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DIPLÔME D'ÉTAT DE DOCTEUR EN MÉDECINE

Qualification en Hépatogastroentérologie

The Easy Liver Fibrosis Test (eLIFT) avoids unnecessary specialized evaluations of liver fibrosis in NAFLD and ALD patients

Le *easy LIver Fibrosis Test* (eLIFT) permet d'éviter des évaluations spécialisées inutiles de fibrose chez les patients NAFLD et/ou alcooliques

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Liste des abréviations

ALD	Alcoholic Liver Disease
NAFLD	Non-Alcoholic Fatty LIver Disease
eLIFT	Easy LIver Fibrosis Test
GGT	Gamma Glutamyl Transpeptidase
AST	Aspartate Serum Transaminase
TP	Prothrombin Time
FM	FibroMeter
LSM	Liver Stiffness Measurement
BMI	Body Mass Index
ALT	ALanine Amino Transferase
APRI	AST to Platelet Ratio Index
FIB 4	FIBrosis-4
NPV	Negative Predictive Value
PPV	Positive Predictive Value

Plan

ABSTRACT

Background and Aims: Liver fibrosis evaluation is mandatory to evaluate disease severity in non-alcoholic fatty liver disease (NAFLD) and alcoholic liver disease (ALD), but most of these patients are seen by non-specialists. The easy liver fibrosis test (eLIFT) is a very simple blood test specifically developed for non-specialists with result ≥8 indicating the need for further specialized evaluation of liver fibrosis. We aimed to evaluate whether using the eLIFT helps to reduce unnecessary referrals for specialized liver fibrosis evaluations in NAFLD and ALD patients.

Method: NAFLD and/or ALD patients newly referred to our centre for a non-invasive evaluation of liver fibrosis between 10/2014 and 03/2017 were retrospectively included. The FibroMeter^{VCTE} (combination of blood markers with Fibroscan result) was taken as the reference test for specialized liver fibrosis evaluation, with result <0.384 indicating no/mild fibrosis and thus "unnecessary referral".

Results: 558 patients were included (NAFLD: 283, ALD: 156, mixed NAFLD+ALD: 119). FM^{VCTE} result was <0.384 (unnecessary referral) in 58.8% of patients, ≥0.715 (advanced fibrosis) in 29.7%, and 0.384-0.714 (undetermined diagnosis) in 11.5%. eLIFT was <8 in 47.7% of patients, of whom 85.3% had also FM^{VCTE} <0.384 and only 6.0% had FM^{VCTE} <0.715. 90.4% of patients with FibroMeter ≥0.715 had eLIFT ≥8. Compared to the strategy "all patients referred", the use of eLIFT as first-line test saved 40% of costs directly linked to liver fibrosis evaluations.

Conclusion: Used by non-specialists for their NAFLD and ALD patients, the eLIFT improve the relevance of patient referrals for specialized evaluation of liver fibrosis.

Introduction

Non-alcoholic fatty liver disease (NAFLD) and alcohol-related liver disease (ALD) represent the two most frequent causes of chronic liver disease in France (respectively 25% and 12% of the general adult population) [1, 2]. NAFLD and ALD expose patients to the risk of cirrhosis and its life-threatening complications. An accurate staging of liver fibrosis in order to evaluate the disease severity is mandatory in NAFLD and ALD patients as the result will strongly impact their clinical management[3, 4]. Particularly, the presence of advanced fibrosis requires to refer to the specialist for a specific management of the liver disease. Liver biopsy remains the reference for this purpose but, due to its invasiveness added to the risk of severe complications and death, this procedure can't be used as first line test in large populations[5, 6]. Non-invasive tests of liver fibrosis such as blood tests and liver stiffness measurement (LSM) by elastography have been developed for the non-invasive evaluation of liver fibrosis and provide an attractive alternative to biopsy[4]. Elastography devices have the advantage of quick and painless examination with immediate result whilst the consultation. Accessibility to this technology remains nevertheless limited, due to the low number of devices with regards to the very large NAFLD and ALD populations**.** On the contrary, blood tests are widely accessible but the most accurates of them include specialized and expensive blood markers which limits their use in clinical practice. Furthermore their use on the front line by GPs to avoid addressing all patients to the hepatogastroenterologist seems impossible since about 30% of patients are included in the grey zone of the tests[7,8]. For all these reasons, liver fibrosis is currently not evaluated in most of NAFLD and ALD patients.

In clinical practice, non-specialists decide to refer their NAFLD and ALD patients for a specialized liver evaluation mainly because of the presence of liver-risk factors (such as

excessive alcohol consumption or liver steatosis) and/or non-specific biochemical abnormalities (such as chronically elevated transaminases or hyperferritinemia). However, these conditions are not very specific of advanced forms of liver disease. As a consequence, a large rate of referred patients has no/mild liver lesions, which requires only lifestyle modification and no specialized liver management. These unnecessary referrals consume the resources of healthcare systems and represent high costs that should be prevented. A first round of selection with a simple fibrosis test would be very interesting to limit the specialized liver evaluations to a subset of at-risk patients.

With this aim in mind, we recently developed "the Easy Liver Fibrosis Test",[9] a cheap and simple score able to identify patients at-risk of advanced liver fibrosis who require further referral to the specialist. The eLIFT has the advantage to include simple biological parameters available to all physicians (aspartate serum transaminase, gammaGT, platelets, prothrombin time index) and to be easily calculated by head without any computer. When the eLIFT is <8, there is a low risk of advanced liver fibrosis, the patient is not to be addressed for specialized evaluations. On the other hand, when the eLIFT is ≥ 8, there is a high risk of advanced liver fibrosis and the patients should attend a specialized evaluation **(Table I)**. The study in which the eLIFT has been developed was performed in a large yet selected population of patients with chronic liver disease who had undergone liver biopsy.

In the present work, we aimed to evaluate if the eLIFT helps in 'real-life' to appropriately reduce unnecessary specialized evaluations of liver fibrosis in NAFLD and ALD patients. The secondary objective is to compare several strategies in order to minimize the number of unnecessary specialized assessments.

Patients and methods

1. Study population

We included retrospectively ALD and/or NAFLD patients referred for the first time to our center for a first liver stiffness measurement with Fibroscan between October 2014 and March 2017. History of alcohol consumption was specifically investigated by interviewing the patients. ALD was defined by excessive alcohol consumption, i.e., >210 g/week in men or >140 g/week in women. Patients were considered to have mixed ALD and NAFLD when they met all the following criteria: excessive alcohol consumption, overweight (BMI ≥25 kg/m^2), and at least one of the following treatment: antidiabetic, antihypertensive or lipid-lowering. All patients undergo a blood test measuring : prothrombine (TP), Aspartate aminotransferase (AST), Alanine aminotransferase (ALT) platelets, alpha-2 microglobuline, gammaGT, hyaluronic acid, urea, bilirubin.

Patients with history of hepatocellular carcinoma or cirrhosis decompensation (liver failure, encephalopathy, ascites, variceal bleeding, systemic infection) or having biological or liver stiffness measurement data missing were excluded. Clinical data, biological data and stiffness were collected during the same consultation. When the patient's treatments were not registered in their medical records, we collected it by their general practitioner. The study protocol conformed to the ethical guidelines of the current Declaration of Helsinki and was approved by local Ethic Committees. All patients gave written informed consent to participate to our local cohort SNIFF whose aim is to evaluate non-invasive tests in chronic liver diseases.

2. Non-invasive evaluation test

2.1. Liver stiffness measurement

Liver stiffness measurement (LSM) was performed using a Fibroscan 502 Touch device (Echosens, Paris, France) by a specialized nurse experienced with the procedure (>500 examinations) and blinded for patient data. Examination conditions were those recommended by the manufacturer[10]. LSM was stopped when 10 valid measurements were recorded and the result (kilo Pascal: kPa) was expressed as the median of these valid measurements. XL probe of the Fibroscan was used in case of LSM failure (no valid measurement) with the M probe.

2.2. Blood Test

Three blood fibrosis tests were available in our study: the eLIFT, the FibroMeter^{V}, and the FibroMeter^{VCTE}.

2.2.1. The Easy LIver fibrosis test (eLIFT)

The eLIFT is a very simple fibrosis test including common parameters (age, gender, gammaglutamyl transferase, aspartate aminotransferase (AST), platelets and prothrombin time). An eLIFT ≥8 identifies patients at-risk of advanced (i.e., histological fibrosis stage Metavir F≥2 or NASH CRN F≥3) liver fibrosis who require further specialized liver evaluation **(table I)**[9].

Table I. The Easy LIver Fibrosis Test

The eLIFT correspond to the sum of points attributed to its six composite parameters.

VARIABLES	POINTS
Age (years)	
- ≥40	3
Gender	
- Male	1
AST (IU/L)	
- 35 – 69	2
- ≥70	4
Gamma-GT (IU/L)	
- 35 – 89	1
- ≥90	2
Platelets (G/L)	
- 170 – 249	1
- <170	4
Prothrombin time (%)	2
- 84 – 96	4
- <84	

AST : aspartate aminotransferase

2.2.2. The Fibrometer^{Virus} (FM^{V})

The FM^{V} is a blood test combining indirect (aspartate aminotransferase, platelets, prothrombin time, urea) and direct (hyaluronate, apha2macroglobulin) markers of liver fibrosis with age and sex[11]. The diagnostic cut-off used for FM^{V} to diagnose advanced liver fibrosis was ≥0.46[12].

2.2.3. The FibroMeter^{VCTE} (FM^{VCTE})

FM^{VCTE} is a combination of the FM^{V} blood markers with LSM result in a single test[13]. The FM^{VCTE} is based on the following parameters : age, gender, Platelets, Prothrombin index, AST, Alpha-2-macroglobulin, Gamma-GT, Liver stiffness measured by fibroscan. FM^{VCTE} was considered as the reference for the non-invasive evaluation of liver fibrosis[9]. FM^{VCTE} is interpreted using two diagnostic cut-offs: <0.384 to rule-out advanced fibrosis with 90% sensitivity, and ≥0.715 to rule-in advanced fibrosis with 90% specificity[13].

FibroMeter^{V} (FM^{V}) and FibroMeter^{VCTE} (FM^{VCTE}) were collected in the patient files and came from the calculation performed in clinical practice using the commercial Echosens website.

2.3. Costs evaluation

Costs were based on reimbursement rates by the French Health Insurance. Only costs directly linked to the non-invasive evaluation of liver fibrosis (blood tests, Fibroscan examination, and specialized consultation) were included in the analysis. The total cost was calculated for the whole study population and divided by the sample size to obtain the mean cost per patient in euros.

3. Statistics

Quantitative variables were expressed as mean ± standard deviation, or median with 1st and 3rd quartiles when appropriate, and compared using the Mann-Withney or Wilcoxon test. Qualitative variables were expressed as percentage and compared using the Fisher exact test or McNemar test. We have recently shown that FM^{VCTE} was the most accurate non-invasive test of liver fibrosis in a large series including 1,964 patients with biopsy-proven chronic liver

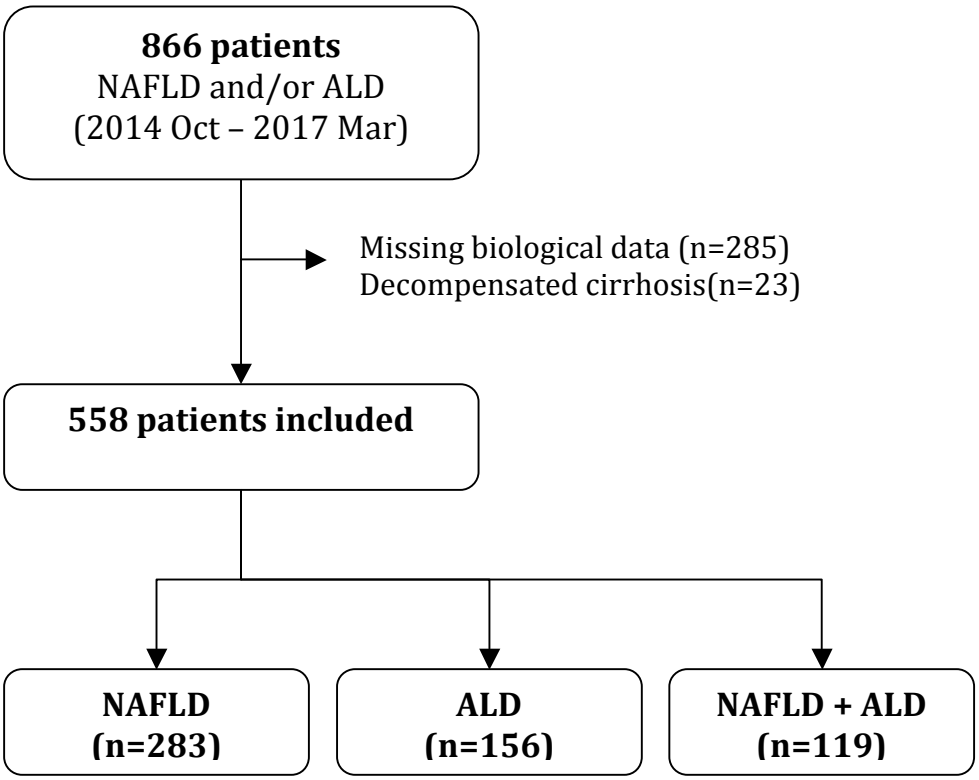
disease[9]. Therefore, in the present work, we chose FM^{VCTE} as the reference test for non-invasive evaluation of liver fibrosis. Because our primary aim was to determine if the eLIFT helps to avoid unnecessary specialized liver fibrosis evaluations in NAFLD/ALD patients, we took FM^{VCTE} <0.384 as primary outcome and evaluated whether a eLIFT <8 indicates a FM^{VCTE} <0.384 and thus no need for referral to the hepatologist. Statistical analyses were performed using SPSS version 18.0 software (IBM, Armonk, NY, USA).

Results

1. Patients

A total of 866 patients NAFLD and/or ALD underwent a first LSM with Fibroscan in our Department between October 2014 and March 2017. 23 patients were excluded because of history of hepatocellular carcinoma or decompensated cirrhosis. Blood markers for FM^{VCTE} calculation were missing in 285 patients **(Figure 1).**

Figure 1. Flowchart



The characteristics of the 558 remaining patients finally included in the study are detailed in **Table II**.

Table II. Patients characteristics at inclusion

	All (n=558)	**NAFLD (n=283)**	**ALD (n=156)**	**Mixed NAFLD + ALD (n=119)**	**p**
Age (years)	57.5 ± 12.2	56.5 ± 12.7	55.5 ± 11.5	62.4 ± 10.4	<0.001
Male Sex (%)	68.6	53.4	78.8	91.6	<0.001
Diabetic treatment (%)	30.1	38.1	5.4	43.5	<0.001
BMI (kg/m^2)	30.8 ± 6.9	32.9 ± 6.6	25.6 ± 5.1	32.4 ± 6.4	<0.001
AST (IUL)	35 (26 – 50)	33 (25 – 44)	37 (26 – 57)	40 (29 – 59)	0.002
ALT (IU/l)	39 (25 – 64)	42 (29 – 69)	31 (22 – 52)	39 (25 – 57)	<0.001
GammaGT (IU/l)	76 (40 – 161)	53 (33 – 107)	95 (47 – 197)	109 (55 – 271)	<0.001
Bilirubin (µmol/l)	10 (8 – 15)	10 (7 – 13)	10 (8 – 16)	12 (8 – 17)	0.062
Prothrombin time (%)	99 (88 – 109)	101 (93 – 109)	95 (85 – 109)	93 (78 – 105)	<0.001
Platelets (G/l)	225 (181 – 275)	238 (193 – 286)	223 (177 – 277)	196 (152 – 254)	<0.001
LSM result (kPa)	7.2 (5.4 – 15.5)	6.8 (5.0 – 12.0)	6.9 (5.1 – 18.8)	11.2 (6.2 – 21.5)	<0.001
FM^{VCTE} (%)					<0.001
- <0.384	58.8	67.5	57.1	40.3	
- 0.384-0.714	11.5	11.7	12.2	10.1	
- ≥0.715	29.7	20.8	30.8	49.6	

BMI: body mass index; AST: aspartate aminotransferase; ALT: alanine aminotransferase; LSM: liver stiffness measurement with Fibroscan; FM^{VCTE}: FibroMeter^{VCTE}

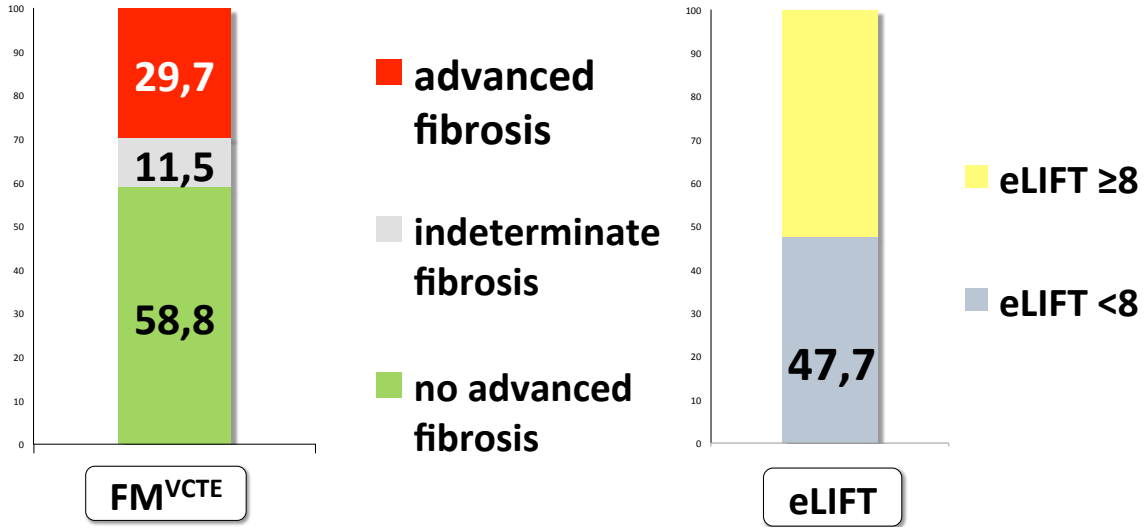
The mean age was 57.5±12.2 years, 68.6% of the patients were male, mean BMI was 30.8±6.9 kg/m^2, 30.1% were diabetic, and median LSM was 7.2 kPa (interquartile range: 5.4 - 15.5). The cause of chronic liver disease was NAFLD in 283 patients, ALD in 156, and mixed NAFLD/ALD in 119. Patients with mixed NAFLD/ALD had more severe liver disease with significantly higher LSM result, lower prothrombin time, and lower platelet count than patients with NAFLD alone or ALD alone.

2. eLIFT versus FibroMeter^{VCTE}

FM^{VCTE} was <0.384 suggesting no/mild liver fibrosis in 328 patients (58.8%), and ≥0.715 suggesting advanced fibrosis in 166 (29.7%).

eLIFT was <8 suggesting a low risk of advanced fibrosis and therefore no need for referee to the specialist 266 patients (47.7%) **(Figure 2)**.

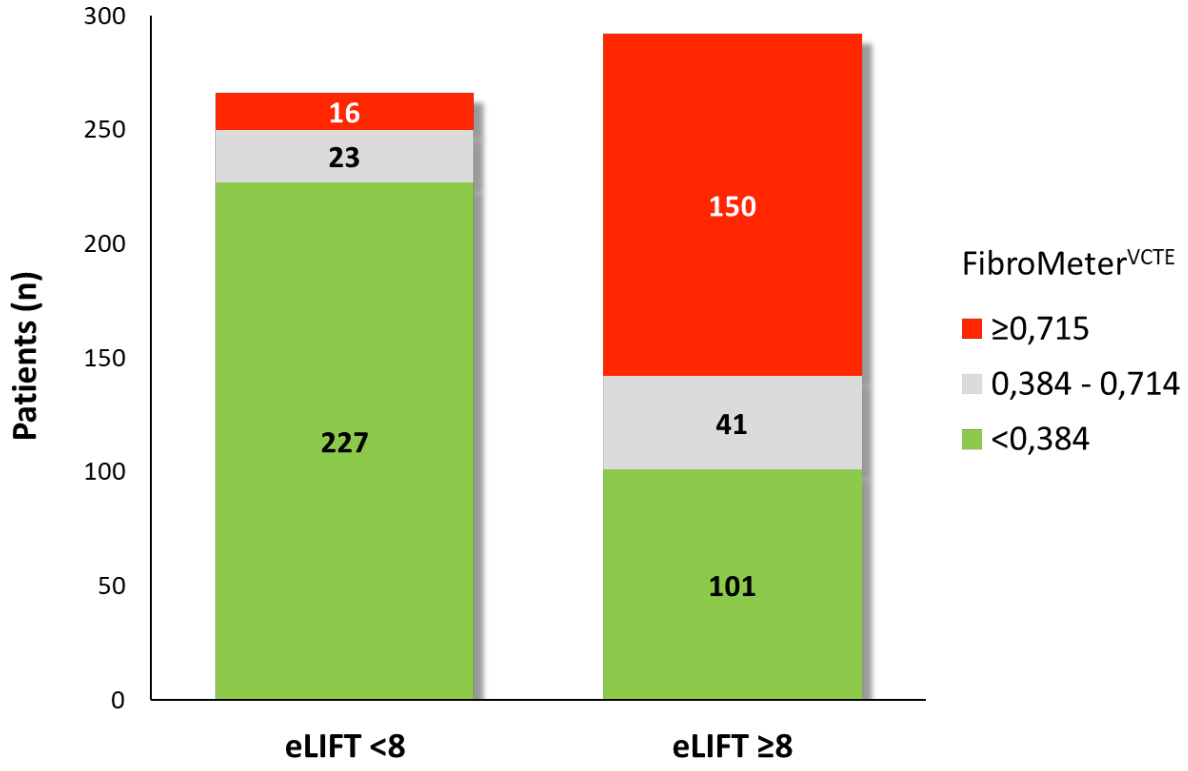
Figure 2. Results of FM^{VCTE} and eLIFT



FM^{VCTE}: FibroMeter^{VCTE}, eLIFT : easy LIver Fibrosis Test

The eLIFT was ≥8 in 191 of the 230 patients having FM^{VCTE} ≥0.384 (sensitivity: 83.0%). Among the patients with eLIFT <8, 227 had FM^{VCTE} <0.384 (negative predictive value: 85.3%) and only 16 (6.0%) had FM^{VCTE} ≥0.715 **(Figure 3).** Therefore, had the eLIFT been used to select the patients for referee to the specialist, nearly half of the specialized liver fibrosis evaluations would have been avoided with a very low rate of potential advanced liver disease missed.

Figure 3. Results of the FibroMeter^{VCTE} as a function of eLIFT



eLIFT : easy LIver Fibrosis Test

Regardless of the etiology, 171 NAFLD patients had eLIFT <8 and 140 of them (NPV : 81.9%) had no/mild fibrosis according to FM^{VCTE}. 58 of the 63 ALD patients with eLIFT <8 (NPV : 92,1%) had no/mild fibrosis according to FM^{VCTE}, and 29 of the 32 NAFLD+ALD patients (NPV : 90.1%). **(table III).**

Table III. Results of the FibroMeter^{VCTE} as a function of eLIFT according to the etiology

Cause of CLD	**eLIFT**	**FMVCTE**		
		<0.384	**0.384-0.714**	**≥0.715**
NAFLD	<8	140	18	13
	≥8	51	15	46
Alcohol	<8	58	3	2
	≥8	31	16	46
NAFLD	<8	29	2	1
+ alcohol	≥8	19	10	58

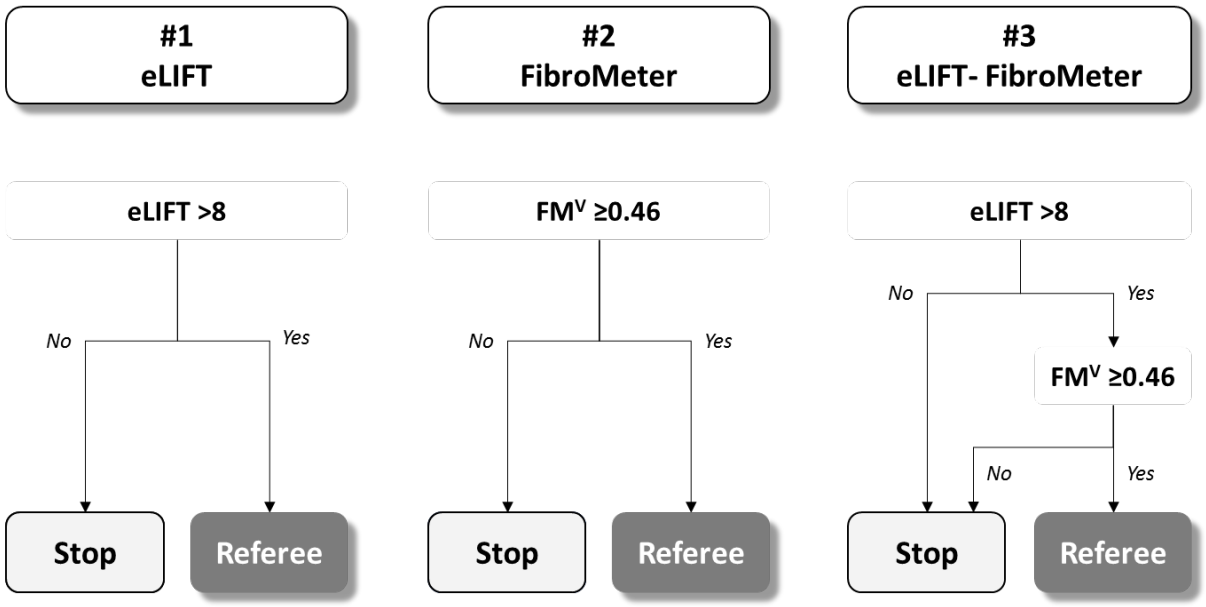
CLD : Chronic Liver Disease, eLIFT : easy LIver Fibrosis Test, FM^{VCTE}: FibroMeter^{VCTE}

3. Other strategies to select patient for referee to the specialist

The use of eLIFT decreased by three-fold the number of patients with FM^{VCTE} <0.384 referred to the specialist (from 328 to 101, **Figure 3**). However, FM^{VCTE} <0.384 still represented 101 of the 292 patients with eLIFT ≥8, and thus 34.6% of the referred patients. We therefore evaluated a second strategy using the FM^{V} as first-line test (**Figure 4**). 320 patients had FM^{V} <0.46, of whom 275 had FM^{VCTE} <0.384 (negative predictive value: 85.9%, **Table IV**) and only 5.6% had FM^{VCTE} ≥0.715. FM^{V} was ≥0.46 in 80.4% of patients with FM^{VCTE} ≥0.384 and in 89.2% of patients with FM^{VCTE} ≥0.715. Among the 238 patients with FM^{V} ≥0.46 (referral rate: 42.7%), 53 had FM^{VCTE} <0.384 (unnecessary referral rate: 22.3%).

We also evaluated a third strategy using a sequential use of eLIFT then FM^{V} (**Figure 4**). 361 patients had negative first-line testing (eLIFT <8 or eLIFT ≥8 with FM^{V} <0.46), of whom 299 had FM^{VCTE} <0.384 (negative predictive value: 82.8%, **Table IV**) and 8.0% had FM^{VCTE} ≥0.715. First-line testing was positive (eLIFT ≥8 and FM^{V} ≥0.46) in 73.0% of patients with FM^{VCTE} ≥0.384 and in 82.5% of patients with FM^{VCTE} ≥0.715. Among the 197 patients with positive first-line testing (referral rate: 35.3%), only 29 had FM^{VCTE} <0.384 (unnecessary referral rate: 14.7%).

Figure 4: Different strategies evaluated to select patients for referee to the specialist



eLIFT : easy LIver Fibrosis Test, FM^{V} : FibroMeter^{Virus}

Table IV: Results of the FibroMeter^{VCTE} as a function of first-line testing using eLIFT, FibroMeter^{V}, or a sequential strategy combining eLIFT then FibroMeter^{V}

First-line testing	Threshold	FibroMeter^{VCTE}		
		<0.384	**0.381 – 0.714**	**≥0.715**
eLIFT	<8	227	23	16
	≥8	101	41	150
FibroMeter^{V}	<0.46	275	27	18
	≥0.46	53	37	148
eLIFT then FibroMeter^{V}	Negative [a]	299	33	29
	Positive [b]	29	31	137

[a] eLIFT <8 or eLIFT ≥8 with FibroMeter^{V} <0.46
[b] eLIFT ≥8 and FibroMeter^{V} ≥0.46
eLIFT : easy LIver Fibrosis Test, FibroMeter^{V} : FibroMeter^{Virus}

Table V summarizes and compares the three study strategies. The sensitivity for FM^{VCTE} ≥0.384 was significantly higher with eLIFT and FM^{V} strategies compared to the sequential eLIFT-FM^{V} strategy. Compared to the eLIFT strategy, the FM^{V} strategy better identify patients who don't need referee to the specialist with significantly higher specificity, and significantly lower rates of referrals and unnecessary referrals.

Table V: Comparison of the three strategies evaluated to select patients for referee to the specialist

Strategy		Referral (%) [a]	Se (%)	Spe (%)	NPV (%)	PPV (%)	Unnecessary referral (%) [b]
#1.	eLIFT ≥8	53.3	83.0	69.2	85.3	65.4	34.6
#2.	FibroMeter^{V} ≥0.46	42.7	80.4	83.8	85.9	77.7	22.3
#3.	eLIFT ≥8 then FibroMeter^{V} ≥0.46	35.3	73.0	91.2	82.8	85.3	14.7
Comparison (p)							
#1 vs #2		<0.001	0.430	<0.001	-	-	-
#1 vs #3		<0.001	<0.001	<0.001	-	-	-
#2 vs #3		<0.001	<0.001	<0.001	-	-	-

Se: sensitivity (%), i.e. rate of patients with positive result for the strategy among those with FM^{VCTE} ≥0.384
Spe: specificity (%), i.e. rate of patients with negative result for the strategy among those with FM^{VCTE} <0.384
NPV: negative predictive value (%), i.e. rate of patients with FM^{VCTE} <0.384 among negative results for the strategy
PPV: positive predictive value (%), i.e. rate of patients with FM^{VCTE} ≥0.384 among positive results for the strategy
[a] Rate of patients with positive result for the strategy (#1: eLIFT ≥8; #2: FibroMeter^{V} ≥0.46; #3: eLIFT ≥8 and FibroMeter^{V} ≥0.46)
[b] Rate of patients with FM^{VCTE} <0.384 among those with positive result for the strategy but (i.e. 1- positive predictive value)
eLIFT : easy LIver Fibrosis Test

4. Costs evaluation

The mean cost per patient was not significantly different between the eLIFT and the FM^V strategies with, respectively, 73.15±58.53 versus 71.62±39.25 euros (p=0.473). Compared to the strategy "all patients referred to the specialist" (117.09 euros per patient) the use of eLIFT or FM^V to select patients for referee significantly decreased the costs by 40% (p<0.001).

DISCUSSION AND CONCLUSION

Cirrhosis has become the eleventh leading cause of mortality among non-communicable diseases worldwide, and hepatocellular carcinoma the second leading cause of cancer-related death[14]. At the time of diagnosis, 75% of cirrhosis are already decompensated with poor short-term survival and two third of hepatocellular carcinoma are already at the palliative stage[15, 16, 17]. These data underline the crucial need for a widespread diagnosis and early management of advanced forms of chronic liver diseases, especially in NAFLD and ALD which are the two main causes. Given the high prevalence of NAFLD and ALD in the general population, achieving this ambitious goal will require a close collaboration between hepatologists and many other physicians such as primary care practitioners, addictologists, or diabetologists. Our study shows that the eLIFT, a simple and cheap blood test available to all these physicians, can help them to improve their patient referrals for specialized liver fibrosis evaluations. A negative eLIFT <8 indicates a very high probability of no/mild fibrosis diagnosis by specialized tests and therefore no need for referral to the hepatologist.

A first remarkable result of our work is that 59% of NAFLD/ALD patients referred to our tertiary centre for a specialized liver fibrosis evaluation had a final diagnosis of no/mild liver fibrosis with no need for further specialized management. This demonstrates that the patient selection by non-specialists using classical liver risk factors or abnormal liver function tests is suboptimal. If physicians had used the eLIFT before referring their patients, the rate of referral to our tertiary centre would have been halved and "unnecessary referrals" would have decreased from 59% to 35%. As a result, this would have allowed us to double our capacity to manage patients with advanced liver disease over the same period. Similarly,

a recent work has shown that using eLIFT in type 2 diabetic patients would spare two third of specialized liver fibrosis evaluation [18].

Using the eLIFT to decide patient referral would have missed 16 among the166 patients with FMVCTE ≥0.715. We have previously demonstrate that the liver-related prognosis of patients with eLIFT <8 is excellent at middle-term. In these patients, eLIFT can be monitored during follow-up and, should the result become ≥8, spark a referral for a specialized liver fibrosis evaluation. Further longitudinal studies with long term follow-up and repeated eLIFT measurements are required to validate this attitude in clinical practice.

Simple blood fibrosis tests have the advantage to be cheap and widely available but complex blood fibrosis tests are more accurate[18, 19]. Using the FM^V as first-line test instead of the eLIFT would have even more reduced the rate of referrals to 43% and unnecessary referrals to 22%. However, this improvement in patient selection was not associated with a reduction in costs which were not significant different between the eLIFT and FM^V strategies. In fact, the savings linked to the reduced rates of specialized liver fibrosis evaluations following FM^V evaluation are counterbalanced by the higher costs linked to the use of this test as first-line procedure. This demonstrates that diagnostic tests and strategies must be evaluated not only in terms of accuracy, but also for the costs they induce. In our analysis, we only considered the direct costs linked to the non-invasive evaluation of liver fibrosis using French pricing. Further studies considering also indirect costs, country-specific pricing, and the impact in term of mortality and quality of life of managements based on the results of non-invasive tests of liver fibrosis are mandatory to make stronger conclusions. For now, in France, FM^V is reimbursed in the setting of chronic hepatitis C and not for NAFLD or ALD patients who therefore must pay for the online calculation of the test. In such context, the eLIFT strategy

using a simple and free first-line test will most likely be preferred by patients and physicians.

Only a minority of NAFLD and ALD patients develop advanced liver fibrosis and, given the very large NAFLD and ALD populations, this could seen as looking for a needle in a haystack. Moreover, the diagnosis of advanced liver fibrosis is very difficult because patients have no symptoms, physical examination is normal, and usually observed biological or radiological abnormalities are non-specific. Our results show that the eLIFT represents thus a very simple and attractive solution to help non-specialists identifying those NAFLD and ALD patients who don't need to be refer to the hepatologist because of high likelihood of no/mild fibrosis, and those who need further specialized evaluation because of increased risk of advanced liver fibrosis. Due to its design (retrospective analysis of our patient files), our study population was limited to patients for whom the decision of referral to the specialist was already made. Further work is now required to evaluate whether a more widespread and systematic use of eLIFT in patients from primary care or in at-risk populations such as diabetics will help to accurately and cost-effectively screen for advanced liver fibrosis. Such screening will probably become very soon relevant in NAFLD with the upcoming arrival in clinical practice of the new treatments that are currently evaluated in therapeutic trials[20]. Finally, survey data demonstrates that most of non-specialists do not use non-invasive tests in their patients having liver risk factors[21, 22]. Therefore, the validation of the concept of screening for advanced liver fibrosis using non-invasive tests of liver fibrosis will have to be accompanied with a lot of work in education to familiarize non-specialist physicians with the concept and the use of these tests in their daily clinical practice.

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BROUSSIER Thomas

Le easy LIver Fibrosis Test (eLIFT) permet d'éviter des évaluations non-invasives de fibrose spécialisées chez les patients NAFLD et/ou alcooliques

RÉSUMÉ

L'évaluation de la fibrose hépatique est nécessaire pour évaluer la gravité de la maladie dans la stéatose hépatique non alcoolique (NAFLD) et de maladie hépatique alcoolique (ALD). Cependant, la plupart de ces patients sont vus par des non-spécialistes. Le « easy liver fibrosis test (eLIFT) » est un test sanguin très simple, spécifiquement développé pour les non-spécialistes. En cas de score ≥ 8, le test indique la nécessité d'une évaluation spécialisée de la fibrose hépatique. Nous avons cherché à évaluer si l'utilisation de l'eLIFT permet de réduire les évaluations spécialisées « inutiles » de la fibrose hépatique chez les patients NAFLD et ALD.

Méthode: Les patients NAFLD et / ou ALD adressés pour la première fois dans notre centre pour une évaluation non invasive de la fibrose hépatique entre 10/2014 et 03/2017 ont été inclus rétrospectivement. Le FibroMeter^{VCTE} (combinaison de marqueurs sanguins avec le résultat de Fibroscan) a été utilisé comme test de référence pour l'évaluation spécialisée de la fibrose hépatique. Un résultat <0,384 signifie l'absence de fibrose ou fibrose minime et donc une «évaluation spécialisée inutile».

Résultats: 558 patients ont été inclus (NAFLD: 283, ALD: 156, mixte NAFLD + ALD: 119). Le résultat du FM^{VCTE} était <0,384 (évaluation spécialisée inutile) chez 58,8% des patients, ≥ 0,715 (fibrose avancée) chez 29,7% et entre 0,384-0,714 (diagnostic indéterminé) chez 11,5%. Le eLIFT était inférieur à 8 chez 47,7% des patients, dont 85,3% avaient également un FM^{VCTE} <0,384 et seulement 6,0% avaient un FM^{VCTE} >0,715. 90,4% des patients inclus avec un FibroMètre ≥ 0,715 avaient un eLIFT ≥ 8. Comparé à la stratégie «tous les patients sont adressés», l'utilisation du eLIFT comme test de première ligne aurait permis d'économiser 40% des coûts directement liés aux évaluations de la fibrose hépatique.

Conclusion: Utilisé par des non-spécialistes pour leurs patients atteints de NAFLD et d'ALD, le eLIFT améliore la pertinence des patients adressés pour une évaluation spécialisée de la fibrose hépatique.

Mots-clés : NAFLD, ALD, eLIFT, non-invasive evaluation

The Easy Liver Fibrosis Test (eLIFT) avoids unnecessary specialized evaluations of liver fibrosis in NAFLD and ALD patients

ABSTRACT

Background and Aims: Liver fibrosis evaluation is mandatory to evaluate disease severity in non-alcoholic fatty liver disease (NAFLD) and alcoholic liver disease (ALD), but most of these patients are seen by non-specialists. The easy liver fibrosis test (eLIFT) is a very simple blood test specifically developed for non-specialists with result ≥8 indicating the need for further specialized evaluation of liver fibrosis. We aimed to evaluate whether using the eLIFT helps to reduce unnecessary referrals for specialized liver fibrosis evaluations in NAFLD and ALD patients.

Method: NAFLD and/or ALD patients newly referred to our centre for a non-invasive evaluation of liver fibrosis between 10/2014 and 03/2017 were retrospectively included. The FibroMeter^{VCTE} (combination of blood markers with Fibroscan result) was taken as the reference test for specialized liver fibrosis evaluation, with result <0.384 indicating no/mild fibrosis and thus "unnecessary referral".

Results: 558 patients were included (NAFLD: 283, ALD: 156, mixed NAFLD+ALD: 119). FM^{VCTE} result was <0.384 (unnecessary referral) in 58.8% of patients, ≥0.715 (advanced fibrosis) in 29.7%, and 0.384-0.714 (undetermined diagnosis) in 11.5%. eLIFT was <8 in 47.7% of patients, of whom 85.3% had also FM^{VCTE} <0.384 and only 6.0% had FM^{VCTE} <0.715. 90.4% of patients with FibroMeter ≥0.715 had eLIFT ≥8. Compared to the strategy "all patients referred", the use of eLIFT as first-line test saved 40% of costs directly linked to liver fibrosis evaluations.

Conclusion: Used by non-specialists for their NAFLD and ALD patients, the eLIFT improve the relevance of patient referrals for specialized evaluation of liver fibrosis.

Keywords : NAFLD, ALD, eLIFT, non-invasive evaluation

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