eISSN 2255-0569

ORIGINAL

Relationship between nonalcoholic fatty liver disease and liver fibrosis risk scales and various cardiometabolic risk scales in 219.477 Spanish workers

Relación entre escalas de riesgo de higado graso no alcohólico y fibrosis hepática con diversas escalas de riesgo cardiometabólico en 219.477 Trabajadores españoles

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Received: 18 - IV - 2023
Accepted: 15 - V - 2023

doi: 10.3306/AJHS.2023.38.05.138

Abstract

Introduction: Non-alcoholic fatty liver disease (NAFLD) is the main cause of chronic liver disease in the West, and in late stages it can lead to cirrhosis, which is expected to become the most frequent indication for liver transplantation in the next decade.
Material and methods: Descriptive and cross-sectional study in 219.477 Spanish workers in which the risk of presenting NASH and liver fibrosis was determined with 7 different scales and the cardiometabolic risk established from atherogenic indices, metabolic syndrome, atherogenic dyslipidemia, lipid triad and risk of prediabetes applying the PRISQ scale.
Results: There was an increase in the mean values and in the prevalence of high-risk values of all the NASH and liver fibrosis scales in persons at high cardiometabolic risk compared to those at lower risk.
Conclusions: There is a good relationship between the NASH and liver fibrosis risk scales and the cardiometabolic risk scales analyzed.

Keywords: non-alcoholic fatty liver disease (NAFLD), cardiometabolic disease, metabolic syndrome, atherogenic dyslipidemia, atherogenic indices, prediabetes.

Resumen

Introducción: La enfermedad del hígado graso no alcohólico (EHGNA) es la principal causa de hepatopatía crónica en occidente, pudiendo cursar en estadios tardíos con cirrosis por lo que se prevé que se convierta en la indicación más frecuente para el trasplante de hígado para la próxima década.
Material y métodos: Estudio descriptivo y transversal en 219.477 trabajadores españoles en los que se determina el riesgo de presentar EHGNA y fibrosis hepática con 7 escalas diferentes y el riesgo cardiometabólico establecido a partir de los índices aterogénicos, síndrome metabólico, dislipemia aterogénica, triada lipídica y riesgo de prediabetes aplicando la escala PRISQ.
Resultados: Se aprecia un incremento en los valores medios y en la prevalencia de valores de alto riesgo de todas las escalas de EHGNA y fibrosis hepática en las personas con alto riesgo cardiometabólico frente a las personas con menor riesgo.
Conclusiones: Existe una buena relación entre las escalas de riesgo de EHGNA y fibrosis hepática y las escalas de riesgo cardiometabólico analizadas.

Palabras clave: Enfermedad del hígado graso no alcohólico (EHGNA), enfermedad cardiometabólica, síndrome metabólico, dislipemia aterogénica, índices aterogénicos, prediabetes.

Introduction

Cardiometabolic diseases are highly prevalent in all countries of the world and not only in developed countries[1] and are responsible for high morbidity and mortality rates[2].

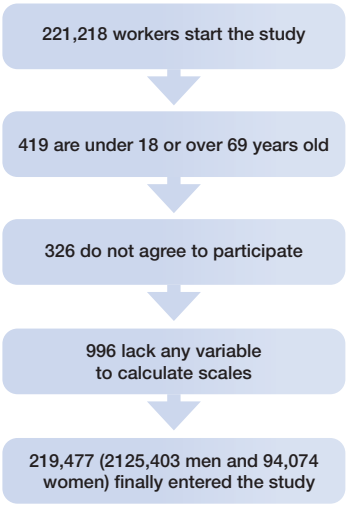
2 Non-alcoholic fatty liver disease (NAFLD) is a pathological entity that is also very common throughout the world today and its prevalence is increasing[3]. Its histological basis is an excessive accumulation of fat in the hepatocytes[4] which, left to its natural evolution, can develop into a picture of steatohepatitis[5] and even liver cirrhosis[6]. In contrast to other histologically similar pathological pictures very frequent in heavy alcohol consumers, NASH is observed in people who do not consume any or only small amounts of alcohol.

NASH can be considered a cardiometabolic disease and for this reason the aim of this study was to assess the relationship between different risk scales for NASH and liver fibrosis and other cardiometabolic risk scales.

Methods

A descriptive and cross-sectional study was performed on 219,477 Spanish workers belonging to different labor groups and Spanish regions. The workers were selected from those who attended occupational medical examinations 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 variables (height, weight and waist circumference), analytical and clinical, were carried out by the occupational health professionals of the participating companies after standardization of the processes to avoid interobserver bias.

Weight and height were obtained with a SECA 700 model scale-measuring scale. Waist circumference was measured with a tape measure placed parallel to the floor at the level of the last floating rib and with the person standing, abdomen relaxed, upper limbs hanging down and feet together.

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Blood pressure was obtained with the person seated and after 10 minutes of rest. Three measurements were obtained one minute apart and the mean was calculated.

Blood analysis was performed after at least 12 hours. Enzymatic techniques were used to determine cholesterol, triglycerides and glycemia, and precipitation techniques were used for HDL. LDL was calculated indirectly with the Friedewald formula (total cholesterol -HDL-c- triglycerides/5), which is only applicable for triglycerides up to 400.

Seven risk scales for nonalcoholic fatty liver disease and liver fibrosis were determined:

- Fatty liver index (FLI)[7].

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

High risk is considered to be 60 or more.

- Hepatic steatosis index (HSI)[8]

HSI = 8 × GOT/GPT + BMI + 2 if diabetes, + 2 if female. Risk is high from 36.

- Zhejian University index (ZJU index)[9]
ZJU = BMI + Glycemia (mmol L) + Triglycerides (mmol L) +3 GOT/GPT +2 if female.
The cut-off point to consider high risk is 38.

- Fatty liver disease index (FLD)[10]
FLD = BMI+Triglycerides+3 × (GOT/GPT) +2 × Hyperglycemia (present=1; absent=0).
Values above 37 is high risk.

- Framingham Steatosis Index (FSI)[11]
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 GOT/GPT ratio ≥1.33 (yes = 1, no =0) There are no cut-off points.

- Lipid accumulation product (LAP)[12]
Men: (waist (cm) - 65) x (triglycerides (mMol)).
Women: (waist (cm) - 58) x (triglycerides (mMol)).
The risk is high from 42.7.

- BARD score13 This is a risk scale for liver fibrosis.

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

- Different cardiometabolic risk scales are calculated:
  - Atherogenic indices present different cut-off points[14]: Total cholesterol/HDL-c ratio: low risk: < 5 in men and < 4.5 in women; moderate risk: between 5 and 9 in men and between 4.5 and 7 in women; and high risk: > 9 in men and > 7 in women. LDL-c/HDL-c ratio: low risk: < 3 and high risk ≥ 3. The triglyceride/HDL-c ratio is considered high risk as from 3%.
  - The metabolic syndrome is determined by applying three criteria[15]: (a) NCEP ATP III (National Cholesterol Educational Program Adult Treatment Panel III). Metabolic syndrome is considered to exist when at least three of the following factors are present: waist circumference > 88 cm in women and > 102 cm in men, triglycerides greater than 150 mg/dL or specific treatment for this lipid disorder, blood pressure greater than 130/85 mm Hg, HDL less than 50 mg/dL in women or less than 40 mg/dL in men or specific treatment, and fasting blood glucose greater than 100 mg/dL or specific treatment for blood glucose. b) International Diabetes Federation (IDF) Requires the presence of central obesity (waist circumference greater than 80 cm in women and 94 cm in men), in addition to two of the other factors mentioned above for ATP III (triglycerides, HDL, blood pressure and blood glucose). c) The JIS model16 uses the same criteria as the NCEP ATPIII but with waist circumference cut-off points starting at 80 cm in women and 94 cm in men.
  - Prediabetes risk score Qatar (PRISQ)[16] is a scale that assesses the risk of prediabetes. It is considered low risk (0-16 points), moderate risk (17-27 points) and high risk (>27 points).
  - Deuremberg fat mass index[17]. It is obtained by applying the formula: fat mass %= 1.2 x (BMI) + 0.23 x (Age) - 10.8 x (sex) - 5.4 Women are given a value of 0 and men a value of 1. Obesity is considered to be 25% or more in men and 32% in women.

- Relative fat mass (RFM)18 is obtained by applying these formulas: women: 76 - (20 × (height/waist)) and men: 64 - (20 × (height/waist)).

- We considered atherogenic dyslipidemia19 if: triglycerides ≥ 150 mg/dL, HDL < 40 mg/dL in men and <45 mg/dL in women and normal LDL. If LDL levels were > 160 mg/dL, it was considered LT.

A smoker is a person who has smoked at least one cigarette (or its equivalent in another type of consumption) in the last month or has quit less than 12 months ago.

To obtain the social class, we used the proposal of the Spanish Society of Epidemiology based on the 2011 National Classification of Occupations[20]. Three groups were established: class I (executives, managers and university professionals), class II (intermediate occupations and self-employed workers) and class III (manual workers).

Statistical analysis

A descriptive analysis of the categorical variables was performed, calculating the frequency and distribution of the responses for each of them. For quantitative variables, the mean and standard deviation were calculated following a normal distribution.

Bivariate association analysis was performed using the chi2 test (corrected by Fisher's exact statistic when conditions required it) and Student's t test for independent samples (for comparison of means). Multivariate techniques were used to establish the most significant variables associated with the risk factors. Logistic regression was used for multivariate analysis, with calculation of the odds ratio and the Hosmer-Lemeshow goodness-of-fit test. Statistical analysis was performed with the Statistical Package for the Social Sciences (SPSS) version 28.0 (IBM Company, New York, NY, USA) for Windows, with an accepted statistical significance level of 0.05.

Ethical considerations and/or aspects

The research team undertook at all times to follow the ethical principles of health sciences research established nationally and internationally (Declaration of

Helsinki), paying special attention to the anonymity of the participants and the confidentiality of the data collected. Approval was requested from the Ethics and Research Committee of the Balearic Islands (CEI-IB), which was obtained with indicator IB 4383/20. Participation in the study was voluntary, so the participants gave their written and oral consent to participate in the study after receiving sufficient information about the nature of the study. For this purpose, they were given an informed consent form, as well as an information sheet explaining the objective of the study.

The data collected for the study were identified by a code and only the person responsible for the study can relate these data to the participants. The identity of the participants will not be disclosed in any report of this study. The investigators will not disseminate any information that could identify them. In any case, the research team is committed to strict compliance with the Organic Law 3/2018, of December 5, on the protection of personal data and guarantee of digital rights, guaranteeing the participant in this study that they may exercise their rights of access, rectification, cancellation and opposition of the data collected.

Results

The average age of the sample is over 40 years (41.8 years in men and 39.9 years in women), the largest group being 30-49 years. All the variables analyzed show more unfavorable values in men. The most prevalent social class is III. One third of the workers smoke. The data are presented in **table I**.

Tables 2a and **2b** show how all the NASH and liver fibrosis risk scales increase their mean values in parallel to the increases in the different cardiometabolic scales analyzed. In all cases these mean values are higher in men.

Table IV shows the results of the multivariate analysis using multinomial logistic regression. The risk of presenting elevated values for all the nonalcoholic fatty liver disease and liver fibrosis risk scales increased in parallel to the increase in the values of the different cardiometabolic risk scales. The greatest increases are seen with the obesity scales (Deuremberg and RFM).

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 IIa: Mean values of NASH and liver fibrosis risk scales according to values of cardiometabolic risk scales in men.

		FLI	HSI	ZJU	FLD	FSI	LAP	BARD
Men	n	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
CT/HDL low	107718	36.4 (25.5)	36.3 (6.6)	36.6 (5.4)	31.5 (5.1)	0.2 (0.2)	29.8 (23.8)	1.0 (1.0)
CT/HDL moderate	17544	59.7 (25.4)	39.8 (7.0)	40.7 (5.9)	35.3 (5.5)	0.3 (0.2)	57.1 (43.3)	1.9 (1.1)
CT/HDL high	141	70.3 (25.6)	40.4 (6.7)	44.2 (7.3)	36.7 (5.2)	0.5 (0.2)	90.8 (47.4)	2.1 (1.1)
TG/HDL normal	92151	31.5 (22.9)	35.7 (6.3)	35.8 (5.0)	30.8 (4.8)	0.1 (0.1)	23.2 (14.0)	0.8 (0.8)
TG/HDL high	33252	62.4 (23.4)	39.8 (7.0)	40.8 (5.7)	35.5 (5.4)	0.4 (0.2)	62.6 (38.7)	2.1 (1.0)
LDL/HDL normal	97914	36.2 (25.7)	36.2 (6.6)	36.5 (5.4)	31.4 (5.2)	0.2 (0.2)	29.9 (23.5)	1.0 (1.0)
LDL/HDL high	27489	52.1 (26.9)	38.8 (6.9)	39.5 (5.9)	34.2 (5.5)	0.3 (0.2)	46.9 (40.7)	1.6 (1.1)
PRISQ low	52974	22.8 (18.1)	33.4 (5.4)	33.7 (3.9)	28.8 (3.8)	0.1 (0.1)	21.3 (17.0)	0.5 (0.7)
PRISQ moderate	53811	46.2 (22.9)	38.1 (5.9)	38.4 (4.5)	33.2 (4.3)	0.2 (0.2)	37.4 (27.0)	1.4 (1.0)
PRISQ high	18618	68.8 (24.4)	42.7 (7.1)	43.3 (6.2)	37.7 (5.8)	0.4 (0.2)	58.0 (41.0)	2.21 (0.9)
Normalweight Deuremberg	22125	12.4 (8.5)	30.5 (4.1)	31.0 (2.6)	26.1 (2.4)	0.06 (0.05)	14.9 (10.8)	0.3 (0.5)
Overweight Deuremberg	38502	26.1 (15.6)	34.3 (4.6)	34.6 (2.8)	29.6 (2.6)	0.12 (0.09)	23.7 (16.8)	0.6 (0.7)
Obesity Deuremberg	64776	57.1 (23.5)	40.4 (6.3)	40.8 (5.0)	35.5 (4.7)	0.31 (0.20)	46.0 (33.1)	1.8 (1.0)
No obesity RFM	116964	36.3 (24.3)	36.0 (6.1)	36.4 (4.8)	31.3 (4.6)	0.2 (0.2)	30.6 (24.9)	1.1 (1.0)
Yes obesity RFM	8439	86.3 (11.9)	47.6 (6.4)	47.8 (5.5)	42.3 (5.1)	0.5 (0.2)	75.5 (45.3)	2.2 (0.9)
No atherogenic dyslipidemia	117276	37.6 (25.8)	36.4 (6.6)	36.7 (5.4)	31.7 (5.2)	0.2 (0.2)	30.7 (25.0)	1.0 (1.0)
Yes atherogenic dyslipidemia	8127	70.3 (22.0)	41.8 (7.0)	43.0 (6.0)	37.4 (5.5)	0.4 (0.2)	76.2 (45.4)	2.5 (0.9)
No lipid triad	123519	39.2 (26.5)	36.7 (6.7)	37.0 (5.6)	31.9 (5.3)	0.2 (0.2)	32.7 (26.9)	1.1 (1.0)
Yes lipid triad	1884	74.3 (20.6)	41.5 (6.8)	43.8 (6.3)	38.0 (5.7)	0.5 (0.3)	96.1 (67.7)	2.6 (0.8)
No MS NCEP ATPIII	105330	33.9 (23.4)	35.7 (6.1)	35.9 (4.7)	31.0 (4.6)	0.2 (0.1)	27.4 (20.0)	0.9 (0.9)
Yes MS NCEP ATPIII	20073	70.0 (22.6)	42.4 (7.1)	43.4 (6.0)	37.6 (5.7)	0.4 (0.2)	66.8 (43.2)	2.3 (0.9)
No MS IDF	108318	33.6 (22.8)	35.6 (6.0)	35.9 (4.7)	30.9 (4.5)	0.2 (0.1)	27.3 (19.6)	1.0 (0.9)
Yes MS IDF	17085	78.3 (15.6)	44.2 (6.7)	44.8 (5.5)	39.1 (5.1)	0.5 (0.2)	74.3 (42.9)	2.3 (0.9)
No MS JIS	93204	30.5 (21.4)	35.1 (5.8)	35.3 (4.4)	30.4 (4.3)	0.1 (0.1)	24.5 (16.8)	0.8 (0.8)
Yes MS JIS	32199	66.2 (22.8)	41.6 (7.0)	42.4 (5.7)	36.7 (5.4)	0.4 (0.2)	60.1 (39.1)	2.1 (1.0)

FLI Fatty liver index. HSI hepatic steatosis index. ZJU Zhejianng University index. FLD Fatty liver disease index. FSI Framingham steatosis index. LAP Lipid accumulation producto. CT Total colesterol. HDL High density lipoprotein. LDL Low density lipoprotein. PRISQ Prediabetes score Qatar. RFM Relative fat mass. MS ATPIII. Metabolic syndrome Adult Treatment Panel III. MS IDF Metabolic syndrome International Diabetes Federation. Metabolic syndrome Joint Interim Statement

Table IIa: Mean values of NASH and liver fibrosis risk scales according to values of cardiometabolic risk scales in women.

		FLI	HSI	ZJU	FLD	FSI	LAP	BARD
Women	n	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
CT/HDL low	84117	17.7 (21.2)	35.9 (6.7)	36.5 (5.9)	29.7 (5.7)	0.1 (0.1)	17.7 (15.9)	0.6 (0.8)
CT/HDL moderate	9825	33.9 (27.4)	36.3 (6.9)	40.5 (6.5)	33.3 (6.2)	0.2 (0.2)	32.5 (27.8)	1.3 (1.0)
CT/HDL high	132	51.9 (29.4)	40.6 (8.9)	43.1 (8.7)	35.8 (8.4)	0.4 (0.3)	60.0 (54.5)	1.7 (1.0)
TG/HDL normal	86841	17.2 (20.4)	35.9 (6.7)	36.4 (5.8)	29.6 (5.6)	0.1 (0.1)	16.6 (13.1)	0.5 (0.7)
TG/HDL high	7233	47.0 (27.9)	41.2 (7.6)	42.8 (6.8)	35.5 (6.5)	0.4 (0.2)	51.9 (33.4)	2.0 (0.9)
LDL/HDL normal	83238	18.1 (21.5)	36.0 (6.8)	36.5 (6.0)	29.7 (5.8)	0.1 (0.2)	18.1 (16.4)	0.6 (0.8)
LDL/HDL high	10836	30.2 (26.6)	38.8 (7.2)	39.7 (6.5)	32.6 (6.2)	0.2 (0.2)	28.5 (26.8)	1.1 (0.9)
PRISQ low	65310	11.8 (15.3)	34.2 (5.8)	34.8 (4.8)	28.1 (4.7)	0.1 (0.1)	14.0 (12.9)	0.3 (0.6)
PRISQ moderate	22764	32.8 (24.3)	40.2 (6.5)	40.8 (5.8)	33.7 (5.6)	0.2 (0.2)	28.8 (20.6)	1.2 (0.8)
PRISQ high	6000	51.6 (28.4)	44.0 (7.5)	44.7 (6.9)	37.3 (6.6)	0.4 (0.2)	40.9 (26.3)	1.9 (0.8)
Normalweight Deuremberg	5373	2.9 (1.9)	28.2 (3.1)	29.0 (1.9)	22.4 (1.7)	0.03 (0.02)	7.1 (6.0)	0.1 (0.3)
Overweight Deuremberg	20754	4.7 (3.0)	31.1 (3.4)	31.8 (2.1)	25.1 (2.0)	0.05 (0.03)	9.2 (6.3)	0.1 (0.3)
ObeYesdad Deuremberg	67947	25.3 (24.0)	38.5 (6.6)	39.1 (5.7)	32.2 (5.5)	0.18 (0.17)	23.3 (19.7)	0.9 (0.9)
No obeYesdad RFM	85293	14.4 (15.6)	35.1 (5.7)	35.7 (4.8)	28.9 (4.6)	0.1 (0.1)	16.1 (13.6)	0.5 (0.8)
Yes obeYesdad RFM	8781	68.7 (19.1)	48.1 (5.9)	48.7 (5.1)	41.5 (4.9)	0.5 (0.2)	50.5 (26.2)	1.6 (0.7)
No atherogenic dyslipidemia	90057	18.0 (21.1)	36.0 (6.7)	36.6 (5.9)	29.8 (5.7)	0.1 (0.1)	17.6 (14.8)	0.6 (0.7)
Yes atherogenic dyslipidemia	4017	51.6 (28.0)	42.0 (7.4)	43.8 (6.9)	36.4 (6.5)	0.4 (0.2)	57.8 (36.6)	2.2 (0.8)
No lipid triad	93060	19.1 (22.2)	36.2 (6.9)	36.8 (6.1)	30.0 (5.9)	0.1 (0.2)	18.8 (17.1)	0.6 (0.8)
Yes lipid triad	1014	50.0 (27.1)	41.1 (6.9)	43.5 (6.6)	35.9 (6.1)	0.4 (0.3)	62.7 (47.9)	1.2 (0.8)
No MS NCEP ATPIII	85026	15.5 (17.9)	35.4 (6.2)	35.9 (5.3)	29.2 (5.1)	0.1 (0.1)	16.1 (12.9)	0.5 (0.7)
Yes MS NCEP ATPIII	9048	57.0 (26.4)	44.9 (7.1)	46.0 (6.4)	38.4 (6.2)	0.4 (0.2)	49.3 (30.0)	1.9 (0.9)
No MS IDF	84996	15.1 (17.6)	35.3 (6.1)	35.9 (5.2)	29.1 (5.1)	0.1 (0.1)	15.9 (12.7)	0.5 (0.7)
Yes MS IDF	9078	59.8 (23.1)	45.7 (6.7)	46.5 (5.8)	39.0 (5.5)	0.4 (0.2)	51.2 (28.5)	1.8 (0.9)
No MS JIS	83280	15.1 (17.9)	35.3 (6.2)	35.8 (5.3)	29.1 (5.1)	0.1 (0.1)	15.8 (12.7)	0.5 (0.7)
Yes MS JIS	10794	53.2 (25.8)	44.2 (7.0)	45.2 (6.2)	37.7 (5.9)	0.4 (0.2)	46.5 (28.7)	1.8 (0.9)

FLI Fatty liver index. HSI hepatic steatosis index. ZJU Zhejianng University index. FLD Fatty liver disease index. FSI Framingham steatosis index. LAP Lipid accumulation producto. CT Total colesterol. HDL High density lipoprotein. LDL Low density lipoprotein. PRISQ Prediabetes score Qatar. RFM Relative fat mass. MS ATPIII. Metabolic syndrome Adult Treatment Panel III. MS IDF Metabolic syndrome International Diabetes Federation. Metabolic syndrome Joint Interim Statement

Table IIIa: Prevalence of high values of the NASH and liver fibrosis risk scales according to values of the cardiometabolic risk scales in men.

		FLI high	HSI high	ZJU high	LAP high	BARD high
Men	**n**	**%**	**%**	**%**	**%**	**%**
CT/HDL low	107718	20.8	46.2	33.7	36.1	28.7
CT/HDL moderate	17544	52.5	69.3	65.9	73.1	64.8
CT/HDL high	141	74.5	72.3	78.7	91.5	74.5
TG/HDL normal	92151	14,0	42.2	27.8	25.4	19.9
TG/HDL high	33252	56.8	69.6	67.3	85.4	72.2
LDL/HDL normal	97914	20.8	45.7	33.4	36.2	28.5
LDL/HDL high	27489	41.2	62.9	55.6	59.5	52.5
PRISQ low	52974	5.9	25.3	12.5	19.2	10.9
PRISQ moderate	53811	29,0	61.3	48.5	50.4	41.6
PRISQ high	18618	69.9	84.3	82.1	78,0	76.3
Normalweight Deuremberg	22125	0.2	7.7	0.7	6.2	2.4
Overweight Deuremberg	38502	14.2	28.2	9.4	23.7	11.1
Obesity Deuremberg	64776	46.5	76.4	68.2	63.8	57.9
No obesity RFM	116964	20.2	45.9	33.9	37.4	30.7
Yes obesity RFM	8439	95.3	98.9	98.6	95.3	76.1
No atherogenic dyslipidemia	117276	22.2	47.4	35.4	37.8	30.1
Yes atherogenic dyslipidemia	8127	70.1	80,0	80.5	91.9	86,0
No lipid triad	123519	24.5	49.1	37.6	40.5	32.9
Yes lipid triad	1884	77.1	79,0	83.3	93,0	89.2
No MS NCEP ATPIII	105330	16.9	43.1	29.7	32.9	24.5
Yes MS NCEP ATPIII	20073	69.7	82.9	83,0	85.7	82.3
No MS IDF	108318	15.7	42.6	29.7	33,0	26.1
Yes MS IDF	17085	86.3	93.4	92.8	93.9	82.1
No MS JIS	93204	39.9	38.8	24.4	27.3	19.6
Yes MS JIS	32199	64.1	80.4	78.5	81.9	74.7

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Table IIIa: Prevalence of high values of the NASH and liver fibrosis risk scales according to values of the cardiometabolic risk scales in women.

		FLI high	HSI high	ZJU high	LAP high	BARD high
Women	**n**	**%**	**%**	**%**	**%**	**%**
CT/HDL low	84117	20.8	46.2	33.7	36.1	28.7
CT/HDL moderate	9825	52.5	69.3	65.9	73.1	64.8
CT/HDL high	132	74.5	72.3	78.7	91.5	74.5
TG/HDL normal	86841	14,0	42.2	27.8	25.4	19.9
TG/HDL high	7233	56.8	69.6	67.3	85.4	72.2
LDL/HDL normal	83238	20.8	45.7	33.4	36.2	28.5
LDL/HDL high	10836	41.2	62.9	55.6	59.5	52.5
PRISQ low	65310	5.9	25.3	12.5	19.2	10.9
PRISQ moderate	22764	29,0	61.3	48.5	50.4	41.6
PRISQ high	6000	69.9	84.3	82.1	78,0	76.3
Normalweight Deuremberg	5373	0.2	7.7	0.7	6.2	2.4
Overweight Deuremberg	20754	14.2	28.2	9.4	23.7	11.1
ObeYesdad Deuremberg	67947	46.5	76.4	68.2	63.8	57.9
No obeYesdad RFM	85293	20.2	45.9	33.9	37.4	30.7
Yes obeYesdad RFM	8781	95.3	98.9	98.6	95.3	76.1
No atherogenic dyslipidemia	90057	22.2	47.4	35.4	37.8	30.1
Yes atherogenic dyslipidemia	4017	70.1	80,0	80.5	91.9	86,0
No lipid triad	93060	24.5	49.1	37.6	40.5	32.9
Yes lipid triad	1014	77.1	79,0	83.3	93,0	89.2
No MS NCEP ATPIII	85026	16.9	43.1	29.7	32.9	24.5
Yes MS NCEP ATPIII	9048	69.7	82.9	83,0	85.7	82.3
No MS IDF	84996	15.7	42.6	29.7	33,0	26.1
Yes MS IDF	9078	86.3	93.4	92.8	93.9	82.1
No MS JIS	83280	39.9	38.8	24.4	27.3	19.6
Yes MS JIS	10794	64.1	80.4	78.5	81.9	74.7

FLI Fatty liver index. HSI hepatic steatosis index. ZJU Zhejianng University index. FLD Fatty liver disease index. FSI Framingham steatosis index. LAP Lipid accumulation producto. CT Total colesterol. HDL High density lipoprotein. LDL Low density lipoprotein. PRISQ Prediabetes score Qatar. RFM Relative fat mass. MS ATPIII. Metabolic syndrome Adult Treatment Panel III. MS IDF Metabolic syndrome International Diabetes Federation. Metabolic syndrome Joint Interim Statement

Table IV: Multinomial logistic regression.

	FLI high OR (95% CI)	HSI high OR (95% CI)	ZJU high OR (95% CI)	LAP high OR (95% CI)	BARD high OR (95% CI)
CT/HDL low	1	1	1	1	1
CT/HDL moderate	1.15 (1.09-1.22)	1.32 (1.19-1.45)	1.07 (1.03-1.11)	1.23 (1.16-1.30)	1.35 (1.28-1.42)
CT/HDL high	1.28 (1.10-1.47)	1.47 (1.26-1.62)	1.22 (1.14-1.30)	1.50 (1.44-1.56)	1.69 (1.63-1.75)
TG/HDL normal	1	1	1	1	1
TG/HDL high	7.83 (7.52-8.15)	1.46 (1.41-1.51)	2.52 (2.43-2.62)	14.85 (14.26-15.46)	8.31 (8.01-8.62)
LDL/HDL normal	1	1	1	1	1
LDL/HDL high	1.22 (1.16-1.29)	1.05 (1.01-1.10)	1.08 (1.04-1.13)	1.26 (1.26-1.30)	1.11 (1.05-1.16)
PRISQ low	1	1	1	1	1
PRISQ moderate	2.27 (2.17-2.37)	1.10 (1.06-1.15)	1.36 (1.30-1.42)	1.21 (1.16-1.26)	3.04 (2.93-3.16)
PRISQ high	5.45 (5.17-5.74)	2.00 (1.91-2.09)	2.46 (2.35-2.58)	2.77 (2.64-2.90)	9.52 (9.10-9.96)
Normalweight Deuremberg	1	1	1	1	1
Overweight Deuremberg	4.35 (4.10-4.60)	4.36 (4.25-4.47)	11.05 (10.65-11.48)	2.54 (2.47-2.63)	3.82 (3.67-3.97)
Obesity Deuremberg	40.59 (30.22-54.52)	13.76 (13.08-14.48)	88.72 (76.11-103.42)	6.84 (6.43-7.27)	8.80 (8.02-9.65)
No obesity RFM	1	1	1	1	1
Yes obesity RFM	16.20 (15.42-17.03)	52.98 (44.11-63.63)	77.48 (65.47-91.71)	17.72 (16.53-19.00)	1.13 (1.08-1.18)
No atherogenic dyslipidemia	1	1	1	1	1
Yes atherogenic dyslipidemia	1.15 (1.08-1.20)	1.22 (1.13-1.31)	1.23 (1.13-1.33)	1.24 (1.13-1.35)	2.12 (1.97-2.29)
No lipid triad	1	1	1	1	1
Yes lipid triad	1.20 (1.07-1.34)	1.20 (1.09-1.29)	1.29 (1.17-1.41)	1.22 (1.16-1.28)	1.17 (1.01-1.35)
No MS NCEP ATPIII	1	1	1	1	1
Yes MS NCEP ATPIII	1.18 (1.14-1.23)	1.10 (1.03-1.17)	1.34 (1.26-1.43)	1.18 (1.14-1.23)	1.11 (1.06-1.17)
No MS IDF	1	1	1	1	1
Yes MS IDF	3.76 (3.56-3.95)	4.50 (4.22-4.81)	5.29 (4.94-5.66)	7.15 (6.69-7.64)	1.18 (1.12-1.24)
No MS JIS	1	1	1	1	1
Yes MS JIS	1.57 (1.49-1.66)	1.32 (1.26-1.40)	1.47 (1.39-1.56)	1.32 (1.24-1.39)	2.13 (2.03-2.24)

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Discussion

Our results show that the mean values and the prevalence of high-risk values of all the NASH and liver fibrosis scales analyzed increased in parallel with the cardiometabolic risk scales.

Multivariate analysis showed that the variable that most increased the risk of presenting high values of the different NASH and liver fibrosis risk scales were the scales that assessed obesity (RFM and Deuremberg).

Many authors consider obesity and dyslipidemia to be the main risk factors for NAFLD, and it is known that they increase cardiometabolic diseases, which are the main cause of death in these patients. A study by Tutunchi et al[21] in 256 individuals concluded that the severity of hepatic steatosis and fibrosis correlated very well with the atherogenic lipid profile. The Raine study[22] in adolescents also found similar results indicating that the presence of atherogenic lipoproteins increased the risk of NASH in adulthood. A study by Katsiki et al[23] showed that NASH was associated with various risk factors, including dyslipidemia.

The association that we have found between NAFLD and metabolic syndrome has also been described by other authors, and Sheka et al[24] concluded that there is a strong relationship between the two entities. Other authors such as Yki-Järvinen[25] and Wainwright[26] expressed the same opinion, although in the latter case the relationship was bidirectional.

The same relationship that we have found between NAFLD and risk of prediabetes has been observed by some authors. Insulin resistance, which is common to both pathologies, seems to be involved in the genesis of this association27. A study of more than 2000 individuals with a 10-year follow-up showed that increased risk of NAFLD assessed with the FLI was associated with increased risk of prediabetes and diabetes mellitus.

Strengths and limitations

The strengths of the study include the large sample size, more than 200,000 individuals, and the large number of NASH 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 our population there is a direct relationship between the values of the different NASH and liver fibrosis risk scales and the values of the cardiometabolic risk scales analyzed.

Conflict of Interest

The authors declare that no competing interests exist.

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