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Usefulness of noninvasive methods including assessment of liver stiffness by 2-dimensional shear wave elastography for predicting esophageal varices

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ABSTRACT

Background: The aim of this study was to predict the presence of esophageal varices (EVs) by noninvasive tools combined with 2-dimensional shear wave elastography (2D-SWE), and to compare the diagnostic capabilities of 2D-SWE with those of transient elastography (TE).
Methods: Between January 2015 and December 2017, 289 patients with compensated advanced chronic liver disease (cACLD) who underwent consecutive 2D-SWE and EGD were enrolled. Capabilities for predicting the presence of EVs of 2D-SWE and models combining 2D-SWE with other noninvasive tools (modified LS-spleen-diameter-to-platelet-ratio score [mLSPS], platelet-spleen ratio score) were compared. A subgroup analysis was performed on 177 patients who also underwent simultaneous TE.
Results: The area under receiver operating characteristics (AUROCs) for detecting EVs for 2D-SWE alone vs. mLSPS, which included 2D-SWE, were 0.757 (95% confidence interval [CI], 0.701–0.810) and 0.813 (95% CI, 0.763–.857), respectively. The AUROCs for predicting varices needing treatment (VNT) for 2D-SWE and mLSPS were 0.712 (95% CI, 0.621–0.738) and 0.834 (95% CI, 0.785–0.875), respectively. For the 195 patients who underwent simultaneous TE and 2D-SWE, no differences in diagnostic performance were observed.
Conclusions: The diagnostic performance of 2D-SWE is similar to that of TE for predicting the presence of EVs. The mLSPS, which includes 2D-SWE, seemed to be useful for predicting EVs.

1. Introduction

The prognosis of cirrhosis is closely related to the progression of portal hypertension. The degree of portal hypertension is associated with the development of complications such as variceal bleeding, hepatic encephalopathy, hepatorenal syndrome, and ascites [1], which are the main cause of death in patients with liver cirrhosis (LC) [2]. Since variceal bleeding has high rebleeding and high mortality rates, predicting the presence of esophageal varices (EVs) and subsequently preventing variceal bleeding are the major concerns in patients with LC [3]. The prevalence of high-risk EVs in LC patients is approximately 15%–25%; therefore, most patients who undergo screening endoscopy either do not have varices or have varices that do not require preventive therapy [4].

The 2015 Baveno VI consensus suggested that esophagogastroduodenoscopy (EGD) for variceal screening could be avoided if liver stiffness (LS), as measured by transient elastography (TE), was less than 20 kPa and the platelet count was higher than 150,000/μL [5]. In addition, Abraldes et al. [6] and others [7–10] have shown that the predictive ability for EVs was further improved by combining TE with other noninvasive tools.

TE was the first shear wave imaging method introduced for the assessment of LS, and it has been used clinically for the noninvasive assessment of liver fibrosis. TE estimates liver elasticity from the velocity of a low-frequency elastic wave that is propagated through the liver [11]. Many studies have shown that TE measurements have

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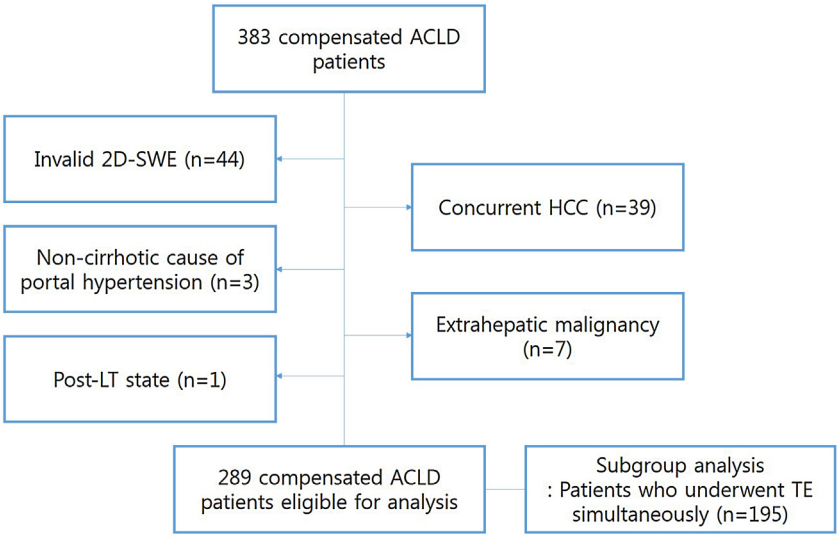

Fig. 1. Flow diagram for patient selection. ACLD: advanced chronic liver disease; 2D-SWE: 2-dimensional shear wave elastography; HCC: hepatocellular carcinoma; LT: liver transplantation; TE: transient elastography.

excellent correlation with clinically significant portal hypertension (CSPH) [6,12–14] and the presence of EVs [6,15]. The good correlations might be due to the fact that portal hypertension is a direct consequence of the fibrotic transformation of the liver tissue [13].

TE is limited, however, because it cannot be used to assess patients with ascites or a high body mass index. The results are also inaccurate if the alanine aminotransferase (ALT) level is elevated [9]. Although TE is an ultrasound-based technique, it is performed without direct B-mode imaging guidance, which can impede identification of the appropriate region for assessment [16].

The newest shear wave imaging method is 2D-SWE, which uses acoustic radiation. It can be performed simultaneously with conventional ultrasonography (USG), which is convenient, since patients with chronic liver disease frequently undergo USG examinations [16].

Several studies have shown that 2D-SWE is equivalent to TE for liver fibrosis assessment [17], similarly predicting CSPH [18] and the presence of EVs [19,20]. However, these claims have not yet been sufficiently validated. Specifically, there have been few studies confirming the usefulness of 2D-SWE for predicting the presence of EVs. The aim of this study was to predict the presence of EVs by 2D-SWE and to compare the diagnostic capabilities of 2D-SWE with those of TE. We also aimed to assess the prediction capability of data consisting of a combination of the LS value provided by 2D-SWE with data from other noninvasive assessments.

2. Materials and methods

2.1. Patients

We retrospectively analyzed consecutively collected data from 383 patients with compensated advanced chronic liver disease (cACLD) seen at a single tertiary care hospital in Korea from January 2015 to December 2017.

Among patients without symptoms or signs of decompensation such as jaundice, ascites, hepatic encephalopathy, and history of variceal bleeding, imaging findings from modalities such as computed tomography, USG, or TE that suggested cACLD or histologic findings of cirrhosis or severe fibrosis were used to identify participants to include in the study. Patients were considered to have cACLD with the following findings: a TE value $\geq$10 kPa, based on the Baveno VI recommendation, or with surface nodular irregularity and marginal blunting on computed tomography or USG [21].

Suggested cACLD patients with suspicious findings that included EGD paired with 2D-SWE and other noninvasive tests (laboratory tests, TE, or USG) occurring within 6 months were included. Exclusion criteria included the following: invalid 2D-SWE reading (n = 44), noncirrhotic cause of portal hypertension (n = 3), history of liver transplantation (n = 1), or concurrent hepatocellular carcinoma (HCC) (n = 39) or other extrahepatic malignancy (n = 7). Finally, a total of 289 patients were included in this study. Among these, a subgroup analysis was also performed for 195 patients who underwent simultaneous TE and 2D-SWE (Fig. 1).

2.2. LS by 2D-SWE

The 2D-SWE was performed by the LOGIQ E9 system (GE Healthcare, Chalfont St Giles, United Kingdom), with the patient in a fasting state. The examination was performed with the patient in the supine position with his or her right arm in maximum abduction. All measurements were performed using the intercostal approach and the best acquired acoustic window for liver evaluation on segment 5 or 6 of the right hepatic lobe [17]. The region of interest (ROI) consisted of the trapezoid window, located in a homogenous region of parenchyma that was free of any vascular structure and situated at least 1–2 cm below the hepatic surface [17]. A total of 10 measurements were performed, with each patient instructed to hold his or her breath during each measurement. The measurements were expressed in kPa, and the median value was considered to be valid and used for analysis for an interquartile range (IQR) <30% [22]. Two different examiners (Y.S. Kim and S.G. Kim) carried out the LS assessments.

2.3. USG assessment

While undergoing LS by 2D-SWE, every patient underwent USG of the upper abdomen, which included measurement of the spleen bipolar diameter in millimeters. The spleen bipolar diameter was measured on the monitor by electronic calibers. It was defined as the greatest longitudinal dimension at the level of splenic hilum [22].

2.4. EGD

EVs were staged according to the staging system of the Japanese Research Society for Portal Hypertension, as follows: (1) F0, no varices; (2) F1, small and non-tortuous varices; (3) F2, tortuous varices but with a radius <50% of the esophageal radius; and (4) F3, very large and tortuous varices. Varices needing treatment (VNTs) were defined as varices with a grade F2 and F3 or the presence of a red-color sign.

2.5. LS by TE

TE was measured by the FibroScan device (Echosense, Paris, France), with the patient in a fasting state. The examination was performed via the intercostal approach, with the patient in the supine position and the right arm in maximum abduction. A total of 10 measurements were performed. The measurements were expressed in kPa, and the median value was considered to be valid and used for analysis for an IQR < 30% and a success rate >60% [23].

2.6. Laboratory parameters

The collected laboratory parameters included albumin, bilirubin, prothrombin time expressed as international normalized ratio (INR), ALT, aspartate aminotransferase, creatinine, hemoglobin, and platelet count. Each patient's Child–Pugh score was calculated.

2.7. Predictive model

The LS-spleen-diameter-to-platelet-ratio score (LSPS) described previously by Kim et al. [4], was modified as follows: LS by 2D-SWE × spleen diameter/platelet ratio. We termed this model the "modified LSPS (mLSPS)".

The platelet-spleen ratio (PSR) described previously by Giannini et al. [24] was calculated as the ratio between platelet number of platelets/mm^3 and the bipolar diameter of the spleen in millimeters.

The Lok Index [25], AST to platelet ratio index (APRI) [26], FIB-4 [27] were computed according to previous research.

2.8. Statistical analysis

Univariate logistic regression analysis was performed to identify the parameters with significant discriminating capacity ($p \leq 0.05$) for predicting the presence of all-size varices and VNTs. Statistically significant parameters by multivariate logistic regression analysis were subjected to the receiver operating characteristics (ROC) curve analysis. Models of a combination of factors were also evaluated by ROC curve analysis. The Youden equation was used to identify the optimal cut-off value, which was used to determine the sensitivity, specificity, and positive and negative predictive values of each variable measured. For patients who underwent simultaneous TE and 2D-SWE, we identified all the relevant factors by logistic regression, calculating each probability when the influence of other variables had been corrected; the diagnostic performances of 2D-SWE and TE were compared. We used DeLong equations to compare the ROC curves of these elastographic methods.

A cut-off p-value of 0.05 was adopted for all analyses. SPSS 25.0 (IBM Corp., Armonk, NY, USA) and Medcalc, version 12.5.0.0 (MedCalc Software, Ostend, Belgium) were used for statistical analysis.

Table 1
Baseline characteristics.

Variables	All patients (n = 289)	EVs (n = 125)	No EVs (n = 164)
Age (years)	56.8 ± 10.2	56.4 ± 10.6	57.2 ± 9.8
Sex (male)	177 (61.2%)	78 (62.4%)	99 (60.4%)
Etiology			
HBV	137 (47.4%)	44 (35.2%)	93 (56.7%)
HCV	23 (8.0%)	8 (6.4%)	15 (9.1%)
Alcohol	94 (32.5%)	55 (44.0%)	39 (23.8%)
Others	35 (12.1%)	18 (14.4%)	17 (10.3%)
Spleen diameter (cm)	11.40 ± 2.51	12.54 ± 2.57	10.56 ± 2.11
Hemoglobin (g/dL)	13.0 ± 2.4	12.4 ± 2.6	13.48 ± 2.19
Platelet count (10^9/L)	139.4 ± 80.8	106.4 ± 68.8	165.0 ± 80.3
AST (IU/L)	44.4 ± 33.1	44.9 ± 28.3	44.0 ± 36.5
ALT (IU/L)	30.7 ± 26.5	25.8 ± 16.1	34.5 ± 31.8
Bilirubin (mg/dL)	1.13 ± 1.15	1.21 ± 0.62	1.05 ± 1.43
Albumin (mg/dL)	3.94 ± 0.67	3.74 ± 0.62	4.10 ± 0.66
Sodium	140.9 ± 5.6	140.0 ± 3.0	141.6 ± 6.8
Creatinine (mg/dL)	1.34 ± 1.55	1.35 ± 1.73	1.33 ± 1.40
PT, INR	1.14 ± 0.15	1.19 ± 0.16	1.09 ± 0.12
CTP class (A)	238 (83.5%)	99 (79.8%)	139 (86.3%)
LS by 2D-SWE (kPa)	11.19 ± 3.98	13.0 ± 4.17	9.79 ± 3.20

The continuous variables were presented as mean ± standard deviation. The nominal variable were presented as n (%).
EVs: esophageal varices; HBV: hepatitis B virus; HCV: hepatitis C virus; AST: aspartate aminotransferase; ALT: alanine aminotransferase; PT: prothrombin time; INR: international normalized ratio; CTP: Child-Turcotte-Pugh; LS: liver stiffness; 2D-SWE: 2-dimensional shear wave elastography.

3. Results

3.1. Patient's characteristics

This study included 289 patients who satisfied the inclusion criteria. The baseline characteristics of these patients are summarized in Table 1. The mean age was 56.8 ± 10.2 years, and the most common etiology of cACLD was chronic hepatitis B (47.4%), followed in order of frequency by alcoholic liver disease and hepatitis C. Child–Pugh–Turcotte class A and B disease occurred in 83.5% and 16.5% of patients, respectively. Among patients with chronic hepatitis B, 67.2% of patients had been treated with nucleotide or nucleoside analogues for more than 3 months. Five patients with hepatitis C were treated with PEGylated interferon and ribavirin and 6 patients were treated with direct-acting antivirals. Among patients with hepatitis B, the mean LS value of the group taking NUC was 9.67 ± 3.15 kPa while the mean value of the other patients was 10.66 ± 3.31 kPa, There was no statistically significant difference in LS between the two groups (p = 0.872).

3.2. Prediction of EVs by LS as assessed by 2D-SWE and other models that used additional noninvasive markers for predicting the presence of varices

The prevalence of any-size varices was 43.2%. The mean value of LS by 2D-SWE was 11.2 kPa. The mean values of 2D-SWE in patients with or without EVs were 13.0 kPa and 9.79 kPa, respectively.

Univariate analysis showed that LS measured by 2D-SWE, spleen diameter, platelet count, the etiology of cACLD, the levels of hemoglobin, ALT, sodium, and albumin, INR, and Child-Pugh score were all significantly associated with the presence of EVs. The 2D-SWE LS value, platelet count, spleen thickness, ALT level, sodium level, and the etiology of cACLD were all found to be parameters significantly associated with the presence of EVs by stepwise multivariate analysis (Table 2). Among patients with chronic hepatitis B, the association between NUCs treatment and presence of EVs was not statistically significant (p = 0.179).

The area under ROC (AUROC) (95% confidence interval [CI]) of 2D-SWE for predicting the presence of varices was 0.757 (95% CI,

Table 2
Univariate and multivariate logistic analysis for predicting presence of varices.

Variables	Univariate analysis		Multivariate analysis	
	OR (95% CI)	p	OR (95% CI)	p
Age	0.992 (0.970–1.105)	0.285		
Sex				
Male	Ref.			
Female	0.918 (0.569–1.481)	0.725		
Etiology				
HBV	Ref.	<0.001	Ref.	0.116
HCV	1.113 (0.445–2.857)	0.800	0.989 (0.325–3.010)	0.985
Alcohol	2.981 (1.729–5.140)	<0.001	2.291 (1.076 – 4.877)	0.032
Others	2.238 (1.053–4.755)	0.036	1.999 (0.734–5.447)	0.176
Spleen diameter	1.448 (1.283–1.633)	<0.001	1.206 (1.045–1.392)	0.010
Hemoglobin	0.816 (0.735 – 0.906)	<0.001	0.867 (0.856–1.140)	0.867
Platelet count	0.986 (0.981–0.991)	<0.001	0.991 (0.986–0.996)	0.001
Sodium	0.860 (0.784–0.942)	0.001	0.919 (0.814–1.039)	0.176
AST	1.001 (0.994 – 1.008)	0.828		
ALT	0.983 (0.971 – 0.996)	0.007	0.982 (0.986–0.996)	0.024
Bilirubin	1.146 (0.874–1.500)	0.324		
Albumin	0.430 (0.291–0.634)	<0.001		
Creatinine	1.009 (0.868–1.172)	0.910		
PT, INR	240.372 (27.129–2129.784)	<0.001		
CTP score				
5	Ref.	0.021	Ref.	0.372
6	2.299 (1.241–4.261)	0.008	1.102 (0.485–2.505)	0.817
7	2.791 (1.245–6.260)	0.013	1.371 (0.438–4.292)	0.588
8	1.364 (0.354–5.256)	0.651	0.397 (0.090–1.744)	0.221
9	0.853 (0.207–3.521)	0.826	0.285 (0.051–1.593)	0.153
LS by 2D-SWE	1.340 (1.228–1.462)	<0.001	1.208 (1.078–1.353)	0.001

OR: odds ratio; CI: confidence interval; Ref.: reference; HBV: hepatitis B virus; HCV: hepatitis C virus; AST: aspartate aminotransferase; ALT: alanine aminotransferase; PT: prothrombin time; INR: international normalized ratio; CTP: Child-Turcotte-Pugh; LS: liver stiffness; 2D-SWE: 2-dimensional shear wave elastography.

Table 3
Prediction of all size varices and varices needing treatment using various models.

EVs	AUROC	95% CI	p	COV	Se (%)	Sp (%)	PPV	NPV
2D-SWE	0.757	0.701–0.810	<0.01	11.05	77.6	66.5	63.8	79.6
PLT	0.758	0.704–0.807	<0.01	118000	69.6	72.8	66.4	75.6
Spleen diameter	0.729	0.674–0.780	<0.01	10.19	81.8	51.2	55.3	79.2
PSR	0.785	0.732–0.831	<0.01	11.73	76.0	69.8	65.2	79.6
APRI	0.594	0.535–0.652	<0.01	0.92	34.4	85.2	64.2	62.7
Lok index	0.762	0.708–0.810	<0.01	0.68	80.8	65.9	64.3	81.8
FIB-4	0.757	0.703–0.805	<0.01	3.20	76.8	68.5	65.3	79.3
LS * spleen diameter	0.795	0.744–0.841	<0.01	120	78.5	67.7	64.2	81.0
mLSPS	0.813	0.763–0.857	<0.01	0.83	85.1	64.8	64.4	85.4
VNT	AUROC	95% CI	p	COV	Se (%)	Sp (%)	PPV	NPV
2D-SWE	0.712	0.656–0.764	<0.01	11.72	69.1	65.1	37.9	87.3
PLT	0.781	0.729–0.828	<0.01	108000	75.00	73.1	46.4	90.4
Spleen diameter	0.743	0.688–0.793	<0.01	11.83	69.2	70.0	40.5	88.5
PSR	0.816	0.766–0.860	<0.01	9.41	76.9	71.6	44.6	91.2
APRI	0.676	0.618–0.729	<0.01	0.92	44.1	83.1	44.8	82.7
Lok Index	0.687	0.630–0.740	<0.01	0.68	82.4	54.3	35.7	90.9
FIB-4	0.725	0.670–0.776	<0.01	3.20	80.9	58.0	37.4	90.7
LS * spleen diamter	0.784	0.732–0.830	<0.01	120	76.9	71.6	38.1	93.5
mLSPS	0.834	0.785–0.875	<0.01	1.65	69.2	83.5	55.6	90.1

EVs: esophageal varices; VNT: varices needing treatment; AUROC: area under receiver operating characteristics; CI: confidence interval; COV: cut-off value; Se: sensitivity; Sp: specificity; PPV: positive predictive value; NPV: negative predictive value; 2D-SWE: 2-dimensional shear wave elastography; PLT: platelet count; PSR: platelet-spleen ratio; APRI: aspartate aminotransferase to platelet ratio index; LS: liver stiffness; mLSPS: modified liver stiffness-spleen-diameter-to-platelet-ratio score.

0.701–0.810). The cut-off values for LS by 2D-SWE, platelet count and spleen diameter that were used to identify patients with EVs are shown in Table 3. In addition, we calculated the AUROCs of various models of noninvasive parameters suggested by a previous study [25–27], as shown in Table 3. We also plotted the ROC curves of these parameters and models (Fig. 2). Based on the ROC curves, 2D-SWE alone shows good ability for identifying varices (AUROC, 0.757; 95% CI, 0.701–0.810) similar to the ability of the FIB-4 and Lok index. The combination of an LS cut-off value of <11.05 kPa by 2D-SWE and platelet count cut-off of >118,000/μL missed only 13 (4.5% of 289) patients with varices. Models that included 2D-SWE showed better predictive ability than other models. The modified LSPS, which consisted of 2D-SWE, spleen diameter, and platelet count, was found to produce the largest AUROC (0.813; 95% CI, 0.763–0.857) and the highest negative predictive value for detecting the presence of varices.

3.3. Prediction of VNT by LS as assessed by 2D-SWE and other models that use noninvasive markers

The prevalence of VNTs was 23.5%. The AUROC of 2D-SWE for predicting the presence of VNTs was 0.712 (95% CI, 0.656–0.764).

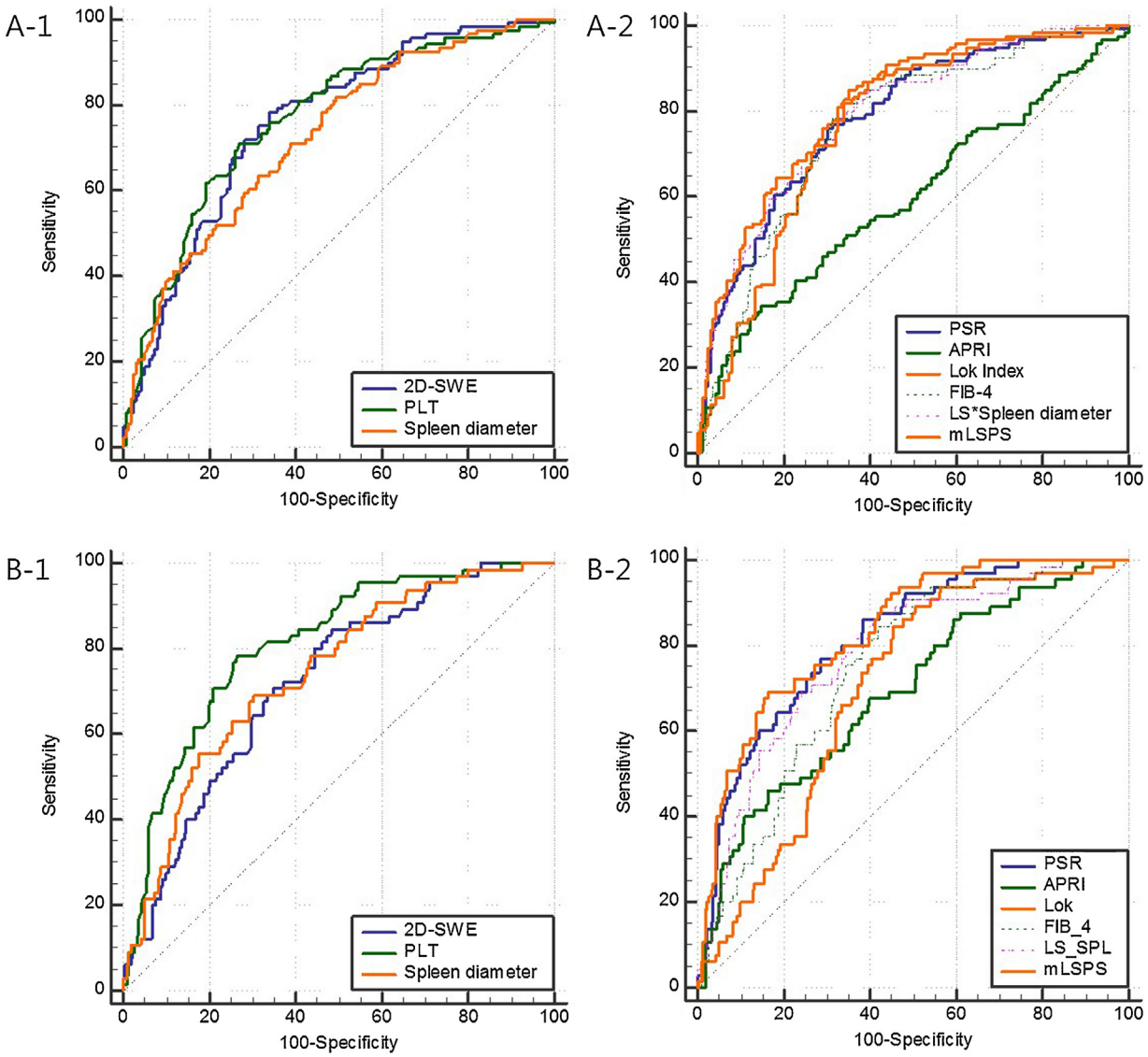

Fig. 2. Receiver operating characteristic curves for all-size varices and varices needing treatment prediction in various models. (A) All-size varices prediction. (A-1) Single parameter, and (A-2) model combining non-invasive tools. (B) varices needing treatment prediction. (B-1) Single parameter, and (B-2) model combining non-invasive tools. 2D-SWE: 2-dimensional shear wave elastography; PLT: platelet count; PSR: platelet-spleen ratio; APRI: aspartate aminotransferase to platelet ratio index; LS: liver stiffness; mLSPS: modified liver stiffness-spleen-diameter-to-platelet-ratio score.

The cut-off LS value determined by 2D-SWE for predicting VNT was 11.72 kPa. The 2D-SWE alone did not show better predictive power than other single parameters, including the platelet count and spleen diameter for predicting the presence of VNT. The 2D-SWE combined with other noninvasive tools showed better predictability. When combining LS by 2D-SWE and platelet together, LS less than 11.72 kPa and platelet count more than 108,000/μL, 7 cases (2%) had VNTs. The mLSPS produced the highest AUROC values as follows: 0.834 (95% CI, 0.785–0.875). The AUROCs and cut-off values of various models are shown in Table 3, and the ROC curves are shown in Fig. 2.

3.4. Comparison of diagnostic performance for varices and VNT as assessed by 2D-SWE and TE

Univariate and multivariate analyses were performed for 195 patients who underwent simultaneous TE and 2D-SWE. After adjustment for associated factors, including albumin, INR, ALT, platelet count, hemoglobin, sodium level, spleen diameter and etiology of cACLD, LS values as determined by 2D-SWE and TE both had good predictive ability for the presence of varices (Fig. 3), with AUROCs of 0.844 and 0.898, respectively. The difference between their predictive abilities based on their ROC curves was not significant ($p = 0.146$ by DeLong method). Likewise, after adjusting for confounding factors to predict VNT including INR, albumin, platelet count, hemoglobin, spleen diameter and etiology of cACLD, LS values by 2D-SWE and TE both had good diagnostic performance for predicting VNT (Fig. 3), with AUROCs of 0.844 and 0.898, respectively. There were no differences in their predictive abilities ($p = 0.352$ by DeLong method).

4. Discussion

In this study, we validated the usefulness of 2D-SWE alone and combined with other noninvasive markers for predicting the presence of varices in patients with cACLD. We also found that the predictive ability of 2D-SWE was similar to that of TE.

In this study, proposed cut-off values are low in comparison to the cut-off values reported by other elastography methods (TE or 2D-SWE by SuperSonic image for example), but this may fit into

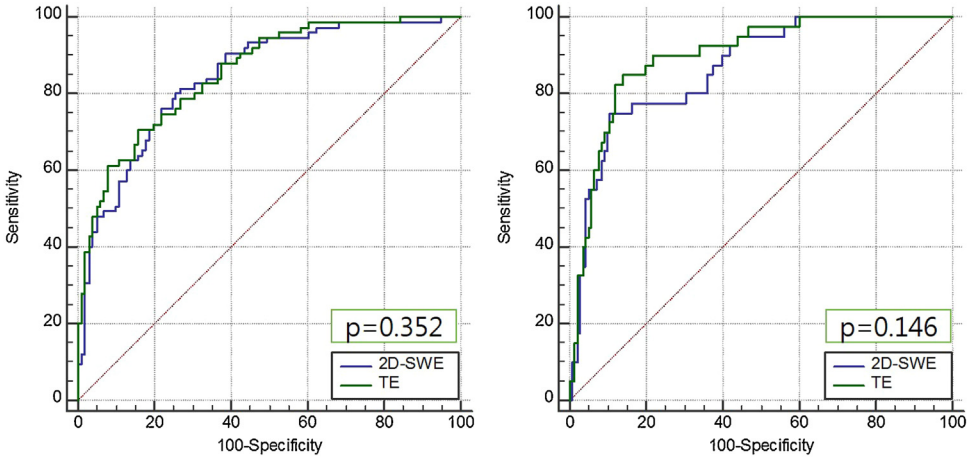

Fig. 3. Comparison of receiver operating characteristic curves for 2-dimensional shear wave elastography (2D-SWE) and transient elastography (TE) after adjusting for other confounding factors. (A) For predicting all-size varices (confounding factors: albumin, international normalized ratio of prothrombin time prothrombin time, hemoglobin, alanine aminotransferase, spleen diameter, sodium level, platelet count, and etiology of compensated advanced chronic liver disease (cACLD)). (B) For predicting varices needing treatment (confounding factors: platelet count, etiology of cACLD, hemoglobin level, albumin level, spleen diameter, and international normalized ratio of prothrombin time).

the general pattern of 2D-SWE by GE healthcare since low cut-off values for fibrosis stages by this method were reported as well [17].

LS estimated by 2D-SWE, spleen diameter, and platelet count are strongly associated with the presence of EVs in both univariate and multivariate analysis. Similar results were obtained for patients who underwent both TE and 2D-SWE. Although ALT showed statistical significance on logistic regression analysis, the odds ratio and cut-off-value for ALT were not associated with clinical significance.

The 2D-SWE alone showed good predictive capacity for predicting EVs (AUROC, 0.757). However, models combining other factors showed better diagnostic characteristics. In particular, mLSPS showed good predictive power for identifying the presence of EVs (AUROC 0.834).

The 2D-SWE, which can measure LS by USG, has more methodological advantages than TE in that USG can be performed simultaneously. In our study, the predictive power of 2D-SWE was similar to that of TE for predicting the presence of EVs, a finding that is consistent with previous studies. Based on the results of our study, 2D-SWE might eventually replace TE. In addition, the spleen diameter is a noninvasive parameter that is easy to measure by USG. Conventional LSPS requires 2 separate instruments, whereas mLSPS can be assessed by a single instrument. Therefore, mLSPS assessment described in this study could be easily obtained during the same ultrasound examination and it also will provide high predictive power.

On the other hand, 2D-SWE alone did not show good predictive capacity for VNTs compared to other models based on noninvasive tools. In general, the AUROC for predicting VNT is expected to be higher than the AUROC for predicting EV, but not only in our study, shear wave seems to predict all-size varices better than VNT. Kim et al. [19] using SuperSonic imaging showed an AUROC for all-size varices of 0.887, while the AUROC for VNT was 0.880. Also, Kazemi et al. [15] and Abraldes et al. [6] who used TE also reported similar results, showing higher AUROC for predicting all-size varices than VNT (AUROC for all-size varices vs. VNT, 0.84 vs. 0.83, 0.71 vs. 0.67). These results may suggest that shear wave elastography does not correlate well with advanced cirrhosis, which often shows high grade varices. Studies evaluating the association between 2D-SWE and progression of cirrhosis are lacking, and further studies are needed on this subject. 2D-SWE alone showed lower predictive power than spleen diameter or platelet count for predicting VNTs. However, a model combining noninvasive methods with 2D-SWE still showed good predictive ability for predicting VNTs, and among the various models, mLSPS showed the best predictive power. In addition, in our study, when the cut-off values of <11.72 kPa for LS combined with a platelet count >108,000/μL were used, only 7 cases of VNTs (2%) were missed.

Kim et al. [19], investigated the diagnostic performance of 2D-SWE and PSR for predicting EVs. The AUROC obtained in their study for 2D-SWE alone was 0.887, which was higher than the value in our study. The disparity is probably attributable to the difference between studies in the prevalence of EVs and in the number of study patients, which was higher in our study than in the study of Kim et al. [19]. Mahmoud Hashim et al. [20] evaluated the predictive capacity of 2D-SWE in 100 patients with chronic hepatitis C. They found an AUROC for predicting EVs of 0.775 for 2D-SWE alone, which is consistent with our study. Stefanescu et al. [28] reported a study of 73 patients with cirrhosis that showed an AUROC for predicting EVs with 2D-SWE of 0.753.

Recent studies have shown that spleen stiffness measured by 2D-SWE could also be useful for predicting CSPH and EVs [20,29]. Grgurević et al. [30] reported that both LS and spleen stiffness showed good diagnostic performance for predicting EVs. Their AUROCs was 0.796 (95% CI, 0.701–0.891) and 0.790 (95% CI, 0.690–0.890) respectively. This study differs from ours in that they included patients with decompensated cirrhosis. Procopet et al. [18] reported a success rate for the measurement of spleen stiffness as low as 66%. A report by Stefanescu et al. [28] showed that liver stiffness had a better diagnostic accuracy than spleen stiffness (AUROCs of 0.753 and 0.747, respectively). Additional studies are needed to characterize the diagnostic power of spleen stiffness measured by 2D-SWE.

Our study has several strengths compared with other studies. Our study cohort consisted of patients with cACLD. Few studies have enrolled this type of patients; most studies [8,10,12,13,24] have focused instead on cirrhotic patients. Furthermore, this study is different because it compared the diagnostic performances of TE and 2D-SWE in 195 patients, which is a relatively larger sample than the samples of previous studies. This study also calculated the diagnostic characteristics of various models of noninvasive markers, which were not evaluated in other studies. In addition, we used a combination of well -known and easily accessible non-invasive markers for predicting the presence of EVs, including LS measured by 2D-SWE, spleen diameter, spleen thickness, and platelet count.

There are some limitations in this study. First, it was retrospective, and should be confirmed by prospective studies with larger

samples. We also plan to confirm the results of this study in a validation cohort. Second, various endoscopists performed EGD, but because the study was retrospective, we could not determine the degree of interobserver agreement. Also, air insufflation during endoscopy, which may affect the size of varices, may have influenced the assessment of variceal grade. This point should be taken into account in interpreting the results of the study. Third, the mLSPS, which consisted of 2D-SWE, spleen diameter and platelet count achieved the highest AUROC with a good negative predictive value for detecting the presence of all-size varices and varices needing treatment. However this score includes the use of 2D-SWE which is not broadly available. Even if 2D-SWE is not widely used to date, due to the fact that it can be performed simultaneously with conventional USG and that its diagnostic performance for detecting varices and VNT is equivalent to that of transient elastography, we expect that this equipment will be more widely used than transient elastography in the future. Fourth, the suggested cut-off values for predicting all-size EV and VNT (11.05 vs. 11.72 kPa) by 2D-SWE showed a little difference. It is hard to distinguish between the two categories in daily practice with these values alone. This result may have been influenced by the presence in our study of patients with high body mass index and other characteristics that were expected to increase the occurrence of inadequate LS measurements. Further studies are needed to obtain more precise cut-off values to differentiate between the two categories of varices.

In summary, 2D-SWE is a useful method for predicting the presence of all-size varices in patients with cACLD. The utility of 2D-SWE has been shown to be more useful in models, notably mLSPS, that consist of easy-to-obtain noninvasive markers such as platelet counts and spleen diameters. Additional studies with larger samples should be performed to validate the usefulness of these models for predicting the presence of EVs, and validation of these models through external samples is required.

Conflict of interests

None declared.

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