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Original Article

Role of shear wave elastography of liver and spleen "as noninvasive method" in prediction of oesophgeal varices in Egyptian patients with liver cirrhosis

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ABSTRACT

Background: Upper gastrointestinal endoscopy (UGIE) screening for esophageal varices (EVs) is expensive for the health care system and invasive for the patients. Elastography has been recently used for prediction of liver cirrhosis and its complications.

Objective: To identify the reliability of liver stiffness (LS) and spleen stiffness (SS) using point shear wave elastography (PSWE) as noninvasive predictors of EVs.

Methodology: This case-control study was carried was conducted on sixty patients divided into two groups (cirrhotics without EVs (30 patients) and cirrhotics with EVs (30 patients)) were subjected to: Demographic, clinical, laboratory tests, abdominal ultrasound and LS and SS measured by shear wave elastography (PSWE), and finally UGIE.60 healthy control subjects were also included in the study.

Results: There was highly significant increase of liver, spleen stiffness, and liver stiffness x splenic size/platelet count (LSPS) in group with EVs in comparison to group without EVs and control group, and in patients group with cirrhosis without EVs in comparison to control. Also there was significant increase of spleen stiffness in cases with large EVs than in those with mild and moderate EVs while there was no significant difference as regard liver stiffness.

Conclusion: LS and SS are reliable predictive tools for EVs. These results could be used to reduce the need for routine upper gastrointestinal endoscopy screening.

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INTRODUCTION

In cirrhotic patients with acute variceal bleeding esophageal varices (EVs) are present in 40% of patients with Child-Pugh A and up to 85% with Child-Pugh C cirrhosis and mortality rate is as high as 20%, despite endoscopic and medical treatment ^[1]. Several guidelines such as American Association for the Study of Liver Diseases (AASLD) recommend that esophagastroduodenoscopy (EGD) should be performed in all newly diagnosed cirrhotic patients to screen for EV, and subsequent surveillance EGD should be performed according to result of the initial EGD. Although this approach was found to be cost-effective, surveillance EGD remains expensive and its risk of complications cannot be negligible ^[2].

Historically, several non-invasive measurements such as aspartate transaminase to platelet ratio index, platelet count/spleen diameter ratio, and Lok index have been extensively studied. However, their performance is far from perfect for detection of EV and, therefore, cannot be universally recommended ^[3]. Liver stiffness (LS) and spleen stiffness (SS) measured by elastography has been

shown to correlate with degree of fibrosis, presence of significant portal hypertension, and EVs in the past decade. Additionally, combination of LS, spleen size, and platelet count (LS-spleen diameter to platelet ratio score [LSPS]) has been initially shown to further improve the performance in the detection of Evs^[2].

Transient elastography (TE) or FibroScan is a new technique for rapid and non-invasive measurement of tissue stiffness. It has been largely accepted that liver stiffness (LS) is reflective of the degree of fibrosis and also predictive of EV. Measurement of LS by TE has been considered a useful but not excellent method for predicting EV. Although most of these outcomes have been related to the liver stiffness (LS) as assessed by TE, spleen stiffness (SS) has recently attracted attention as well. SS correlates even better with portal hypertension and the presence of esophageal varices ^[4]. On the other hand, TE has limitations due to the fact that it cannot be applied in patients with ascites, does not allow twodimensional imaging of the investigated structures, and investigation of the spleen can be performed only when proper spot has been chosen by conventional ultrasound. These limitations have been overcomed by shear wave elastography which is a new technique that is based on shear waves Implemented on a diagnostic US system. Shear wave elastography relies on the generation of shear waves determined by the displacement of tissues induced by the force of a focused ultrasound beam or by external pressure ^[5].

The shear waves are lateral waves, with a motion perpendicular to the direction of the force that has generated them. They travel slowly (between 1 and 10 m/s) and are rapidly attenuated by tissue. The propagation velocity of the shear waves correlates with the elasticity of tissue; i.e., it increases with increasing stiffness of the liver or spleen parenchyma^[5]. With SWE, it is possible to perform gray-scale, Doppler, and elastographic investigations at the same time, in the same patient, with the same US probe ^[6]. SWE has been tested in different patient populations, mainly with chronic viral hepatitis, and the results were comparable to TE $^{[7]}$. The aim of this study is to identify the reliability of liver stiffness (LS) and spleen stiffness (SS) using point shear wave elastography (PSWE) as noninvasive predictors of EVs.

SUBJECTS AND METHODS

This case-control study was carried out at Infectious Hepatogastroenterology and diseases department and Diagnostic Radiology, Al-Zharaa University hospital, Cairo during the period from November 2017 till November 2018. It included 60 cirrhotic patients as well as 60 controls. Adult patients of both sexes with liver cirrhosis (with and without esophgeal varices) were included while patients with BMI >35, heart failure, renal failure cholestasis, patients with blood diseases that affect the platelet count, HCC and acute hepatic failure were excluded. Informed consent was obtained from all patients, and the study was approved by the Ethics Committee of Hepatogastroenterology and Infectious Diseases Department, Al-Azhar University. The studied groups were classified into:

- **Group I:** Included 30 cirrhotic patients without esophageal varices (EVs).
- **Group II:** Included 30 cirrhotic patients with esophageal varices (EVs).
- Group III: Included 60 volunteer subjects as a control group. They were negative for HBs Ag, HCV Ab, Bilharzial Ab, with normal liver function tests and normal abdominal ultrasonography.

Ethical approval

All authors hereby declare that the study protocol has been examined and approved by the appropriate ethics committee and has therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

All patients were subjected to:

Detailed history, complete physical examination, Laboratory investigations(complete blood picture, liver function tests, kidney function tests (urea and creatinine), fasting blood sugar (FBS),viral hepatitis markers: hepatitis B surface antigen (HBVsAg.), HBC Ab, hepatitis C virus antibody (HCV Ab.) were measured by ELISA technique, (ANA) for autoimmune liver disease and Alpha feto protein (AFP) for patients groups .Also upper GIT endoscopy for detection and grading of EVs according to Chinese Society o Gastroenterology (2008)(as well as Liver and spleen stiffness measurements using pSWE after routine abdominal US. Child pugh classification was calculated for patients groups.

Liver and spleen stiffness measurement by p-SWE

Shear wave elastography (pSWE) using (Philips Affinity 70-G ultrasonography device) at Diagnostic radiology department, AlZahraa university hospital, was done to control group (60 subjects) and patient groups (60 patients) fullfing inclusion and excluding exclusion criteria. Measurements were performed after overnight fasting.

Procedure

Measurements were performed in the right lobe of the liver through the intercostal spaces, on patients lying in the dorsal decubitus position with the right arm in maximal abduction to facilitate access to the right liver. The tip of the probe is in contact with the intercostal skin through a coupling gel in the 9^{th} to 11^{th} intercostal space. The operator, assisted by a time-motion image, locates a liver portion 2 cm away from liver capsule and free of large vascular structures. Once the measurement area had

been located, the operator pressed the probe button to start an acquisition ("shot")^[6].

Successful measurements were validated using the following criteria: 1) number of shots ≥ 10 , 2) Interquartile range (IQR, reflecting the variability of measurements) less than 30% of the median liver stiffness measurement (LSM) value (IQR/LSM \leq 30%) The results are expressed in kilopascal (kPa). The median value of the successful measurements was kept as representative of LS^[8].



Figure (1): Shear wave elastography for liver in cirrhotic patient with esophageal varices. It shows pSWE for liver in cirrhotic patient with EVs, the shear waves displayed inside a sample box over a conventional B-mode image. The stiffness was 20.83kpa.

Splenic stiffness was performed by investigator, radiologist. The patient was lying in the supine decubitus position with the left arm in maximum abduction. Through a left-side intercostal space access, the ROI was placed in the parenchyma of the lower pole, which was the portion of the spleen that is easily visualized on B-mode ultrasound and is of adequate thickness for assessing shear wave velocity⁹. The observers kept a perpendicular ROI depth whenever possible, at least 1 cm below the spleen capsule. Each patient was asked to stop breathing for few seconds to minimize motion. For each subject studied, both observers obtained 10 samples, with median values expressed in kilopascal.



Figure (2): Shear wave elastography for spleen in patient with esophageal varices. It shows pSWE for spleen in patient with EVs, the shear waves displayed inside a sample box over a conventional B-mode image. The stiffness was 31.80kpa.

Statistical Analysis

Data were collected, reviewed and fed to the computer where statistical analysis was done using the Statistic Package for Social Science version 20.0 (SPSS Inc., Chicago, Illinois, USA) for windows. Comparing groups was done using Student's t- test. Study of the relationship between variables was done using correlation coefficient (Pearson correlation), also (ANOVA), Post Hoc test, Chi-square (x^2) were used. The level of significance was taken at P-value of <0.05". P1: GI vs. G II, P2: GII vs. GIII and P3: GI vs. GIII

RESULTS

The results and data were collected and analyzed in tables 1-4 and figure 1-2.

Group I (GI): Their age ranged between 35 and 70 years with a mean of 55.57 years (50% were females and 50% were males). Group II (GII): Their age ranged between 38 and 76 years with a mean of 58.43 years (60% were females and 40% were males) .Group III (GIII): included 60 apparently healthy individuals as a control group. Their age ranged between 22 and 75 years with a mean of 56.7 years (63.3% were females and 36.7% were males). HCV was the predominant cause of liver cirrhosis. Child A and Child C were the pre dominant in G I and II respectively (Table 1). There was highly significant difference among the studied groups as regard the shear wave values (kPa) (Table 2). There were significant Positive correlations between liver stiffness (kPa) with spleen stiffness (kPa), PC%, urea and LSPS, while there were significant negative correlations with PC% and blood urea in group I while in group II a significant positive correlation between liver stiffness (kPa) with LSPS was detected. Also, there was significant positive correlation of spleen stiffness (kPa) with FBS, PV and spleen size (Table 3). There were variations in the diagnostic performance of shear wave among the studied groups (Table 4). There was highly significant increase of PV diameter and spleen size in GII in comparison to G I and G III respectively and in G I in comparison to G III. Ascites was found only in G II (60%) of patients (Figure 3). Also there was a

statistically significant difference in spleen stiffness with increase the grade of EVs, while there was no statistically significant difference between liver stiffness measurements in different grades of Evs (Figure 4)

Table (1): Demographic data	, Etiology of liver cirrl	hosis, Child class, ar	mong the patients	groups
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Items		Group I	Group II
	Age (years)	35-70	38-76
	Mean ± SD	55.57±9.68	58.43±8.70
Demographic Data	Sex		
	Female	15 (50%)	18 (60%)
	Male	15 (50%)	12 (40%)
	HCV	28 (93.3%)	27 (90.0%)
Etiology of liver cirrhosis G I and	HBV	2 (6.7%)	2 (6.7%)
GII	Bilharziasis	10 (33.3%)	11 (36.7%)
	Autoimmune	0 (0%)	1 (3.3%)
	А	27 (90.0%)	10 (33.3%)
Child class	В	3 (10.0%)	7 (23.3%)
	С	0 (0.0%)	13 (43.3%)

Table (2): Comparison of shear wave values (kPa) among the studied groups

Shear Wave	Group I	Group II	Group III	Post hoc analysis				
		010up 111	P1	P2	P3			
Liver Stiffness (kPa)								
Range	9.21-32.2	8.29-43.8	1.55-0.74					
Mean ± SD	15.61±4.57	24.85±6.92	4.54±2.19	0.001	0.001	0.001		
Spleen Stiffness (kPa)								
Range	8.68-33.9	21.86-153	1.35-14.2	0.001	0.001	0.001		
Mean ± SD	21.82±6.01	44.74±17.94	6.09 ± 2.08	0.001				
LSPS								
Range	0.54-3.55	1.14-13.54	0.05-0.53	0.001	0.001	0.001		
Mean ± SD	1.33±0.59	5.92±3.12	0.20±0.12	0.001	0.001	0.001		



Figure (3): Comparison of liver size, PV and spleen size among the studied groups

Table (3): The positive Correl	ations of liver stiffness a	and spleen stiffness (l	kPa), using Pearson	correlation coefficient
in group I and II				

	Group I: Cirrhotics without EVs				Group II: Cirrhotics with EVs			
Item	Liver Stiffness (kPa)		Spleen Stiffness (kPa)		Liver Stiffness (kPa)		Spleen Stiffness (kPa)	
	r	Р	r	р	R	р	R	р
Liver Stiffness kPa)	-	-	0.40	0.025	-	-	-0.09	0.60
Spleen Stiffness (kPa)	0.40	0.025*	-	-	-0.09	0.60	-	-
PC %	-0.42	0.019*	-0.02	0.90	-0.31	0.085	-0.03	0.86
FBS	0.06	0.737	-0.10	0.59	-0.30	0.108	0.42	0.020*
Urea	0.37	0.042*	0.050	0.79	0.10	0.566	-0.02	0.882
PV (mm)	0.03	0.86	-0.11	0.55	-0.19	0.292	0.51	0.004*
Spleen size (cm)	0.13	0.48	0.02	0.89	-0.30	0.108	0.40	0.029*
LSPS	0.86	0.001*	0.16	0.38	0.53	0.002*	0.27	0.149

Table (4): Diagnostic performance of shear wave

Discrimination of cirrhotic patients	Shear Wave (kPa)	Cut-off	Sen.	Spe.	PPV	NPV	Accuracy
Without Evs and control (GI and GIII).	Liver Stiffness	≥8.5	100%	96.7%	93.8%	100%	99.8%
	Spleen Stiffness	≥14.2	90%	100%	100%	95.2%	98.0%
With Evs and control (GII,	Liver Stiffness	≥10.74	96.7%	100%	100%	98.4%	99.8%
GIII).	Spleen Stiffness	≥14.2	100%	100%	100%	100%	100%
With, without Evs (GI, GII).	Liver Stiffness	≥17.2	93.3%	76.7%	80%	92%	89.6%
	Spleen Stiffness	≥32	90%	96.7%	96.4%	90.6%	96.7%
Prediction of large EVs	Liver Stiffness	≥18.5	71%	20%	38%	50%	40%
	Spleen Stiffness	≥37.12	77%	69%	67%	50%	67%



Figure (4): Comparison of (liver stiffness and spleen stiffness) among the different grades of Evs (GII)

DISCUSSION

Esophageal varices) resulting from portal hypertension is a serious complication of cirrhosis, screening for EVs is crucially important in the management of the cirrhotic patients to prevent bleeding event and death ^[10]. Upper gastrointestinal endoscopy is the best method to determine the presence of oesophageal and gastric varices, and allows the identification of additional signs used to stratify bleeding risk .In order to avoid the endoscopic burden, cost, drawbacks, unpleasant and repeated examinations to the patients, several noninvasive parameters have been investigated for prediction of the presence and the size of EVs ^[11]. As it was postulated that the progressive fibrotic remodeling of the liver increases the resistance to hepatic sinusoidal blood flow and hence, it increases portal venous pressure causing esophageal and gastric varices ^[12]. The arrival of transient elastography (TE) in 2003 represented a milestone in hepatology, giving the possibility to clinicians to non-invasively evaluate these features through the measurement of liver stiffness $(LS)^{[4]}$.

Since 2008, this quantification becomes possible with shear wave elastography (SWE). Different technologies introduced have been later on classified by European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB)^[6]. De Franchis ^[13] mentioned that among elastographic methods, transient elastography has been studied the most. However, transient elastography has limited effectiveness, especially in patients with ascites and obesity which is overcomed by shear wave elastography.

Shear wave elastography (SWE) is a novel technology involving the remote generation of transient mechanical forces into the tissue by a transducer. The resulting shear waves are imaged with the same transducer at an ultra-fast imaging sequence to provide quantitative elasticity maps ^[9]. Shear wave elastography is integrated into an ultrasound machine which provides real-time two dimensional B-mode images to identify the area of interest ^[10].

The current study was done to evaluate the reliability of liver stiffness (LS) and spleen stiffness (SS) measured by point shear wave elastography (pSWE) as noninvasive predictors of oesophgeal varices. As regard the etiological cause of cirrhosis, our study reported that HCV was the predominant cause of liver cirrhosis, HCV ab was present in (93.3%) and (90%), of patients in G I and GII respectively. Two patients (6.7%) were HBV in GI and GII while autoimmune was only 1 (3.3%) of patients in GII. In Egypt hepatitis C infection considered to be one of the most important health problems. The overall prevalence of anti HCV antibodies is estimated at 14.7%. Kandeel et al. ^[14] reported that the demography health survey (DHS) in 2015 showed 29% reduction in HCV RNA prevalence has been seen since 2008, which is largely attributable to the aging of the group infected 40-50 years ago during the mass schistosomiasis treatment campaigns and it is expected to decrease after the use of DAAS.

Our study revealed that (33.3%) and (36.7%) of patients in group I and group II respectively had positive Anti-Bilharzial Abs., and this in agreement with El-Tawil^[15] who reported that Bilharziasis is a common cause of varices in the setting of developing countries as Egypt.

As regard abdominal ultrasound examination, the current study found that there was a high statistically significant increase in splenic diameter in group II in comparison to group I and III. Several studies have demonstrated that splenic longitudinal diameter (with various cutoff values >11.3 to >15cm) could predict the presence of Evs^[16].

In our study we noticed a highly significant increase in portal vein diameter in group II in comparison to group I and III. Several studies have shown that portal vein diameter increase with the presence of oesophgeal varices¹⁷ but other studies did not identify any statistical significant difference ^[18]. In G I child A was the predominance while in G II child c was the predominance and this is in agreement with Sakr et al.^[19] who reported that oesophgeal varices in the studied patients increased with the increase of their Child classification. The measuring unit for stiffness used in some systems in studies of shear wave elastography was m/s and ultrasound system used in our study used kpa as a measuring unit, so we used the equation Young's modulus ($E = 3 \rho V s^2$), where E is Young's modulus, Vs is shear wave velocity and ρ is the density of the tissue (whose approximate value in the human body is 1 g/cm3)⁸ to convert their results to kpa to be able to compare our study results with their results

The mean shear wave values for liver stiffness were (15.61±4.57), (24.85±6.92), (4.54±2.19) kpa in group I, II and III respectively with highly significant increase in group II in comparison to group I and III and in group I in comparison to group III. These results are close to results obtained by Friedrich-Rust et al. ^[20] who reported liver stiffness values of 1.13 ± 0.23 m/s $\approx 3.8 \pm 0.12$ kpa in healthy volunteers. Also, Ye et al.²¹ in their study found that mean liver stiffness was 1.13 ± 0.12 m/s ≈ 3.8 ±0.12 kpa in healthy subjects. Also, Ferraioli et al.^[9] found that the mean liver stiffness in healthy volunteers was 3.5±0.12 kPa. Our results were more or less similar to Piscaglia et al.^[22] who found that mean liver stiffness was 10.2 kpa in patients with liver cirrhosis. Friedrich-Rust et al. ^[20] reported liver stiffness of 2.38 ± 0.74 m/s \approx 16.9kpa in 81 patients with HCV and HBV liver cirrhosis.

In our study we found a cut off value of liver stiffness of 8.8 kpa for discrimination of cirrhotic patients without EVs from control. Ye et al. ^[21] found that the mean liver stiffness value was 2.50 ± 0.50 m/s ≈ 14.5 kpa and the cut off value was $1.88 \approx 10.3$ kpa for patients with HBV related cirrhosis while Ferraioli et al. ^[9] found the cutoff values for advanced fibrosis and cirrhosis were 9.54 and 11.34 kPa, respectively.

In our study the cut off value of liver stiffness was 17.2kPa with 93.3%sensitivity, 76.7% specificity, 80% PPV and 92% NPV and 89.6% diagnostic accuracy for prediction of the presence of EVs. This is supported by the study done by Lucchina et al.^[8] who had a prospective study on 42 patients (mixed causes of liver cirrhosis) concluded that L-SWE cut off: 12.27 kPa for EVs with100%sensetivity and 66.6%specificity and) S-SWE cut off: 23.87kPa with 73. 81% sensitivity and 59.5% specificity. Attia et al.^[23] had a study on 78 patients with liver cirrhosis (mixed causes) and found

that L-SWE cut off for portal hypertension was 2,29 m/s (~15.73kpa) with 91%sensitivity and 85%specificity, PPV 95% and NPV 74% and S-SWE cut off was 2.71m/s (~22.03kpa)with 95%sensetivity and 92%specificity, PPV97% and NPV 85%. Another study by Park et al.[^{24]} on 366 patients (ALD and viral hepatic cirrhosis and S-SWE: 29.9kpa with sensitivity 58.1% and 79.1 specificity % <0.001 With P PV:81.6% and N PV:82.8%. The mean shear wave values for spleen stiffness were (21.82 \pm 6.01), (44.74 \pm 17.94) and (6.09 \pm 2.08)kpa in group I, II and III respectively with highly significant increase in group II in comparison to group I and III and in group I in comparison to group III

Our study revealed a cut off value of spleen stiffness was 14.2kpa for discrimination of cirrhotic patients without EVs and control. Bota et al. ^[25] reported spleen stiffness of 2.04 \pm 0.28 m/s \approx 12.4kpa in 15 healthy volunteers and 3.1m/s \approx 28.8kpa and cut off value of 2,55m/s \approx 19.5 kpa for predicting liver cirrhosis. Also Grgurevic et al. $^{[26]}$ showed a cutoff value 2.55 m/s \approx 19.5 kpa for predicting cirrhosis with a good AUROC (0.91). Ye et al. ^[21] reported a mean spleen stiffness $3.24 \pm 0.44 \approx 31.4$ kpa and a cut off value 2.72m/s \approx 22.19kpa in patients with HBV related cirrhosis. Results obtained by the different elastography techniques is challenging because terminology, shear-wave frequency, reported parameters, and other technical factors are not standardized. For example, some SWE-based techniques report different units (e.g., m/s or kPa) and apply different cut-off values which are defined by each manufacturer and can vary between systems ^[27].

In our study we found Spleen stiffness cut off value was 32kPa with 90%sensitivity, 96.7% specificity, 96.4% PPV and 90.6% NPV and 96.7% diagnostic accuracy for prediction of EVs. As regard role of pSWE in prediction of the presence of EVs, we found some studies using different ultrasound devices. Takuma et al. ^[28] found that spleen stiffness cutoff value of 3.18 m/s (≈ 30.3 kpa) was identified in patients with EVs with a 98.4% negative predictive value, 98.5% sensitivity, 75.0% accuracy. They suggested that spleen stiffness had the greatest diagnostic accuracy for the identification of patients with EVs or high-risk EVs compared with other noninvasive parameters, independent of the etiology of cirrhosis. Rossi et al.²⁹ Kim et al.^[30] found almost the same SS cutoff for predicting EVs they would avoid endoscopy in about 45% of cirrhotic patients, with significant time and cost savings.

In our study we found that mean LSPS in patients with EVs was 5.92 ± 3.12 . This is in concordance with Kim et al. ^[31] in their prospective study who concluded that Patients with LSPS < 3.5 may avoid endoscopy safely, whereas those with LSPS > 5.5 should be considered for appropriate prophylactic treatments. While Berzigotti et

al. ^[32] found mean LSPS was 4.83 ± 4.30 with cutoff 3.21 for the prediction of EVs with sensitivity of 81.1, specificity of 86%, 73.2% PPV, 90.8% NPV.

We recorded a cut off value of >37.12kpa o for spleen stiffness for prediction of large EVs. Our results are close to results obtained by Ye et al. [21] who found a significant linear correlation between SS and grade of varices and no correlation between liver stiffness and varix grade with cut off value 3.39m/s (34.47kpa)for prediction of sever EVs.(sensitivity 78.9% and specificity 78.3%). On the contrary to our study Bota et al.^[25] observed no significant differences in the mean spleen stiffness values between patients with and without varices of between those with different varix grades. The difference in the results may be explained by the following possible reasons. The interval between spleen stiffness measurements and the distribution of patients according to varix grades was unequal and the relative small number of the patients group.

CONCLUSIONS

Liver and spleen stiffness measured by point shear wave elastography are valuable non-invasive parameters for prediction of esophageal varices in patients with liver cirrhosis. Liver and spleen stiffness were much higher among cirrhotic patients than controls, denoting the potential prediction of liver cirrhosis. Both liver stiffness and spleen stiffness were significantly associated with presence of esophageal varices among cirrhotic patients. Moreover, spleen stiffness increases with the severity of esophageal varices. Liver stiffness × splenic size /platelet count was higher in patients with liver cirrhosis and higher in patients with esophageal varices, so it could be used to predict cirrhosis and esophageal varices.

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Conflict of interest:

The authors declared that there is no conflict of interest to be declared

REFERENCES

- 1. El-Serag HB and Everhart JE: Improved survival after variceal hemorrhage over an 11-year period in the Department of Veterans Affairs. Am. J. Gastroenterol. 2000, 95: 3566–357.
- 2. Manatsathit W, Samant H, Kapur H, Ingviya T, Esmadi M., Wijarnpreecha K, et al. Accuracy of liver stiffness, spleen stiffness, and LS-spleen diameter to platelet ratio score in detection of esophageal varices: Systemic review and metaanalysis. Journal of Gastroenterology and Hepatology; 2018, 33: 1696-1706.
- 3. Deeks JJ, Macaskill P, and Irwig L. The performance of tests of publication bias and other sample size effects in systematic reviews of diagnostic test accuracy was assessed. J. Clin. Epidemiol. 2005, 58: 882–893.
- 4. Colecchia A, Montrone L, Scaioli E, Bacchi-Reggiani, ML, Colli A, Casazza, G, et al.

Measurement of spleen stiffness to evaluate portal hypertension and the presence of esophageal varices in patients with HCV-related cirrhosis. Gastroenterology; 2012. 143(3), 646–654.

- 5. Sarvazyan AP, Rudenko OV, and Nyborg WL. Biomedical applications of radiation force of ultrasound: historical roots and physical basis. Ultrasound Med Biol; 2013, 36: 1379–1394.
- 6. Dietrich CF, Bamber J, Berzigotti, A, Bota S, Cantisani V, Castera L, et al. EFSUMB Guidelines and Recommendations on the Clinical Use of Ultrasound Elastography. Ultraschall in Med; 2017, 38: e16–e47.
- Cassinotto C, Charrie A, Mouries A, Lapuyade B., Hiriart JB, Vergniol, J, et al. Liver and spleen elastography using supersonic shear imaging for the non-invasive diagnosis of cirrhosis severity and oesophageal varices. Dig Liver Dis. 2015, 47: 695– 701.
- 8. Lucchina N, Recaldini C, Macchi M, Molinelli V, Montanari M, Segato, et al. point shear wave elastography of the spleen and its role in portal hypertention. World Federation for Ultrasound in Medicine and Biology; 2018, 44.4: 771-778.
- 9. Ferraioli G, De Silvestri A, Reiberger T, Taylor-Robinson SD, de Knegt RJ, Maiocchi L et al. Adherence to quality criteria improves concordance between transient elastography and ElastPQ for liver stiffness assessment-A multicenter retrospective study. Dig Liver Dis; 2018, 50:1056-1061.
- 10. Paternostro R, Reiberger T, and Bucsics TH. Elastography-based screening for esophageal varices in patients with advanced chronic liver disease. World Journal of Gastroenterology; 2019, 25: 3,.308-329;
- 11. Hassan EM, Omran DA, El Beshlawey ML, Abdo M, and El Askary A. Can transient elastography, Fib-4, Forns Index, and Lok Score predict esophageal varices in HCV-related cirrhotic patients? Gastroenterol. Hepatol. 2014, 37: 58-65.
- 12. Park DK, Um SH, Lee JW, Lee JB, Kim YS, Park CH, et al. Clinical Significance of Variceal Hemorrhage in Recent Years in Patients with Liver Cirrhosis and Esophageal Varices. Journal of Gastroenterology and Hepatology; 2004, 19, 1042-1051.
- 13. **De Franchis R.** Expanding consensus in portal hypertension: report of the Baveno VI Consensus Workshop: stratifying risk and individualizing care for portal hypertension. J Hepatol. 2015, 63:743-52.
- 14. Kandeel A, Genedy M, El-Refai S, Funk, AL, Fontanet A, and Talaat M. the prevelance of hepatitis C virus infection in Egypt 2015: implication for future policy on prevention and treatment, liver international journal; 2017, 37:1,45-53.

- 15. El-Tawil M A: Trends on gastrointestinal bleeding and mortality. Where are we standing? World Journal of Gastroenterology; 2012, 18(11): 1154-1158.
- 16. Esmat S and Rashid L. A comparative study between three noninvasive predictors of oesophageal varices in post hepatitis C virus liver cirrhosis in Egypt. Acta Gastroenterol Belg; 2011, 74(4):497-502.
- 17. Cherian JV, Deepak N, Ponnusamy RP, Somasundaram A, and Jayanthi V. Non-invasive predictors of esophageal varices. Saudi J Gastroenetrol; 2011,17(1):64-8.
- Berzigotti A, Gilabert R, Abraldes JG, Nicolau C, Bru C, Bosch J, et al. Noninvasive prediction of clinically significant portal hypertension and esophageal varices in patients with compensated liver cirrhosis. Am. J. Gastroenterol; 2008, 103(5):1159–67;
- 19. Sakr MA, Hamed WA, El Gafaary MM, EL-Folly RF, and EL-Hamamsy M. Role of Sucralfate in Promoting Healing of Post Band Variceal Ulcer. Advances in Natural Science; 2011, 4 (2): 7-14.
- 20. Friedrich-Rust M, Wunder K, Kriener S, Sotoudeh F, Richter S, Bojunga J et al. Liver fibrosis in viral hepatitis: non invasive assessment with acoustic radiationforce impulse imaging versus transient elastography. Radiology; 2009, 252: 595-604.
- 21. Ye XP, Ran HT, Cheng J, Zhu YF, Zhang DZ, Zhang P, et al. Liver and spleen stiffness measured by acoustic radiation force impulse elastography for noninvasive assessment of liver fibrosis and esophageal varices in patients with chronic hepatitis B. J Ultrasound Med; 2012, 31:1245–1253.
- 22. Piscaglia F, Salvatore V, Mulazzani L, Cantisani V, Colecchia A, Di Donato R, et al. Differences in liver stiffness values obtained with new ultrasound elastography machines and Fibroscan: a comparative study. Dig Liver Dis. 2017 Jul;49(7):802-808
- 23. Attia D, Schoenemeier B, Rodt T, Negm AA, Lenzen, H, Lankisch TO, et al. Evaluation of liver and spleen stiffness with acoustic radiation force impulse quantification elastography for diagnosing clinically significant portal hypertension. Ultraschall Med.2015, 36: 603-610.
- 24. Park J, Kwon H, Cho J, Oh J, Lee S, Han S, et al. Is the spleen stiffness value acquired using acoustic radiation force impulse (ARFI) technology predictive of the presence of esophageal varices in patients with cirrhosis of various etiologies? Med Ultrason; 2016, 18:11–17.
- 25. Bota S, Herkner H, Sporea I, Salzl P, Sirli R, Neghina AM, et al. Meta-analysis: ARFI elastography versus transient elastography for the

evaluation of liver fibrosis. Liver Int 2013; 33: 1138–1147.

- 26. Grgurević I, Bokun T, Mustapić S, Trkulja V, Heinzl R, Banić M, et al. Real-time twodimensional shear wave ultrasound elastography of the liver is a reliable predictor of clinical outcomes and the presence of esophageal varices in patients with compensated liver cirrhosis. Croat. Med. J. 2015, 56: 470–481.
- 27. Barr RG, Ferraioli G, Palmeri ML, Goodman ZD, Garcia-Tsao G, Rubin J, et al. Elastography assessment of liver fibrosis: society of radiologists in ultrasound consensus conference statement. Radiology; 2015, 276(3):845-861.
- 28. Takuma Y, Nouso K, Morimoto Y, Tomokuni J, Sahara A, Takabatake H, et al. Portal hypertension in patients with liver cirrhosis: diagnostic accuracy of spleen stiffness. Radiology; 2016, 279: 609–619.

- 29. Rossi S, Rosa L, Ravetta V, Cascina A, Quaretti P, Azzaretti A, et al. Contrast-enhanced versus conventional and color Doppler sonography for the detection of thrombosis of the portal and hepatic venous systems. AJR. Am. J. Roentgenol.2006, 186(3), 763–773.
- 30. Kim TY, Jeong WK, Sohn JH, Kim J, Kim MY, and Kim Y. Evaluation of portal hypertension by real-time shear wave elastography in cirrhotic patients. Liver Int.2015, 35: 2416–2424.
- 31. Kim BK, Han KH, Park JY, Ahn SH, Kim JK, Paik YH, et al. A liver stiffness measurementbased, noninvasive prediction model for high-risk esophageal varices in B-viral liver cirrhosis. Am J Gastroenterol. 2010, 105: 1382–1390.
- 32. Berzigotti A¹, Seijo S, Reverter E, Bosch J. Assessing portal hypertension in liver diseases. Expert Rev Gastroenterol Hepatol. 2013, 7: 141– 155.

الملخص العربى

دور قياس صلابة الكبد و الطحال "كطريقة غير تداخليه" في التنبؤ بدوالي المريء في المرضى المصريين المريين

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ملخص البحث:

ا**لخلفية:** يعد فحص تنظير الجهاز الهضمي العلوي الفحص دوالي المريء مكلفًا لنظام الرعاية الصحية وفحص إختراقي المرضى. تم استخدام قياس الصلابة مؤخرًا للتنبؤ بتليف الكبد ومضاعفاته.

ا**لهدف:** تحديد موثوقية تصلب الكبد وتصلب الطحال باستخدام موجات القص الموجية كمتنبئات غير تداخلية تداخليه للتنبؤ بدوالي المريء.

الطرق: أجريت دراسة الحالات والشواهد هذه على ستين مريضاً تم تقسيمهم إلى مجموعتين (ثلاثين مريضا بالتليف بدون دوالى مرئً) (ثلاثين مريضا بالتليف مع دوالى مرئً). تم تسجيل صفات الديمو غرافية و العلامات السريرية ، كما تم عمل تحاليل مخبرية، موجات فوق صوتية على البطن وقياس تصلب الكبد وتصلب الطحال تقاس بواسطة موجات القص الموجية ، تنظير الجهاز الهضمي العلوي لكل المرضى المشاركين في الدراسة.

النتائج : كان هناك زيادة كبيرة في الكبد وتصلب الطحال وتصلب الكبد و حجم الطحال / عدد الصفائح الدموية في مجموعة دوالى المرئ مقارنة مع المجموعة بدون دوالى المرئ و المجموعة الضابطة على التوالي وفي المجموعة بدون دوالى مقارنة من المجموعة الضابظة. كما وجد زيادة فى تصلب الطحال فى الحالات المصاحبة بتليف مرئ كبير مقارنة مع حالات دوالى المريض البسيطة و المتوسطة بينما لم يوجد أخللاف فى تصلب الكبد.

الأستنتاجات: تصلب الكبد و الطحال أدوات تنبؤية موثوق بها لدوالى المرئ و يمكن استخدام موجات القص الموجية لتقليل الحاجة إلى إجراء فحص روتيني عمل منظار علوي

الكلمات المفتاحية: غير تداخلي - موجات الشير ويف-تصلب الكبد ، تصلب الطحال ، دوالي المريء

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