.5	59.4
Women	**n**	**n**	**%**	**%**	**%**	**%**	**%**
REGICOR low	63018	8.7	46.8	37.3	46.6	29.7	15.7
REGICOR moderate	13551	10.6	48.9	39.5	46.6	31.2	20.6
REGICOR high-very high	1371	10.7	51.2	40.9	45.1	31.9	19.5
SCORE low	46626	9.5	50.9	41.2	50.5	32.0	21.8
SCORE moderate	1479	17.4	69.8	62.1	60.0	49.3	58.4
SCORE high	414	24.6	66.7	64.5	45.7	51.4	64.5
ERICE low-mild	73515	9.0	46.8	37.4	46.5	29.5	15.6
ERICE moderate	2136	15.7	73.3	64.7	54.9	50.6	60.8
ERICE high-very high	153	20.2	80.4	68.6	57.4	51.0	61.5
DORICA low-mild	84063	8.4	44.9	35.4	45.1	28.0	13.5
DORICA moderate	2586	26.8	75.5	71.9	51.7	59.6	67.3
DORICA high-very high	75	52.0	88.0	92.0	72.1	88.0	92.0
ALLY VA Framingham <10 years	61797	6.4	42.1	32.4	45.0	24.8	11.1
ALLY VA Framingham ≥10 years	14007	22.3	72.1	64.3	54.9	53.7	43.0
ALLY VA SCORE <10 years	42006	8.7	49.7	39.9	50.1	30.8	19.8
ALLY VA SCORE ≥10 years	6513	17.2	64.2	55.7	54.8	45.0	45.6

FLI Fatty liver index. HSI Hepatic steatosis index. ZJU Zhejiang University index. FLD Fatty liver disease. FSI Framingham Steatosis index. LAP Lipid accumulation product. REGICOR (Registro Gironi del corazón). SCORE Systematic Coronary Risk Evaluation. DORICA Dislipemia Obesidad y Riesgo Cardiovascular en España ERICE Ecuación de Riesgo Cardiovascular Española. ALLY VA Avoidable lost life años vascular age. Statistically significant differences (p<0.001) in all cases.

Table IV: Multinomial logistic regression.

	FLI high OR (95% CI)	HSI high OR (95% CI)	ZJU high OR (95% CI)	FLD high OR (95% CI)	LAP high OR (95% CI)	BARD high OR (95% CI)
REGICOR low	1	1	1	1	1	1
REGICOR moderate	1.08 (1.02-1.17)	1.09 (1.00-1.19)	1,08 (1.02-1.15)	1.09 (1.05-1.15)	1.06 (1.02-1.11)	1.11 (1.06-1.17)
REGICOR high-very high	1.27 (1.17-1.38)	1.14 (1.07-1.22)	1.17 (1.09-1.25)	1.22 (1.14-1.30)	1.14 (1.07-1.22)	1.30 (1.21-1.40)
SCORE low	1	1	1	1	1	1
SCORE moderate	1.21 (1.15-1.26)	1.34 (1.29-1.38)	1.31 (1.26-1.35)	1.05 (1.00-1.10)	1.05 (1.01-1.09)	1.30 (1.25-1.34)
SCORE high	1.31 (1.26-1.36)	1.47 (1.43-1.51)	1.46 (1.42-1.50)	1.25 (1.16-1.34)	1.35 (1.30-1.40)	1.47 (1.42-1.52)
ERICE low-mild	1	1	1	1	1	1
ERICE moderate	1.09 (1.03-1.116)	1.23 (1.12-1.36)	1.18 (1.08-1.30)	1.14 (1.04-1.25)	1.06 (1.01-1.11)	1.04 (1.00-1.09)
ERICE high-very high	1.27 (1.15-1.40)	1.84 (1.67-2.04)	1.62 (1.47-1.78)	1.17 (1.06-1.28)	2.45 (2.20-2.72)	1.23 (1.12-1.35)
DORICA low-mild	1	1	1	1	1	1
DORICA moderate	1.79 (1.63-1.96)	1.16 (1.04-1.28)	1.65 (1.49-1.83)	1.29 (1.22-1.35)	1.63 (1.44-1.84)	1.88 (1.70-2.09)
DORICA high-very high	3.14 (2.84-3.47)	1.39 (1.25-1.54)	2.53 (2.28-2.82)	1.35 (1.28-1.41)	3.24 (2.87-3.67)	3.37 (3.03-3.76)
ALLY VE Framingham <10 years	1	1	1	1	1	1
ALLY VE Framingham ≥10 years	2.49 (2.41-2.58)	2.41 (2.34-2.49)	2.48 (2.41-2.55)	1.02 (1.00-1.05)	1.99 (1.93-2.05)	2.33 (2.27-2.40)
ALLY VE SCORE <10 years	1	1	1	1	1	1
ALLY VE SCORE ≥10 years	1.08 (1.04-1.13)	1.06 (1.01-1.12)	1.12 (1.05-1.19)	1.05 (1.01-1.09)	1.20 (1.15-1.24)	1.17 (1.08-1.26)

FLI Fatty liver index. HSI Hepatic steatosis index. ZJU Zhejiang University index. FLD Fatty liver disease. FSI Framingham Steatosis index. LAP Lipid accumulation product. REGICOR (Registro Gironi del corazón). SCORE Systematic Coronary Risk Evaluation. DORICA Dislipemia Obesidad y Riesgo Cardiovascular en España. ERICE Ecuación de Riesgo Cardiovascular Española. ALLY VA Avoidable lost life años vascular age. Statistically significant differences (p<0.001) in all cases.

Figure 2: ROC curve.

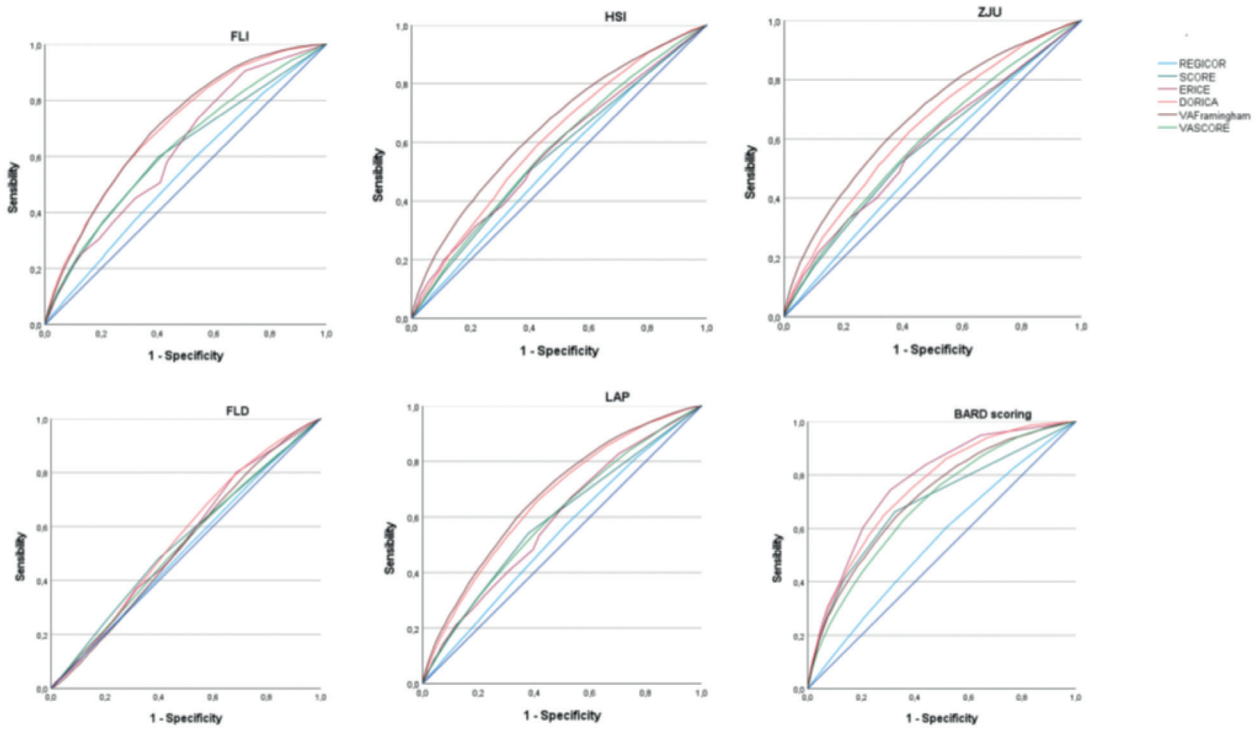


Table V: Areas under the curve (ROC curves).

	FLI high AUC (95% CI)	HSI high AUC (95% CI)	ZJU high AUC (95% CI)	FLD high AUC (95% CI)	LAP high AUC (95% CI)	BARD high AUC (95% CI)
REGICOR	0.541 (0.537-0.545)	0.531 (0.527-0.534)	0.534 (0.530-0.537)	0.511 (0.508-0.515)	0.536 (0.533-0.539)	0.554 (0.551-0.557)
SCORE	0.613 (0.609-0.617)	0.556 (0.553-0.560)	0.572 (0.568-0.575)	0.541 (0.538-0.545)	0.588 (0.585-0.592)	0.695 (0.692-0.698)
ERICE	0.625 (0.622-0.629)	0.571 (0.567-0.574)	0.579 (0.575-0.582)	0.545 (0.542-0.549)	0.590 (0.587-0.593)	0.774 (0.772-0.777)
DORICA	0.704 (0.701-0.707)	0.610 (0.607-0.613)	0.637 (0.634-0.640)	0.558 (0.555-0.561)	0.665 (0.662-0.668)	0.752 (0.749-0.755)
ALLY VA Framingham	0.709 (0.706-0.712)	0.651 (0.648-0.654)	0.674 (0.671-0.677)	0.530 (0.527-0.533)	0.678 (0.675-0.681)	0.715 (0.712-0.718)
ALLY VA SCORE	0.626 (0.623-0.630)	0.574 (0.571-0.578)	0.592 (0.589-0.596)	0.529 (0.526-0.533)	0.596 (0.593-0.599)	0.691 (0.688-0.694)

FLI Fatty liver index. HSI Hepatic steatosis index. ZJU Zhejiang University index. FLD Fatty liver disease. FSI Framingham Steatosis index. LAP Lipid accumulation product. REGICOR (Registro Gironi del corazón). SCORE Systematic Coronary Risk Evaluation. DORICA Dislipemia Obesidad y Riesgo Cardiovascular en España ERICE Ecuación de Riesgo Cardiovascular Española. ALLY VA Avoidable lost life años vascular age.

Discussion

In our study, the mean values and the prevalence of high values for all the NAFLD and liver fibrosis risk scales analyzed increase as the cardiovascular risk scales increase.

Multivariate analysis showed that the variable that most increased the risk of presenting elevated values of the different non-alcoholic fatty liver disease and liver fibrosis risk scales was the DORICA scale followed by vascular age with the Framingham model. The areas under the curve of all the cardiovascular risk scales show low values that only in some cases exceed 70%.

We have not found studies like ours that assess the relationship between NAFLD and liver fibrosis risk scales with cardiovascular risk scales but there is abundant literature showing the relationship between NAFLD and cardiovascular disease.

A review by Targher et al[20] concluded that there is increasing evidence that NAFLD is strongly associated with an increased risk of severe cardiovascular disease such as cardiomyopathy, cardiac valvular calcifications, and arrhythmias, independent of traditional cardiovascular risk factors.

A subsequent review by Kasper et al[21] also obtained similar results, indicating that increasing evidence suggests that individuals with NAFLD are at increased risk of developing hypertension, coronary artery disease, cardiomyopathy and cardiac arrhythmias, which will lead to increased cardiovascular morbidity and mortality.

A review by Caussy et al[22] provided evidence that NAFLD could be considered an independent risk factor for cardiovascular disease based on its relationship with diabetes mellitus. People with diabetes and NAFLD were found to have a higher risk of cardiovascular disease than diabetics without NAFLD, suggesting a possible synergistic effect of both conditions on cardiovascular risk. This synergy could be explained because both entities share several pathophysiological pathways.

Strengths and limitations

The strengths of the study include the large sample size, more than 200,000 individuals, and the large number of NAFLD and liver fibrosis risk and cardiovascular risk scales used. The main limitation is that no objective diagnostic techniques for NAFLD or liver fibrosis other than the risk scales were used.

Conclusions

Taking into account the results obtained in our study, we can conclude that in this Spanish working population there is a direct relationship between the values of the different NAFLD and liver fibrosis risk scales and the values of the cardiovascular risk scales. The power of the cardiovascular risk scales to predict the presence of elevated values of the different NAFLD and liver fibrosis scales is low and only in some cases moderate.

Conflict of Interest

The authors declare that no competing interests exist.

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