CORRELATION OF LIVER STIFFNESS IN CHRONIC LIVER DISEASES BETWEEN FIBROSCAN AND 2D SHEAR WAVE ELASTOGRAPHY IN PHRAMONGKUTKLAO HOSPITAL

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Abstract

Background: Noninvasive assessment of liver stiffness has been increasingly used to evaluate fibrosis instead of liver biopsy among patients with chronic liver diseases. FibroScan has been widely used as an alternative tool to assess liver stiffness. Several studies have shown significant correlation between the performance in staging liver fibrosis using 2D shear wave elastography (2D-SWE) technique, FibroScan method and the histological analysis of liver biopsy. The information using 2D-SWE is not well established in Thailand because this rather new technology can be obtained using high-end ultrasound machines.

Objective: The study aimed to evaluate the correlation of liver stiffness in chronic liver diseases obtained by the 2D-SWE method and a reference standard method, FibroScan.

Methods: A prospective observational study was conducted between March and December 2018. A total of 30 consecutive participants aged 18-80 years having chronic liver diseases were enrolled. Liver stiffness (LS) was evaluated in the same session using two elastographic methods: FibroScan (transient elastography) and 2D-SWE techniques. The conventional 2D ultrasound of the liver was also performed simultaneously. The assessment of fibrosis is described below: significant fibrosis (F >2), advanced fibrosis (F>3) and cirrhosis (F=4). The cut off values were 6.6, 9.4 and 11.2 kPa, respectively.

Results: Moderate to strong positive correlations were observed between measurements obtained by FibroScan and 2D-SWE in all stages of liver fibrosis ($r= 0.66$, $p < 0.01$) especially in fibrosis stages 2-3.

Conclusion: The 2D-SWE technique could be another alternative tool to evaluate liver fibrosis especially during the main targeted early stages for further medical therapeutic prevention of liver stiffness progression. This 2D-SWE may be added in routine sonographic studies in particular cases of chronic liver disease.

Keywords : Cirrhosis, Liver stiffness, 2D-shear wave elastography, FibroScan, Transient elastography

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Introduction

Cirrhosis is the 8th leading cause of death in Thailand. The Thai Association for the study of the liver has reported that cirrhosis is caused by inflammation or other harmful effects on the liver. Many causes of liver fibrosis include alcoholism, chronic hepatitis B, chronic hepatitis C, autoimmune hepatitis, bile duct obstruction and fatty liver disease. [1]

The mild degree of liver fibrosis and early stage of cirrhosis can be completely asymptomatic. Thus, the timely diagnosis of liver fibrosis has an important value in treatment and prognostic assessment of chronic liver diseases. The standard tool to assess the severity for pretreatment planning is liver biopsy. However, this involves an invasive procedure that can result in complications including death. Presently, due to the development of noninvasive methods and their high accuracy, the number of liver biopsies has decreased.

These noninvasive techniques comprise multiparameter blood tests (FibroTest) including haptoglobin, bilirubin, GGT, apolipoprotein A-I and alpha2 macroglobulin; radiographic examinations such as transient elastography (TE) (FibroScan) and magnetic resonance elastography (MRE). In addition interest has increased in acoustic radiation force impulse imaging and ultrasound in the imaging program, 2D shear wave elastography (2D-SWE).[2] Several studies have reported that the measurements of liver stiffness by 2D-SWE significantly correlated with the measurement by FibroScan and liver biopsy. [3, 4, 9, 10] In addition, 2D-SWE allows more area of screening, up to 20 cm^3 (7 cm).

All patients with chronic liver diseases received TE (FibroScan) at the Division of Gastroenterology and Hepatology, Department of Internal Medicine, Phramongkutklao Hospital to assess of liver fibrosis. They were also screened for liver tumors at the Department of Radiology using ultrasound on the upper abdomen. The process was costly and time-consuming for the patient to complete at multiple appointments. Therefore, we were interested to study whether 2D-SWE could be performed with accuracy at the time of performing conventional ultrasound. Thus, there would be no need to change tools, location or staff for the inspection. The aim of this study was to evaluate the diagnostic performance of the 2D-SWE using FibroScan as the reference method.

Methods

This study employed a prospective observational design approved by the Ethics Committee, Institutional Review Board, Royal Thai Army Medical Department (R217h/60). All subjects signed informed consent forms to undergo elastographic measurement. All patients with chronic liver disease aged from 18 to 80 years who had undergone TE (FibroScan) between March 2018 and December 2018 were included. Patients presenting a history of hepatocellular carcinoma, other hepatic tumors, hepatobiliary disease, liver transplantation or poor performance status were excluded.

Transient elastography (TE)

TE was performed in all subjects under fasting conditions using a FibroScan device (Echosens 502 Touch). Each patient was placed in the supine position using the right intercostal approach (around the 4th to 5th rib), right arm in maximal abduction using the M probe (standard frequency 3.5 MHz). The median value of ten valid liver stiffness (LS) measurements was calculated and the results were shown in kilopascals (kPa) (**Fig. 1**). To discriminate between various stages of fibrosis, the cut off values were used according to Metavir score of TE (FibroScan) [4,11-13] which differ in each disease status of the patients. The hepatic steatosis measurement was used from the study of Sasso et al. as the reference. [7] Because TE is a validated method for liver fibrosis evaluation, it served as the reference method to compare with the performance of 2D SWE.

Shear wave elastography (SWE)

2D SWE was performed using a Toshiba Aplio 500 system. All fasting patients were placed in the supine position with right arm maximal abduction. The probe was placed using the intercostal approach on the right chest wall to assess the right hepatic lobe. The patients held their breath for 5 to 10 seconds before the examiner pushed the acoustic pulse using the sample box size 3x3 cm (**Fig. 2**) and placed it 1 to 2 cm below the liver capsule. Ten regions of interest (ROI) measurements were taken in circular and 1 cm in diameter. The median value of ten consecutive measurements

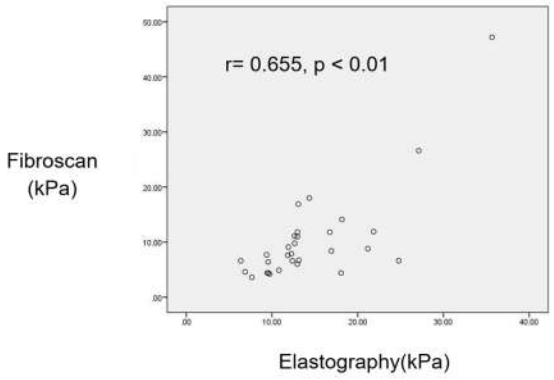

Figure 1. The correlation between FibroScan and elastography data

was used for statistical analysis, and the results were shown in kilopascals (kPa) and meters per second (m/s). The assessment of fibrosis is described below: significant fibrosis (F >2), advanced fibrosis (F>3) and cirrhosis (F=4). The cut off values of 6.6, 9.4 and 11.2 kPa, respectively, were used according to the study of Ferraioli et al.[5] Conventional ultrasound of the liver was also performed using the same ultrasound equipment (Toshiba Aplio500 system). All fasting patients were placed in the supine position. The cirrhotic ultrasound characteristics were investigated including the right hepatic lobe and/or the medial segment of the left lobe atrophy, the lateral segment of the left hepatic lobe hypertrophy, increased caudate to the right lobe ratio (>0.65), increased distance of the gallbladder fossa, coarse heterogeneous liver parenchymal echo, evidence of portal hypertension and ascites. The ultrasound findings of fatty change were also recorded including increased liver echogenicity, obscuring of the hepatic and portal veins walls and impaired evaluation of the deep liver parenchyma and diaphragm.[6] Statistical analysis All data was analyzed using IBM SPSS statistics, Version 22.0 for Windows. Normal distribution was checked using the Kolmogorov-Smirnov test. All data on continuous variables were presented as mean, standard deviation (SD) or median and interquartile range (IQR). The correlation between FibroScan and elastography data were represented in Spearman's rank correlation coefficients. The sensitivity, specificity, positive predictive value and negative predictive value were calculated, and a *p*-value less than 0.05 was considered statistically significant. Results Thirty participants were evaluated for liver stiffness by means of TE and 2D-SWE among patients with viral hepatitis B (6 cases), viral hepatitis C (17 cases) and nonalcoholic steatohepatitis (NASH) (7 cases) as shown in **Table 1**.

Table 1. Demographic data of enrolled participants (N=30)

Characteristics	Number
Sex	
Male	21
Female	9
Underlying diseases	
Hepatitis B	6
Hepatitis C	17
NASH	7
Alcoholism	0
Steatosis stage from fibroScan	
(Control attenuated attenuation parameter,dB/m)	
Stage 0	15
Stage 1	2
Stage 2	6
Stage 3	7
Age (years, mean±SD)	49.6 ± 11.65 (28-72)*
BMI (Kg/m^2, mean±SD)	25.3 ± 3.76 (18.5-32.4)*

BMI =Body mass index, NASH= non alcoholic steatohepatitis

*(Min-Max)

Stage of fibrosis was obtained from 2D-SWE of which 2 individuals were at stage 2, 6 were at stage 3 and 22 were at stage 4 (**Table2**). Moderate to strong positive correlation was observed among liver stiffness values (kPa) assessed by means of FibroScan and by 2D-SWE (Spearman's rank correlation coefficient = 0.66, p <0.01) as shown in **Fig. 1**. Almost one half (13/30) were categorized as FibroScan stage 1. Another 5, 6 and 6 participants were categorized as stage 2, 3 and 4, respectively. The correlation between liver stiffness values obtained from FibroScan and 2D-SWE at each stage is shown in **Table 2**. The best correlation between the two methods was observed in fibrosis stage 2 (r = 0.9, p = 0.03) and stage 3 (r = 0.83, p = 0.04). Additionally, most patients in the group of strong correlation had normal BMI (r =.76, p = 0.049).

The 2D-ultrasound appearances at each fibrosis stage using FibroScan are shown in **Table 3** whereas the fatty change appearance from 2D ultrasound at each fibrosis stage using the 2D-SWE is shown in **Table 4**.

Table 2. Fibrosis staging and correlation of liver stiffness values by FibroScan and 2D-shear wave elastography

	Number of participants			
Fibrosis stage	Fibroscan	2D-SWE	Spearman's rank correlation coefficient (r)	p-value
Mild /no fibrosis (F<2)	13	0	0.34	0.25
Significant fibrosis (F2)	5	2	0.90	0.03
Advanced fibrosis (F3)	6	6	0.83	0.04
Liver cirrhosis (F4)	6	22	0.54	0.27
Total	30	30		

Table 3. Ultrasound characteristics in each fibrosis stage using FibroScan

Fibrosis stage	Normal	Coarse parenchyma	Nodular contour	Increased caudate to right lobe ratio	Lateral segment hypertrophy	Mild steatosis	Moderate steatosis
0/1	2	8	3	0	0	3	4
1/2	1	3	1	0	0	2	1
2/3	3	3	3	0	1	1	1
3/4	2	3	1	0	1	0	2

Table 4. The fatty change appearance from 2D ultrasound in each fibrosis stage from 2D-shear wave elastography

Fibrosis stage From 2D-SWE	No steatosis	Mild steatosis	Moderate steatosis
1	0	0	0
2	1	0	1
3	2	2	2
4	13	3	6

Discussion

To our knowledge, limited numbers of studies in Thailand have evaluated the correlation between transient elastography, 2D-SWE and ultrasound characteristics of the liver in different stages of fibrosis. In this study, the correlation rate between transient elastography and 2D-SWE stiffness data was moderate to strong positive ($r = 0.66$, $p = 0.01$) in all chronic liver diseases for which fibrosis stage 2 and 3 revealed the most significant strong correlation ($r = 0.9$, $p = 0.03$ and $r = 0.83$, $p = 0.042$, respectively). The results of this study were similar to the related study of Bende et al.[7] showing a strong correlation (r=0.83) between liver stiffness value assessed by means of TE and by 2D-SWE. Thus, we could use 2D-SWE as an alternative tool to assess liver stiffness.

The advantage of 2D-SWE compared with TE is that the technique is guided by B-mode imaging using a color-coded map. The operator can choose where to place the ROIs in which LS is measured in the most homogeneous area, and can use the color homogeneity as a qualitative criterion for the evaluation. It also allows avoiding large vessels and placing the measuring box far enough from the liver capsule to avoid interference with the liver capsule and subcutaneous fat. In addition, 2D-SWE also provides are larger ROI than TE.

After using BMI for subgroup analysis, the best correlation between TE and 2D-SWE was in the group having normal BMI ($r = 0.76$, $p = 0.049$). The result was similar to the study of Bende et al. [8] which reported the reliability of LS measurement depended on BMI.

The comparison between 2D-sonographic characteristics of cirrhotic change and degree of liver stiffness using TE showed that nine patients had cirrhotic appearance. Four participants (44.4%) were categorized having early fibrosis stage (F1-2) and five participants (55.6%) were categorized having severe fibrosis. These results might imply that the cirrhotic appearance from 2D-ultrasound may not be the only good criterion to represent severe degree of liver stiffness.

In this study, moderate correlation was observed between FibroScan and 2D-SWE in fibrosis stage 4, which might be due to a confounding factor such as fatty infiltration of the liver. The statistical analysis showed the liver stiffness data (kPa) tended to increase in high grades of hepatic steatosis (S0 = 13.94 ± 5.71, S1 = 15.02 ± 8.52, S2 = 15.21 ± 2.63) and 9 of 22 patients presenting severe fibrosis (stage 4) using 2D-SWE showed fatty liver. Thus, further study of the relationship between abnormal high liver stiffness data (kPa) among patients with fatty liver would be interesting.

In conclusion, 2D-SWE could serve as another alternative tool to detect early stages of liver stiffness (stages 2 to 3), which constitute the main targeted stages for further medical therapeutic prevention of liver stiffness progression. This 2D-SWE may be added in the routine sonographic study of particular cases of chronic liver disease.

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Potential conflicts of interest

The authors declare they have no conflict of interest.

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