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Prevalence of metabolic dysfunction-associated steatotic liver disease (MASLD) in a middle-aged population with overweight and normal liver enzymes, and diagnostic accuracy of noninvasive proxies

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Abstract

The prevalence of metabolic dysfunction-associated steatotic liver disease (MASLD) is increasing at an alarming rate. Elevated liver enzymes are a primary reason to refer patients for further testing. However, liver enzymes within the normal range do not exclude the presence of MASLD. We examined the prevalence of MASLD in a middle-aged population with overweight and normal liver enzymes. In addition, we examined the accuracy of 4 sets of noninvasive proxies for MASLD.

We included 1017 participants from the Netherlands epidemiology of obesity cohort study with body mass index ≥ 25 kg/m² and liver enzymes (aspartate aminotransferase, alanine aminotransferase, gamma-glutamyltranspeptidase) within normal range. The diagnostic accuracy of biomarker scores (fatty liver index, liver fat score [LFS], STEATO-ELSA, and hepatic steatosis index) was determined against elevated hepatic triglyceride content measured by ¹proton magnetic resonance spectroscopy.

Participants (mean age 56 years, 49% women), had a median body mass index of 29.6 kg/m² and a median hepatic triglyceride content of 4.4%. MASLD was present in 42% of participants and was more common in men than women, with respectively 47% and 36% being affected. The LFS showed the highest accuracy with an area under the curve of 0.72. We identified metabolic syndrome as the prime predictor for MASLD with an odds ratio of 2.95 (95% confidence interval 2.20–3.98).

The prevalence of MASLD in middle-aged men and women with overweight and liver enzymes within the normal range is over 40%. LFS showed the highest accuracy to detect MASLD, but, overall, biomarker scores performed relatively poor. The presence of metabolic syndrome was the prime predictor of MASLD.

Abbreviations: ALT = alanine aminotransferase, AST = aspartate aminotransferase, AUC = area under the curve, BMI = body mass index, CI = confidence interval, FLI = fatty liver index, HDL = high density lipoprotein, H-MRS = proton magnetic resonance spectroscopy, HSI = hepatic steatosis index, HTGC = hepatic triglyceride content, IQR = interquartile range, LFS = liver fat score, LUMC = Leiden university medical center, MASLD = metabolic dysfunction-associated steatotic liver disease, MRI = magnetic resonance imaging, NAFLD = non-alcoholic fatty liver disease, NEO = Netherlands epidemiology of obesity, OR = odds ratio, ULN = upper limit of normal, VCTE = vibration controlled transient elastography.

Keywords: biomarkers scores, MASLD, metabolic syndrome, NEO study, noninvasive tools

KCVS and LCTN-N have contributed equally to this work.

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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1. Introduction

Metabolic dysfunction-associated liver disease (MASLD), formerly known as nonalcoholic fatty liver disease (NAFLD),^[1] is an increasingly prevalent disease and has been linked to metabolic, cardiovascular and malignant morbidity.^[2] MASLD is defined as the presence of hepatic steatosis with the presence of metabolic risk factors, most notably type 2 diabetes mellitus and overweight.^[1,3] It is considered to be more than a single entity, since it encompasses a range of phenotypes, starting from isolated steatosis, in which the predominant histological characteristic is lipid accumulation in hepatocytes, to metabolic dysfunction-associated steatohepatitis, characterized by the addition of hepatic inflammation and/or fibrosis, and metabolic dysfunction-associated steatohepatitis-related cirrhosis and hepatocellular carcinoma.^[4,5] Abdominal, particularly visceral, obesity leading to insulin resistance is strongly associated with MASLD, both via increased delivery of free fatty acids to the liver and through increases of hepatic lipogenesis associated with hyperglycemia and hyperinsulinemia.^[6–8] For this reason, MASLD is regarded as the hepatic manifestation of metabolic syndrome.^[9–11] Metabolic syndrome is a cluster of metabolic abnormalities that increase the risk of cardiovascular disease and type 2 diabetes mellitus. It is typically diagnosed when an individual has at least 3 of the following 5 criteria: abdominal obesity, hypertension, elevated fasting glucose, high, and low high density lipoprotein cholesterol.^[12]

The prevalence of MASLD ranges from 25% in the general population to 60% in high-risk populations, such as individuals with obesity and/or type 2 diabetes mellitus. The prevalence increases with age, obesity and lack of physical activity.^[13,14] MASLD, when diagnosed at an early stage, is reversible when lifestyle modifications are implemented and causative factors are corrected.^[15] Yet progression into fibrotic stages of MASLD is strongly associated with liver-related and overall mortality.^[16,17] Thus, timely detection of MASLD is clearly called for. However, because MASLD commonly remains asymptomatic until the cirrhotic stage,^[18] it is often overlooked and, consequently, undertreated.^[19] Identifying individuals at high-risk of MASLD is needed to effectively treat patients and to prevent progression of disease, thus reducing liver-related and overall mortality.

To date, liver biopsy remains the gold standard for diagnosing and grading MASLD. However, liver biopsy is an invasive procedure that can be painful, has a risk of post-biopsy bleeding (up to 2%) and might convey a sampling error, due to only about 1/50,000th of the liver tissue being analyzed, while MASLD is often not equally distributed throughout the liver.^[20,21] Proton magnetic resonance spectroscopy (¹H-MRS) is regarded as the most robust and accurate measure of hepatic triglyceride content (HTGC) and is consistent with liver biopsy in diagnosing and grading MASLD.^[2,11,22–24] Although repeated assessments can be performed without safety concerns,^[24,25] it is a time-consuming, costly procedure and only available in a few academic centers worldwide.^[23] Many patients with MASLD express elevated serum liver enzymes, in particular alanine aminotransferase (ALT) and gamma-glutamyltranspeptidase (GGT). However, liver enzymes within the normal range do not exclude MASLD,^[26] and although elevated liver enzymes may serve as a diagnostic clue for the presence of liver disease, they fail to predict the presence and severity of hepatic steatosis, inflammation and fibrosis.^[5,27] The present European association for the study of the liver guideline recommends to screen for MASLD by liver enzymes and/or ultrasound as part of routine work-up in subjects with obesity or metabolic syndrome.^[28] This may however underestimate the number of patients with MASLD.

The objective of this study was to examine the prevalence of MASLD in middle-aged people with overweight and, most notably, liver enzymes within the normal range. Additionally, we will assess predictive factors for MASLD in this cohort, and assess

the diagnostic accuracy of 4 distinct noninvasive biomarker scores for MASLD, namely fatty liver index (FLI),^[29] liver fat score (LFS),^[30] STEATO-ELSA^[31] and hepatic steatosis index^[32] compared to HTGC measured by ¹H-MRS.

2. Methods

2.1. Study design and study population

Data from the Netherlands epidemiology of obesity (NEO) study was used for this study. The NEO study is an ongoing population-based cohort study, with baseline measurements between 2008 and 2012. The study included 6671 participants living in the greater area of Leiden (in the west of the Netherlands), aged 45 to 65 years and predominantly with overweight (body mass index [BMI] ≥ 25 kg/m²).^[33]

Participants attended a baseline visit at the NEO study center at the Leiden university medical center (LUMC) after an overnight fast. Before this study visit, participants completed a general questionnaire at home to report the medical history of relevant morbidities and demographic, lifestyle, and clinical information. At the visit, participants underwent an extensive physical examination, including anthropometry, and blood sampling. Furthermore, they completed a screening form to rule out contra-indications for magnetic resonance imaging (MRI) (most notably a body circumference >170 cm, claustrophobia or metal implants). Of the participants who were eligible for MRI, approximately 40% were randomly selected for a direct assessment of ¹H-MRS. In the present analysis, we excluded participants without ¹H-MRS assessment, technical failure of the ¹H-MRS or because of missing data other than ¹H-MRS. A detailed description of the study design and data collection of the NEO study has previously been published.^[33] The medical ethics committee of the LUMC approved the study and all participants gave written informed consent.

Presence of type 2 diabetes mellitus was defined as a self-reported history of type 2 diabetes mellitus, the use of glucose-lowering drugs or a fasting plasma glucose ≥ 7.0 mmol/L. Prediabetes was defined as fasting plasma glucose between 5.6 and 7.0 mmol/L. Cardiovascular disease was defined as (history of) myocardial infarction, angina, congestive heart failure, stroke, or peripheral vascular disease. HTGC was quantified by ¹H-MRS of the liver (1.5 Tesla whole-body MR scanner, Philips Medical Systems, the Netherlands).^[33] Participants with excessive alcohol consumption, defined as ≥ 30 g/day and ≥ 20 g/day for men and women, respectively, and participants with liver enzymes above the upper limit of normal (ULN) (ALT ≥ 45 U/L, aspartate aminotransferase [AST] ≥ 35 U/L and/or GGT ≥ 55 U/L for men and ALT ≥ 34 U/L, AST ≥ 31 U/L and/or GGT ≥ 38 U/L for women^[34]). The ULN of our academic hospital (LUMC) was used as reference. Participants without overweight (BMI <25 kg/m²) were excluded from final analyses.

2.2. Literature search

A literature search was performed which identified 59 biomarker scores, developed between 1988 and 2018, that predicted NAFLD, the precursor of MASLD.^[8,11,20,22,23,31,32,35–93] Fifty-four biomarker scores were excluded because they reported biomarkers not measured in the NEO study, had patented formulas, or had a lack of cutoff values for NAFLD. Finally, 4 combinations of biomarkers were suitable for investigation, namely the FLI,^[29] LFS,^[30] STEATO-ELSA^[31] and hepatic steatosis index.^[32] We use proxies for NAFLD to assess the presence of MASLD as previous studies have demonstrated that 98% to 99% of patients with NAFLD would fulfill the new criteria for MASLD.^[1,94]

2.3. Statistical analyses

Baseline characteristics were expressed as a mean with standard deviation (SD) when normally distributed, as a median with interquartile range (IQR) when not-normally distributed, or as a frequency accompanied by a percentage in categorical data. HTGC measured by ¹H-MRS was dichotomized, where a cutoff value of 5.56% or higher indicated MASLD.^[33] The following variables are reported for the entire study population and the groups after dichotomization for HTGC: age, sex, menopausal status, alcohol consumption, smoking behavior, height, body weight, BMI, waist and hip circumference, blood pressure, laboratory findings (fasting glucose, insulin, total cholesterol, low density lipoprotein and high density lipoprotein cholesterol, triglycerides and liver enzymes AST, ALT, and γ GT), homeostatic model assessment for insulin resistance, and factors of comorbidity and drug usage. To examine the performance of the aforementioned biomarker scores to rule in or rule out MASLD, sensitivity, specificity, predictive values and area under the curve (AUC) were calculated. Published cutoff values were used for each set of biomarkers.^[29–32,46] Both the lower (≥ 30) and higher (≥ 60) cutoffs were used for FLI.^[29] We stratified for sex to examine the accuracy of the sets of biomarkers in men and women separately.^[44,95] A logistic regression analysis was performed to evaluate predictive factors for MASLD.

For all analyses, STATA statistical software (StataCorp, College Station, TX), version 14 was used.

3. Results

3.1. Baseline characteristics of the study population

From the 6671 participants included in the NEO study, a random sample of 2083 participants without contra-indications for MRI were invited for ¹H-MRS. After exclusion because of excessive alcohol consumption ($n = 459$) and missing data ($n = 34$), 711 (45%) participants had an elevated HTGC ($n = 1590$). When subsequently excluding individuals with BMI $< 25 \text{ kg/m}^2$ ($n = 186$), or with liver enzymes outside the normal range ($n = 387$), 686 (50%) and 444 (37%) participants had an elevated HTGC, respectively. After exclusion of participants with BMI $< 25 \text{ kg/m}^2$ and liver enzymes outside the normal range, a total of 1017 participants were eligible to be included in the final analyses, of whom 424 (42%) had an elevated HTGC. The flow of inclusion is shown in Figure 1. All baseline characteristics are shown in Table 1.

Table 1 also shows the participants divided into 2 groups; with HTGC $< 5.56\%$ and HTGC $\geq 5.56\%$, defined as normal and elevated, respectively. In total, 424 (42%) participants had an elevated HTGC. There was a difference in age, with the group with elevated HTGC having a higher mean age, and the group with elevated HTGC had a higher percentage of men. Weight, BMI, and waist and hip circumference were higher in the participants with elevated HTGC. Median HTGC was 2.4% (IQR 1.6–3.7) and 11% (IQR 7.3–15.7) in the normal and elevated HTGC groups, respectively. More participants in the elevated HTGC group had metabolic syndrome (according to adult treatment panel III definition^[12]), type 2 diabetes mellitus, prediabetes and hypertension, 64% compared to 29%, 11%

compared to 5%, 40% compared to 26%, and 64% compared to 46% in the normal HTGC group, respectively.

3.2. Regression analysis

Table 2 shows the results of the multiple logistic regression analysis. The odds ratio (OR) of metabolic syndrome and BMI as a predictor for MASLD were 2.95 (95% confidence interval (CI) 2.20–3.98, $P < .00$) and 1.14 (95% CI 1.06–1.24, $P = .00$), respectively. Age and waist circumference were also statistically significant predictors of MASLD, both yielding an OR of 1.03 (95% CI 1.01–1.06, $P = .01$). The OR of type 2 diabetes mellitus as a predictor for MASLD was 1.18 (95% CI 0.69–2.03, $P = .55$) and thus not statistically significant. The OR of type 2 diabetes mellitus or prediabetes as a predictor for MASLD was 1.12 (95% CI 0.80–0.54, $P = .51$), see supplementary Table 3, <http://links.lww.com/MD/J692>.

3.3. Diagnostic accuracy

Table 3 shows the diagnostic accuracy of the 4 noninvasive biomarker scores compared to HTGC, for the entire studied population. Supplementary Tables 1, <http://links.lww.com/MD/J693> and 2, <http://links.lww.com/MD/J694> shows the diagnostic accuracy of the biomarker scores for men and women, respectively. The LFS had the biggest AUC both before (0.72 (95% CI 0.69–0.75)) and after stratification for sex (0.72 (95% CI 0.68–0.75)) and 0.72 (95% CI 0.68–0.76) for men and women, respectively).

4. Discussion

Although liver enzymes above the ULN are currently an indication for referral by general practitioners, in our study population of middle-aged people with overweight and, notably, liver enzymes within the normal range, 42% of participants had HTGC $\geq 5.56\%$ and could therefore be diagnosed with MASLD. This percentage was even higher among men, at 47%. Our findings demonstrate that relying upon liver enzymes as an indication for screening for MASLD will greatly underestimate the disease prevalence in this middle-aged population with overweight.

Our results complement the results of previously performed studies such as the Rotterdam study which sought to determine the prevalence of MASLD in an elderly population. In their cohort of 2811, 35.1% had MASLD, diagnosed using abdominal ultrasonography. Interestingly, in their cohort participants with MASLD had a median ALT of 21 U/L (IQR 16–17), whereas participants without MASLD had a median ALT of 17 U/L (IQR 14–21) which, although significantly different, is clinically irrelevant. AST was not significantly different between both groups.^[14] These findings, together with the prevalence of 42% found in our study cohort of individuals without liver test abnormalities, underscore the inability of liver enzymes to exclude disease. Most screening programmes for MASLD aim to detect severe stages of disease, such as significant ($\geq F2$) or even advanced ($\geq F3$) fibrosis.^[5,96] This follows

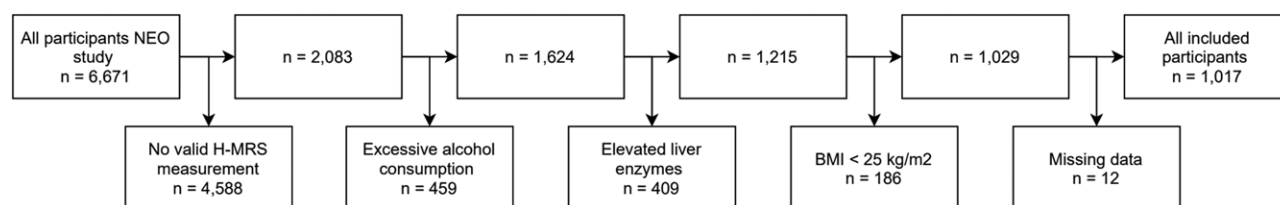


Figure 1. Flow chart of inclusion.

Table 1**Baseline demographics, clinical and histological characteristics of the participants, categorized by normal and increased HTGC.**

		All included participants (n = 1017)	HTGC < 5.56% (n = 593)	HTGC ≥ 5.56% (n = 424)	P value
Age, yr*		56 (50–61)	55 (49–60)	57 (51–62)	.00‡
Female, n (%)		503 (49.46)	323 (54.47)	180 (42.45)	.00§
Alcohol consumption	Alcohol intake per d, g/d*	5.06 (0.88;14.24)	4.73 (0.52–13.04)	5.84 (1.22–14.50)	.05‡
Smoking behavior	Never smoked, n (%)	414 (40.71)	261 (44.01)	153 (36.08)	.04§
	Former smoker, n (%)	479 (47.10)	266 (44.86)	213 (50.24)	
	Current smoker, n (%)	124 (12.19)	66 (11.13)	58 (13.68)	
Height, m*		1.73 (1.67–1.81)	1.72 (1.67–1.80)	1.75 (1.68–1.82)	.01‡
Weight, kg†		91.23 (13.12)	88.22 (11.94)	95.44 (13.54)	.00II
BMI, kg/m²*		29.59 (27.72–31.98)	28.90 (27.32–30.95)	30.73 (28.62–33.13)	.00II
Hepatic triglyceride content, %*		4.37 (2.15–9.09)	2.44 (1.57–3.69)	10.65 (7.27–15.69)	.00‡
Waist circumference, cm†		102.05 (10.27)	99.23 (9.46)	105.99 (10.07)	.00II
Hip circumference, cm†		110.65 (7.76)	109.62 (7.30)	112.09 (8.16)	.00II
Blood pressure	Systolic blood pressure, mm Hg†	132.32 (16.51)	129.70 (16.35)	136.00 (16.03)	.00II
	Diastolic blood pressure, mm Hg†	85.13 (10.30)	83.51 (10.40)	87.39 (9.72)	.00II
Laboratory findings	Fasting glucose, mmol/L*	5.41 (5.11–5.87)	5.30 (5.01–5.69)	5.63 (5.24–6.10)	.00‡
	Fasting insulin, mU/L*	10.40 (7.07–15.00)	8.75 (6.09–12.10)	13.40 (9.68–18.80)	.00‡
	Fasting total cholesterol, mmol/L†	5.63 (1.06)	5.63 (1.04)	5.64 (1.10)	.94II
	Fasting LDL cholesterol¶, mmol/L†	3.60 (0.98)	3.61 (0.96)	3.60 (1.00)	.83II
	Fasting HDL cholesterol, mmol/L†	1.38 (0.38)	1.46 (0.39)	1.27 (0.34)	.00II
	Fasting triglycerides, mmol/L*	1.27 (0.92–1.68)	1.11 (0.83–1.47)	1.46 (1.10–2.03)	.00‡
	ASAT, U/L*	22.10 (19.40–25.70)	21.80 (18.90–25.10)	22.70 (19.85–26.60)	.00‡
	ALAT, U/L*	22.60 (18.00–28.60)	20.80 (16.60–25.80)	25.80 (20.50–31.10)	.00‡
	γGT, U/L*	22 (16–30)	20 (14–27)	25 (20–33)	.00‡
HOMA-IR*		2.52 (1.68–3.74)	2.05 (1.43–2.99)	3.40 (2.39–4.97)	.00‡
Medical history	Metabolic syndrome#, n (%)	446 (43.85)	174 (29.34)	272 (64.15)	.00§
	Cardiovascular disease, n (%)	95 (9.34)	46 (7.76)	49 (11.56)	.04§
	Type 2 diabetes				
	Yes, n (%)	75 (7.37)	27 (4.55)	48 (11.32)	.00§
	Prediabetes, n (%)	323 (31.76)	154 (25.97)	169 (39.86)	
	No, n (%)	619 (60.08)	412 (69.48)	207 (48.82)	
	Hypertension, n (%)	543 (53.39)	272 (45.87)	271 (63.92)	.00§
Drugs usage	Lipid lowering drugs, n (%)	130 (12.78)	62 (10.46)	68 (16.04)	.01§
	Glucose lowering drugs, n (%)				
	None, n (%)	979 (96.26)	581 (97.98)	398 (93.87)	.00§
	Oral medication, n (%)	33 (3.24)	10 (1.69)	23 (5.42)	
	Oral medication and insulin, n (%)	5 (0.49)	2 (0.34)	3 (0.71)	
	Antihypertensive drugs, n (%)	267 (26.25)	128 (21.59)	139 (32.78)	.00§

HDL = high density lipoprotein, HOMA-IR = Homeostatic model assessment for insulin resistance, HTGC = hepatic triglyceride content, LDL = low density lipoprotein.

*Value not normally distributed, therefore presented as median with interquartile range (median [IQR]).

†Value normally distributed, therefore presented as means with standard deviation (mean [SD]).

‡Mann–Whitney *U* test.

§Chi-square test.

IIUnpaired *t* test.

¶Calculated using Friedewald formula.

#According to ATP III definition.^[12]**Table 2****Multiple logistic regression analysis.**

Variable	Units of increase	OR (95% CI)	Standard error	P value
BMI	1 kg/m²	1.143 (1.057–1.236)	0.046	.00
Sex	0 = male; 1 = female	0.720 (0.498–1.041)	0.136	.08
Age	1 yr	1.034 (1.010–1.058)	0.012	.01
Metabolic syndrome	0 = no; 1 = yes	2.952 (2.201–3.978)	0.442	.00
Type 2 diabetes mellitus	0 = no; 1 = yes	1.181 (0.686–2.032)	0.327	.55
Waist circumference	1 cm	1.032 (1.008–1.057)	0.013	.01
Hip circumference	1 cm	0.971 (0.941–1.002)	0.016	.07

BMI = body mass index, CI = confidence interval, OR = odds ratio.

Table 3

Diagnostic performance of biomarker scores compared to proton magnetic resonance spectroscopy (¹H-MRS).

		MASLD			Sens	Spec	PPV	NPV	AUC
		+	–	Total					
FLI	+	405	479	884	0.955 (0.931–0.973)	0.192 (0.161–0.226)	0.458 (0.425–0.492)	0.857 (0.786–0.912)	0.574 (0.555–0.592)
	–	19	114	133					
	Total	424	593	1017					
FLI	+	332	299	551	0.759 (0.716–0.799)	0.614 (0.573–0.653)	0.584 (0.542–0.626)	0.781 (0.741–0.818)	0.687 (0.645–0.726)
	–	102	364	466					
	Total	424	593	1017					
LFS	+	305	167	472	0.719 (0.674–0.762)	0.718 (0.680–0.754)	0.646 (0.601–0.689)	0.782 (0.745–0.816)	0.719 (0.691–0.747)
	–	119	426	545					
	Total	424	593	1017					
STEATO-ELSA	+	394	420	814	0.929 (0.901–0.952)	0.292 (0.255–0.330)	0.484 (0.449–0.519)	0.852 (0.796–0.898)	0.610 (0.588–0.633)
	–	30	173	203					
	Total	424	593	1017					
HSI	+	388	428	816	0.915 (0.884–0.940)	0.278 (0.243–0.316)	0.475 (0.441–0.510)	0.821 (0.761–0.871)	0.597 (0.574–0.619)
	–	36	165	201					
	Total	424	593	1017					

AUC = area under the curve, FLI = fatty liver index, HSI = hepatic steatosis index, LFS = liver fat score, NPV = negative predictive value, PPV = positive predictive value.

the notion that progression into fibrotic stages is strongly correlated with liver-related and overall mortality.^[16,17] Yet, MASLD is associated with adverse outcomes even before fibrosis occurs, and MASLD may be a precursor for the future development of metabolic syndrome components, including type 2 diabetes mellitus.^[97,98] Ultrasonographic changes in MASLD status over time may affect the risk of incident type 2 diabetes mellitus, hypertension and other components of the metabolic syndrome.^[98–101] This emphasizes the central role the liver plays within systemic homeostasis and underscores why MASLD should not be overlooked. Moreover, the finding of MASLD may encourage early lifestyle changes including increased physical activity, decreased caloric intake (especially fructose-containing beverages), and adherence to a healthier diet, such as a Mediterranean diet.^[102,103]

We identified the presence of metabolic syndrome as the prime predictor for MASLD. Participants who met the criteria for metabolic syndrome were at almost 3 times higher risk of MASLD than those who did not meet the criteria.^[12,104] BMI was also identified as a statistically significant predictor of MASLD with the chance of having MASLD increasing 1.14-fold for every added 1 kg/m². Surprisingly, type 2 diabetes mellitus and prediabetes were not statistically significant predictors for MASLD in our study population. Age, male sex and waist circumference were all statistically significant predictors of MASLD, but to a lesser extent than metabolic syndrome or BMI.

The LFS was best able to differentiate between participants with and without MASLD in our population with normal liver enzymes, as it yielded the largest AUC of the investigated biomarker scores. The other biomarker scores had low specificities and would thus lead to more excessive referral rates and diagnostic testing. It needs to be stressed that other diagnostic modalities, such as vibration controlled transient elastography (VCTE) which yields an AUC of 0.87 for the detection of >5% steatosis,^[105] outperform the studied sets of biomarkers. Moreover, VCTE may provide health care providers with an additional point of care effect as it allows for direct counseling of the patient and thus may aid in eventual lifestyle changes. Unfortunately, these more intricate diagnostic tools have limited availability, especially for general practitioners.^[96]

Of course, our study design comes with its limitations. Firstly, by excluding patients without overweight there is a clear oversampling of individuals with metabolic syndrome, type 2 diabetes mellitus and hypertension in our data compared to the general population. The study population, however, does represent a population at risk of MASLD. Enrollment for the NEO

study was limited to people between the ages of 45 and 65 years old. This limits the possibility of translating recommendations to the wider public as findings cannot be extrapolated to other age groups. An important strength of our study is the large number of participants and the robust assessment of hepatic steatosis using ¹H-MRS.

5. Conclusion

MASLD is taking epidemic forms and remains mostly undiagnosed and, therefore, untreated which may lead to severe consequences. Our data indicate that over 40% of individuals with overweight and between the ages of 45 and 65 years old may have undiagnosed MASLD, even when liver enzymes are within the normal range. In our NEO study cohort, the presence of metabolic syndrome was the biggest predictor for MASLD, followed by BMI and waist circumference. The LFS appears to be best able to detect MASLD in our study population. However, performance remains relatively poor compared to other noninvasive testing modalities such as VCTE.

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