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Prevalence and association of metabolism-associated steatotic liver disease across age groups and gender

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ABSTRACT

Background and aim: Metabolic dysfunction-associated steatotic liver disease (MASLD) marks a fundamental advancement in understanding hepatic steatosis within the context of metabolic dysfunction. It evolved from the previous term, "non-alcoholic fatty liver disease" (NAFLD). MASLD specifically includes hepatic steatosis with metabolic risk factors, excluding legacy NAFLD subtypes, thus enabling a more precise characterisation of this condition. This study aimed to evaluate the prevalence of MASLD across diverse age and gender groups, focusing on metabolic factors contributing to the condition.

Methods and results: In this cross-sectional study, 338 patients with metabolic disorders were recruited from the Department of Internal Medicine outpatient ambulatory in Palermo, Italy. Data collection involved comprehensive anthropometric measurements, blood pressure assessments, laboratory analyses and abdominal echography. Liver stiffness was measured through 2-D shear wave elastosonography. The study found MASLD to be more prevalent in older male patients, with central obesity (OR 2.44, 95 % CI 1.37–4.34) (OR = 1.17, 95 % CI 1.09–1.24) as significant predictors. While age was not significantly associated with MASLD, central obesity and male gender increased risk.

Conclusions: MASLD prevalence is influenced by gender, central obesity, and BMI. The strong correlation between MASLD and central obesity underscores an urgent need for targeted interventions focusing on lifestyle modification and weight management.

1. Introduction

Metabolic dysfunction-associated steatotic liver disease (MASLD) marks a substantial evolution in the comprehension and classification of steatotic liver disease, highlighting the complex interplay between metabolic dysfunction and hepatic steatosis. MASLD has emerged as a prominent term in recent literature, serving as a replacement for non-alcoholic fatty liver disease (NAFLD) [1]. This shift in terminology underscores an increasing awareness of the relationship between metabolic dysfunction and hepatic steatosis. Firstly, in 2020, an international committee of experts agreed to rename NAFLD to MAFLD. This definition did not exclude patients with alcohol consumption or other chronic liver diseases, encompassing individuals with hepatic steatosis who also present at least one of the following metabolic conditions: type 2 diabetes mellitus (T2DM), overweight or obesity, and metabolic abnormalities [2]. Finally, the term MASLD includes hepatic steatosis alongside various cardiometabolic risk factors, distinguishing it from other subtypes of steatotic liver disease (SLD). A new classification of fatty liver disease has recently been published based on a multi-society Delphi consensus. It represents the most comprehensive classification of SLD to date [3,4]. MASLD has undergone significant changes in nomenclature and diagnostic criteria. The newly proposed criteria for

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MASLD include various subtypes, such as metabolic alcohol-associated/related liver disease (MetALD), where MASLD is linked to substantial alcohol consumption, MASLD-viral hepatitis, and cryptogenic SLD. This underscores the necessity for a comprehensive approach to diagnosing MASLD, considering its diverse aetiologies and risk factors. The transition from NAFLD to MASLD has implications for diagnostic criteria, as over 95 % of patients previously diagnosed with NAFLD meet the revised diagnostic criteria for MASLD. This shift highlights the importance of recognising metabolic dysfunction as a critical factor in diagnosing steatotic liver disease.

The prevalence of metabolic dysfunction-associated steatotic liver disease (MASLD) is on the rise, with studies indicating a high prevalence among middle-aged individuals who are overweight and have normal liver enzyme levels [5]. Furthermore, MASLD, similar to non-alcoholic fatty liver disease (NAFLD) and metabolic dysfunction-associated fatty liver disease (MAFLD), has been associated with conditions such as diabetes mellitus and heart failure, highlighting its significant overlap with other metabolic disorders [6]. Research has also linked MASLD to adverse health outcomes, suggesting associations with clinically significant fibrosis and frailty in elderly [7].

In the United States, approximately 80.19 million individuals are affected by steatotic liver disease, resulting in an age-adjusted prevalence of 35.7 % (95 % CI, 33.2%–37.6 %) [8]. Among this population, 14.32 million individuals present with clinically significant fibrosis, corresponding to an age-adjusted prevalence of 6.5 % (95 % CI, 5.2%–7.7 %). Regarding the elderly population, a study on 9097 Australian participants aged ≥70, showed a prevalence of MASLD of about 33 %, decreasing with increasing age [7].

The understanding of the clinically relevant features defining sex differences in NAFLD is still limited. A multitude of factors contribute to gender differences.

Gender differences are related to sex hormones, sex chromosomes, gut microbiota and insulin resistance. Obesity and menopausal status are the main factors contributing to the occurrence of NAFLD and progression to NASH in women. Sex hormones are involved in the different distribution of adiposity in men and women. Women have a more significant subcutaneous fat deposition, whereas men have a more visceral distribution. In addition, sex hormones are involved in the regulation of hepatic glucose and lipid metabolism. The increased risk of NAFLD in postmenopausal women is due to decreased estrogen levels that alter the visceral fat distribution and promote the dyslipidemic milieu. Estrogens play a protective role against the development of insulin resistance and are involved in decreasing triglyceride synthesis and increasing the oxidation of free fatty acids in the liver [9]. Many aspects of obesity, including body composition, lipid metabolism, endocrine function, and chronic low-grade inflammation, are influenced by gender differences [10]. Obesity and hepatic steatosis are both components of the metabolic syndrome and are closely related. Men have a higher prevalence and severity of NAFLD than women during reproductive age. However, NAFLD affects women more frequently after menopause, indicating that oestrogen may offer some protection [11]. According to these data, our study aimed to verify the prevalence of MASLD across different genders and age groups and the factors associated with it.

2. Methods

2.1. Study design

At the Internal Medicine outpatient clinic of ARNAS Civico Di Cristina Benfratelli, Palermo, 338 consecutive patients were enrolled. Inclusion criteria were consecutive outpatients with at least one of the metabolic syndrome conditions according to the NCEP criteria. In addition, all patients had one or more of the following diagnoses: hypertension, type 2 diabetes mellitus, dyslipidaemia and related conditions. Anthropometric measurements such as height, weight, body mass index (BMI) and waist circumference were recorded. Blood pressure was measured, and laboratory variables including HDL, LDL, triglycerides, creatinine, eGFR (by CKD-EPI formula), fasting blood glucose, AST, ALT and γ-GT were performed. In addition, elastosonography was performed to assess tissue stiffness or elasticity. Stages of hepatic steatosis and visceral fat thickness were evaluated for each patient by ultrasonography. All patients attending the centre whose data are entered into a database for research purposes, have signed an informed consent.

2.2. Hepatic steatosis and visceral fat measurement

Steatosis was assessed using first-line imaging techniques [12]. Increased liver echogenicity compared to the kidney indicates steatosis, though this assessment is qualitative and operator-dependent. The diaphragm can attenuate (weaken) the ultrasound signal during abdominal ultrasound due to its tissue composition and location. Diaphragmatic attenuation refers to the reduction in the intensity of ultrasound waves as they pass through the diaphragm. Diaphragmatic attenuation helps distinguish between moderate and severe steatosis. It is important to note that the diaphragm may not be visible in severe steatosis [13]. This study discusses how hepatic steatosis affects liver echogenicity and visibility of surrounding structures like the diaphragm on ultrasound). Finally, visceral fat thickness was taken from the inner edge of the posterior rectus abdominis muscle to the anterior wall of the aorta. This distance in millimetres represented the thickness of the visceral fat layer [14].

2.3. Elastosonography

Elastosonography (2D-Shear Wave Elastography, SWE method) measures the stiffness or elasticity of tissues [15]. Different liver tissues have varying stiffness levels; elastography uses ultrasound waves to induce mechanical stress in tissue. It provides additional information about tissue characteristics, more than conventional ultrasound can. SWE generates shear waves within the tissue using focused ultrasound pulses. It measures the speed of these shear waves to quantify tissue stiffness (faster waves indicate stiffer tissue). This technique has been particularly useful in evaluating liver stiffness (LS). The tissue's response to this stress was measured to determine its stiffness. The ultrasound transducer was placed on the skin of the area of interest and generated focused ultrasound pulses to create shear waves within the tissue. Elastosonography software processes the tissue's response to mechanical stress or shear waves. The resulting images showed the stiffness of the tissue, often colour-coded (red for stiff tissue, blue for soft tissue). Quantitative measurements, such as Young's modulus (a measure of stiffness), were obtained. It provided visual (qualitative) and numerical (quantitative) information about the stiffness of tissues. Young's modulus can be expressed in kilopascals (kPa), a unit of pressure and stress measurement, especially regarding softer materials such as biological tissue. In a diagnosis, patients with a normal liver typically have a stiffness of about ≤5.3 kPa, while a fibrotic liver (F) was measured from ≥5.31 kPa to 6.9 kPa, (F1), ≥7 kPa–8.9 kPa, (F2), ≥9 kPa–11.9 kPa, (F3) and ≥12 kPa measured an F4 (cirrhosis) [16].

2.4. Criteria for diagnosing metabolic syndrome (MS)

Several organisations, including the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) and the International Diabetes Federation (IDF), have established criteria for diagnosing metabolic syndrome, strongly emphasising central obesity. According to the IDF's 2006 criteria [17], central obesity, defined by ethnicity-specific waist circumference values (greater than 94 cm in men and 80 cm in women), is a primary requirement, alongside the presence of at least two additional factors: elevated triglycerides (greater than 150 mg/dl or receiving treatment), reduced HDL cholesterol levels (less than 40 mg/dl in men and 50 mg/dl in women, or on treatment), elevated blood pressure (greater than 130/85 mmHg or on treatment),

and elevated fasting blood glucose (greater than 100 mg/dl or on treatment). In contrast, the NCEP ATP III criteria [18], diagnose metabolic syndrome based on the presence of any three of the following five factors: increased waist circumference (greater than 102 cm in men and 88 cm in women), elevated triglycerides (greater than 150 mg/dl or on treatment), reduced HDL cholesterol levels (less than 40 mg/dl in men and 50 mg/dl in women, or on treatment), elevated blood pressure (greater than 130/85 mmHg or on treatment), and elevated fasting blood glucose (greater than 100 mg/dl or on treatment).

2.5. Adults' criteria used for MASLD diagnosis

MASLD was diagnosed based on the criteria of the Delphi consensus [3], steatotic liver was confirmed by ultrasound in conjunction with at least one of the following five cardiometabolic risk factors (CMRF): BMI $\geq$25 kg/m^2 or waist circumference >94 cm in males or >80 cm in females; fasting serum glucose $\geq$5.6 mmol/L, 2-h post-load glucose $\geq$7.8 mmol/L (140 mg/dl), HbA1c $\geq$ 5.7 % (39 mmol/mol), or a diagnosis or treatment for type 2 diabetes mellitus; blood pressure $\geq$130/85 mmHg or specific antihypertensive treatment; plasma triglycerides $\geq$1.70 mmol/L (150 mg/dl) or lipid-lowering treatment; plasma HDL $\leq$1.0 mmol/L (40 mg/dl) in males or $\leq$1.3 mmol/L (50 mg/dl) in females, or lipid-lowering treatment. Patients with hepatic steatosis who do not meet any CMRF criteria were diagnosed with cryptogenic SLD.

2.6. Statistical analysis

Data are presented as percentages in the case of categorical variables and as median (interquartile range) in the case of continuous variables. The non-parametric U Mann-Whitney Test and the test for proportion were used to compare groups as it is appropriate. Multivariable logistic regression assessed the relationship between dichotomous outcomes and the variables examined. Multivariable linear regression was performed for continuous outcomes. Odds ratios (ORs) or coefficients were calculated with 95 % confidence intervals (95 % CI) and p-value. The significance level used was 0.05 two-tailed. Stata Statistical Software, release 18 (College Station, TX: StataCorp LLC; 2023) was used for database management and all analyses.

3. Results

A total of 338 patients were enrolled. Table 1 shows the median age was 66 years (55–73), and men were 56.2 %. Median Body Mass Index (BMI) was 27.8 kg/m^2 (24.7–31.2), and the median waist circumference was 102 cm (93–110). Clinical characteristics and laboratory variables were compared between two groups of outpatients: young adults <65 years (n = 152; 55.26 % men) and elderly $\geq$65 years (n = 186, 56.98 % men). The elderly had a significantly higher prevalence of hypertension (72.6 % vs. 40.7 %, p < 0.001) and coronary artery disease (13.4 % vs. 3.9 %, p < 0.003). In addition, laboratory variables indicated that elderly patients had significantly lower levels of alanine aminotransferase (ALT) [18 vs 29 U/L, (p < 0.0001)], estimated glomerular filtration rate (eGFR) [82.6 vs 98 ml/min/1,73 m [2] (p < 0.0001)] and total cholesterol (158 vs 180 mg/dl, p < 0.0029). Significant differences were found in the prevalence of type 2 diabetes mellitus (39 % vs 25 %, p < 0.006) and alcoholic hepatitis (2.2 % vs 6.57, p < 0.042) between the age groups. As described in Table 2, the prevalence of body mass index (BMI), overweight and first-class obesity were slightly higher in the elderly group, and these differences were statistically significant. Notably, the elderly had lower rates of severe hepatic steatosis (5.9 % vs. 15.8 %, p < 0.03). These findings indicate that the elderly were less likely to have severe hepatic steatosis, which could contribute to a reduced risk of MASLD and related liver dysfunction with increasing age. However, no significant differences were found between age groups in the different fibrosis stages, except grade 1, which was prevalent in the elderly population. Central obesity, defined by NCEP-ATPIII, was more common in the elderly (74.2 % vs. 58.6 %, p = 0.002). The prevalence of metabolic syndrome was higher in the elderly groups (52, 7 % vs. 34.9 %, p = 0.001), making it statistically significant. In the elderly, statin use was higher compared to the population <65 years old (51.61 % vs. 35.5 %, p < 0.003). There were no significant differences between the two groups regarding using ezetimibe employed in 44 % of the total population (23.7 % vs. 22.4 %, p = 0.780).

Table 1
Demographic characteristics of the population with comorbidities and laboratory variables according to the age groups.

	All patients	Patients <65 yrs	Patients ≥65 yrs	p =
n.	338	152	186	-
Men (%)	56.21	55.26	56.98	= 0.750
[a] Age	66(55–73)	53(42–60)	72(68–77)	-
Type 2 diabetes mellitus (%)	32.8	25	39.2	**<0.006**
Arterial Hypertension (%)	52.3	40.7	72.6	**<0.001**
COPD (%)	6.2	3.9	8.1	= 0.134
Coronary artery disease (%)	9.2	3.9	13.4	**<0.003**
Chronic vascular encephalopathy (%)	1.2	0.66	1.6	= 0.430
Hepatitis HCV (%)	9.2	9.9	8.6	= 0.614
Hepatitis HBV (%)	10.1	12.5	8	= 0.169
Alcoholic Hepatitis (%)	4.14	6.57	2.2	**<0.042**
Autoimmune Hepatitis (%)	0.6	0.66	1.1	= 0.692
[a] AST (U/L)	22 (17–32)	23 (18–36)	20(16–29.8)	**<0.0117**
[a] ALT (U/L)	21.5 (14–39)	29 (17–50.5)	18(18–27)	**<0.0001**
[a] GGT (U/L)	26 (19–50)	32 (19–60)	23(18–35.7)	**<0.0404**
[a] Bilirubin (mg/dl)	0.7 (0.4–1.05)	0.51 (0.4–0.84)	0.8(0.6–1.1)	**=0.0001**
[a] Direct bilirubin (mg/dl)	0.26 (0.19–0.40)	0.2 (0.16–0.32)	0.3(0.2–0.4)	**<0.0001**
[a] Alkaline phosphatase (U/L)	83 (62–102)	76 (52–102)	83(67–101)	= 0.2761
[a] eGFR CDK EPI (ml/min/1,73 m)^2	87.8 (73–100)	98 (81.6–106.7)	82.6 (64.4–93.7)	**<0.0001**
[a] Glycemia (mg/dl)	100 (89–115)	92 (83–104)	106 (94–125.8)	**<0.0001**
[a] Albumin (g/dl)	4.1 (3.7–4.4)	4.3 (3.9–4.5)	3.96 (3.68–4.22)	**<0.0157**
[a] Total cholesterol (mg/dl)	169.5 (127–203.8)	180 (148–217)	158 (119.5–191)	**<0.0029**
[a] HDL Cholesterol (mmol/l)	46.2 (39–55)	47 (41–55.7)	45(39–55)	= 0.2475
[a] Triglycerides (mg/dl)	110.5 (76–144)	121 (81.5–172.5)	101 (75–131)	**<0.0148**
[a] LDLCholesterol (mg/dl)	95 (70–127)	98 (79–136)	88 (60–123)	= 0.0936

[a] Data are reported as median (interquartile range Q1-Q3).

Regarding the main aim of our study, MASLD was higher in men over> 65 (45.7 % vs. 36.2 %, p = 0.068) but not statistically significant. In addition, Fig. 1 represents the prevalence of MASLD across different age and gender groups in a population with metabolic conditions.

A multivariable logistic regression analysis evaluated the association between MASLD and the variables according to various models, as shown in Table 3. Age was not statistically associated with MASLD (OR = 1.01, 95 % CI: 0.99–1.03, p = 0.244), probably due to the sample size. Male gender was associated with MASLD (OR = 2.01, 95 % CI 1.21–3.63, p < 0.008).

Central obesity and BMI were independently associated with MASLD, despite being in the same logistic regression model. Central obesity was associated with MASLD (OR 2.44, 95 % CI 1.37–4.34, p < 0.002). BMI was also positively associated with MASLD (OR = 1.17, 95 % CI 1.09–1.24, p < 0.0001). The association between severe steatosis

Table 2
Adiposity and liver features in our population sample.

	All patients	Patients <65 yrs	Patients ≥65 yrs	p =
[a] BMI $^{2}_{(kg/m)}$	27.8 (24.7–31.2)	26.5 (23.4–30.8)	28.1 (25.1–31.8)	**<0.0239**
[a] Waist circumference (cm)	102 (93–110)	97(91–108)	104 (96–110)	**<0.0034**
Overweight (%)	34.9	30.9	38.2	**<0.010**
Obesity 1st class (%)	24.3	19.7	27.9	**<0.006**
Obesity 2nd class (%)	6.8	5.3	8.1	= 0.057
Obesity 3rd class (%)	2.4	3.9	1.2	= 0.331
[b] Central obesity (%)	67.2	58.6	74.2	**<0.002**
Central obesity IDF (%)	83.4	77.6	87.2	**<0.010**
[a] Visceral fat (mm)	56.45 (35–75)	44 (32.6–70.6)	60 (41.9–76.6)	**<0.0072**
[b] Metabolic Syndrome (%)	44.7	34.9	52.7	**<0.001**
MASLD %	68.3	63.2	72.6	= 0.064
Men MASLD (%)	41.42	36.2	45.70	= 0.068
MetALD(%)	2.9	4.6	1.6	= 0.106
ALD (%)	0	0	0	–
Specific SLD (%)	12.4	12.5	12.4	= 0.970
Cryptogenic SLD (%)	0	0	0	–
Steathosis (%)	71.9	69.1	74.2	= 0.298
Steathosis mild (%)	29.6	25	33.3	= 0.209
Steathosis moderate (%)	31.7	29.6	33.3	= 0.490
Steathosis severe (%)	10.4	15.8	5.9	**<0.030**
[a] Liver Stiffness (Kpa)	4.7 (4.1–5.7)	4.5 (3.83–5.55)	4.9 (4.21–5.7)	**<0.0043**
Fibrosis (%)	36.4	31.6	40.3	= 0.106
Fibrosis grade 1 (%)	19.8	13.2	25.3	**<0.007**
Fibrosis grade 2 (%)	4.1	3.3	4.8	= 0.345
Fibrosis grade 3 (%)	4.1	6.6	2.2	= 0.113
Fibrosis grade 4 (%)	7.1	6.6	7.5	= 0.504

[a] Data are reported as median (interquartile range Q1-Q3).
[b] According to NCEP-ATPIII criteria.

and its variables was also evaluated by logistic regression.

Severe steatosis was not found to be significantly associated with LS. In contrast, there was a significant association with age (OR = 0.96, 95 % CI 0.93–0.99, $p < 0.004$), gender male (OR = 2.77, 95 % CI 1.19–6.41, $p < 0.018$), central obesity (OR = 16.53, 95%CI 2.1–129.74, $p < 0.008$) and BMI (OR 1.16, 95 % CI 1.08–1.26, <0.0001).

As reported in Table 3, only BMI was significantly associated with LS (Coefficient = 0.31, 95 % CI 0.09–0.54, $p < 0.006$) in a model with age, gender and central obesity.

4. Discussion

Based on our findings, we analysed a cohort of 338 patients to explore clinical characteristics and risk factors associated with MASLD and related metabolic conditions. The cohort's median age was 66 years, and men represented 56.2 % % of the population. BMI and waist circumference were also assessed, with median values indicating a tendency toward overweight and central obesity.

The primary goal of our study was to determine how common MASLD is in different age groups and genders and to identify factors linked to the disease. According to our findings, the prevalence of MASLD showed a trend towards higher prevalence in men over 65, although this was not statistically significant. Logistic regression analysis indicated that male gender, central obesity, and BMI were significantly associated with MASLD, highlighting the importance of these factors in predicting disease risk. Age, however, was not significantly associated with MASLD, which could be attributed to the sample size limitations.

Our findings highlighted a higher association of MASLD with male gender, consistent with previous research indicating that men are at increased risk of MASLD compared to women, especially in populations with similar metabolic profiles. Studies like Lonardo et al. [19], have demonstrated that men generally exhibit a higher prevalence of MASLD, which may be attributed to differences in fat distribution, hormonal influences, and lifestyle factors. These gender differences are particularly prominent in the presence of central obesity, as observed in our sample. These results highlight the importance of gender-and age-specific approaches to the prevention and management of MASLD, with particular attention to the older male population, which appears to be at higher risk.

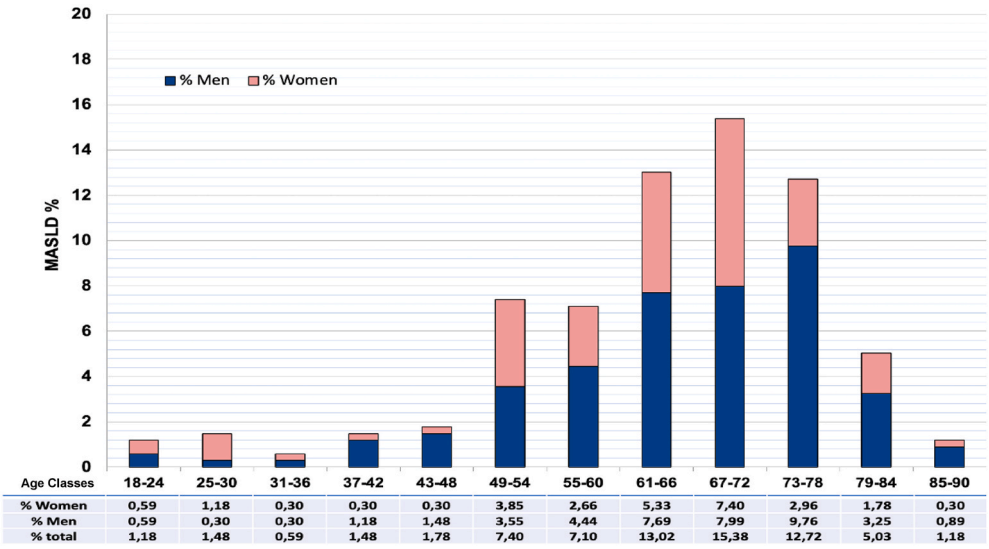
When comparing young adults (<65 years) with the elderly (≥65 years), significant differences emerged in cardiovascular comorbidities and laboratory variables. The elderly showed a markedly higher prevalence of hypertension and coronary artery disease, consistent with an age-related increase in cardiovascular risk. Alqahtani et al. have underlined that several risk factors for the development of NAFLD, such as hypertension, diabetes, and obesity, are higher in the elderly [20]. Regarding metabolic health, the elderly group had a lower rate of severe hepatic steatosis. The reduced prevalence of severe hepatic steatosis in elderly patients may imply a lower MASLD risk with aging, though this could also reflect survivor bias or differences in metabolic adaptations. Although the prevalence of metabolic syndrome was similar in both age groups in our sample, metabolic syndrome remains a significant contributor to MASLD risk. Ford E. et al. [21] demonstrated an increase with age in metabolic syndrome, according to NCEP criteria.

The lack of age-related differences in metabolic syndrome prevalence in our study may indicate a consistent metabolic burden across age groups, contributing to MASLD regardless of age.

On the other hand, laboratory findings revealed significantly lower levels of ALT, as shown by Dong et al. [22], estimated glomerular filtration rate (eGFR), and total cholesterol among elderly, reflecting possible age-related metabolic shifts.

Statin use was higher in the elderly population, which mirrors findings in cardiovascular literature where statins are frequently prescribed in elderly for primary and secondary prevention of cardiovascular diseases. Statins have shown potential protective effects on liver steatosis progression in MASLD patients, as documented by Pastori et al. [23], where statin use was associated with reduced liver fat and fibrosis progression. However, our study found no significant difference in ezetimibe use, which is consistent with the limited impact of ezetimibe on MASLD in comparison to statins [24]. Emerging evidence suggests that adipose tissue dysfunction is the first step in the pathogenesis of MASLD [4]. Visceral adipose tissue (VAT) and subcutaneous adipose tissue (SAT) compartments may contribute to different degrees to the development and progression of MASLD, as VAT mainly appears to have deleterious metabolic effects [25]. Central obesity was independently associated with MASLD in our cohort, supporting the well-established link between visceral adiposity and liver steatosis. According to the literature, central obesity is a significant risk factor for MASLD, as visceral fat contributes to increased free fatty acid flux and hepatic fat [26].

Our study found no significant association between age and MASLD prevalence, although there was a non-significant trend toward higher MASLD prevalence in older men. This aligns with some literature suggesting that while MASLD prevalence increases with age, it is primarily driven by metabolic factors, such as obesity and insulin resistance, rather than age alone. For instance, Younossi et al. [27] reported that



Age Classes	18-24	25-30	31-36	37-42	43-48	49-54	55-60	61-66	67-72	73-78	79-84	85-90
% Women	0,59	1,18	0,30	0,30	0,30	3,85	2,66	5,33	7,40	2,96	1,78	0,30
% Men	0,59	0,30	0,30	1,18	1,48	3,55	4,44	7,69	7,99	9,76	3,25	0,89
% total	1,18	1,48	0,59	1,48	1,78	7,40	7,10	13,02	15,38	12,72	5,03	1,18

Fig. 1. Distribution frequency of MASLD according to Age Classes and Gender.
Notes: Percentage of women and men with MASLD within each age class.

Table 3
Multivariable regression models about the association between outcome variables and related predictors.

[c] Outcome variable: MASLD		
	OR (95%CI)	p =
[a] Age	1.01 (0.99–1.03)	= 0.244
[a] Gender (Male)	2.01 (1.21–3.63)	**<0.008**
[b] Central obesity	2.44 (1.37–4.34)	**<0.002**
[a] BMI (kg/m2)	1.17 (1.09–1.24)	**<0.0001**
[b] Metabolic Syndrome (%)	1.34 (0.74–2.45)	= 0.337
[c] Outcome variable: Severe Steatosis		
	OR (95%CI)	p =
[a] Age	0.96 (0.93–0.99)	**<0.004**
[a] Gender male	2.77 (1.19–6.41)	**<0.018**
[a] Liver Stiffness (Kpa)	1 (0.98–1.03)	0.817
[b] [a] Central obesity	16.53(2.1–129.74)	**<0.008**
[a] BMI (kg/m2)	1.16 (1.08–1.26)	**<0.0001**
[°] Outcome variable: Liver Stiffness (Kpa)		
	Coeff. (95%CI)	p =
[a] Age	0.06 (−0.01 [c] 0.14)	= 0.099
[a] Gender (Male)	1.06 (−1.25 [c] 3.39)	= 0.368
[b] Central obesity	0.92 (−1.72 [c] 3.55)	= 0.494
[a] BMI (kg/m2)	0.31 (0.09–0.54)	**<0.006**

[°] Multivariable model by linear regression.
[a] Data are reported as mean (95 % confidence interval).
[b] According to NCEP-ATPIII criteria.
[c] Multivariable model by logistic regression.

metabolic risk factors, particularly obesity and type 2 diabetes, are stronger predictors of MASLD than age in most populations.

Data in the literature on prevalence in age groups are controversial. Epidemiological studies have shown that men have a higher prevalence of MASLD than premenopausal women [28]. These data support our results. Lonardo et al. [19] reported that postmenopausal women have a similar prevalence of MASLD as men and show more rapid disease progression, placing them at a comparable or even higher risk of developing cardiovascular disease.

Our study's age groups are segmented from 18 to 90 years, covering various ranges.

The percentage of men with MASLD increases in elderly age groups, peaking at 9.76 % in the 73–78 age group and maintaining relatively high percentages in the 67–72 age group (7.99 %). The lowest percentages are observed in the younger age groups (0.30 % for 25–30 and 31–36).

The peak percentage for women occurs in the 67–72 age group, where women make up 7.40 % of the total population. The lower prevalence of metabolic-associated steatotic liver disease (MASLD) in women within the 31–48 and 85–90 age groups can be attributed to several biological, hormonal, and lifestyle factors.

Women in the 31–48 age range are typically premenopausal, and oestrogen appears to protect against fat accumulation in the liver. Oestrogen enhances lipid metabolism, reduces inflammation, and promotes insulin sensitivity, lowering the risk of MASLD.

Premenopausal women generally tend to store fat subcutaneously rather than viscerally. This type of fat storage is less associated with MASLD than visceral fat, which is more common in men and linked to a higher risk of metabolic diseases [29].

While steatosis is a hallmark of fatty liver disease, it is the progression to fibrosis that leads to more serious liver damage. This study might indicate that severe steatosis can occur even without substantial fibrosis, at least in this population. The negative association between severe steatosis and age may indicate that interventions could be more effective in younger populations. Our finding of a lower prevalence of severe hepatic steatosis in elderly is noteworthy, as some studies have reported a decrease in steatosis severity with advancing age. This could reflect age-related metabolic changes, survivor bias, or the protective effect of lifestyle adjustments commonly adopted with age. The significantly increased risk in males point to a need for gender-specific strategies in the screening and management of severe steatosis. The very high odds associated with central obesity highlight it as a crucial target for prevention and treatment efforts. Regular monitoring of BMI and implementing weight management strategies should be integral parts of patient care to mitigate the risk of severe steatosis. The data indicates several critical factors influencing the risk of severe steatosis, particularly central obesity and male gender. Logistic regression also explored factors linked to severe hepatic steatosis, where age, male gender, central obesity, and BMI emerged as significant predictors. The lack of association between LS and severe steatosis underscores the complexity of MASLD progression and highlights the need for further research. The results on BMI underline its role as a critical marker in assessing the risk of MASLD.

Elevated BMI is strongly associated with hepatic steatosis, which doesn't necessarily equate to advanced fibrosis. In Table 3 is reported a

significant negative association between BMI and LS, suggesting that higher BMI might be protective or associated with lower LS. In our study, BMI was significantly associated with liver stiffness, independent of age, gender, and central obesity. This observation is consistent with reports in the literature indicating that higher BMI, particularly in cases of obesity, is associated with increased liver stiffness and fibrosis progression [30]. Research has suggested that BMI's impact on liver stiffness may be due to the associated inflammatory and fibrotic processes within hepatic tissue.

Our study's findings align with the broader literature on MASLD, confirming that metabolic factors like BMI, central obesity, and gender play a critical role in disease development. While age alone may not directly increase MASLD risk, age-related changes in metabolism and comorbidities may still influence disease progression. These comparisons underscore the importance of targeting modifiable metabolic risk factors for effective MASLD prevention and management, especially in high-risk groups such as men with central obesity.

The originality of our model can be emphasised by the use of unconventional variables or interactions specifically selected for the MASLD context, as well as the detailed analysis between LS and BMI, accounting for the independent impact of central obesity. We have implemented an innovative multivariable analysis considering multiple risk factors to model the association with important variables with MASLD. The methodological choices reflect a unique adaptation of regression models to address specific clinical questions about MASLD, integrating elements like the analysis of severe steatosis about LS, which few studies have tackled comparably.

Our study has various strengths. It uses original multivariable regression analysis to provide valuable insights into the factors influencing MASLD prevalence and risk. It emphasises gender-specific approaches and unexpected findings related to BMI and LS, highlighting the need for continued research to refine our understanding and improve patient care. Finally, it represents a piece of our real world.

However, our study is single-centre and has a limited sample size and it is not representative of the general population.

Further epidemiological studies focused on gender and age are needed to understand the best approach to diagnosing and treating MASLD. Complications related to MASLD can be an important source of morbidity and health care utilisation. Furthermore, risk stratification and evaluation of patients with MASLD should incorporate cardiometabolic comorbidities, muscle mass and quality and frailty assessments. Longitudinal studies would help identify which frailty phenotypes are the best predictors of MASLD in elderly populations.

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