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TOPIC HIGHLIGHT

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Transient elastography in chronic hepatitis B: An Asian perspective

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Abstract

Transient elastography (TE) is a new non-invasive tool for assessing liver stiffness, which is correlated with the histologic stage of liver fibrosis. Many studies have reported a good accuracy of TE in predicting significant fibrosis and an optimal accuracy in predicting cirrhosis. Furthermore, the potential role of TE in screening the general population has also been proven. TE thus helps physicians to decide treatment strategies, predict prognosis, and monitor disease progression in patients with chronic liver disease and to screen the general population to identify high risk patients with potential liver disease. However, most data on the clinical roles of TE have been gathered in European patients with chronic hepatitis C (CHC), because TE was first developed in France. Accordingly, much data on the usefulness of TE in patients with CHC has accumulated. Recently, however, vigorous efforts have been made to apply TE to patients with chronic hepatitis B (CHB), and TE has also proved to have acceptable accuracy in diagnosing liver fibrosis and cirrhosis in these patients. Thus, we focused on TE in the Asian population with CHB in comparison with the European population with CHC and found that the diagnostic performance and cutoff values were different between the 2 populations possibly as a result of several different confounders between Asian and European populations (the etiology of chronic liver disease, histologic features, major fluctuation in alanine aminotransferase levels, and the prevalence of high body mass index and metabolic syndrome). Therefore, further studies tailored to the Asian population with CHB should be performed before the widespread application of TE in Asian populations with CHB.

Key words: Asia; Chronic hepatitis B; Fibroscan; Hepatitis B virus; Liver stiffness measurement; Transient elastography

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INTRODUCTION

Transient elastography (TE) using FibroScan® (EchoSens, Paris, France) is a newly introduced non-invasive tool, that generates an elastic wave using a vibrator applied to the thoracic wall at the level of the right lobe of the liver and measures the propagation velocity of the wave,

which is directly associated with liver stiffness (LS)[1]. To date, the clinical utility of TE has been widely reviewed, and it is regarded as having considerable accuracy for predicting liver cirrhosis in patients with chronic liver disease (CLD) of diverse etiologies[2-5]. TE is quick, highly reproducible, and completely harmless to patients. In addition, it can be learned and performed easily after a short training period (by nurses or technicians) without consuming the time of clinicians. For these reasons, TE has become popular in clinical practice as a tool for aiding in the diagnosis and follow-up of liver disease.

Because TE was first developed in France, most studies on its benefits have been explored in European countries where chronic hepatitis C (CHC) is prevalent. Accordingly, extensive data on the clinical roles of TE in assessing liver fibrosis in patients with CHC have been gathered. Recently, several meta-analysis studies reported that TE is a reliable non-invasive tool to detect advanced liver fibrosis and liver cirrhosis[6-8]. However, most studies included in the meta-analysis investigated European populations with CHC. Data from Europe cannot be extrapolated to the Asian population, as subsequent trials of TE in Asian countries where hepatitis B virus (HBV) infection is more prevalent than hepatitis C virus (HCV), displayed divergent results. In this Topic Highlight, we will focus on TE in the Asian population with chronic hepatitis B (CHB).

METHODOLOGICAL CONSIDERATION OF TE IN THE ASIAN POPULATION

LS values are defined as the median of 10 valid measurements and at least 60% of TE shots should be successful for each examination according to the manufacturer's recommendations. Accordingly, to date, only the results of TE examinations satisfying the above criteria have been considered as reliable and have been included for the analysis in reported studies.

Another important parameter for confirming the validity of LS values is the interquartile range (IQR), which is defined as the values between which 50% of observations fall. The lower boundary is the 25th percentile (lower quartile), the upper boundary is the 75th percentile (upper quartile). Generally, the IQR/median LS value ratio (IQR/M) should not exceed 30% if the reliability of LS values is to be preserved. However, recently, Lucidarme *et al*[9] proposed new criteria for reliable LS values, using the IQR/M based on the data from more than 250 French patients with CHC. They found, in a multivariate analysis, the fibrosis stage (F0-2 *vs* F3-4) and IQR/M were significantly associated with significant discordances between TE and liver biopsy (LB), with an optimal discriminant cutoff value of 0.21. They thus concluded that the IQR/M can overestimate liver fibrosis using TE, irrespective of success rate, when the significance discordance was defined as a discordance of at least 2 stages of fibrosis between LS values by TE examination and the METAVIR scoring system. From these results, they suggested a novel algorithm for clinical practice as first-line assessment of liver fibrosis in patients with CHC (Figure 1).

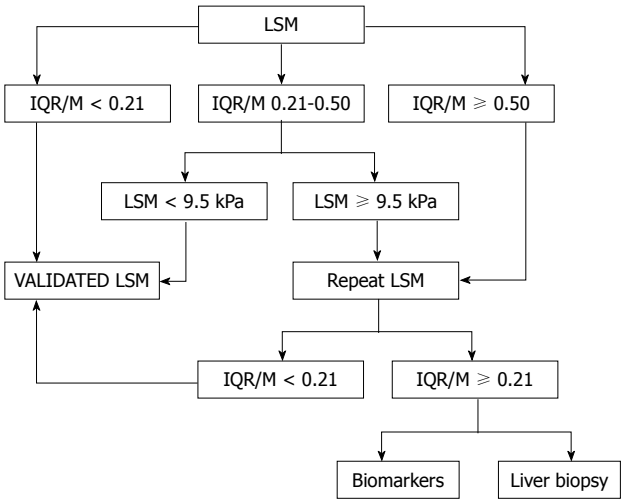

Figure 1 Suggested algorithm for clinical practice as first-line assessment of hepatic fibrosis in patients with chronic hepatitis C. IQR/M: Interquartile range/median liver stiffness value ratio; LSM: Liver stiffness measurement.

Because the IQR/M was confirmed in only one European study with CHC showing relatively high body mass index (BMI) (25 ± 4.1 kg/m^2), its application to the Asian population with CHB (who generally show a lower BMI) is difficult and requires further validation. Although the data are preliminary, we have attempted to validate the IQR/M for our cohort of 156 patients with CHB (mean age 38.8 years, male 75.0%, mean BMI 23.2 kg/m^2) who underwent LB and TE prior to starting antiviral treatment. In this study, we selected the cutoff LS values of Marcellin *et al*[10] (7.2 kPa for ⩾ F2, 8.1 kPa ⩾ F3, and 11.0 kPa for F4) as the reference values between 2 external studies that investigated the performance of TE and then set up the optimal cutoff LS values for each fibrosis stage in patients with CHB[10,11]. We identified 28 (18.0%) patients showing significant discordance between TE and LB. However, the IQR/M was not significantly different between patients with discordance and those with non-discordance (0.125 ± 0.083 *vs* 0.129 ± 0.079, $P = 0.831$), and the success rate also failed to show a significant difference.

Interestingly, the mean IQR/M of our study population was greatly reduced compared to that of subjects in Lucidarme *et al*[9] (0.30 in patients with discordance and 0.22 in those with non-discordance) and the proportion of patients with an IQR/M > 0.03 ($n = 7$, 4.5%) was very small. The reasons are not clear why the IQR/M in our study was reduced in comparison with that in the previous study, and was not selected as a discriminant factor to predict discordance. However, we think that the optimal cutoff value of the IQR/M will be lower than that from patients with CHC even if the IQR/M can be validated in the future for the Asian population with CHB, or that the IQR/M is not a predictor of discordance in the Asian population with CHB due to other potential confounders that overwhelm the influence of the IQR/M, such as the inhomogeneous histological features of CHB which often

Table 1 Normal liver stiffness values of transient elastography

	Asian study		European study				
	Kim *et al*[14]	Fung *et al*[19]	Corpechot *et al*[15]	Roulot *et al*[13]	Sirli *et al*[16]	Colombo *et al*[17]	Colombo *et al*[18]
Type	Full article	Full article	Letter	Full article	Full article	Abstract	Abstract
No. of subjects	69	28	71	429	144	327	746
Population	Liver and kidney donors	Liver donors	Healthy volunteers	Medical check-up	Healthy volunteers	Blood donors	Blood donors
Liver stiffness (kPa)	4.6 (mean)	4.6 (median)	4.8 (median)	5.5 (mean)	4.8 (mean)	4.9 (mean)	4.4 (median)
95th percentile (kPa)	4.7	-	-	8.6	-	7.8	6.7
BMI (kg/m^2)	22.6 (mean)	-	22.5 (median)	25.8 (mean)	-	-	-
Effects on TE							
Age	No	-	No	No	No	No	No
Gender	M = F	-	M > F	M > F	M > F	M = F	M > F
High BMI	No	-	No	Increased TE values	No	Increased TE values	No
Metabolic syndrome	-	-	-	Increased TE values	-	-	-
Fatty liver	-	-	-	-	-	Increased TE values	Increased TE values

BMI: Body mass index; TE: Transient elastography.

makes liver texture inherently macronodular. This would result in LS values that vary depending on the area of the liver and necroinflammatory activity, which has been demonstrated to raise LS values. Therefore, the validation of the IQR/M in the Asian population with CHB requires further studies using increased sample sizes to allow sufficient cases with a spectrum of IQR/M values.

Several issues still remain to be resolved regarding the Asian population with CHB: How many valid measurements do we need to maintain the performance of TE[12]? What is the optimal success rate of the TE measurement to accurately exclude unreliable LS values? Can the IQR/M alone be applied to increase the performance of TE without a sufficient number of valid measurements and an adequate success rate?

WHAT ARE THE NORMAL LS VALUES FOR THE ASIAN POPULATION

Before discussing data on TE in the Asian population with CHB, it is important to first confirm that TE can reliably identify patients with CLD from the normal population. If TE cannot, the clinical meaning of further analysis on the performance of TE in grading the severity of CLD would be significantly lessened. Despite the importance of this, to date, most studies on TE have focused on patients with CLD.

The concept of "what are normal LS values assessed by TE?" is a critical issue that should be addressed to determine whether TE can be used for screening the general population and for subsequent selection of high-risk patients who require periodic follow-up and adequate treatment measures. Indeed, concerns regarding normal LS values are increasing, and several studies (including 2 Asian studies) have proposed normal LS values despite variations in study design[13-19].

In a study by Corpechot *et al*[15], the authors found that the normal LS values in the healthy population were significantly higher in men than in women and that the median LS value was 4.8 kPa (range, 2.5-6.9 kPa). Roulot *et al*[13] examined a large cohort of 429 apparently healthy subjects to establish normal LS values [5.81 ± 1.54 kPa (range, 3.8-8.0 kPa) in men *vs* 5.23 ± 1.59 kPa (range, 3.3-7.8 kPa) in women, $P < 0.01$]. Another study conducted in Romania demonstrated that the mean values of TE in 144 normal subjects were 4.8 ± 1.3 kPa (range, 2.3-8.8 kPa) and that the normal LS values were significantly different between genders[16]. Colombo *et al*[17] also assessed the LS values of 327 voluntary blood donors and found that the mean LS value was 4.9 kPa (95% CI: 4.6-5.1 kPa) and the normal LS values showed no significant differences between genders. However, Colombo *et al*[18] in their follow-up study that enrolled more than 1000 healthy blood donors reported that the normal LS value was 4.4 kPa (95th percentile, 6.7 kPa) and that the male gender presents with increased LS values.

All the aforementioned studies were conducted in Europe. However, normal LS values in the Asian population are now available. Fung *et al*[19] reported a mean LS value in 28 healthy living-related liver donors of 4.6 kPa (range, 2.0-7.1 kPa), and all subjects had LS values of < 7.2 kPa, which indicated that they had no significant fibrosis. We have previously reported that the normal range of LS values was 3.9-5.3 kPa, which was calculated from 69 strictly selected living liver and kidney donors[14].

Table 1 indicates the results of all studies on normal LS values. The upper normal range of LS values was consistently lower than the range generally used for identifying significant liver disease (7-8 kPa) in the majority of previous studies[20-22]. These data demonstrated that TE can perform reliably in identifying high-risk subpopulations without an overlap between the normal and abnormal ranges of LS values. Interestingly, the mean LS values in Asian studies appear lower in comparison with European studies, and the effects of gender on the performance of TE are variable among studies. The discrepancy cannot be fully explained, because the complete histological data of the normal subjects were largely unavailable except a small

Table 2 Failure rate of transient elastography measurement

	Asian study				European study		
	Kim *et al*[14]	Chan *et al*[24]	Masuzaki *et al*[25]	Wong *et al*[26]	Ziol *et al*[2]	Marcellin *et al*[10]	Maimone *et al*[27]
Etiology	HBV	HBV	HCV	HBV	HCV	HBV	HBV
Total patients (*n*)	74	1136	876	487	327	202	230
Excluded patients (*n*)	5	30	10	34	76	29	10
Excluded patients due to TE failure (*n*)	1	30	10	17	23	14	10
TE failure rate (%)	1.4	2.6	1.1	3.5	7	6.9	4.3
Enrolled patients (*n*)	69	1106	866	453	251	173	220
Age (yr)	38.9 (mean)	47 (mean)	66.2 (mean)	37 (median)	47.5 (mean)	40.1 (mean)	45.2 (mean)
Male, *n* (%)	35 (50.7)	-	398 (46.0)	270 (60.0)	155 (61.8)	115 (66.5)	99 (45.0)
BMI (kg/m^2)	22.6 (mean)	-	22.5 (mean)	22.4 (median)	23.9 (mean)	24.5 (mean)	-
Failure criteria							
Success rate	< 60%	< 60%	< 60%	< 60%	< 60%	< 50%	< 60%
The number of VMs	< 10 VMs	< 10 VMs	< 8 VMs	< 10 VMs	< 10 VMs	< 7 VMs	< 10 VMs

HBV: Hepatitis B virus; HCV: Hepatitis C virus; TE: Transient elastography; BMI: Body mass index; VM: Valid measurement.

number of liver donors in the studies by our group[14] and Fung *et al*[19]. Lower mean BMI, younger age, and lower prevalence of metabolic syndrome in the Asian studies can explain, at least in part, the lower mean LS values observed. Another reasons are that other confounders of TE performance, such as high alanine aminotransferase (ALT) levels and fatty liver, were not sufficiently excluded[17,18] and that the hepatic imaging studies and/or cardiologic evaluation were not fully completed in European studies[13,16]. These reasons may have increased the normal range of LS values in the European studies.

More carefully designed studies with a large number of subjects are thus still required to fully assess the normal LS values for both Western and Asian populations. However, it should be remembered that the actual normal range of LS values cannot be precisely defined without a definition of a "normal liver", sufficient histological evaluation of normal subjects, and further stratified analysis with lifestyle factors between genders (such as alcohol consumption). If these issues are resolved, we can identify the true normal LS value and use this as a reference for future studies.

INFLUENCE OF BMI ON THE PERFORMANCE OF TE IN THE ASIAN POPULATION

Previous work has demonstrated that BMI can affect the performance of TE. This can be explained in 2 ways. First, BMI influences the failure rate of TE, and second, BMI acts to increase LS values. Although previous studies have reported that the success rate of TE decreases in subjects displaying higher BMI[13,23], TE failure may not be significant, because these patients were largely excluded from the analysis. However, in another point of view, this effect of high BMI on TE failure can be a significant pitfall of TE, as the majority of patients with high BMI have an increased chance of suffering from fatty liver and, if TE examination fails, they miss the opportunity to receive rapid and non-invasive methods to exclude significant fibrosis. From the knowledge of the varying failure rates between Asian and European study populations, we can discern the possible influence of BMI on TE failure rate according to the study population.

Table 2 summarizes the failure rates of previous studies conducted in Asian and European populations. Overall, TE failure rates and BMI both appear to be lower in Asian compared to European studies, indicating that the lower BMI found in Asian populations is possibly associated with a lower TE failure rate.

In spite of debate, several European studies have reported that a high BMI (which might cause hepatic steatosis) could potentially increase LS values[13,17], although research to date has not determined whether steatosis itself increases LS value in patients with chronic viral hepatitis[28-30]. For the Asian population, the effects of high BMI on TE performance have not been fully validated, because most Asian studies on TE lack sufficient numbers of patients with high BMI (> 30 kg/m^2). In our previous study, BMI did not influence LS values, although our study population was younger and showed lower BMI values than European studies[14]. This potential effect of high BMI on TE performance should therefore be further investigated for the Asian population.

INFLUENCE OF METABOLIC SYNDROME ON THE PERFORMANCE OF TE IN THE ASIAN POPULATION

Recently, the effects of metabolic syndrome (MS) on TE have been examined in a French study[13]. Here, BMI > 30 kg/m^2 was more frequent among subjects with MS than among normal subjects (49.1% *vs* 8.9%, respectively, $P < 0.001$). The mean LS value was higher in subjects with MS compared to controls (6.51 ± 1.64 kPa *vs* 5.33 ± 1.51 kPa, $P < 0.001$). In a multivariate analysis, LS values were still significantly different between subjects with and without MS, irrespective of BMI and other variables. Because MS

has been demonstrated to increase LS values significantly, and hepatic steatosis which can result in histological progression to cirrhosis and hepatocellular carcinoma is strongly associated with MS[31-33], a potential role of TE in detecting MS was proposed. However, 88% of the subjects with MS had LS values within the defined normal range. This result indicated that not only could TE not precisely perform in the diagnosis of MS, but also that hepatic steatosis differentially affected by MS may have influenced LS values differently for different individuals. One drawback of the study[13] was a lack of ultrasonographic evaluation of hepatic steatosis. It is thus unclear whether the increased LS values in the subjects with MS were dependent on MS itself or on hepatic steatosis associated with MS. Other studies in Italy[17,18] attempted to overcome this drawback by including ultrasonographic evaluation of the healthy blood donors and concluded that the severity of hepatic steatosis was independently related to LS values.

The association between MS or hepatic steatosis and LS values was investigated primarily in healthy subjects, because the effects of MS or hepatic steatosis on TE can be attenuated if the study population presented with background fibrotic liver (the most significant factor for high LS values). Therefore, it is difficult to identify the main factors that increase LS values among MS, hepatic steatosis, associated steatofibrosis, and background fibrosis, if the study enrolls patients already presenting with CLD.

As mentioned above, only one published European study reporting the effects of MS on TE in healthy individuals is currently available. Furthermore, no available European and Asian data address the effects of MS on TE performance in patients with chronic viral hepatitis. Considering the different clinicopathological course of hepatic steatosis in patients with CHC and CHB and the varied distribution of body fat according to race, further studies on the effects of MS and hepatic steatosis should be performed with the Asian populations.

INFLUENCE OF ALT ON THE PERFORMANCE OF TE IN THE ASIAN POPULATION WITH CHB

The most important confounding factor of TE is serum ALT levels. Hepatic inflammation, as reflected by higher ALT levels, tends to increase LS values[11,20,34]. Even minor changes in ALT levels have been shown to influence LS values[35]. Because HBV, unlike HCV, frequently exhibits acute ALT flares[36,37], the interpretation of LS values becomes increasingly difficult in the setting of CHB when major fluctuations of necrosis and inflammatory activity occur[24,38]. It thus becomes more relevant to consider ALT levels when examining TE in the Asian population with CHB.

Considering the significant effects of high ALT levels, several Asian studies with CHB patients attempted to establish varying cutoff LS values according to ALT levels. Chan *et al*[11] proposed ALT-based algorithms when interpreting LS results, and established different optimal cutoff values according to ALT levels (one group with normal ALT *vs* the other group with ALT > upper limit of normal (ULN) and ≤ 5 × ULN). In our previous study, we also stratified the study population according to ALT levels and calculated the optimal cutoff values for each group[34]. For patients with normal ALT levels, 6.0, 7.5 and 10.1 kPa were selected as the optimal cutoff values for ≥ F2, ≥ F3, and F4, respectively, whereas 8.9, 11.0, and 15.5 kPa were selected in those with ALT > ULN and ≤ 2 × ULN. Considering this unreliability of TE performance in patients with high ALT levels, more recent studies began to exclude patients displaying ALT > 5 × ULN for analysis[24]. In addition, the optimal time interval for TE to recover its reliability in patients who experience acute exacerbation of CHB was recently reported[38].

Although it seems reasonable to use different cutoff values according to ALT levels, large-scale validation of these LS values has not been performed for Asian patients with CHB. Furthermore, some issues still remain unresolved, such as how we stratify patients with CHB according to ALT levels to establish the cutoff values, and who should be excluded for TE examination because of unreliability of TE among patients with high ALT levels.

DIAGNOSTIC PERFORMANCE OF TE IN THE ASIAN POPULATION WITH CHB

Few studies have investigated the performance of TE in the Asian population with CHB[4,11,39-43]. The characteristics of studies and the identified performance of TE to predict significant fibrosis and cirrhosis are summarized in Tables 3 and 4 (Marcellin *et al*[10] is listed for comparison with other Asian studies). The listed Asian studies were selected if they evaluated TE in Asian populations with CHB, they used LB as a reference standard, and they assessed the diagnostic accuracy of TE [using area under the receiver operating characteristic curve (AUROC)] for F ≥ 2 or F = 4 fibrosis stage and/or diagnostic indexes (sensitivity, specificity, positive predictive value, or negative predictive value based on some cutoff LS values). Most Asian studies were conducted in Korea and China (Hong Kong) and some studies were available in abstract form from Korea, Singapore, and Thailand.

The AUROCs for predicting F ≥ 2 fibrosis and F = 4 fibrosis stage in patients with CHC were reported as 0.79-0.83 and 0.97-0.95, respectively in the studies by Ziol *et al*[2] and Castera *et al*[44]. However, the AUROCs in Asian studies seems to be lower than those reported in European studies (0.76-0.88 for F ≥ 2 and 0.80-0.93 for F4, Table 4), although TE diagnosed cirrhosis more accurately than significant fibrosis in Asian studies.

Overall, TE is accepted as a promising and accurate tool for the early detection of cirrhosis irrespective of the etiology of CLD, although the optimal cutoff values remain debatable. The range of the optimal cutoff values for diagnosing HBV-related cirrhosis in the Asian population were between 9.0 and 10.1 kPa based on the full-length articles[4,11,39] (Table 4) and the range for cirrhosis was less than 11.0 kPa, which is consistently lower than in

Table 3 Characteristics of studies evaluating the performance of transient elastography for the diagnosis of liver fibrosis in patients with chronic hepatitis B

	Type	Country	Total sample (*n*)	Sample size (*n*)	Excluded due to failure		Age (yr)	Male (%)	BMI (kg/m^2)	LB length (mm)	Staging
					TE (reason)	LB (reason)					
Kim *et al*[4]	Original	Korea	194	103	0 (SR < 60%, < 10 VMs)	4 (< 10 mm, < 10 PTs)	40.0	80.2	23.8	16.7	METAVIR
Chan *et al*[11]	Original	China	186	161	1 (SR < 60%, < 10 VMs)	22 (< 15 mm, < 6 PTs)	45.0	76.0	24.0	19.0	METAVIR
Kim *et al*[36]	Original	Korea	130	130	0 (SR < 60%, < 10 VMs)	0 (< 10 mm, < 6 PTs)	42.5	79.2	25.3	14.5	METAVIR
Marcellin *et al*[10]	Original	France	202	173	14 (SR < 50%, < 7 VMs)	15 (< 10 PTs)	40.1	66.5	24.5	16.6	METAVIR
Chang *et al*[40]	Abstract	Singapore	35	33	2 (obesity, narrow ICS)	0 (-)	43.0	-	25.6	-	Ishak
Tanwandee *et al*[41]	Abstract	Thailand	104	104	0 (-)	0 (-)	44.0	63.0	23.6	-	METAVIR
Choi *et al*[42]	Abstract	Korea	48	48	0 (-)	0 (-)	41.7	58.3	23.3	-	-
Chang *et al*[43]	Abstract	Singapore	88	84	3 (-)	1 (-)	49.0	71.6	-	-	-

TE: Transient elastography; VM: Valid measurement; LB: Liver biopsy; BMI: Body mass index; SR: Success rate; PT: Portal tract; ICS: Intercostal space.

Table 4 Histologic distribution and the performance of transient elastography for the diagnosis of liver fibrosis in patients with chronic hepatitis B

	n (%)					METAVIR and other scoring system (≥ F2/F4)							
	F0	F1	F2	F3	F4	AUROC	Cutoff (kPa)	Se (%)	Sp (%)	PPV (%)	NPV (%)	LR (+)	LR (-)
Kim *et al*[4]	0	9 (9.9)	33 (36.3)	10 (11.0)	39 (42.9)	-/0.803	-/9.7	-/82	-/62	-/63	-/76	-/4.97	-/0.13
Chan *et al*[11]	10 (6.2)	27 (16.8)	47 (29.2)	37 (23.0)	40 (24.8)	-/0.93	-/9	-/98	-/75	-/57	-/98	-/1	-/0.01
Kim *et al*[36]	0	10 (7.7)	37 (28.5)	16 (12.3)	67 (51.5)	-/0.84	-/10.1	-/76	-/81	-/76.1	-/80.9	-/-	-/-
Marcellin *et al*[10]	16 (9.2)	70 (40.5)	44 (25.4)	29 (16.8)	14 (8.1)	0.81/0.93	7.2/11	70/98	83/75	80/57	73/98	4/1	-/0.01
Chang *et al*[40]	7 (20.0)	16 (45.7)	F2-3 (5, 14.3)		7 (20.0)	-/-	11.8/-	90/-	78/-	-/-	-/-	-/-	-/-
Tanwandee *et al*[41]	-	-	-	-	-	0.757/-	6.9/7.3	70/93	79/61	82/31	66/98	-/-	-/-
Choi *et al*[42]	-	-	-	-	-	0.88/0.86	7.7/10.4	88/79	88/83	-/-	-/-	-/-	-/-
Chang *et al*[43]	-14.8	-30.7	-14.8	-21.6	-17.1	0.801/-	8.8/-	-/-	-/-	-/-	-/-	-/-	-/-

AUROC: Area under the receive operating characteristic curve; Se: Sensitivity, Sp: Specificity; PPV: Positive predictive value; NPV: Negative predictive value; LR: Likelihood ratio.

patients with CHC[45,46]. These findings can be explained in several ways. The histopathological characteristics of CHC (including portal lymphoid follicles, bile duct damage, lobular activity, and steatosis) may contribute to the variations in cutoff values compared with those in patients with CHB[47]. Another explanation is that the total fibrotic material in CHB may be lower than that in CHC, because CHB tends to make the liver macronodular and heterogeneous[48]. Other researchers have proposed that the different types and extent of liver inflammatory infiltrate within the liver may account for the different cutoff LS values between CHB and CHC[20].

The performance of TE in prediction of cirrhosis is acceptable for the Asian population with CHB, but increased performance in prediction of significant fibrosis and subsequent precise staging, particularly for patients with CHB who are candidates for antiviral treatment, is needed and should be pursued through future studies. This is particularly important, because the decision to start antiviral treatment and the type of antiviral agents to be used may be affected by fibrosis stage.

CONCLUSION

Because of limitations of LB, prohibiting its routine use for the evaluation of liver fibrosis in patients with CHB, interest in the use of noninvasive TE has increased. Ideally, TE can be used to screen the general population to detect high-risk patients with potential liver disease, to identify patients with significant fibrosis who could benefit from the initiation of antiviral treatment, to select patients with cirrhosis who are at a high risk of developing HCC[25], and to identify patients with cirrhosis and portal hypertension. To date, although numerous European studies have demonstrated that this is possible, data on TE for the Asian population are scarce.

We are now fully armed with nuggets of knowledge that the etiologies of CLD, BMI, MS, cardiac function, cholestasis, hepatic steatosis, and ALT levels can influence the performance of TE, and also that several confounders vary between Asian and European populations, for example, the etiology of CLD, major fluctuation in ALT levels, and the prevalence of high BMI and MS. However, because almost all information on TE has thus far originated from European data, for the Asian population with CHB, TE is not popular clinically. Therefore, further studies tailored to the Asian population with CHB will restore the confidence of Asian clinicians to utilize TE.

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