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Clinical applications of transient elastography

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Chronic liver disease represents a major public health problem, accounting for significant morbidity and mortality worldwide. As prognosis and management depend mainly on the amount and progression of liver fibrosis, accurate quantification of liver fibrosis is essential for therapeutic decision-making and follow-up of chronic liver diseases. Even though liver biopsy is the gold standard for evaluation of liver fibrosis, non-invasive methods that could substitute for invasive procedures have been investigated during past decades. Transient elastography (TE, FibroScan®) is a novel non-invasive method for assessment of liver fibrosis with chronic liver disease. TE can be performed in the outpatient clinic with immediate results and excellent reproducibility. Its diagnostic accuracy for assessment of liver fibrosis has been demonstrated in patients with chronic viral hepatitis; as a result, unnecessary liver biopsy could be avoided in some patients. Moreover, due to its excellent patient acceptance, TE could be used for monitoring disease progression or predicting development of liver-related complications. This review aims at discussing the usefulness of TE in clinical practice. **(Clin Mol Hepatol 2012;18:163-173)**

Keywords: Chronic liver disease; Cirrhosis; Decompensation; Fibroscan; Fibrosis; Hepatocellular carcinoma; Liver stiffness measurement; Transient elastography

INTRODUCTION

As liver fibrosis is closely related to the prognosis of patients with chronic liver diseases (CLD), assessment of the extent and progression of liver fibrosis is important in deciding treatment strategies for patients with CLD.[1,2] Although liver biopsy (LB) has been considered as the golden standard for evaluation of liver fibrosis to date, several issues such as sampling errors, intra- and inter-observer variability, and potential life-threatening complications have prevented wide use of LB in clinical practice.[3,4] Moreover, serial LB examinations to monitor the dynamic changes in liver fibrosis or disease progression is impossible because of the inherent invasiveness. Therefore, the need for a non-invasive method of liver fibrosis assessment has increased and various surrogate models using blood or clinical parameters have been proposed.[5]

Recently, liver stiffness measurement using transient elastography (TE; FibroScan®, EchoSens, Paris, France), which is an ultrasound-based modality for quantitative assessment of liver fibrosis, has been introduced and had gained increasing attention globally. First reported in 2003, its clinical usefulness has been investigated in a large number of studies.[6-13] Most studies have demonstrated diagnostic accuracy of TE for assessing liver fibrosis in various etiology of CLDs cross-sectionally.[14-16] Recently, an additional role of

Abbreviations:

ALT, alanine aminotransferase; APRI, aspartate aminotransferase -to-platelet ratio index; ASPRI, age-spleen-platelet ratio index; AST, aspartate aminotransferase; AUROC, areas under the receiver operating characteristics curve; BMI, body mass index; CHB, chronic hepatitis B; CHC, chronic hepatitis C; CLD, chronic liver disease; HCC, hepatocellular carcinoma; HEV, high risk esophageal varices; HVPG, hepatic venous pressure gradient; IQR, the interquartile range; IQR/M, the interquartile range/median value; kPa, kilopascals; LB, liver biopsy; LRE, liver related events; LSPS, LSM spleen diameter to platelet ratio score; TE, transient elastography

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TE, monitoring disease progression has begun to attract attention, which indicates that the role of TE is not merely limited in lessening unnecessary LB, but TE can enable establishment of tailored management strategies by providing more detailed prognostic information.[17]

Here, we review currently available data regarding the role of TE in liver fibrosis assessment and prognosis prediction.

TRANSIENT ELASTOGRAPHY

The basic principle of TE is that the propagation velocity of a wave through a homogenous tissue is proportional to its elasticity, which is correlated with the amount of fibrosis in the liver.[18] Briefly, TE consists of an ultrasound transducer mounted on the axis of the vibrator, which produces vibration of a mild amplitude and low frequency (50 Hz), consequently inducing an elastic shear wave that propagates through the liver. Pulse-echo ultrasound follows the propagation of the shear wave and measures its velocity, which is related to liver tissue stiffness. It is reported that the velocity of elastic waves is faster in fibrotic liver than normal livers in previous study.[6]

Performance of TE takes only a few minutes, and it is well tolerated by most patients. TE is performed on the right lobe of the liver, through intercostal spaces, with the patient lying in dorsal decubitus with the right arm in maximal abduction. The operator, assisted by time motion ultrasound images, locates the probe in a liver portion at least 6 cm thick and free of large vascular structures and gallbladders and presses the probe button to commence the measurement. Usually, 10 valid measurements should be performed to examine a patient with TE. The median value of the ten valid measurements is considered representative of liver elasticity. The success rate is calculated as the number of valid measurements divided by the total number of measurements. Examinations with a success rate higher than 60% are considered reliable. The results are immediately obtained after performance of TE and expressed in kilopascals (kPa), corresponding to the median value of 10 validated measurements (range 2.5-75 kPa). The interquartile range (IQR), which represents the intrinsic variability of TE, <30% of the median indicates a high-quality result.

However, in a recent study, the IQR/median value (IQR/M) was recently proposed as a factor that determines the accuracy of TE irrespective of the success rate, in patients with chronic hepatitis C (CHC).[19] In contrast, regarding patients with chronic hepatitis B (CHB), advanced liver fibrosis stage on LB (F3-4) was significantly associated with non-discordance with LB data, regardless of IQR/M and success rate.[20] Thus, further studies are necessary to resolve this controversial issue.

NORMAL TE VALUES

Besides assessment of liver fibrosis, it is also important to confirm whether TE can reliably identify patients with CLD in the normal population. Nevertheless, only few studies have been available. Roulot et al examined a large cohort of 429 apparently healthy French subjects to establish normal TE values (5.81±1.54 [range, 3.8-8.0] kPa in men vs. 5.23±1.59 [range, 3.3-7.8] kPa in women, $P<0.01$).[21] Normal TE values for Asian subjects have been also reported. Fung et al reported a mean TE value in 28 healthy living-related liver donors of 4.6 (range, 2.0-7.1) kPa, and all subjects had TE values of <7.2 kPa, which indicated that they had no significant fibrosis.[22] Our group has also reported that the normal range of TE values is 3.9-5.3 kPa, which was calculated from 69 strictly selected living liver and kidney donors.[23] All these data demonstrated that TE can reliably identify high-risk subpopulations without overlap between the normal and abnormal ranges of TE values and indicated that the use of TE can be extended as a screening tool.[24]

However, it is also noticeable that the mean LS values in Asian studies seem to be slightly lower than those in European studies; furthermore, the influence of gender and metabolic syndrome on TE value remains controversial.[25] Thus, further large-scale confirmative studies are still required.

DIAGNOSTIC PERFORMANCE OF ASSESSING LIVER FIBROSIS

Most studies on TE have focused on its ability to identify significant fibrosis and cirrhosis, because the presence of significant fibrosis is an indication for antiviral treatment and the presence of cirrhosis is cornerstone for initiating surveillance program for the early detection of hepatocellular carcinoma (HCC) development. As the current gold standard for liver fibrosis assessment, LB is the reference for calculation of the diagnostic accuracy of TE. The accuracy of TE has been estimated by calculating areas under the receiver operating characteristics curve (AUROC) for prediction of each fibrosis stage based on LB and comparing these with the AUROC values of other non-invasive models.

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Hepatitis C

A considerable number of studies from Western nations have demonstrated that TE values are significantly correlated with histological fibrosis stage and have high diagnostic accuracy superior or similar to other non-invasive methods such as FibroTest in patients with CHC (Table 1).[7,8,26-29] In these studies, the AUROC of TE ranged from 0.77 to 0.90, with a cutoff value of 6.2-8.7 kPa for assessment of significant fibrosis (F≥2), and an AUROC of 0.90-0.97 and cutoff value of 9.6-14.8 kPa for assessment of cirrhosis (Table 1). In South Korea, one multi-center cohort study reported the diagnostic performance of TE in populations with CHC (Table 1).[29] In this study, the optimal cutoff value for significant fibrosis was 6.2 kPa and that for cirrhosis was 11.0 kPa, which were more accurate than other non-invasive parameters such as aspartate aminotransferase (AST)-to-platelet ratio index (APRI).[29]

Hepatitis B

Marcellin et al first reported the diagnostic accuracy of TE in populations with CHB.[14] In this study, the AUROC was 0.81 for significant fibrosis and 0.93 for cirrhosis. Several other studies have also reported the diagnostic accuracy of TE in patients with CHB (Table 1).[14-16,30-33] The performance and corresponding cutoff TE values for predicting significant fibrosis (AUROC, 0.81-0.95; cutoff value, 6.3-7.9 kPa)[31-33] and cirrhosis (AUROC, 0.80 to 0.98; cutoff value, 9-13.8 kPa) are shown in Table 1.[14-16,30-33] Currently, TE is considered to have an acceptable diagnostic accuracy in patients with CHB,[34] although the overall AUROCs seem slightly lower than those reported from populations with CHC (Table 1).

In general, the cutoff values for cirrhosis in patients with CHB tend to be lower than those for CHC. This phenomenon can be explained by the fact that the amount of liver fibrosis is lower because hepatitis B virus tends to generate macronodular cirrhosis. In addition, the physician should also keep in mind the overestimating influence of alanine aminotransferase (ALT) flare, which is frequent in CHB.[35] Thus, TE values in populations with CHB should be interpreted cautiously due to the simultaneous possibility of false negatives (low fibrotic extent) and false positives (high ALT). To overcome the confounding effect of high ALT, several studies have suggested varying cutoff values according to ALT levels in patients with CHB.[32,16]

Other etiologies

Other studies have reported the accuracy of TE in patients with CLD related to etiologies other than CHB and CHC.[36-46] First, the role of TE was investigated in patients with hepatitis C and HIV co-infection.[36,40-42] In these studies, the AUROC of TE for significant fibrosis ranged from 0.72 to 0.87, with cutoff values of 4.5-9.3 kPa, and the AUROC for cirrhosis from 0.87 to 0.99, with cutoff values of 11.8-14.0 kPa, which are similar to those in

Table 1. Diagnostic performance of transient elastography in predicting significant fibrosis (≥F2) and cirrhosis (F4) in patients with chronic hepatitis C and B

Authors	Etiology	Country	Patients (n)	≥F2 (%)	F4 (%)	Cut-offs (kPa) ≥F2/F4	AUROC ≥F2/F4	Se (%) ≥F2/F4	Sp (%) ≥F2/F4	+LR ≥F2/F4	-LR ≥F2/F4
Castera et al (2005)	HCV	France	183	74	25	7.1/12.5	0.83/0.95	67/97	89/91	6.09/9.66	0.37/0.14
Ziol et al (2005)	HCV	France	251	65	19	8.7/14.5	0.79/0.97	56/86	91/96	6.63/23.05	0.48/0.14
Arena et al (2008)	HCV	Italy	150	56	19	7.8/14.8	0.91/0.98	83/94	82/92	4.58/11.27	0.20/0.07
Nitta et al (2009)	HCV	Japan	165	60	14	7.1/9.6	0.88/0.90	80/91	80/78	4.1/-	4.2/-
Sirli et al (2010)	HCV	Romania	150	89	10	6.8/13.3	0.77/0.97	60/93	73/96	3.53/24.08	0.64/0.07
Kim et al (2011)	HCV	Korea	91	55	9	6.2/11.0	0.90/0.97	76/77	97/93	30.4/0.3	12.8/0.2
Marcellin et al (2009)	HBV	France	173	50	8	7.2/11.0	0.81/0.93	70/98	83/75	4/1	-/0.01
Kim et al (2009)	HBV	Korea	91	90	42	-/9.7	-/0.80	-/82	-/62	-/4.97	-/0.13
Chan et al (2009)	HBV	China	161	77	24	-/9	-/0.93	-/98	-/75	-/1	-/0.01
Kim et al (2009)	HBV	Korea	130	92	67	-/10.1	-/0.84	-/76	-/81	-/-	-/-
Zhu et al (2010)	HBV	China	175	45	16	7.9/13.8	0.95/0.98	88/93	90/91	-/-	-/-
Ogawa et al (2011)	HBV	Japan	44	45	9	6.3/12.0	0.86/0.89	95/75	74/88	3.66/-	6.58/-

AUROC, area under the receiver operating characteristic curve; HCV, hepatitis C virus; HBV, hepatitis B virus; Se, sensitivity; Sp, specificity; +LR, positive likelihood ratio; -LR, negative likelihood ratio.

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patients with CHC only. Additionally, recent studies have investigated the usefulness of TE in patients with non-viral liver disease such as primary biliary cirrhosis, primary sclerosing cholangitis, or Wilson's disease.[37,38,43,44]. Although the diagnostic accuracy was considerable (AUROC, range 0.81-0.95 for significant fibrosis and 0.91-0.96 for cirrhosis), its usefulness requires further validation. Interestingly, recent studies have suggested the ability of TE to assess fibrosis stage in patients taking methotrexate with potential hepatotoxicity due to rheumatoid arthritis, inflammatory bowel disease, or psoriasis.[39,45,46]

Meta-analysis

Four meta-analyses have assessed the diagnostic performance of TE.[47-50] In the most large-scaled study including 50 studies, the mean AUROCs for the diagnosis of significant fibrosis and cirrhosis were 0.84 and 0.94, respectively, with optimal cutoff values of 7.6 and 13.01 kPa, respectively.[48] Although previous meta-analyses suggested that TE is a reliable method for assessment of liver fibrosis stage irrespective of etiology, it should be noted that most studies included in the meta-analysis was based on Western populations with CHC. Consequently, it would be unwise to apply these cutoff values from previous meta-analysis to patients with diverse CLD etiologies.

Combination with other fibrosis prediction models

To increase the accuracy of liver fibrosis assessment, new approaches using a combination of TE and other fibrosis prediction models have been proposed in several studies.[51-56] A recent study by Castera et al suggested that the number of LB for assessment of significant fibrosis could be significantly reduced through the use of combinations of TE and FibroTest in populations with CHC.[51] Similarly, our group also demonstrated that the performance of TE can be enhanced when combined with other fibrosis prediction models such as FibroTest in patients with CHB.[54-56] However, the cost-effectiveness of combining other non-invasive models with TE needs to be clarified in the future.

CHANGES IN TE VALUES DURING ANTIVIRAL TREATMENT

Due to the ease, safety, and rapidity of performing, it can be assumed that TE can be used for monitoring of the dynamic changes of liver fibrosis during anti-viral or anti-fibrotic treatment. Indeed, several studies have reported the clinical usefulness of TE for monitoring of the potential fibrosis regression during antiviral treatment in patients with CHC and CHB.[33,57,58]

Hepatitis C

The clinical implications of changes in TE values during antiviral treatment for patients with CHC have been investigated in several studies. Two prospective studies by Vergniol et al[57] and Ogawa et al[58] demonstrated that patients with CHC showing sustained virological responses to pegylated interferon-ribavirin combination therapy had significantly reduced TE values at the end of follow-up. Moreover, Ogawa et al reported that patients with non-sustained virological responses but with a biochemical response showed a greater reduction in TE values than did those with a non-biochemical response.[58] Subsequent studies reported similar results, suggesting that changes in TE values during antiviral treatment in patients with CHC may represent alterations in liver fibrosis severity.[59,60] However, it was not clearly indicated in these studies whether the reduction in TE values was closely correlated with regression of liver fibrosis based on paired biopsy and with favorable long-term clinical outcomes.

Hepatitis B

Dynamic changes in TE values during antiviral treatment in patients with CHB have been mostly reported in Asian countries.[30,61-63] In a large prospective cohort study of 426 patients, Fung et al reported that a significant decline in TE value occurred in patients with CHB after 3 years of antiviral treatment using oral agents.[61] However, the significant reduction in TE values at follow-up compared with baseline (6.1 kPa vs. 7.8 kPa respectively) was limited in patients who had elevated ALT levels at baseline and subsequent normalization after 3 years. As liver histology was not available in this study, it was not certain that decline in TE values reflected liver fibrosis regression or ALT stabilization of by antiviral treatment. To exclude the confounding effect of high ALT, our group investigated changes in TE values during antiviral treatment in 41 patients with CHB showing low ALT levels (≤2× upper limit of normal).[30] After 1-2 years of antiviral treatment, TE values significantly decreased compared with baseline, whereas ALT levels were unchanged (Fig. 1). Interestingly, 3 patients with reduced TE values experienced concomitant fibrosis regression on follow-up

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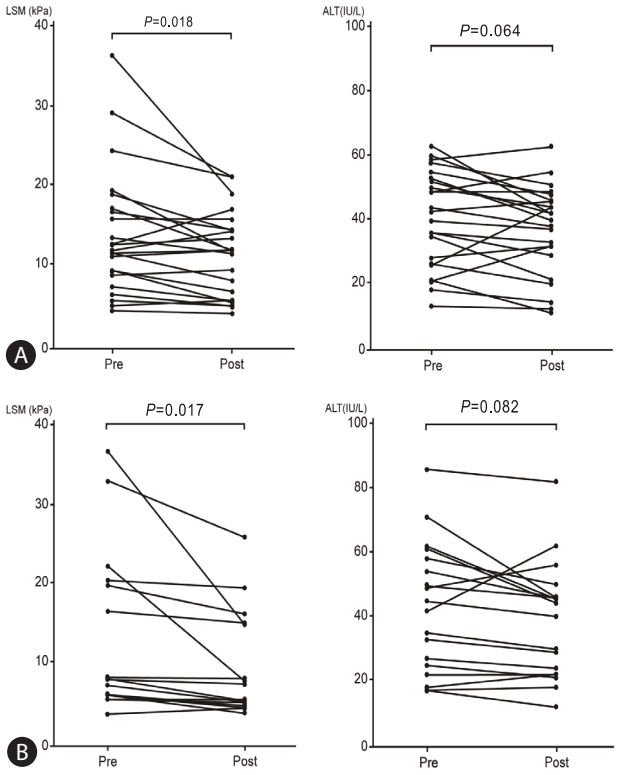

Figure 1. Changes in TE values and ALT levels between pre-and post antiviral treatment in patients with CHB who underwent follow-up TE after 1 year (n=23, A) or 2 years (n=18, B) of antiviral treatment using nucleoside analogs. In both groups, TE values decreased significantly after antiviral treatment, whereas ALT levels were unchanged. TE, transient elastography; ALT, alanine aminotransferase (adapted from reference 30).

biopsy, suggesting the potential fibrosis regression by long-term antiviral treatment can be monitored using TE.

However, whether changes in TE values indicate fibrosis regression remains controversial, because a recent study by Lim et al, which compared serial TE values and paired LB in 15 patients with CHB undergoing antiviral treatment, reported that the reduction in TE values was correlated with improved necroinflammatory scores, not with fibrosis regression.[62]

PREDICTION OF HEPATIC DECOMPENSATION

Foucher et al[64] reported that the cutoff value of 27.5, 37.5, 49.1, 53.7, and 62.7 kPa had >90% negative predictive values for the presence of large esophageal varices (stage 2/3), Child-Pugh score B or C, past history of ascites, HCC, and esophageal bleeding, respectively. Subsequently, correlations between TE values and hepatic decompensation due to increased portal hypertension have been investigated in several studies.

A significant correlation between TE values and portal hypertension, expressed as the hepatic venous pressure gradient (HVPG), was demonstrated by Vizzutti et al,[65] suggesting that TE may reflect a progressive rise in portal pressure mainly due to increased hepatic vascular resistance caused by fibrillar extracellular matrix accumulation. As variceal bleeding is the most important complication of portal hypertension, the relationship between TE values and the presence of esophageal varices has been also investigated

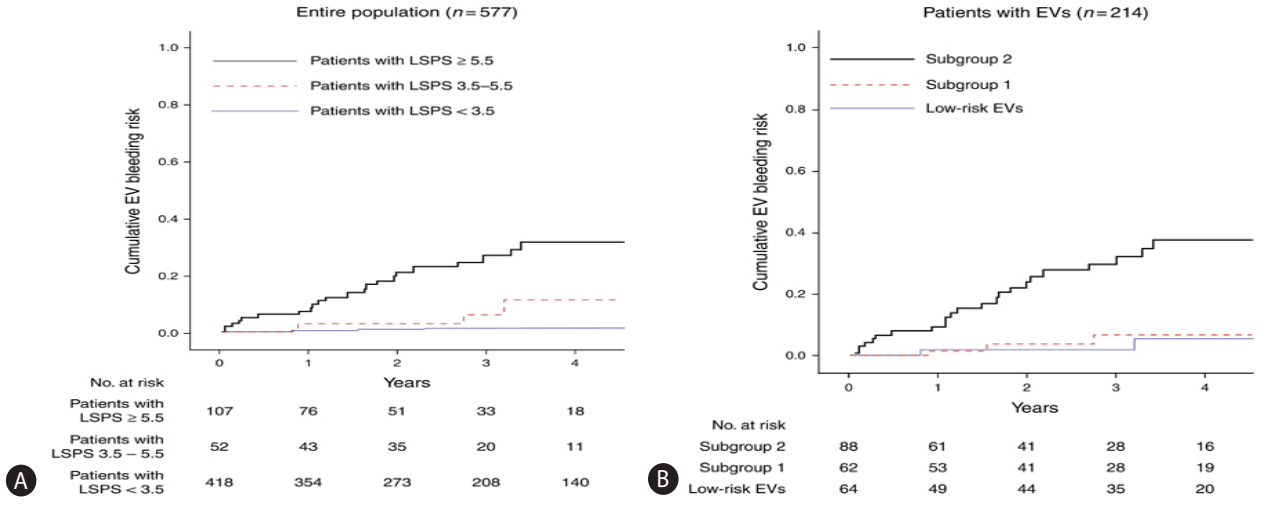

Figure 2. Cumulative incidence rates of EV bleeding based on LSPS values. The incidence of variceal bleeding increased significantly in association with higher LSPS value (long-rank test, $P<0.001$; A) Among patients with high-risk EV, the incidence rate of variceal bleeding was significantly higher in patient with LSPS ≥6.5 (subgroup 2; B) than those with LSPS <6.5 (subgroup 1; B). EV, esophageal varice; LSPS, liver stiffness-spleen diameter to platelet ratio score (adapted from reference 70).

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in several studies.[66-68] All of these studies demonstrated that there is a significant correlations between TE values and the presence of esophageal varices and that TE values could predict the presence of large varices (more than grade 2).[66,67] Although TE can predict the presence of esophageal varices and consequently assist in selection of candidates for endoscopic screening or prophylactic treatment, several issues still remain unresolved. First, the cutoff values (range, 13.9-21.5 kPa) and performance of TE were varied among the studies (AUROC range, 0.76-0.85).[66-68] Second, TE alone seems insufficient to predict the presence of esophageal varices.

To achieve more high accuracy, Kim et al recently proposed a novel prediction model (liver stiffness-spleen diameter to platelet ratio score [LSPS]) using TE values and other parameters that reflect portal hypertension as constituent variables in patients with CHB.[69] Overall, this model had excellent diagnostic accuracy for prediction of high risk esophageal varices (HEV, AUROC=0.953; negative predictive value 94.7%, positive predictive value 93.3%). Beyond this cross-sectional analysis, a subsequent study by same group recently reported that LSPS can be a reliable predictor of the development of variceal bleeding.[70] In this prospective, longitudinal study of 577 patients with CHB, those with LSPS ≥5.5 had higher cumulative incidence rates of esophageal variceal bleeding during the follow-up period and LSPS score ≥6.5 was an independent risk factor of variceal bleeding from HEV, indicating that prophylactic treatment should be considered in these high risk patients (Fig. 2).

PREDICTION OF HCC DEVELOPMENT

Given that advanced liver fibrosis and cirrhosis are the most important risk factors of HCC development, several Asian studies have investigated the clinical role of TE for predicting HCC development.[71-73] The first large prospective study of 866 Japanese patients with CHC was conducted to investigate whether TE could predict the risk of HCC development.[71] In this study, TE value was selected as one of independent risk factors for HCC development, and patients with higher TE values had a significantly higher risk of HCC development, with a hazard ratio of 16.7 with 10.1-15 kPa, 20.9 with 15.1-20 kPa, 25.6 with 20.1-25 kPa, 45.5 with over 25 kPa, as compared to under 10 kPa (Fig. 3A). Similarly, in populations with CHB, the similar role of TE was confirmed in large cohort study of 1,130 Korean patients with CHB.[72] In this study, stratified TE value was also identified as an independent risk factor for HCC development, with relative risks of 3.07, 4.68, 5.55, and 6.60 for respective TE values of 8-13 kPa, 13-18 kPa, 18-23 kPa, and >23 kPa compared TE value to under 8 kPa (Fig. 3B). Interestingly, when patients with available follow-up TE values were analyzed, the risk of HCC development can be changed according to the pattern of the changes in TE values, which proposed the potential role for TE as a dynamic monitoring tool for risk estimation of HCC development. In addition, another prospective study by Fung et al also demonstrated the usefulness of TE for prediction of HCC development in patients with 528 HBeAg-negative CHB.[73] Although the performance of TE and a TE based model (LSPS)

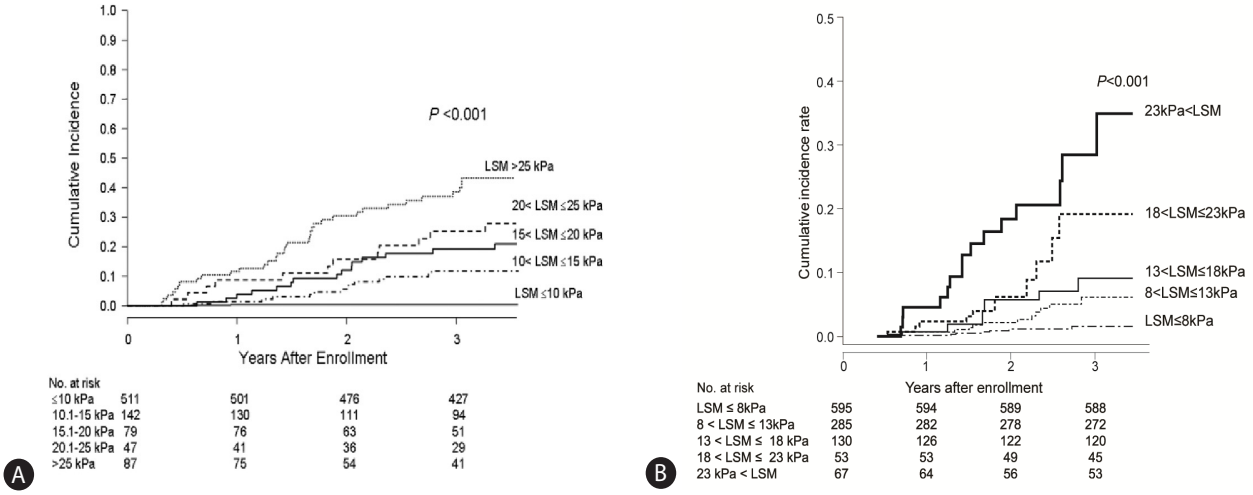

Figure 3. Cumulative incidence of HCC development based on stratified TE values in patients with CHC (n=866; A) and those with CHB (n=1,130, B) (Kaplan-Meier plot). The cumulative incidence rates increased significantly in association with higher TE values (log-rank test, all *P*<0.001). HCC, hepatocellular carcinoma; TE, transient elastography; CHC, chronic hepatitis C; CHB, chronic hepatitis B; kPa, kilopascal (A: adapted from reference 71, B: adapted from reference 72).

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for prediction of HCC was superior to other non-invasive fibrosis prediction models, such as APRI, age-spleen-platelet ratio index (ASPRI), P2/MS, and FIB-4,[74] the role of TE in this setting need to be validated in other ethnicities.[71-73]

Lastly, a recent study by Kim et al reported that the TE could predict the development of liver-related event (LREs) including hepatic decompensation and HCC development in patients with CHB with histologically advanced liver fibrosis (≥F3).[75] TE values was selected as independent predictor of LRE development and patients with a TE value>19 kPa were at significantly greater risk than those with a TE value ≤19 kPa.

USEFULNESS OF TE IN SURGICAL SETTING

Because, TE values show significant correlations with portal hypertension and HCC development, prediction of postoperative short term outcomes such as hepatic insufficiency and long-term outcomes such as recurrence or liver-related death using TE has been tested in several pilot studies.[76-78] If further studies validate these results, TE will facilitate stratification of patients according to different prognosis assessed using TE values.

Postoperative hepatic insufficiency

Recently, our group has investigated whether preoperative TE values could predict the development of postoperative hepatic insufficiency after curative resection of HCC.[76] In this study, multivariate analysis revealed that TE values >25.6 kPa was identified as the only predictor of postoperative insufficiency. The AUROC of 25.6 kPa was higher than that of ICG R15 (0.824 vs. 0.620, respectively). Similar results were obtained in a subsequent investigation by our group.[77] In this study, the performance of TE was superior to that of diffusion-weighted MRI, which has also been known as a noninvasive fibrosis prediction tool, for assessment of liver fibrosis and prediction of postoperative hepatic insufficiency.[77]

HCC recurrence after curative resection

Our group also investigated whether preoperative TE could predict recurrence after curative resection of HCC, based on the assumption that the severity of liver fibrosis assessed using TE is correlated with de novo recurrence of HCC.[78] In an analysis of 133 patients who underwent preoperative TE and curative resection

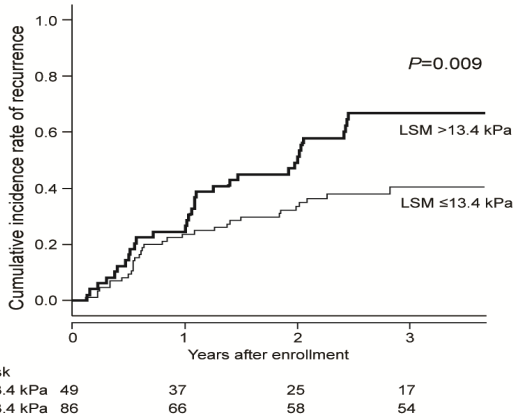

Figure 4. Cumulative incidence rates of HCC recurrence based on stratified TE values (Kaplan-Meier plot). The cumulative incidence rates increased significantly in patients with TE >13.4 kPa than in those with TE ≤13.4 kPa (log-rank test, *P*=0.009). HCC, hepatocellular carcinoma; TE, transient elastography (adapted from reference 78).

(HCC recurred in 62 patients), TE was selected as an independent predictor of recurrence, whereas the histological fibrosis status was not. In the study, patient with preoperative TE values >13.4 kPa were at greater risk for recurrence with a hazard ratio of 1.925 (*P*=0.010, Fig. 4). More specifically, when recurrence was stratified into early (<2 year) and late (≥2 year) recurrence, TE values were significantly related to late recurrence. These results suggest that preoperative TE could reveal the potential influence of liver fibrosis on recurrence and explain multicentric carcinogenesis from a fibrotic liver. However, more data are needed to clarify this issue.[78]

Recurrence of hepatitis C after transplantation

Several studies have suggested that TE could predict fibrosis progression in patients with recurrent hepatitis C after liver transplantation.[79,80] Initial study by Carrión et al reported that an AUROC was 0.90 for significant fibrosis and 0.98 for cirrhosis in 124 liver transplant recipients with recurrent hepatitis C infection. Using a cutoff value of 8.5 kPa, the sensitivity, specificity, negative predictive value, and positive predictive value for diagnosis of significant liver fibrosis were 90%, 81%, 79%, and 92%, respectively.[80] Similar results were reported in several subsequent studies.[81,82] In addition, Rigamonti et al showed that TE values changed in parallel with fibrosis staging in patients with paired LB during the post-liver transplantation follow-up period.[79]

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LIMITATIONS AND FAILURE

Although TE has revealed excellent diagnostic accuracy with excellent inter-observer and intra-observer agreement, there are some confounding factors which influence the results of TE. At first, the extent of necroinflammatory activity has been known to influence TE results in patients with viral hepatitis, resulting in an overestimation of TE values that increases in parallel with the degree of histological activity.[16,83-85] Therefore, in patients with acute flare, TE examinations should be delayed until ALT levels are stabilized. Regarding this issue, several studies have tried to investigate the optimal period (3 to 6 months) to restore of reliability of TE values in patients with acute flare.[16,86,87]

In addition, the performance of TE can be limited in patients with a high body mass index (BMI), or narrow intercostal space, and it is impossible in patients with ascites.[5] In a previous study, BMI>28 kg/m^2 and waist circumference were significantly associated with TE failure.[88] To achieve technological improvement in these patients, new TE probe (XL Probe) was recently introduced to lessen TE failure rate in obese patients, however its efficacy should be further validated.[89]

CONCLUSION

Over the past decade, significant progress has been made in regarding non-invasive assessment of liver fibrosis in patients with CLD. Of the methods now available, TE appears to be an excellent tool for assessment of liver fibrosis, particularly for diagnosis cirrhosis, and also has prognostic value in longitudinal perspectives. Although TE cannot completely abolish the need for LB, it can be used as an important noninvasive tool which enables us set up a more efficient and tailored management strategies for patients with CLD.

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Conflicts of Interest

The authors have no conflicts to disclose.

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