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DIPLÔME D'ÉTAT DE DOCTEUR EN MÉDECINE

Qualification en Radiologie et Imagerie médicale

VALIDATION OF THE 2021 EASL ALGORITHM FOR THE NON INVASIVE ASSESSMENT OF LIVER FIBROSIS WITH ULTRASOUND DEVICES

VALIDATION DE L'ALGORITHME DE L'EASL DE 2021 CONCERNANT LE DIAGNOSTIC NON INVASIF DE LA FIBROSE HEPATIQUE AVEC APPAREILS D'ECHOGRAPHIE

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Sous la direction de M. le Professeur AUBE Christophe

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« Au moment d'être admise à exercer la médecine, je promets et je jure d'être fidèle aux lois de l'honneur et de la probité. Mon premier souci sera de rétablir, de préserver ou de promouvoir la santé dans tous ses éléments, physiques et mentaux, individuels et sociaux. Je respecterai toutes les personnes, leur autonomie et leur volonté, sans aucune discrimination selon leur état ou leurs convictions. J'interviendrai pour les protéger si elles sont affaiblies, vulnérables ou menacées dans leur intégrité ou leur dignité. Même sous la contrainte, je ne ferai pas usage de mes connaissances contre les lois de l'humanité. J'informerai les patients des décisions envisagées, de leurs raisons et de leurs conséquences. Je ne tromperai jamais leur confiance et n'exploiterai pas le pouvoir hérité des circonstances pour forcer les consciences. Je donnerai mes soins à l'indigent et à quiconque me les demandera. Je ne me laisserai pas influencer par la soif du gain ou la recherche de la gloire.

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Liste des abréviations

MASLD	Metabolic Dysfunction Associated Steatotic Liver Disease
NAFLD	Non Alcoholic Fatty Liver Disease
MASH	Metabolic Dysfunction SteatoHepatitis
VCTE	Vibration Controlled Transient Elastography
p-SWE	Point Shear Wave Elastography
VTQ	Virtual Touch Quantification
ARFI	Acoustic Radiation Force Impulse
2D-SWI	2D-Shear Wave Elastography
SSI	Supersonic Shear Imagine
EASL	European Association for the Study of the Liver
FIB-4	Fibrosis-4
FMV2G	FibroMeter
ELF	Enhanced liver Fibrosis
kPa	KiloPascals
m/s	meters per second
ROI	Region Of Interest
Se	Sensitivity
Sp	Specificity
IQRm	InterQuartile to Median Ratio
BMI	Body Mass Index

Plan

VALIDATION OF THE 2021 EASL ALGORITHM FOR THE NON-INVASIVE ASSESSMENT OF LIVER FIBROSIS WITH ULTRASOUND DEVICES

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Contexte : En 2021, l'EASL a proposé un algorithme diagnostic non invasif de la fibrose hépatique chez les patients MASLD reposant sur la concordance positive successive des FIB4, FibroScan et tests sanguins et permettant de se passer de la biopsie hépatique.

Objectif : Validation de l'algorithme de l'EASL concernant le diagnostic non-invasif de la fibrose hépatique chez les patients MAFLD utilisant VTQ et/ou SSI en lieu et place du FibroScan.

Matériels et Méthodes : 867 patients MASLD ayant bénéficié d'une élastographie par VTQ et 698 patients MASLD ayant bénéficié d'une élastographie par SSI ont été inclus dans cette étude rétrospective. Chacun d'entre eux a bénéficié d'une biopsie hépatique dont les résultats étaient connus ainsi que de FIB4, FibroScan et tests sanguins (FibroMètre, FibroTest ou ELF) le jour ou dans les 48h suivant la biopsie. Les performances diagnostiques des VTQ et SSI seuls et intégrés dans l'algorithme ont été évaluées par des AUROCs et comparées à celles du FibroScan par le test de Delong via le R package pROC.

Résultats : La sensibilité de l'algorithme de l'EASL est significativement meilleure avec le SSI qu'avec le FibroScan (P<0,001) et aucune différence significative n'est retrouvée entre FibroScan et VTQ (P=0,678). La spécificité de l'algorithme est meilleure avec le Fibroscan qu'avec le VTQ (P<0,001) et aucune différence significative n'est retrouvée entre FibroScan et SSI (P=0,074). Le taux de biopsie passe de 7% avec le FibroScan à 10% avec les VTQ et SSI. Le sexe est le seul facteur influant significativement sur le bon classement des patients avec toutes les modalités l'élastographie.

Conclusion : La substitution du FibroScan par les VTQ ou SSI permet de rendre l'algorithme de l'EASL plus accessible sans perte de sensibilité ou spécificité ni majoration du recours à la biopsie.

INTRODUCTION

Metabolic Dysfunction Associated Steatotic Liver Disease (MASLD), formerly known as Non-Alcoholic Fatty Liver Disease (NAFLD), is nowadays the most frequent liver pathology, with a growing incidence representing nearly 30% of the population today[1,2]. MASLD is characterized by an accumulation of fat within liver cells, linked to genetic factors but also acquired factors such as an excessively rich diet or a sedentary lifestyle[3]. In 25% of cases, steatotic liver disease leads to Metabolic Dysfunction SteatoHepatitis (MASH), a breeding ground for the development of hepatic fibrosis, cirrhosis and liver cancer [4]. Liver fibrosis is the main prognostic factor in MASLD. Morbidity and mortality are significantly increased in patients with advanced liver fibrosis, i.e., septal fibrosis on liver biopsy [5,6]. Therefore, the evaluation of liver fibrosis is particularly important. Although the gold standard for hepatic fibrosis assessment is liver biopsy, it is impaired by sampling variability, complications and suboptimal inter-observed reproducibility between pathologists [7,8]. The development of new diagnostic tools, known as non-invasive fibrosis tests have been developed and validated for 20 years, mainly represented by blood-based tests and radiology-based techniques using elastography [9]. Blood tests include either direct or indirect markers of liver fibrosis and have the advantages of good reproducibility and potentially wide availability since they can be prescribed by any physician [9].

As regards elastography, Vibration Controlled Transient Elastography (VCTE) with Fibroscan (Echosens, Paris, France) was the first of the various elastography techniques available and remains to this day the most widely used tool with the highest level of evidence [10]. Other elastography techniques combined with ultrasound scanners have been extensively studied in the literature and have shown similar accuracy to Fibroscan for the assessment of liver fibrosis: Point Shear Wave Elastography (p-SWE) including Siemens' Virtual Touch Quantification (VTQ)-Acoustic Radiation Force Impulse (ARFI) [11–15] and 2D-Shear Wave Elastography (2D-SWE) from Supersonic Shear Imagine (SSI) [4,16–20]. Based on the repeated generation of a shear wave by high-impact ultrasonic waves, their main difference stands in the hepatic volume studied, as the Siemens VTQ technique explores a 10x5 mm limited window, while the Supersonic SSI technique explores a wider one enabling color mapping

of hepatic stiffness with qualitative measurement in regions of interest. Because these devices are readily available in radiology practices, they represent an interesting option to increase the availability of liver elastography in the context of screening.

In 2021, the European Association for the Study of the Liver (EASL) proposed a three-stage algorithm based on blood tests and Fibroscan for the diagnosis of advanced liver fibrosis in patients with risk factors [9]. This algorithm is innovative because liver biopsy is not mandatory for the diagnosis. In fact, in patients with the simple blood test Fibrosis-4 (Fib-4) > 1.30, the diagnosis of advanced fibrosis is based on the concordance of Fibroscan and specialized blood tests like FibroMeter (FMV2G), Fibrotest or Enhanced Liver Fibrosis (ELF). This algorithm provided a diagnostic accuracy of 85% for the diagnosis of advanced fibrosis [21].

While the EASL algorithm has already been validated for the non-invasive diagnosis of advanced fibrosis in MASLD [21], the aim of this study was to evaluate the accuracy of ARFI from Siemens and SSI from Supersonic as replacements for Fibroscan in the EASL algorithm for patients with MASLD.

MATÉRIEL ET MÉTHODES

Patients

This study is a retrospective analysis of a biopsy-proven MASLD adult cohort of patients who were prospectively included in hepatology in the Angers and Bordeaux University Hospitals, France. Inclusion criteria were a biopsy-proven MASLD defined as the presence of hepatic steatosis and of at least one cardio-metabolic risk factor with an alcohol intake of less than 140g/week for women and 210g/week for men[22] . All patients underwent elastography with VCTE and VTQ and/or SSI. Exclusion criteria were concomitant drugs inducing steatosis such as Tamoxifen or Methotrexate, pre- or co-existing liver disease (hemochromatosis, Wilson's disease, autoimmune hepatitis, liver injury induced by drugs or cholestatic liver disease), case history of liver complications (ascites, hepatocellular carcinoma, liver failure, encephalopathy, variceal bleeding or systemic infection) or liver biopsy shorter than 10 mm. None of the biopsies were performed during a bariatric surgery.

The study protocol conformed to the ethics guidelines of the current Declaration of Helsinki and obtained approval from the local Ethics Committees, and patients all gave a written and informed consent before inclusion.

Liver biopsy

Anatomopathological examination was carried out by the same hepatology-specialized senior expert blinded for patient data. The liver fibrosis was evaluated according to the MASH Clinical Research Network criteria [23] as follows F0: no fibrosis; F1: perisinusoidal or portal/periportal fibrosis; F2: perisinusoidal and portal/periportal fibrosis; F3: Bridging fibrosis, and F4: Cirrhosis. F3-4 fibrosis stages were considered as advanced liver fibrosis and were the primary diagnostic targets of the study.

Liver stiffness measurement

Fibroscan, VTQ and SSI measurements were performed the day of the liver biopsy. Patients had to be in fasting conditions 8h before the exam. Experienced operators (>100 examinations) blinded for patient data recorded measurements. The position of each patient was the same for all three devices and was codified, as they had to be lying in a dorsal decubitus position with a right arm abduction.

Vibration-Controlled Transient Elastography (VCTE)

VCTE's technology (Fibroscan device; Echosens, Paris, France) assessment of liver stiffness was made according to the manufacturer's recommendations [24]. The median of 10 valid measurements was used as the liver stiffness result and expressed in KiloPascals (kPa).

p-SWE with VTQ

Liver stiffness measurements were performed using ARFI (VTQ Siemens). Real-time B-mode ultrasound imaging was used to target a right lobe liver area where the tissue's thickness was over 6cm and free of large blood vessels. Apnea or quiet breathing was required during the measurement. The median of 10 valid measurements following international recommendations[25] was used as the liver stiffness result and expressed in meters per second (m/s). The measurement of fewer than 4 valid acquisitions after 10 shots was defined as a failure.

2D-SWE with SSI

Liver stiffness measurements were performed using a 2D-SWE device (SuperSonic; Hologic). Apnea was required during the measurement. Measurements were done in a right lobe liver site free of large vascular or biliary structures and located at least 15 cm from the liver capsule. A homogeneous color of the mapping stiffness was obtained according to the manufacturer's recommendations, and liver stiffness was calculated using a Region Of Interest (ROI) of 20 mm positioned in this color map. The mean stiffness (in kPa) of 5 measurements, including at least 3 valid ones, was used as the liver stiffness result. A failure was defined as the absence or failure to obtain a signal, and a maximum of 10 measurements were allowed.

Blood fibrosis tests

Blood samples were taken in fasting conditions the day of or within 48 hours of the liver biopsy, and the following blood fibrosis tests were calculated according to published or patented formulas: FIB-4[26], Fibrotest[27], FMV2G[28] and ELF[29]. All blood assays were performed in the laboratories of Angers and Bordeaux Hospitals.

2021 EASL algorithm

The aim of the three-tiered EASL algorithm was to diagnose advanced fibrosis by successive association of FIB4, Fibroscan and one of three patented serum tests (Fibrotest, FMV2G or ELF (Figure 1)) [9]. Patients were considered as having no/mild fibrosis (F0-2) if FIB4 < 1.30 or FIB4 ≥1.30 with VCTE <8.0 kPa. Advanced fibrosis was defined as successive association of FIB4 ≥1.30 then Fibroscan ≥ 8.0 kPa and either Fibrotest ≥0.48, FMV2G ≥0.45 or ELF ≥9.8. If the Fibroscan was discordant to patented serum tests, a liver biopsy was required.

Statistical analyses

Continuous variables were expressed as median with first and third quartiles, and categorical variables were expressed as percentages.

The diagnostic accuracy of single tests or EASL algorithm for the advanced fibrosis was assessed though discrimination (AUROC) and compared with the Delong test using the R package *pROC*. Fixed threshold performance was described by sensitivity (Se), specificity (Sp), positive predictive value and negative predictive value, and compared using the R package *testCompareR*.

Finally, a multivariate analysis (stepwise backward binary logistic regression) allowed us to identify parameters that influence the well-classification of patients by the EASL algorithm in

advanced fibrosis. Candidate variables were age, gender, body mass index, diabetes status, length of biopsy, and the InterQuartile to Median Ratio (IQRm) of the imaging device used.

Statistical analyses were performed using R version 4.3.2

RÉSULTATS

Patient characteristics

Two groups were defined. The VTQ group included patients with elastography measurements performed with a pSWE system (VTQ, Siemens), and the SSI group included patients with elastography measurements performed with a 2D SWE system (SSI, Supersonic Shear Imaging).
VTCE and histology were available in both groups.

VTQ group

867 patients were included in the VTQ group. Median age was 59.8 years and there were 61.2% of males. Median Body Mass Index (BMI) was 31.9 kg/m^2 and 54.8% of the population was diabetic.
Median liver stiffness values were respectively 8.6 kPa and 1.26 m/s using VCTE and VTQ, whereas the liver biopsy spectrum of fibrosis was F0: 9.8%, F1: 19.8%, F2: 30.9%, F3: 28.0%, and F4: 11.4%.

SSI group

698 patients were included. Median age was 60.4 years and there were 59.2% of males. Median BMI was 32.0 kg/m^2 and 56.4% of the population was diabetic.
Median liver stiffness values were respectively 8.5 kPa and 9.1 kPa using VCTE and SSI whereas the liver biopsy spectrum of fibrosis was F0: 8.5%, F1: 18.2%, F2: 28.4%, F3: 31.2%, and F4: 13.8%.

Characteristics of the patients of both groups are summarized in Table 1.

Performance of single tests

VTQ group

AUROCs for advanced fibrosis in the VTQ group were 0.806 [0.777; 0.835] and 0.723 [0.689; 0.757] using VCTE and VTQ respectively. AUROCs comparison showed that VCTE performed significantly better than VTQ (P<0.001) (Table 2).

Using the thresholds given by the EASL for the diagnosis of advanced fibrosis (8.0 kPa), VCTE yielded a sensitivity of 82.4% and a specificity of 64.1% (Table 3).

Using thresholds retained by previous studies (1.37 m/s) [30] VTQ yielded a sensitivity of 64.6% and a specificity of 71.6%.

Because of the EASL algorithm's goal to detect patients with advanced fibrosis, we applied the VTQ threshold that provided a similar sensitivity as VCTE, i.e. 85%. This 1.08 m/s threshold returned a sensitivity of 84.8% for a specificity of 43.4%.

SSI group

AUROCs for advanced fibrosis in the SSI group were 0.787 [0.754; 0.821] and 0.795 [0.761; 0.828] using VCTE and SSI respectively. No significant difference was found comparing their AUROCs (P=0.682) (Table 2).

Using the thresholds given by the EASL for the diagnosis of advanced fibrosis (8.0 kPa), VCTE yielded a sensitivity of 82.4% and a specificity of 64.1% (Table 3).

Using thresholds retained by previous studies (8.0 kPa) (20), SSI yielded a sensitivity of 88.2% and a specificity of 59.9%.

Performance of the 2021 EASL algorithm using VTQ or SSI

VTQ group

In the VTQ group, FIB4 was < 1.30 in 338 patients and the other 529 patients underwent second-line elastography (Table 4). Of these patients, 346 (65%) were positive using VCTE and 399 (75%) using VTQ. In the end, the diagnostic accuracy of the EASL algorithm was 75% using VCTE and 67% using VTQ. Liver biopsy was required in 7% and 10% of the patients using respectively VCTE and VTQ. Specificity for advanced fibrosis was significantly higher (P < 0,001) for VCTE (Sp = 87.6%) than for VTQ (Sp = 80.8%) (Table 5). No significant difference was found for sensitivity (P=0.678). Regarding the 342 patients with advanced fibrosis, 36% were not detected by the algorithm (false negatives) using VCTE, while non-detection rate for VTQ was 38%.

SSI group

In the SSI group, FIB4 was < 1.30 in 269 patients and the other 429 patients underwent second-line elastography (Table 4). Of these patients, 283 (66%) were positive using VCTE and 329 (77%) using SSI. In the end, the diagnostic accuracy of the EASL algorithm was 72% using VCTE, and 71% using SSI. Liver biopsy was required in 7% and 10% of the patients using VCTE and SSI respectively. Sensitivity for advanced fibrosis was significantly lower ($p < 0,001$) for VCTE (Se = 69.7%) than for SSI (Se = 76.8%) (Table 5). No significant difference was found for specificity (P=0.074). Regarding the 314 patients with advanced fibrosis, 30% were false negatives using VCTE, and 23% using SSI.

Multivariate analysis

A multivariate analysis was performed to find parameters that could influence the correct filing of patients by the EASL algorithm in advanced fibrosis cases. Gender was the only independent factor selected in all elastography devices. Age was an independent factor when using VCTE and VTQ in the algorithm, whereas IQRm was using VCTE and SSI. BMI was not selected by the analysis regardless of the elastography technique associated in the algorithm (Table 6).

DISCUSSION

This study validated the accuracy of the new EASL algorithm in a large cohort of patients with biopsy-proven MAFLD using both VTQ and SSI as ultrasound elastography techniques as an alternative to FibroScan.

For the first time in international guidelines, the EASL algorithm provides the opportunity to diagnose advanced liver fibrosis in a fully noninvasive way without the need for liver biopsy when the three test lines (FIB4, VCTE and 3 serum tests) concur on diagnosis. The algorithm has been validated by the work of Canivet C and al. [21,31].

Nevertheless, unlike FIB4 and blood tests, VCTE remains not widely available and largely limited to specialized institutions, whereas most of the ultrasound imaging devices are equipped with an elastometry module. Our work demonstrates that substituing VTQ or SSI for VCTE in the EASL algorithm provides similar sensitivity for the diagnosis of advanced fibrosis. Moreover, the algorithm specificity using SSI is better than with VCTE.

False negative rates for advanced fibrosis were lower with SSI (23%) than with VCTE (30%), but quite similar between VCTE (36%) and VTQ (38%).

Accuracy for the diagnosis of advanced fibrosis of the SSI technique used in our study is close to that which is found in the literature using published cut-off (8 kPa) (17,20,25). VTQ cut-off had to be adjusted (1.08 m/s) to provide a sensitivity similar to VCTE. Indeed, the initial cut-off for the VTQ technique (1.37 m/s) [30,32] provided low sensitivity, and because the aim of the EASL algorithm is to detect patients with advanced fibrosis, we adapted the cut-off to reach this goal, although no such low cut-off has been described in the literature. Compared to VCTE (71.8%) and SSI (72.6%), this cut-off provides lower accuracy (59.7%) when used alone, but similar accuracy when integrated in the EASL algorithm. This cut-off difference between standalone use and algorithm-integrated use should be confirmed in different populations and underlined to avoid mistakes.

The strong advantage of the EASL algorithm to reduce the rate of liver biopsy remains using VTQ or SSI instead of VCTE as biopsy requirement is not significantly increased (7% to 10%).

Our work has a wealth of strengths, such as a large retrospective multicenter population, high-quality liver biopsies as reference for liver fibrosis, availability of the FIB4, three serum tests and VCTE results for each patient as recommended in the EASL algorithm, but few limitations. The main limitation lies in the fact that our cohort is drawn from tertiary care centers, which does not reflect the intended use of the EASL algorithm, i.e., to identify advanced liver fibrosis in primary care settings. Another limitation could be the cut-off used with the VTQ, lower than those found in the literature, but which was specially designed to be integrated into the EASL algorithm and not used on its own. Finally, likely to be perceived as a limit but rather corresponding to a strength, the fact that elastography data was collected by different doctors brings it closer to the reality of clinical practice in care centres.

CONCLUSION

The substitution of VTQ or SSI elastography techniques for VCTE makes the EASL algorithm more accessible without any loss of sensitivity or specificity, and does not increase the need for biopsy.

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FIGURES & TABLEAUX

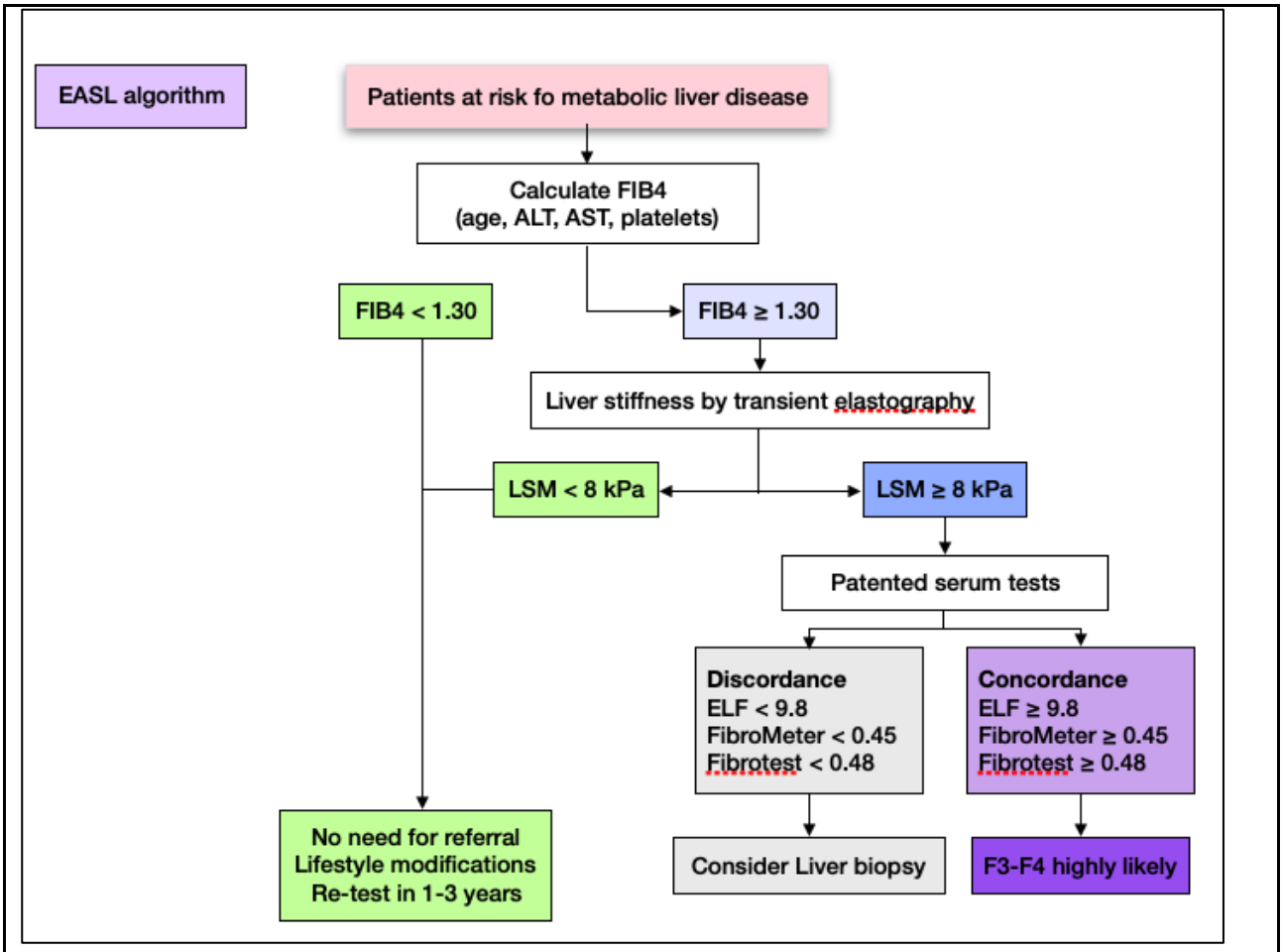

Figure 1. European Association for the Study of the Liver algorithm for the non-invasive diagnostis of advanced-fibrosis in Metabolic Associates Steatosic Liver Disease patients.

FIB4: Fibrosis 4; ALT: Alanine AminoTransferase; AST: Aspartate AminoTransferase; LSM: Liver Stiffness Mesurement; ELF: Enhanced Liver Fibrosis

Characteristics	**VTQ group (n=867)**	**SSI group (n=698)**
Age (years)	59.8 [50.9; 66.4]	60.4 [51.5; 66.9]
Male sex (%)	61.2	59.2
BMI (kg/m²)	31.9 [28.9; 36.5]	32.0 [28.7; 36.7]
T2DM (%)	54.8	56.4
NAS	4.0 [3.0; 5.0]	4.0 [3.0; 5.0]
AST (IU/L)	39.0 [29.0; 55.0]	39.0 [29.0; 55.0]
ALT (IU/L)	52.0 [34.0; 79.0]	51.0 [33.0; 79.0]
GGT (IU/L)	72.0 [41.0; 126.5]	72.0 [42.0; 120.8]
Bilirubin (µmol/L)	10.0 [8.0; 14.0]	10.0 [7.0; 13.0]
Platelets (g/L)	210.0 [169.0; 250.5]	212.0 [169.0; 257.8]
Albumin (g/L)	42.2 [40.0; 45.0]	42.0 [39.1; 45.0]
Prothrombin time (%)	97.0 [89.0; 105.0]	98.0 [90.0; 106.0]
FIB4	1.53 [1.04; 2.24]	1.54 [1.08; 2.30]
FibroMeter	0.45 [0.23; 0.70]	0.47 [0.23; 0.71]
VCTE (kPa)	8.6 [6.2; 12.9]	8.5 [6.1; 12.4]
VTQ (m/s)	1.26 [1.03; 1.80]	1.24 [1.03; 1.63]
SSI (kPa)	9.3 [6.6; 13.4]	9.1 [6.6; 13.3]
Fibrosis stage (%) F0 F1 F2 F3 F4	 9.8 19.8 30.9 28.0 11.4	 8.5 18.2 28.4 31.2 13.8

Table 1. Patients characteristics

BMI: Body Mass Index; T2DM: Type 2 diabetes; NAS: NAFLD Activity Score; AST: Aspartate AminoTransferase; ALT: Alanine AminoTransferase; GGT: Gamma GlutamylTransferase; FIB4: Fibrosis-4; VCTE: Vibration Controlled Transient Elastography (FibroScan); VTQ: Virtual Touch Quantification; SSI: Supersonic Shear Impulse; FM2VG: FibroMeter

Fibrosis test	VTQ group (n=867)	SSI group (n=698)
FIB4 FibroMeter VCTE VTQ SSI	0.768 [0.736; 0.800] 0.790 [0.760; 0.821] 0.806 [0.777; 0.835] 0.723 [0.689; 0.757] -	0.757 [0.721; 0.792] 0.770 [0.735; 0.805] 0.787 [0.754; 0.821] - 0.795 [0.761; 0.828]
Comparison (P) : VCTE vs VTQ VCTE vs SSI	 <0.001 -	 - 0.682

Table 2. AUROCS of non-invasive tests

FIB4: Fibrosis-4; VCTE: Vibration Controlled Transient Elastography; VTQ: Virtual Touch Quantification; SSI: Supersonic Shear Impulse

Test	FIB4	VCTE	VTQ		SSI	FibroMeter
Threshold	1.30	8.0 kPa	1.37 m/s	85% Se (1.08 m/s)	8.0 kPa	0.45
Se (%)	83.4	82.4	64.6	84.8	88.2	75.3
Spe (%)	54.2	64.1	71.6	43.4	59.9	67.2
NPV (%)	81.7	83.3	75.7	81.4	86.1	78.9
PPV (%)	57.1	62.6	59.7	49.4	64.3	62.6
DA (%)	66.5	71.8	68.9	59.7	72.6	70.6
OR	5.9	8.4	4.6	4.3	11.2	6.3
-LR	1.82	2.30	2.28	1.50	2.20	2.30
+LR	0.31	0.27	0.49	0.35	0.20	0.37

Table 3. Diagnostic accuracy of the EASL algorithm tests

FIB4: Fibrosis-4; VCTE: Vibration Controlled Transient Elastography; VTQ: Virtual Touch Quantification; SSI: Supersonic Shear Impulse; Se: Sensitivity; Sp: Specificity; NPV: Negative Predictive Value; PPV: Predictive Positive Value; DA: Diagnostic Acuracy; OR: Odds Ratio; -LR: Negatice Likelihood Ratio; +LR: Positive Likelihood Ratio

Group	Elastography	FIB4 <1.30	FIB4 ≥1.30		
			Elasto neg.	Elasto pos.	
				FM <0.45	FM ≥0.45
VTQ group	VCTE	338 patients F0-2 : 283 F3 : 47 F4 : 8	183 patients F0-2 : 148 F3 : 32 F4 : 3	63 patients F0-2 : 29 F3 : 24 F4 : 10	283 patients F0-2 : 65 F3 : 140 F4 : 78
	VTQ	338 patients F0-2 : 283 F3 : 47 F4 : 8	130 patients F0-2 : 91 F3 : 35 F4 : 4	87 patients F0-2 : 50 F3 : 26 F4 : 11	312 patients F0-2 : 101 F3 : 135 F4 : 76
SSI Group	VCTE	269 patients F0-2 : 215 F3 : 47 F4 : 7	146 patients F0-2 : 105 F3 : 35 F4 : 6	50 patients F0-2 : 17 F3 : 22 F4 : 11	233 patients F0-2 : 47 F3 : 114 F4 : 72
	SSI	269 patients F0-2 : 215 F3 : 47 F4 : 7	100 patients F0-2 : 81 F3 : 15 F4 : 4	67 patients F0-2 : 29 F3 : 26 F4 : 12	262 patients F0-2 : 59 F3 : 130 F4 : 73

Table 4. Agreement between tests in the EASL algorithm

FIB4: Fibrosis-4; FM: FIbroMeter

Group	Elasto.	Se (%)	Spe (%)	NPV (%)	PPV (%)	DA (%)	LB (%)
VTQ group	VCTE	73.7	87.6	83.6	79.5	82.1	7.3
	VTQ	72.5	80.8	81.9	71.1	77.5	10.0
	p	0.678	<0.001	0.121	<0.001		
SSI roup	VCTE	69.7	87.8	78.0	82.3	79.7	7.2
	SSI	76.8	84.6	81.7	80.3	81.1	9.6
	P	<0.001	0.074	0.003	0.272		

Table 5. Whole EASL algorithm accuracy

VTQ: Virtual Touch Quantification; SSI: Supersonic Shear Impulse; Se: Sensitivity; Sp: Specificity; NPV: Negative Predictive Value; PPV: Predictive Positive Value; DA: Diagnostic Acuracy; LB: Liver Biopsy

	Age	Sexe	BMI	Diabète	Longueur biospsie	IQRm	Diabète * Age
VCTE	0.001	0.004	-	<0.001	0.012	0.005	0.001
VTQ	<0.001	0.002	-	-	0.032	-	-
SSI	-	0.026	-	-	-	0.005	

Table 6. Multivariate analysis

BMI: Body Mass Index; IQRm : InterQuartile to mediane ratio

TABLE DES MATIERES

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Validation de l'algorithme de l'EASL concernant le diagnostic non invasif de la fibrose hépatique chez les patients MASLD avec appareils d'échographie

RÉSUMÉ

Contexte : En 2021, L'EASL a proposé un algorithme diagnostic non invasif de la fibrose hépatique chez les patients MASLD reposant sur la concordance positive successive des FIB4, FibroScan et tests sanguins et permettant de se passer de la biopsie hépatique.

Introduction : Validation de l'algorithme de l'EASL concernant le diagnostic non-invasif de la fibrose hépatique chez les patients MAFLD utilisant VTQ et/ou SSI en lieu et place du FibroScan.

Matériels et Méthodes : 867 patients MASLD ayant bénéficié d'une élastographie par VTQ et 698 patients MASLD ayant bénéficié d'une élastographie par SSI ont été inclus dans cette étude restrospective. Chacun d'entre eux a bénéficié d'une biopsie hépatique dont les résultats étaient connus ainsi que de FIB4, FibroScan et tests sanguins (FibroMètre, FibroTest ou ELF) le jour ou dans les 48h suivant la biopsie. Les performances diagnostiques des VTQ et SSI seuls et intégrés dans l'algorithme ont été évaluées par des AUROCs et comparées à celles du FibroScan par le test de Delong via le R package pROC.

Résultats : La sensibilité de l'algorithme de l'EASL est significativement meilleure avec le SSI qu'avec le FibroScan (P<0,001) et aucune différence significative n'est retrouvée entre FibroScan et VTQ (P=0,678). La spécificité de l'algorithme est meilleure avec le Fibroscan qu'avec le VTQ (P<0,001) et aucune différence significative n'est retrouvée entre FibroScan et SSI (P=0,074). Le taux de biopsie passe de 7% avec le FibroScan à 10% avec les VTQ et SSI. Le sexe est le seul facteur influant significativement sur le bon classement des patients avec toutes les modalités l'élastographie.

Conclusion : La substitution du FibroScan par les VTQ ou SSI permet de rendre l'algorithme de l'EASL plus accessible sans perte de sensibilité ou spécificité ni majoration du recours à la biopsie.

Mots-clés : MASLD, fibrose hépatique, tests diagnostiques non-invasifs.

Validation of the 2031 EASL algorithm for the non-invasive assessment of liver fibrosis with ultrasound devices

ABSTRACT

Background : In 2021, the EASL proposed a non-invasive diagnostic algorithm for liver fibrosis in MASLD patients based on the successive positive concordance of FIB4, FibroScan and blood tests, making it possible to dispense with liver biopsy.

Purpose : Validation of the 2021 EASL algorithm for the non-invasive diagnosis of liver fibrosis using VTQ and/or SSI instead of FibroScan.

Materials and methods : 867 MASLD patients with VTQ elastography and 698 MASLD patients with SSI elastography were included in this retrospective study. Each had liver biopsy with known results as well as FIB4, FibroScan and blood-tests (FibroMeter, FibroTest or ELF) on the day or within 48 hours of the biopsy. Diagnostic performance of VTQ and SSI alone and integrated into the algorithm were evaluated by AUROCs and compared with those of FibroScan by Delong's test via the R package pROC.

Results : The EASL algorithm sensitivity was significantly higher with SSI than with FibroScan (P<0.001) and no significant difference was found between FibroScan and VTQ (P=0.678). Algorithm specificity was significantly higher with FibroScan than with VTQ (P<0.001) and no significant difference was found between FibroScan and SSI (P=0 .074). Biopsy rate rose from 7% with FibroScan to 10% with VTQ and SSI. Gender was the only factor significantly influencing the correct classification of patients with all elastography modalities.

Conclusion The substitution of VTQ or SSI elastography techniques for VCTE makes the EASL algorithm more accessible without any loss of sensitivity or specificity, and does not increase the need for biopsy.

Keywords : MASLD, liver fibrosis, non-invasive fibrosis tests.

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