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Developing a non-invasive algorithm for the diagnosis of steatotic liver disease in primary healthcare: a retrospective cohort study

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ABSTRACT

Objective This study aims to develop an algorithm to detect steatotic liver disease (SLD) risk in low-resource settings without requiring imaging.

Methods This retrospective cohort study included 826 measurements from 444 participants aged 45–60 years who participated in the MAUCO+ study. Data included ultrasound, vibration-controlled transient elastography (VCTE), anthropometrics and biomarkers. Logistic multivariable regression was used to develop two predictive models for SLD risk, with and without ultrasound, using VCTE as gold standard. Missing data were minimal and retained in the analysis, as their proportion was not statistically relevant. Predictive performance (sensitivity, specificity, positive predictive value and negative predictive value) was compared with the clinically used Fatty Liver Index (FLI).

Results The algorithm without ultrasound achieved a sensitivity of 81.1% (95% CI 71.7% to 88.4%) and specificity of 71.4% (95% CI 57.9% to 80.4%). The model with ultrasound demonstrated a sensitivity of 91.5% (95% CI 84.1% to 95.6%) and specificity of 70% (95% CI 59.9% to 80.7%). FLI showed an area under the curve (AUC) of 0.762, while our models achieved higher AUCs: 0.878 (with ultrasound) and 0.794 (without ultrasound).

Discussion Our models offer screening tools for SLD in low-resource primary care. The model without ultrasound outperformed FLI, making it a feasible alternative where imaging is unavailable. The ultrasound-based model demonstrated higher performance, underscoring the value of ultrasound when it is accessible. Integrating these algorithms into preventive programmes could improve early diagnosis, especially in populations with a high burden of obesity and diabetes.

Conclusions We developed two predictive models for SLD screening in a Chilean cohort. Both showed strong performance and potential for implementation in primary care to support early detection and better disease management.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Steatotic liver disease (SLD) is highly prevalent in regions like Latin America and is often underdiagnosed in early stages.
⇒ There is a lack of scalable tools for early detection of SLD in low-resource settings, particularly those that can be integrated into primary care infrastructure without requiring advanced imaging.
⇒ Most predictive algorithms for SLD, including the widely used Fatty Liver Index (FLI), were developed in non-Latin American populations and focus on preventing fibrosis rather than early detection.

WHAT THIS STUDY ADDS

⇒ This study developed two predictive models for SLD using data from a Chilean population: one based on clinical and laboratory parameters and the other incorporating ultrasound.
⇒ Both models outperformed the FLI, commonly used in clinical settings, in terms of sensitivity and specificity, with the ultrasound model achieving excellent performance and the non-ultrasound model providing a viable alternative in settings where imaging is not available.
⇒ The models rely on routinely available data in primary healthcare, making them feasible for implementation in public health programmes in Chile and similar contexts.

INTRODUCTION

Steatotic liver disease (SLD) has emerged as a global health priority due to its rising prevalence and association with metabolic risk factors.[1 2] The term SLD adopted in 2023 encompasses a spectrum of subcategories, including metabolic-associated steatotic liver disease (MASLD), metabolic and alcohol-associated liver disease (MetALD), alcohol-associated liver disease (ALD), Specific aetiologies and Cryptogenesis.[3] The distinction between these entities lies primarily in their cause: MASLD occurs in individuals with cardiometabolic dysfunction; MetALD combines cardiometabolic dysfunction

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ These findings support the adoption of SLD screening strategies tailored to local resource availability, thereby addressing a significant gap in liver disease detection in Chile.

⇒ The algorithms could be integrated into Chile's existing adult preventive health primary care programmes, enabling the early identification and management of individuals at risk of SLD, without incurring significant additional costs to the public health system.

⇒ This approach may guide future public health policy and inform scalable screening programmes for SLD in Latin American countries.

with moderate alcohol consumption; ALD results from chronic high alcohol intake; while the remaining categories are linked to specific diseases or remain of unknown origin.[3] MASLD, formerly known as non-alcoholic fatty liver disease (NAFLD),[4] represents the most common form of SDL, affecting approximately 25–30% of the global population.[1 5] Rates of MASLD are particularly high in regions experiencing rapid increases in obesity and type 2 diabetes, such as Latin America.[6 7] Within this region, Chile stands out, with MASLD prevalence rising from 23% among adults aged over 18 years in 2000[8] to 47.5% in adults aged 40–74 years by 2019.[9] These trends underscore a pressing need for public health strategies and diagnostic screening tools to address the growing burden of SLD.

Despite the high burden of disease,[10] early diagnosis of SLD remains challenging. The diagnosis of SLD relies on the presence of hepatic steatosis, defined as fat in more than 5% of hepatocytes.[8 11] Hepatic steatosis is often clinically silent and is frequently identified incidentally or during investigation of abnormal liver tests. Although simple steatosis can be relatively benign, approximately 10–30% of patients progress to stages characterised by inflammation and hepatocellular damage, of whom 25–40% develop some degree of fibrosis and up to 30% progress to cirrhosis.[12] The Latin American Association for the Study of the Liver guidelines highlight that it is typically triggered by three clinical scenarios: altered liver function tests, incidental imaging findings or targeted screening of high-risk populations.[13]

Liver biopsy remains the gold standard for assessing hepatic steatosis and fibrosis.[11] However, its invasive nature, risk of complications and high costs make it unsuitable for large-scale or routine use, particularly in primary healthcare settings.[11 14] Consequently, non-invasive imaging techniques have been developed as alternatives. Ultrasonography is the most widely used due to its non-invasiveness and lower cost; it has limitations in sensitivity and specificity, particularly in the early stages of the disease.[14] Computed tomography (CT) and Magnetic Resonance Imaging (MRI) provide greater sensitivity for detecting minimal fat deposits but are cost-prohibitive and often inaccessible in public health systems.[15] Techniques like vibration-controlled transient elastography (VCTE) combine controlled attenuation parameters (CAP) and elastography to measure steatosis and fibrosis, respectively, showing moderate to high sensitivity and specificity. Current guidelines in the USA and Europe recommend using elastography to diagnose liver steatosis; however, this technology is not routinely available worldwide.[3 16]

Diagnostic algorithms are commonly used in clinical practice as a screening tool, supporting diagnosis and treatment decisions while reducing clinical uncertainty. Model-based algorithms, scores and decision trees are most frequently employed.[17] Given the need to identify at-risk individuals, algorithms are typically designed to prioritise high sensitivity at the expense of specificity, resulting in more false positives but minimising the risk of missed cases.[18] Despite the abundance of algorithm models for SLD, their complexity often limits clinical implementation, favouring simpler scores that rely on easily measured laboratory or anthropometric parameters. Various scores have been proposed for diagnosing fibrosis, including Fibrosis 4,[19] BARD[20] and the NAFLD scale for fibrosis[21]. However, very few scores exist for steatosis, aside from the Fatty Liver Index (FLI).[22] Moreover, these scores were predominantly developed and validated in North American, European or Asian populations, raising concerns about their applicability to Latin American settings.

This study aims to develop a predictive algorithm for screening SLD in Chile, focusing on low-resource settings where advanced imaging technologies are not available. Using a retrospective cohort, we analysed clinical, anthropometric and biochemical data from adults participating in the Maule cohort (MAUCO)+ study, using VCTE as the reference for SLD diagnosis. By integrating accessible diagnostic tools and clinical parameters from Chilean primary healthcare, we aim to enhance early detection in high-risk populations. This approach will help classify patients, guiding clinical decision-making and optimising resource allocation. The findings will contribute to better management of SLD, potentially reducing its progression to more severe stages and associated complications.

METHODS

Study population and design

This study is based on data from the MAUCO+ study, a clinical trial nested within the MAUCO cohort, a prospective population-based cohort initiated in 2014 that follows adults aged 38–74 years located in the Maule Region, Chile.[23] In 2021, MAUCO+ study launched a clinical trial aimed at preventing SLD and cardiovascular disease through lifestyle interventions. The trial seeks to improve sarcopenia, aerobic capacity, body composition, lipid profile, insulin resistance, cardiovascular risk and SLD, while promoting a long-term adoption of healthier lifestyle behaviours through physical activity and nutritional programmes (ClinicalTrials.gov Identifier: NCT05618626). For this analysis, we conducted a retrospective cohort study using baseline and follow-up data collected within the MAUCO+ study.

MAUCO+ study enrolled 444 participants aged 45–60 years with varying degrees of SLD who were not taking medications that affected muscle mass or liver function, and who did not have severe disease or physical conditions that could interfere with the intervention. Participants were invited to join the study and provided written informed consent before enrolment. Trained health technicians administered a health survey, including history of diabetes, hypertension, hepatitis, cancer, medication, alcohol consumption and smoking history, along with sociodemographic information (sex, age, education level and income) and lifestyle data. Anthropometric measurements were collected (height, weight, waist, hip and neck circumference), along with bioelectrical impedance analysis, grip strength testing, step speed and blood pressure measurements. Blood samples were obtained for clinical testing, including fasting glucose, insulin, haemoglobin A1c (HbA1c), homeostatic model assessment for insulin resistance (HOMA-IR), platelet count, high-sensitivity C-reactive protein (CRP), lipid profile (high-density

Table 1 Clinical parameters of the 826 measurements from MAUCO+ study

Health profile		None (n=418)	Mild (n=190)	Moderate (n=111)	Severe (n=107)	Missing*
Age, mean (SD)		54.1 (4.3)	54.3 (4.2)	54.1 (4.1)	53.7 (4.5)	0.1
Sex	Men	102 (24.4)	69 (36.3)	49 (44.1)	52 (48.6)	0.0
	Women	316 (75.6)	121 (63.7)	62 (55.9)	55 (51.4)	
BMI	<25 kg/m^2	66 (15.8)	4 (2.1)	3 (2.7)	1 (0.9)	0.1
	≥25 kg/m^2	351 (84.2)	186 (97.9)	108 (97.3)	106 (99.1)	
Waist circumference‡		366 (88.6)	179 (94.2)	105 (96.3)	104 (100)	1.2
Diabetes†		17 (4.1)	24 (12.7)	18 (16.2)	47 (43.9)	0.1
Pre-diabetes§		79 (19.7)	55 (33.3)	42 (45.2)	31 (51.7)	13.0
Glycaemia (mean (SD))		96.2 (23.2)	106.4 (31.4)	111.9 (40.0)	138.7 (58.9)	0.1
Insulin (mean (SD))		10.2 (7.4)	15.7 (9.7)	18.7 (14.2)	23.5 (16.4)	0.4
ALT (mean (SD))		24.4 (12.1)	26.8 (14.1)	33.1 (25.5)	37.0 (29.6)	0.2
AST (mean (SD))		30.3 (22.2)	37.8 (28.2)	47.0 (34.9)	53.5 (45.0)	0.2
GGT (mean (SD))		34.0 (35.6)	31.7 (22.7)	43.9 (33.8)	63.7 (65.2)	0.2
Total bilirubin		0.5 (0.2)	0.5 (0.3)	0.6 (0.3)	0.5 (0.2)	0.2
Total cholesterol		194.3 (38.2)	197.1 (42.1)	196.1 (38.1)	182.4 (37.4)	0.2
Low HDL¶		192 (45.9)	103 (54.8)	68 (61.3)	80 (74.8)	0.2
C-reactive protein (mean (SD))		0.3 (0.4)	0.3 (0.4)	0.4 (0.4)	0.5 (0.4)	0.4
Ultrasonography	None	301 (71.8)	40 (21.2)	1 (0.9)	2 (1.9)	0.2
	Mild	92 (22.0)	90 (47.6)	36 (32.4)	16 (15.1)	
	Moderate	24 (5.7)	57 (30.2)	71 (64.0)	67 (63.2)	
	Severe	1 (0.2)	2 (1.1)	3 (2.7)	21 (19.8)	
Controlled attenuation parameter	S0	418 (100.0)	10 (5.3)	0 (0.0)	6 (5.6)	0.0
	S1	0 (0.0)	180 (94.7)	2 (1.8)	4 (3.7)	
	S2	0 (0.0)	0 (0.0)	109 (98.2)	6 (5.6)	
	S3	0 (0.0)	0 (0.0)	0 (0.0)	91 (85.0)	
Elastography	Fib1	418 (100.0)	172 (90.5)	94 (84.7)	62 (57.9)	0.0
	Fib2	0 (0.0)	18 (9.4)	11 (9.9)	19 (17.8)	
	Fib3	0 (0.0)	0 (0.0)	6 (5.4)	6 (5.6)	
	Fib4	0 (0.0)	0 (0.0)	0 (0.0)	20 (18.7)	

Absolute numbers are present with their percentages in parentheses unless the mean value is indicated.
*Missings are presented as percentages.
†Diabetes: fasting glucose ≥126 mg/dL or specific drug treatment.
‡Waist circumference: ≥80 cm women, ≥94 cm men.
§Pre-diabetes: fasting glucose 100–125 mg/dL.
¶HDL cholesterol ≤50 mg/dL women, ≤40 mg/dL men.
ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; Fib, Fibrosis; GGT, gamma-glutamyl transferase; HDL, high-density lipoprotein; MAUCO+, MAUCO+ interventional study.

Table 2 Parameters of the predictive model for the risk of SLD without ultrasound

Parameter		OR	CI (95%)	P value
Intercept		0.009	0.0006 to 0.14	<0.001*
Sex (ref. female)		0.762	0.49 to 1.17	0.218
Age		1.004	0.96 to 1.05	0.851
BMI (≥25 kg/m^2) (ref <25 kg/m^2)		3.563	1.52 to 9.59	<0.01*
Bilirubin total (mg/dL)		1.740	0.85 to 3.60	0.132
Cholesterol total/HDL (mg/dL)		1.347	1.13 to 1.60	<0.001*
Insulin (mg/dL)		1.088	1.06 to 1.12	<0.001*
CRP ≥0.2 mg/dL (ref. <0.2 mg/dL)		1.857	1.25 to 2.77	<0.01*
ALT >31 U/L (ref. ≤31 U/L)		1.870	1.28 to 2.73	<0.01*
Diabetes (ref. glycaemia<100 (mg/dL)	Glycaemia ≥100–<126 (mg/dL)	1.937	1.26 to 2.98	<0.001*
	Glycaemia ≥126 (mg/dL)	3.124	1.61 to 6.33	<0.001*

*Statistical significance.
ALT, alanine aminotransferase; BMI, body mass index; CRP, C-reactive protein; HDL, high-density lipoprotein; SLD, steatotic liver disease.

lipoprotein (HDL) cholesterol, total cholesterol, triglycerides), indirect, direct and total bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT) and gamma-glutamyl transferase (GGT). In addition, participants underwent abdominal ultrasound and VCTE assessments to determine the presence and degree of SLD.

Following the baseline evaluation, participants were randomly assigned to either a control group or an intervention group. The control group received standard prevention recommendations based on clinical test results and educational materials on nutrition and physical activity. The intervention group underwent a 6-month personalised physical activity and nutritional plan. Follow-up visits were scheduled at 6, 12, 24 and 36 months, during which both groups repeated the exact studies performed at baseline.

Diagnosis of liver steatosis

Liver steatosis was ascertained through VCTE. The degree of steatosis was classified using CAP measured in dB/m. The classification is as follows: a CAP value of 0–274 dB/m indicates less than 5% steatosis, classified as stage S0 (none); a value of 275–300 dB/m indicates 5–33% steatosis, classified as stage S1 (mild); a CAP value of 301–324 dB/m indicates 34–65% steatosis, corresponding to stage S2 (moderate); and a CAP value of 325 dB/m or higher indicates 66% or more steatosis, corresponding to stage S3 (severe).[16] VCTE elastography was used to classify the presence and severity of hepatic fibrosis, measured in kPa. Depending on abdominal adiposity, different probes were used. For none to mild abdominal adiposity, the M probe was used. Fibrosis classification for the M probe is as follows: 0–7.4 kPa corresponds to stage F1 (no liver fibrosis); 7.5–9.5 kPa corresponds to stage F2 (mild fibrosis); 9.6–11.8 kPa corresponds to stage F3 (moderate fibrosis); and 11.9 kPa or higher corresponds to stage F4 (severe fibrosis).[16] The XL probe was used for higher abdominal adiposity, with the following classification: 0–6.3 kPa corresponds to stage F1 (no liver fibrosis); 6.4–8.4 kPa corresponds to stage F2 (mild fibrosis); 8.5–10.4 kPa corresponds to stage F3 (moderate fibrosis); and 10.5 kPa or higher corresponds to stage F4 (severe fibrosis).[16]

We also assessed liver steatosis diagnosis through ultrasound using Siemens ACUSON P500 and P300 portable machines. Liver steatosis was defined by increased liver echogenicity compared with the kidney. The radiology technician observed the liver parenchyma, and if it appeared more echogenic than the renal cortex ('brighter'), steatosis was confirmed.[24] To determine the degree of steatosis, the radiology technician assessed whether the right hemidiaphragm could be resolved separately from the liver dome. If the structures were resolvable, the condition was classified as 'mild'; if they could be partially distinguished, it was classified as 'moderate'; and if they could not be distinguished, it was classified as 'severe'.[24] Liver steatosis was defined as normal, mild, moderate or severe based on the Rumack criteria.[25] To ascertain the reliability of the ultrasound and VCTE readings, both techniques were performed by the same radiology technician and supervised by a radiologist.

Statistical analysis

Predictive models were developed using multivariable logistic regression with VCTE as the gold standard. We created two models to assess the risk of SLD: one that included ultrasound results and one that did not. Both models predicted the risk of SLD as a binary outcome (0=no risk, 1=risk). Variables initially considered for the model included body mass index (BMI), body roundness index,[26] waist and hip circumference, biomarkers (liver enzymes (GGT, AST, ALT), lipid profile, glycaemia, insulin, HbA1c, HOMA-IR, bilirubin (indirect, direct, total), cholesterol (HDL and total), platelet count, CRP), age and sex. Continuous and categorical variables were

Table 3 Diagnostic accuracy of the predictive model for SLD

Model	Sample	Sensitivity	Specificity	PPV*	NPV*	Youden index
Risk of SLD without ultrasound	820	81.1% (71.7% to 88.4%)	71.4% (57.9% to 80.4%)	79.4%	73.5%	0.52
Risk of SLD with ultrasound	820	91.5% (84.1% to 95.6%)	71.4% (59.9% to 80.7%)	81.1%	86.2%	0.63
Fatty Liver Index	814	80.3% (76.1% to 84.1%)	52.8% (47.8% to 57.7%)	62.3%	73.4%	0.36

NPV, negative predictive value; PPV, positive predictive value; SLD, steatotic liver disease.

standardised or dummy-coded as appropriate. These variables were entered into a stepwise regression analysis, and then manual selection was performed based on biological plausibility and previous literature. Potential confounding was minimised by including biologically relevant variables known to influence SLD risk and by ensuring measurement consistency across all participants. Overfitting was assessed through internal validation, and the models demonstrated stable performance across training and test sets. Missing data were minimal and retained in the analysis, as their proportion was not statistically significant.

To identify the best-fitting model, we used the area under the curve (AUC). The AUC was interpreted as follows: 0.5=no discrimination, 0.7–0.8=acceptable, 0.8–0.9=excellent and 0.9–1.0=outstanding discrimination.[27] Discrimination was evaluated using the AUC with 95% CIs, estimated by the DeLong method. The same logistic regression methodology was applied to the predictive model, including ultrasound as a predictor variable. The dataset was randomly divided into a training set (80%) and a test set (20%) for internal validation. Collinearity among predictors was assessed using the generalised variance inflation factor (GVIF), adjusted for each variable's degree of freedom ($GVIF^{1/(2xDf)}$); all predictors presented adjusted GVIF values <1.2, indicating no multicollinearity (online supplemental table S1). Model calibration was assessed using the calibration intercept and slope from logistic recalibration, the Brier Score and the Hosmer-Lemeshow goodness-of-fit test (10 risk deciles)[28–30] (online supplemental figure S1). Sensitivity, specificity, 95% CI, positive predictive value (PPV) and negative predictive value (NPV) were calculated for each model. The optimal risk threshold for SLD classification was determined using the Youden Index (sensitivity+specificity − 1), identifying the cut-off point that best balances sensitivity and specificity for each model.[31]

We then compared the performance of our models to the FLI, a commonly used clinical algorithm that classifies patients into three groups: low (<30), indicating no risk of liver steatosis; indeterminate (30 to <60), where the risk of steatosis cannot be ruled in or out; and high (≥60), indicating a high risk of liver steatosis.[22] We applied the algorithm to our sample and obtained sensitivity, specificity, 95% CI, PPV and NPV. Receiver operating characteristic (ROC) curves were generated for each model to assess discriminative performance, and the AUC was used as a summary measure of diagnostic accuracy. All statistical analyses were performed using R software V.1.4.1106 (RStudio, PBC), employing the packages *'tidyverse', 'pROC', 'car', 'ResourceSelection'* and *'glmnet'*.[32]

Table 4 Parameters of predictive models for risk of SLD with ultrasound

Parameter	OR	CI (95%)	P value
Intercept	0.13	0.009 to 1.74	0.124
Sex (ref. female)	0.63	0.41 to 0.97	<0.05*
Age	0.99	0.95 to 1.04	0.816
Ultrasound Steatosis (ref. normal)	13.85	8.95 to 21.92	<0.001*
Insulin (mg/dL)	1.07	1.04 to 1.11	<0.001*

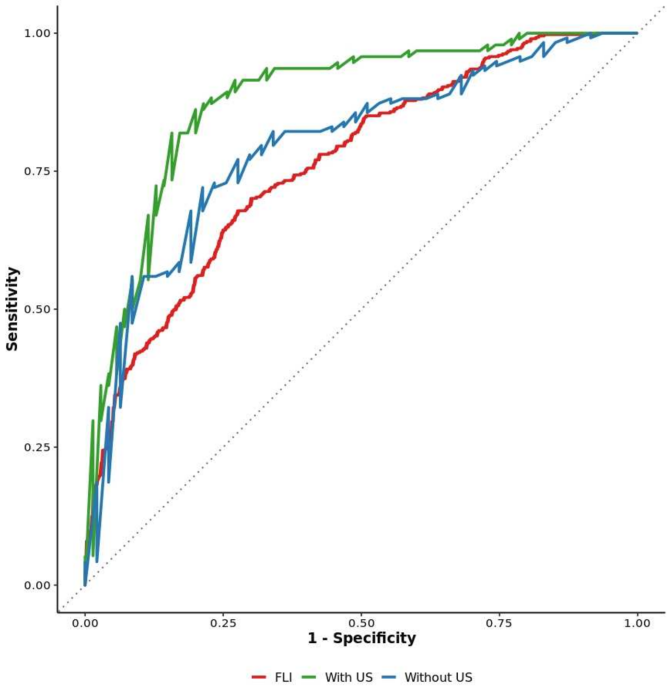
*Statistical significance.
SLD, steatotic liver disease.

RESULTS

The study included 826 measurements from 444 participants in the MAUCO+ study (online supplemental figure S2). All measurements were considered independent. The distribution was as follows: 418 (50.6%) had no SLD, 190 (23.0%) had mild SLD, 111 (13.4%) had moderate SLD and 107 (13.0%) had severe SLD. Across all groups, a higher percentage of participants were women, with a mean age of approximately 54 years. Health profiles showed that participants without steatosis had slightly better profiles than those with mild disease. In contrast, those with moderate and severe disease had higher rates of diabetes, pre-diabetes, obesity, dyslipidaemia, elevated hepatic enzymes and elevated CRP (table 1).

Model without ultrasound

The model without ultrasound included sex (0=women, 1=men), age, BMI (0=<25 kg/m², 1=≥25 kg/m²), total bilirubin (mg/dL), total cholesterol divided by HDL (mg/dL), insulin (mg/dL), CRP (0=≤0.2 mg/dL, 1=>0.2 mg/dL), GPT (0=≤31 U/L, 1=>31 U/L) and diabetes status (0=glycaemia <100 mg/dL, 1=glycaemia 100–125 mg/dL, 2=glycaemia ≥126 mg/dL) (table 2). This model, incorporated 820 measurements, achieved a sensitivity of 81.1% (95% CI 71.7% to 88.4%) and a specificity of 71.4% (95%



Predictive model	AUC
Risk of SLD without ultrasound (US)	0.794
Risk of SLD with ultrasound (US)	0.878
Fatty liver Index (FLI)	0.762

Figure 1 Comparison of ROC curves of the predictive models without and with US and FLI. AUC, area under the curve; ROC, receiver operating characteristic; SLD, steatotic liver disease.

CI 57.9% to 80.4%), with a PPV of 79.4% and an NPV of 73.5% (table 3).

Models with ultrasound

The model incorporating ultrasound findings included sex (0=women, 1=men), age, ultrasound-detected steatosis (0=none, 1=presence of steatosis) and insulin (mg/dL) (table 4). Applied to 820 measurements, this model achieved a sensitivity of 91.5% (95% CI 84.1% to 95.6%) and a specificity of 71.4% (95% CI 59.9% to 80.7%), with a PPV of 81.1% and an NPV of 86.2% (table 3).

Comparison with Fatty Liver Index

The FLI was applied to 814 (98.5%) cohort measurements. Of these, 97 (11.9%) were classified as low-risk, 200 (24.5%) as indeterminate and 517 (63.5%) as high-risk. The FLI identified the risk of SLD with a sensitivity of 80.3% (95% CI 76.1% to 84.1%), a specificity of 52.8% (95% CI 47.8% to 57.7%), a PPV of 62.3% and an NPV of 73.4% (table 3).

When comparing the performance of our models against the FLI, the ROC curves indicated that our algorithms performed better (figure 1). The model with ultrasound achieved an AUC of 0.878, indicating excellent discriminative ability, while the model without ultrasound had an AUC of 0.794, and the FLI had an AUC of 0.762, both of which reflect acceptable discrimination. The Youden Index was highest for the model with ultrasound, 0.63, followed by the model without ultrasound, 0.52, and the FLI (0.36) (table 3), indicating better diagnostic performance of the new models compared with the existing algorithm.

DISCUSSION

Our study aimed to develop predictive models for diagnosing SLD in a Chilean population, with a particular focus on low-resource settings where advanced imaging technologies, such as VCTE, are not available. We used a combination of clinical parameters, biomarkers and ultrasound, all of which are accessible in primary healthcare settings, to develop these models. The results demonstrated that both models provided high sensitivity and specificity for screening and detection of SLD.

Although the model including ultrasound achieved better performance, the one without ultrasound also had an acceptable performance, outperforming the clinically used FLI. Notably, the non-ultrasound model is based on routine clinical and laboratory data available from primary care settings. While the ultrasound-based model demonstrated better performance, one of the main challenges of implementing it is the limited availability of trained personnel to perform abdominal ultrasounds in primary care centres, where radiologists are often scarce.[14 15] Training other healthcare professionals, such as radiology technologists, mitigates this gap. Although the World Health Organization (WHO) has suggested shifting tasks such as imaging techniques to highly qualified healthcare professionals, like radiology technicians, to increase diagnostic efficiency,[33] training costs and infrastructure limitations may not be feasible in all settings. In this context, having a predictive model that does not rely on ultrasound could enhance early detection of SLD in primary healthcare.

Early detection of SLD is crucial, as the condition often progresses silently and is frequently diagnosed incidentally through abnormal liver enzymes or imaging studies.[12] Lifestyle changes can reverse hepatic steatosis in its early stages.[34] In comparison, treating advanced fibrosis or cirrhosis requires substantial weight loss and intensive interventions, which are significantly more challenging to achieve.[35] Therefore, implementing algorithms at the primary care level could help prevent disease progression, reduce the burden of advanced liver disease, lower healthcare costs and promote healthier lifestyles. Importantly, developing an algorithm tailored explicitly to the Chilean population is particularly important, as most existing models, including the widely used FLI, were developed in European, North American or Asian populations and may not accurately capture the risk profiles of Latin American populations. Several studies have explored machine learning-based approaches for predicting hepatic steatosis in non-Latin American regions.[36–39] Although these tools demonstrate strong predictive accuracy, they have not yet been validated in Latin American populations and often rely on data sources that are not consistently available in primary

healthcare settings. In contrast, the FLI remains the most widely used and guideline-endorsed clinical tool for steatosis screening because it relies on four simple, universally available variables.[13 16 40] For this reason, FLI was selected as the comparator in our study to ensure clinical relevance and comparability with existing clinical practice.

We acknowledged that our study has limitations. First, the predictive models were developed and internally validated within the MAUCO+ study, a high-risk population with elevated rates of chronic diseases. Generalisability of the findings to other Chilean populations or regions with different epidemiological profiles may be limited. However, it is essential to note that the burden of risk factors for SLD is not confined to the MAUCO+ study: the 2017 Chilean National Health Survey reported high prevalence of diabetes, obesity and hypertension,[41] all well-established risk factors for SLD. These findings highlight the elevated burden of metabolic risk factors in Chile and the critical need to implement systematic screening strategies specifically targeting high-risk groups.[42] Second, although internal validation was performed, external validation in independent cohorts is necessary to confirm the robustness and applicability of our models. Furthermore, future implementation studies are warranted to assess the feasibility, acceptability and clinical impact of these predictive models in real-world primary healthcare settings. The next step will be to integrate the algorithm into electronic health records, enabling automated risk estimation and identification of patients with SLD risk during routine clinical encounters. This phase will evaluate usability and workflow integration, while continuous data collection from primary care will allow recalibration and improvement of predictive accuracy, ensuring long-term sustainability and clinical utility. Integrating these models into Chile's preventive health framework, particularly the *Examen de Medicina Preventiva del Adulto*,[43] a national programme that provides standardised annual check-ups for adults to detect chronic diseases and related risk factors, would require minimal adaptation, as all input variables are already routinely collected in primary care. Implementation would primarily involve configuring the software and providing brief training to providers on interpretation and follow-up. Given the existing infrastructure, the additional cost of integration would likely be low relative to the potential savings from preventing advanced liver disease and its complications. External validation in urban Chilean and other Latin American populations will further strengthen generalisability and regional adoption. Third, while VCTE was used as the reference standard for diagnosing hepatic steatosis, liver biopsy, the true gold standard, was not feasible due to its invasive nature. Nevertheless, VCTE has been widely validated and recommended by international guidelines from the USA, Europe and Latin America as an accurate tool for SLD diagnostics.[13 16 40]

Despite these limitations, our study is the first to develop and compare predictive models for SLD screening using data from a Chilean cohort. This approach enhances the potential for early diagnosis and meaningful public health impact.

CONCLUSION

Developing a simple and accessible tool for early detection of SLD represents a significant advance for primary healthcare, particularly in low-resource settings. Early diagnosis through these models could enable timely clinical intervention, reduce progression and decrease the burden of liver-related morbidity and mortality. Integrating these algorithms into existing preventive programmes could optimise resource allocation and strengthen public health strategies to combat the growing epidemic of metabolic and liver diseases in Chile and Latin America.[6]

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REFERENCES

1 Barrera F, Uribe J, Olvares N, *et al*. The Janus of a disease: Diabetes and metabolic dysfunction-associated fatty liver disease. *Ann Hepatol* 2024;29:101501.
2 Younossi Z, Henry L. Contribution of Alcoholic and Nonalcoholic Fatty Liver Disease to the Burden of Liver-Related Morbidity and Mortality. *Gastroenterology* 2016;150:1778–85.
3 Rinella ME, Lazarus JV, Ratziu V, *et al*. A multisociety Delphi consensus statement on new fatty liver disease nomenclature. *Ann Hepatol* 2024;29:101133.
4 Chen L, Tao X, Zeng M, *et al*. Clinical and histological features under different nomenclatures of fatty liver disease: NAFLD, MAFLD, MASLD and MetALD. *J Hepatol* 2024;80:e64–6.
5 Younossi ZM, Golabi P, de Avila L, *et al*. The global epidemiology of NAFLD and NASH in patients with type 2 diabetes: A systematic review and meta-analysis. *J Hepatol* 2019;71:793–801.
6 Díaz LA, Villota-Rivas M, Barrera F, *et al*. The burden of liver disease in Latin America. *Ann Hepatol* 2024;29:101175.
7 Pinto Marques Souza de Oliveira C, Pinchemel Cotrim H, Arrese M. Nonalcoholic Fatty Liver Disease Risk Factors in Latin American Populations: Current Scenario and Perspectives. *Clin Liver Dis (Hoboken)* 2019;13:39–42.
8 Riquelme A, Arrese M, Soza A, *et al*. Non-alcoholic fatty liver disease and its association with obesity, insulin resistance and increased serum levels of C-reactive protein in Hispanics. *Liver Int* 2009;29:82–8.
9 Ferreccio C, Huidobro A, Cortés S, *et al*. Cohort Profile: The Maule Cohort (MAUCO). *Int J Epidemiol* 2020;49:760–761i.
10 Stepanova M, Henry L, Younossi ZM. Economic Burden and Patient-Reported Outcomes of Nonalcoholic Fatty Liver Disease. *Clin Liver Dis* 2023;27:483–513.
11 Romero-Gomez M. *NAFLD and NASH: Biomarkers in Detection, Diagnosis and Monitoring*. Springer International Publishing, 2020.
12 Dyson JK, Anstee QM, McPherson S. Non-alcoholic fatty liver disease: a practical approach to diagnosis and staging. *Frontline Gastroenterol* 2014;5:211–8.
13 Arab JP, Dirchwolf M, Álvares-da-Silva MR, *et al*. Latin American Association for the study of the liver (ALEH) practice guidance for the diagnosis and treatment of non-alcoholic fatty liver disease. *Ann Hepatol* 2020;19:674–90.
14 Castera L, Vilgrain V, Angulo P. Noninvasive evaluation of NAFLD. *Nat Rev Gastroenterol Hepatol* 2013;10:666–75.
15 Haas JT, Francque S, Staels B. Pathophysiology and Mechanisms of Nonalcoholic Fatty Liver Disease. *Annu Rev Physiol* 2016;78:181–205.
16 Berzigotti A, Tsochatzis E, Boursier J, *et al*. EASL Clinical Practice Guidelines on non-invasive tests for evaluation of liver disease severity and prognosis – 2021 update. *J Hepatol* 2021;75:659–89.
17 Qian L, Wu L, Zhang L, *et al*. Serum biomarkers combined with ultrasonography for early diagnosis of non-alcoholic fatty liver disease confirmed by magnetic resonance spectroscopy. *Acta Pharmacol Sin* 2020;41:554–60.
18 World Health Organization. Increase effectiveness, maximize benefits and minimize harm screening programmes: a short guide. 2020. Available: https://iris.who.int/bitstream/handle/10665/330829/9789289054782-eng.pdf [Accessed 26 Apr 2025].
19 Sterling RK, Lissen E, Clumeck N, *et al*. Development of a simple noninvasive index to predict significant fibrosis in patients with HIV/HCV coinfection. *Hepatology* 2006;43:1317–25.
20 Harrison SA, Oliver D, Arnold HL, *et al*. Development and validation of a simple NAFLD clinical scoring system for identifying patients without advanced disease. *Gut* 2008;57:1441–7.
21 Angulo P, Hui JM, Marchesini G, *et al*. The NAFLD fibrosis score: a noninvasive system that identifies liver fibrosis in patients with NAFLD. *Hepatology* 2007;45:846–54.
22 Bedogni G, Bellentani S, Miglioli L, *et al*. The Fatty Liver Index: a simple and accurate predictor of hepatic steatosis in the general population. *BMC Gastroenterol* 2006;6:33.
23 Ferreccio C, Roa JC, Bambs C, *et al*. Study protocol for the Maule Cohort (MAUCO) of chronic diseases, Chile 2014-2024. *BMC Public Health* 2016;16:1–7.
24 Hamaguchi M, Kojima T, Itoh Y, *et al*. The severity of ultrasonographic findings in nonalcoholic fatty liver disease reflects the metabolic syndrome and visceral fat accumulation. *Am J Gastroenterol* 2007;102:2708–15.
25 Rumack CM, Wilson SR, Charboneau JW, *et al*. *Diagnostic Ultrasound*. 4th edn. 2011.
26 Zhang X, Ma N, Lin Q, *et al*. Body Roundness Index and All-Cause Mortality Among US Adults. *JAMA Netw Open* 2024;7:e2415051.
27 Mandrekar JN. Receiver operating characteristic curve in diagnostic test assessment. *J Thorac Oncol* 2010;5:1315–6.
28 Steyerberg EW. Clinical Prediction Models. 2009.
29 Surjanovic N, Loughin TM. Improving the Hosmer-Lemeshow goodness-of-fit test in large models with replicated Bernoulli trials. *J Appl Stat* 2024;51:1399–411.
30 Rufibach K. Use of Brier score to assess binary predictions. *J Clin Epidemiol* 2010;63:938–9; .
31 Youden WJ. Index for rating diagnostic tests. *Cancer* 1950;3:32–5.
32 R Core Team. R: a language and environment for statistical computing. R Foundation for Statistical Computing; 2023. Available: https://www.r-project.org/
33 Abrokwa SK, Ruby LC, Heuvelings CC, *et al*. Task shifting for point of care ultrasound in primary healthcare in low- and middle-income countries-a systematic review. *EClinicalMedicine* 2022;45:101333.
34 Wong VW-S, Adams LA, de Lédinghen V, *et al*. Noninvasive biomarkers in NAFLD and NASH - current progress and future promise. *Nat Rev Gastroenterol Hepatol* 2018;15:461–78.
35 Promrat K, Kleiner DE, Niemeier HM, *et al*. Randomized controlled trial testing the effects of weight loss on nonalcoholic steatohepatitis. *Hepatology* 2010;51:121–9.
36 Boncan DAT, Yu Y, Zhang M, *et al*. Machine learning prediction of hepatic steatosis using body composition parameters: A UK Biobank Study. *NPJ Aging* 2024;10:4.
37 Atsawarungruangkit A, Laoveeravat P, Promrat K. Machine learning models for predicting non-alcoholic fatty liver disease in the general United States population: NHANES database. *World J Hepatol* 2021;13:1417–27.
38 Yu Y, Yang Y, Li Q, *et al*. Predicting metabolic dysfunction associated steatotic liver disease using explainable machine learning methods. *Sci Rep* 2025;15.
39 Huang G, Jin Q, Mao Y. Predicting the 5-Year Risk of Nonalcoholic Fatty Liver Disease Using Machine Learning Models: Prospective Cohort Study. *J Med Internet Res* 2023;25:e46891.
40 Rinella ME, Neuschwander-Tetri BA, Siddiqui MS, *et al*. AASLD Practice Guidance on the clinical assessment and management of nonalcoholic fatty liver disease. *Hepatology* 2023;77:1797–835.
41 Departamento de epidemiología división de planificación sanitaria subsecretaría de salud pública. ENCUESTA nacional de salud 2016-2017 primeros resultados. 2017. Available: https://redsalud.ssmso.cl/wp-content/uploads/2018/02/ENS-2016-17_PRIMEROS-RESULTADOS-ilovepdf-compressed.pdf [Accessed 18 Apr 2024].
42 Caussy C. Should We Screen High-Risk Populations for NAFLD? *Curr Hepatology Rep* 2019;18:433–43.
43 Ministerio de Salud. Guía clínica examen medicina preventiva. 2013. Available: https://diprece.minsal.cl/wrdprss_minsal/wp-content/uploads/2014/09/GPC-Medicina-Preventiva.pdf [Accessed 1 Sep 2025].