TOPIC HIGHLIGHT

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Noninvasive assessment of alcoholic liver disease using unidimensional transient elastography (Fibroscan®)

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Abstract

Unidimensional transient elastography (TE) is a noninvasive technique, which has been increasingly used in the assessment of diffuse liver diseases. This paper focuses on reviewing the existing data on the use of TE in the diagnosis of fibrosis and in monitoring disease progression in alcoholic liver disease, on the factors that may influence the result of fibrosis prediction, and last but not least, on its potential use in assessing the steatosis degree. Therefore, this field is far from being exhausted and deserves more attention. Further studies are required, on large groups of biopsied patients, in order to find answers to all the remaining questions in this field.

Key words: Transient elastography; Alcoholic liver disease; Fibrosis; Steatosis; Liver stiffness; Controlled attenuation parameter

Core tip: This review article summarizes the existing data on the use of transient elastography in the noninvasive assessment of fibrosis and steatosis in alcoholic liver disease and highlights the still open questions in this field.

INTRODUCTION

Excessive alcohol consumption is a major public health issue[1,2] as it may lead to liver fibrosis and cirrhosis with life threatening complications[3] such as hepatocellular carcinoma (HCC)[4], liver failure and death[5].

The presence and progression of hepatic fibrosis towards cirrhosis is a main prognostic variable, impacting the survival of people with alcoholic liver disease[6]. Consequently, an important goal in alcoholic patients is to reliably identify those with advanced fibrosis and/or cirrhosis, which not only impact the patients' prognosis but may also be used as an argument to support the necessity to quit drinking.

Many efforts have been devoted lately to the development of noninvasive markers and tests that may reliably predict fibrosis stages in chronic liver diseases. One of the newer developments involve ultrasound elastographic methods for noninvasive liver fibrosis assessment, some of which have been studied and developed for the noninvasive assessment of steatosis, as well. The main method discussed here is the unidimensional transient elastography (TE) - Fibroscan®, one of the best studied elastographic methods.

PRINCIPLE

Unidimensional TE is performed using the Fibroscan® equipment (Echosens, Paris) which consists of a 5 MHz ultrasound transducer probe mounted on the axis of a vibrator. Mild amplitude and low frequency vibrations (50 Hz) are transmitted to the liver tissue, inducing an elastic shear wave that propagates through the underlying liver tissue. The velocity of the wave is directly related to tissue stiffness[7].

The technique measures the stiffness in a cylindrical volume 1 cm in diameter and 4 cm in length, amounting to about 1/500 of the entire liver volume - 100 times larger than the volume of the liver biopsy specimen[8,9].

WHO CAN PERFORM THE EXAMINATION?

The measurement can be performed even by a technician after a certain training period (around 100 cases)[9,10]; the clinical interpretation of the results, however, always requires an expert, who can take into consideration the demographics, disease etiology and biochemical profile of the patient at the moment of the examination[8].

PERFORMANCE PARAMETERS OF THE EXAMINATION

In accordance to the producer recommendations, the success rate (the number of measurements required to obtain 10 valid ones) was for a long time limited to at least 60%, while the IQR (interquartile range) to less than 30% of the median (M) liver stiffness (LS)[7], although the best concordance with the biopsy seems to be obtained when its value does not exceed 20% of the median[11].

According to the latest reports, it is considered that the "success rate $\geq$ 60%" parameter is no longer necessary, and the examination accuracy depends on the IQR/M ratio, influenced by the median LS value. Three reliability categories are therefore defined, with significantly different diagnostic accuracy: "very reliable" (IQR/M $\leq$ 0.10), "reliable" (0.10 < IQR/M $\leq$ 0.30 or IQR/M > 0.30 with median LS < 7.1 kPa), and "poorly reliable" (IQR/M > 0.30 with median LS $\geq$ 7.1 kPa)[12].

REPRODUCIBILITY

FibroScan appears to have good reproducibility[13]. In a series of 195 patients with chronic liver disease of various etiologies and without ascites, using the FibroScan to identify a suitable portion of the liver for examination, Fraquelli *et al*[14] found that overall agreement between two operators was 0.98 (95%CI: 0.977-0.987), and intraobserver agreement was 0.98 for both operators. Increased body mass index (BMI) (> 25 kg/m^2), steatosis (> 24% of fatty liver cells), and histological evidence of none to mild fibrosis (METAVIR stage < F2) were all significantly associated with reduced interobserver agreement.

LIMITATIONS OF THE TECHNIQUE

Because elastic waves do not travel through liquids, FibroScan has no value in patients with ascites[13]. Another important limitation is the impossibility to examine obese patients[13], because the probe is calibrated for a specific distance between the liver and the chest wall[15] and the low frequency vibration induced by the probe and/or the ultrasound wave can be strongly attenuated by the fatty tissue[7]. Castéra *et al*[15] found that a BMI > 30 kg/m^2 had the strongest association with both test failure and unreliable results. A special probe (XL probe) with a measurement depth of 35-75 mm[16] was developed for morbidly obese patients[17]. A study conducted specifically in patients with a BMI $\geq$ 30 kg/m^2 found that the use of the XL specialised probe reduced the rates of failure and unreliable results (LS measurement was successful in 45% of the cases with the M probe, *vs* 76% of the cases with the XL probe)[18].

WHAT ARE THE LS CUT-OFF VALUES FOR THE PREDICTION OF EACH FIBROSIS STAGE IN ALCOHOLIC LIVER DISEASE?

TE assessment of liver fibrosis has already been validated in many people with chronic liver diseases of various etiologies[19-24]. The already published meta-analyses demonstrated that the cause of liver disease is one of the most important factors leading to the heterogeneity of TE results, thus indicating that the different chronic liver diseases should be analysed separately[25-27]. In fact, the cut-off levels for specific stages of hepatic fibrosis vary according to the etiology of the liver disease. This could be easily explained by the fact that LS mainly reflects the amount of liver fibrosis not taking into account its topography and its consequences on liver architecture which are the basis of all semi-quantitative fibrosis staging systems[28].

Compared with other etiologies, few studies have been performed on groups of patients with alcoholic liver diseases (ALD) or, in the studies involving groups of patients with diffuse liver diseases, the ALD cases reach only a small percentage of the entire group[28-38]. The LS cut-off values for fibrosis stage prediction differ quite drastically, mainly due to the presence of inflammation, assessed by transaminase levels[33]. A recent meta-analysis[6], taking into consideration 5 retrospective and 9 prospective studies, with a total of 834 participants, could not identify the optimal cut-off values for the prediction of each fibrosis stage in ALD.

Only one study has established the cut-off values for the prediction of fibrosis stages ⩾ F1 in ALD, namely 5.9 kPa[29], which offered 83% sensitivity and 86% specificity, PPV 97.6%, NPV 35.3% and AUROC 0.84.

For the prediction of stage F2 or above, the TE sensitivity in the studies included in the Pavlov meta-analysis varied from 75% to 100% and the specificity from 80% to 100%, while the cut-off values in the majority of the analysed studies was around 7.5 kPa (range 7.00 to 7.8 kPa)[6]. The following results were obtained when using the 7.5 kPa cut-off in the meta-analysis: sensitivity 0.94 (95%CI: 0.86-0.97); specificity 0.89 (95%CI: 0.76-0.95); positive likelihood ratio (LR+) 8.2 (95%CI: 3.6-18.5); negative likelihood ratio (LR-) 0.07 (95%CI: 0.03-0.17)[6].

In the prediction of stages F3 or above, the sensitivity of the analysed studies in the meta-analysis varied from 72% to 100% and the specificity from 59% to 89% at cut-off values ranging from 8.0 to 17.0 kPa[6]. When considering only the studies yielding LS cut-off values around 9.5 kPa, for the prediction of ⩾ F3 stages, the TE sensitivity varied from 80% to 100% and the specificity from 50% to 80%. In the meta-analysis, when the 9.5 kPa cut-off value was used for the prediction of stages ⩾ F3, the following results were obtained: sensitivity 0.92 (95%CI: 0.83-0.97); specificity 0.68 (95%CI: 0.52-0.80); positive likelihood

ratio (LR+) 2.9 (95%CI 1.8-4.5); negative likelihood ratio (LR-) 0.11 (95%CI: 0.05-0.27)[6].

In alcoholic cirrhosis, the median LS value is higher than that observed in patients with viral cirrhosis[29]. This may be explained by the different spatial distribution of alcoholic fibrosis, which develops in centrolobular and perisinusoidal as well as in periportal regions[39]. Hepatic alcoholic lesions are also characterized by liver cell necrosis, reactive inflammation, steatosis and pericellular fibrosis or steatohepatitis[40].

Concerning the F4 stage prediction, fourteen studies with 834 participants were analysed, using nine different cut-off values ranging from 7.15 to 34.9 kPa. The sensitivity of the TE varied from 75% to 100% and the specificity from 33% to 94%[6]. The most frequently used cut-off value for the prediction of cirrhosis in these studies was 12.5 kPa. Using this value for the prediction of cirrhosis in the meta-analysis yielded the following results: sensitivity 0.95 (95%CI: 0.87-0.98); specificity 0.71 (95%CI: 0.56-0.82); positive likelihood ratio (LR+) 3.3 (95%CI: 2.1-5.0); negative likelihood ratio (LR-) 0.07 (95%CI: 0.03-0.19)[6].

A comment is however required: due to the relatively small number of studies performed on patients with ALD, whose authors agreed to disclose the necessary data, the cited meta-analysis[6] could not establish the optimal cut-off values for the prediction of each fibrosis stage in ALD, which therefore still remains an open subject. The proposed cut-off values for the different stages of hepatic fibrosis may be used in clinical practice, but with caution, since those reported values were simply the most common cut-off values used by the study authors[6]; they are insufficiently validated and there is always the risk of overestimation of LS values in patients who are not abstinent from alcohol consumption[6,7].

The practical conclusion of this meta-analysis[6] is that TE may be used as a diagnostic method to rule out liver cirrhosis (F4) in people with ALD when the pre-test probability is about 51% (range 15% to 79%); TE may also help in ruling out severe fibrosis (F3 or worse). Liver biopsy remains an option if the identification of the stage of hepatic fibrosis or cirrhosis cannot be clearly made after a clinical follow-up or any other noninvasive test considered useful by the clinician[6].

WHAT IS THE SIGNIFICANCE OF LS IN PATIENTS WITH ALCOHOLIC LIVER DISEASES?

LS was proven to correlate well with the grade of fibrosis in various liver diseases[41]. However, the authors of the initial concept have admitted "it is unlikely that only one physical parameter (LS) can describe completely a complex biological system of

which fibrosis is just a part"[42]. Indeed, in a group of biopsied patients with hepatitis C virus infection, although fibrosis is the main predictor of LS, steatosis and necroinflammatory activity cannot be ignored as they could explain the stiffness variability within the same fibrosis stage. The relationship between LS and fibrosis (F), steatosis (S) and necroinflammatory activity (A) is illustrated in the equation[43]:

LS (logarithm) = 0.493 + (0.180 × F) + (0.034 × S) + (0.033 × A)

This is also true of ALD patients. However, the exact relationship between the 3 histopathological parameters and liver stifness still remains to be established in these patients.

Glisson's capsule, covering the liver, is distensible but not elastic. It follows that additional space-occupying tissue abnormalities, such as oedema and inflammation, cholestasis, congestion, cellular infiltrations, and deposition of amyloid may interfere with LS measurement, independently of fibrosis[44]; these confounding factors should be taken into account when interpreting the values of LS.

The necroinflammatory activity

The necroinflammatory activity influences LS, leading to an increase parallel with the histologic activity grade[14,45,46]. As a result, the tissue changes associated to an acute hepatitis may increase stiffness significantly, sometimes up to cirrhotic levels, due to cellular intumescence and sometimes to severe cholestasis[47]. The contribution of these non-fibrotic changes on stiffness was proven by the progressive decrease in stiffness alongside the decrease in transaminase levels[48,49]. On the other hand, in chronic hepatitis patients with transaminase flares, the increased stiffness is caused not only by pre-existing fibrosis but also by superimposed cellular intumescence[50]; consequently, the LS interpretation in patients with high ALT levels must be made with caution: at ALT levels above 2.5 × the normal limit, there is a risk to overestimate the fibrosis stage, which should be stated in the final examination result[19].

The influence of transaminase levels on the accuracy of fibrosis prediction by TE was highlighted by Mueller *et al*[34] in ALD patients, because AST levels > 100 U/L lead to an overestimation of fibrosis stage. The authors cautioned that active inflammation of the liver should first be excluded by blood tests, prior to the noninvasive assessment of fibrosis by TE. By excluding those patients with AST > 100 U/L at the time of LS assessment from this cohort, the area under the receiver operating characteristic (AUROC) for cirrhosis detection by FS improved from 0.921 to 0.945 while specificity increased from 80% to 90% at a sensitivity of 96%. A similar AUROC was obtained for fibrosis stages ≥ F3 if LS measurements were restricted to patients with AST < 50 U/L. If transaminase levels are < 100 U/L, the LS value can identify liver fibrosis and can be used as a diagnostic

tool[34].

Extrahepatic cholestasis

Extrahepatic cholestasis increases LS independently from fibrosis[51], and in patients requiring biliary drainage, the LS decreases with a mean of 1.2 ± 0.56 kPa for each 1 g/dL decrease in bilirubin. For this reason, it is recommended that before interpreting the LS results, a possible cholestasis be excluded through imaging and laboratory tests, in order to avoid the overestimation of fibrosis stage. The reasons underlying the high stiffness in cholestasis are unknown but could be related to tissue swelling, oedema and increased intracellular pressure due to impaired bile flow[44]. In addition, cholestasis may be a general phenomenon leading to higher LS in various chronic liver diseases, since intrahepatic cholestasis has been shown to correlate strongly with LS in patients with acute hepatitis[49] but also with ALD[34].

Congestive heart failure

Congestive heart failure may also lead to increased LS up to cirrhotic levels due to a higher content in hepatic blood, in up to 60% of patients[52-54]. In patients with decompensated congestive heart failure, LS is dramatically elevated and rapidly decreases during clinical recompensation due to diuretic therapy[55].

Liver infiltration, deposits, rare diseases

The rare infiltration with mast cells, also encountered sometimes in ALD patients, can also lead to dramatically increased LS[44]. An important noncancerous differential diagnosis of increased LS is amyloidosis[56,57].

Liver steatosis

The influence of steatosis on LS remains controversial. In some studies, steatosis did not significantly impact the stiffness, even after adjusting for fibrosis stage, but the proportion of patients with severe steatosis was too low to ensure the accurate quantification of any influence[7,17,45]. Other studies proved that for the same fibrosis stage and activity grade, the presence of steatosis lead to a significant increase in LS[43], while the morphometric analysis of the biopsy specimen proved that steatosis does indeed influence LS independently of fibrosis. This influence is negligible in cirrhosis but significant in non-cirrhotic patients[58]. Still, a steatotic, non-inflamed liver is usually softer, not stiffer. Further studies are therefore necessary to explain to what extent does steatosis influence LS values, especially in ALD patients.

LS AND ALCOHOLIC LIVER DISEASE FOLLOW-UP

Effect of detoxification on LS assessed by Fibroscan® in alcoholic patients

Gelsi *et al*[40] studied on a population from an addi-

ctology unit the changes in LS occurring after alcohol weaning over a period of 60 d, and compared these changes in relapser and abstinent patients. They found a rapid decrease in LS [-1.67% ± (-27.6%) on day 8] during detoxification in a high proportion of patients if abstinence was sustained: 41% of patients had lower values on day 8 and 66.7% on day 60. Relapsers were found to have a new increase in LS during follow-up after alcohol relapse.

Similar results were reported in a previous paper by Mueller *et al*[34] on 50 patients undergoing alcohol detoxification. The first finding was a parallel decrease in LS and AST values during alcohol detoxification. The second was that LS was more likely to decrease in patients with alcoholic liver disease with high initial AST levels, but remained stable once AST levels were below 100 U/L. The decrease in LS during alcohol detoxification could not be explained by changes in fibrosis stage given the short observation interval of 5.3 d. Therefore any change in LS must be attributed to other factors, most likely steatohepatitis[34].

Bardou-Jacquet *et al*[3] also confirmed these results during a much longer follow-up period (median 32.5 wk) with a precise control of the addiction. LS decreased after alcohol cessation over a long period of time, and this was of particular importance when the initial LS values varied between 8-16 kPa; these levels indicate significant fibrosis or cirrhosis in chronic hepatitis C, but should be interpreted with caution in ALD[3]. In this study, relapsers were found to have either an increase or a decrease in LS during follow up, possibly due to the level of alcohol consumption after relapse; relapsers could consume less alcohol during follow-up which could lead to a decrease in LS. This particular point should be assessed in a prospective study recording the precise alcohol amount consumed. If these results will be confirmed, then TE would have proven to be a useful tool in monitoring adherence during follow-up and fluctuations in alcohol consumption[3]. Considering that in this study LS and its variation were correlated with AST and GGT levels, the TE performance in estimating the fibrosis stage in ALD may be improved by the use of a coefficient based on liver enzyme values[3].

Prospective studies performed on large groups of biopsied patients followed up during alcohol withdrawal are, however, necessary and they must also establish the best interval between alcohol cessation and TE evaluation. Therefore, the interpretation of Fibroscan results in alcoholics must take into account whether alcohol consumption was continuous, the abstinence period as well as the biochemical tests at the moment of the examination (mainly AST, ALT and GGT).

Use of TE in monitoring disease progression in patients with alcoholic liver disease: Portal hypertension and hepatocellular carcinoma

In alcoholic cirrhosis, the evidence relating to the diagnostic accuracy of TE in relation to portal hypertension and oesophageal varices is weaker than that relating to fibrosis and cirrhosis[13].

Concerning portal hypertension, the studies performed on patients with various etiologies of liver cirrhosis report that TE can be quite effective in detecting patients with a high risk of having developed clinically significant elevations of hepatic venous pressure gradient (HVPG) or varices[41]. Several studies have shown that there is a good correlation between LS values and HVPG in patients with advanced liver diseases[37,59,60]. A recent meta-analysis found an excelent diagnostic performance of TE in predicting clinically significant PH (HVPG $\geqslant$ 10 mmHg) in patients with compensated chronic liver disease/cirrhosis, with an AUROC of 0.93[61]. While the correlation is excellent for HVPG values between 5 and 10-12 mmHg (typical of cirrhosis without evident clinical manifestations related to PH), it hardly reaches statistical significance for values above 12 mmHg[41,60].

Lemoine *et al*[38] analysed a group of 48 patients with alcoholic cirrhosis and 44 with viral C cirrhosis and found that, although all patients had compensated cirrhosis Child-Pugh class A, the LS was significantly higher in the former group (49.9 ± 21.7 kPa *vs* 25.7 ± 14 kPa, P < 0.001) and the area under ROC curve for the prediction of clinically significant portal hypertension was 0.94 ± 0.03; a cutoff value of 34.9 kPa had a sensitivity, specificity, PPV and NPV of 0.90, 0.88, 0.97 and 0.64, respectively, for the diagnosis of clinically significant portal hypertension. The cutoff values were different in the two studied groups, higher in the alcoholic cirrhosis group than in the viral C cirrhosis group (34.9 kPa *vs* 20.5 kPa), suggesting that LS values must be closely interpreted according to the cause of the liver disease[38]; apart from the amount and location of fibrosis, other elementary lesions such as steatosis and inflammation may also influence the LS values in alcoholic patients.

Even more uncertainty and controversy involves the possibility of predicting the presence and size of oesophageal varices (OV) based on LS values[41]. Some studies found a correlation between LS and the presence of oesophageal varices[60,62,63] with AUROCs ranging from 0.74 to 0.85 and cut-offs from 13.9 to 21.5 kPa. Although the sensitivity for the prediction of the presence of OV was high (76%-95%), specificity was in general not satisfactory (43%-78%).

A study by Nguyen-Khac *et al*[63] found that, in alcoholic cirrhosis, using a threshold of 47.2 kPa, FibroScan could predict the presence of large oesophageal varices with a sensitivity of 85% (95%CI: 67%-95%) and a specificity of 64% (95%CI: 53%-74%).

Some studies have highlighted the potential utility of spleen stiffness (SS) assessment for the prediction of the presence of OV and of the PH degree in cirrhotic patients[64,65]. Further validation is needed before the place of SS in clinical practice can be defined[41], especially in alcoholic liver disease.

Hepatocellular carcinoma

Several cross-sectional studies[66-69] identified that high LS values measured by TE are significantly associated with the risk of HCC. One of these studies was performed on a group including patients with alcoholic cirrhosis[69]. However, as mentioned in the EASL-ALEH guidelines on noninvasive tests for evaluation of liver disease severity and prognosis, these cross-sectional studies only describe the "static" phenomenon that patients with HCC have higher LS values than those without HCC, not considering the "dynamic" association between the progression or regression of liver fibrosis and the risk of future HCC development[41]. Several longitudinal prospective studies[70-80] have recently been published and stratified LS values were identified as an independent risk factor for HCC development. For example, in a study performed on patients with hepatitis C, compared with patients with LS values ⩽ 10 kPa, those with higher LS values were at significantly higher risk of developing HCC (LS values, 10.1-15 kPa, HR = 16.7; LS values, 15.1-20 kPa, HR = 20.9; LS values, 20.1-25 kPa, HR = 25.6; and LS values, > 25 kPa, HR = 45.5)[68]. Nevertheless, few studies include ALD patients in their study groups[70,79], meaning that the cutoff values described in HCV and HBV patients cannot be extrapolated for ALD patients.

Concerning ALD patients, further studies are needed to expand the clinical prognostic usefulness of TE. In addition, optimal LS cut-off values to assess the risk of HCC development should be set up in the future in larger longitudinal prospective studies. Using TE to assess and monitor the risk of HCC development will help physicians to establish optimum treatment strategies. Further research should investigate whether the accuracy of the surveillance strategy can be enhanced by incorporating these noninvasive methods into the routine surveillance strategy[41].

NONINVASIVE ASSESSMENT OF STEATOSIS IN ALCOHOLIC LIVER DISEASE USING UNIDIMENSIONAL TE (FIBROSCAN®)

Steatosis is a frequent histological finding in patients with chronic liver diseases[81,82]. Ethanol consumption, the most popular cause for steatosis, induces fatty liver *via* multiple pathways[83]. An accurate method to detect and quantify steatosis would be extremely useful and it has been the subject of extensive research lately. One of the major obstacles in better defining the liver fat has been the lack of an easy, noninvasive and quantitative method to measure steatosis.

A novel noninvasive tool based on the evaluation of ultrasound attenuation using the Fibroscan® device (Echosens, Paris, France) has been developed, using a novel proprietary algorithm called controlled attenuation parameter (CAP)[84]. This parameter is an estimate of the total ultrasonic attenuation (go-and-return path) at the central frequency of the regular or M probe of the Fibroscan® (3.5 MHz) and is expressed in decibel per meter (dB/m). CAP is evaluated using the same radio-frequency data and the same region of interest as the region used to assess LS[85].

Since the development of this method, CAP has been used in some studies performed on patients with various diffuse liver diseases[84,86-94]. Among the histopathological parameters, these studies analyzed mainly the influence of steatosis and fibrosis and, in some studies, also that of necroinflammatory activity on CAP. One study, performed on NASH patients, included the influence of lobular inflammation and ballooning on CAP, apart from that of steatosis and fibrosis[95].

A recent study performed on a series of Romanian patients[96] has confirmed the preliminary results of previous studies[84,86-90,92-94] namely that, among all histopathological parameters assessed during various diffuse liver diseases, CAP is independently influenced only by the amount of steatosis, not by fibrosis, necroinflammatory activity, ballooning or lobular inflammation (quantified according to liver disease etiology). The CAP value increases alongside the increase in steatosis degree. Despite some overlap in adjacent steatosis grades, the overall differences between any two steatosis grades are statistically significant, except between ⩾ 34%-66% and 67%-100% fatty load, which was also reported by several authors[87-89,97,98]. Moreover, this situation is also encountered when quantifying steatosis using ^{1}H-magnetic resonance spectroscopy[98], which raises the suspicion of bias in steatosis quantification for those grades on liver biopsy[96].

In a meta-analysis assessing the CAP accuracy for steatosis detection[99], the median optimal CAP cut-off values were 232.5 dB/m, 255 dB/m and 290 dB/m for steatosis involving ⩾ 11%-33% (S1), ⩾ 34%-66% (S2) and 67%-100% of hepatocytes (S3), respectively, and the summarized sensitivity and specificity values were 0.78 (95%CI: 0.69-0.84) and 0.79 (95%CI: 0.68-0.86) for ⩾ S1, 0.85 (95%CI: 0.74-0.92) and 0.79 (95%CI: 0.71-0.85) for ⩾ S2, and 0.83 (95%CI: 0.76-0.89) and 0.79 (95%CI: 0.68-0.87) for S3.

Few ALD patients have been included in studies performed so far, evaluating the utility of CAP in assessing steatosis in various difuse liver diseases; for this reason, a complete analysis of patients with this etiology was never acomplished. Certain aspects of this analysis still remain to be clarified in future studies in alcoholic patients[44,100]: Which are the CAP cutoff values for the prediction of steatosis grade in ALD? To what extent does the histology of liver steatosis (micro- or macrovesicular) influence CAP? Is there a quantitative relationship between the location and histological type of the hepatitis, the transaminase level and LS? What is the diagnostic value of LS in more complex clinical settings, for example a patient

with combined alcoholic liver fibrosis, steatohepatitis, and cardiomyopathy? How does CAP change in response to fast kinetics such as alcohol detoxification, binge drinking, after meals and the intake of certain drugs?

CONCLUSION

In conclusion, in alcoholic liver disease, unidimensional TE is useful mainly in 2 areas: to identify patients with fibrosis, so that efforts may be made to prevent the development of cirrhosis, and to identify patients with cirrhosis, enabling a better monitorization for the development of complications such as oesophageal varices and HCC. The results may be influenced by factors other than the degree of fibrosis present in the liver, mainly acute alcoholic hepatitis. The current drinking status is also relevant. Prospective studies performed on large groups of biopsied patients are, however, necessary, to establish the optimal cut-off values of LS and CAP for the prediction of each fibrosis and steatosis grade.

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