ORIGINAL RESEARCH PAPER

Gastroenterology

LIVER STIFFNESS MEASUREMENT BY FIBROSCAN PREDICTS THE SIZE OF ESOPHAGEAL VARIES AND BLEEDING RISK IN INDIAN PATIENTS

KEY WORDS: Transient elastography, Liver stiffness, Large esophageal varices

Rohan Mahajan MBBS, MD National Institute of Medical Sciences &R Jaipur, Rajasthan, India (303121)

Kandarp Saxena MBBS, MD,DM National Institute of Medical Sciences &R Jaipur, Rajasthan, India (303121)

Amit Mathur MBBS,MD,DM National Institute of Medical Sciences &R Jaipur, Rajasthan, India (303121)

Ramesh Roop Rai MBBS,MD,DM National Institute of Medical Sciences &R Jaipur, Rajasthan, India (303121)

Rakesh Yadav National Institute of Medical Sciences &R Jaipur, Rajasthan, India (303121)

Shankar Lal Jat* MBBS, MD, DM Assistant Professor, National Institute of Medical Sciences &R Jaipur, Rajasthan, India (303121) *Corresponding Author

ABSTRACT

Background: Transient elastography (TE) may be used to predict the presence of portal hypertension. LS measurement may allow prediction of the presence of large EV in patients with cirrhosis and may help to select patients for endoscopic screening

Methods: One hundred patients with liver cirrhosis prospectively enrolled in the study. Eligible patients were cirrhotics of all etiology and severity who were admitted at department of gastroenterology, NIMS medical college, Jaipur between August 2016 and July 2017. In all patients we performed LS measurement by TE using a FibroScan device (Echosens, Paris). We selected only those cases with EV and we divided them into groups on basis of size of esophageal varices (No large oesophageal varices (no LOV) and patients with large esophageal varices (LOV) and on presence of gi bleeding (No upper GI Bleeding and upper GI bleeding)

Results: Of 100 cirrhotic fibroscan values were available in 82 patients. Mean fibroscan value was 43.07± 22.8 Kpa. Liver stiffness values does not predicts the presence or absence of large oesophageal varices (40.97±3.52 vs. 44.97±3.62, P=0.43, Table 2) Liver stiffness significantly higher in patients with history of GI bleeding than patients with no bleeding (47.28±3.29 vs. 36.81± 3.73, P=0.04, Table 2, Fig 3)

Conclusion: LS measurement by means of TE is accurate for assessing the risk of variceal hemorrhage in cirrhotic patients but its doesn't predicts the presence of large oesophageal varices

INTRODUCTION:

Transient elastography (TE) is a new promising non-invasive and rapid method for the diagnosis and quantification of liver fibrosis in patients with chronic liver disease. It was originally developed to detect solid malignancies in soft tissues such as breast cancer and prostate cancer[1]. Liver stiffness (LS) measurement using TE is reproducible and independent of the operator [2]. Some recent extensive studies have demonstrated that LS measurement with TE is a good alternative for liver biopsy. The amount of fibrosis can be quantified very easily and reliably and is feasible in more than 95% of the patients [3-5]

Development of oesophageal varices is a major complication that may occur in up to 90% of cirrhotic patients [6]. Esophageal varices may lead to variceal bleeding that is a life threatening event that has an incidence of 5% in patients with small oesophageal varices and up to 15% in those with large esophageal varices. Mortality per bleeding episode is around 10%20% [7].Therefore, screening for esophageal varices in cirrhotic patients is a strong recommendation in all consensus statement [8]. The current screening method is endoscopy at 2-3 years in patients without esophageal varices and at 1-2 years in those with small varices, this approach is invasive. That is why selection of patients with large esophageal varices at high risk for bleeding has become an issue of growing importance TE may be used to predict the presence of portal hypertension. LS measurement may allow prediction of the presence of large EV in patients with cirrhosis and may help to select patients for endoscopic screening [9-12]

The purpose of this study was to determine if TE can be used to predict indirectly the presence of portal hypertension and the risk of variceal bleeding. At present the Baveno VI and AASLD Consensuses recommend screening all cirrhotic patients for EV. If LS measurement could predict the presence of large EV in patients with cirrhosis, we could select these patients for endoscopic screening.

MATERIAL AND METHODS:

One hundred patients with liver cirrhosis prospectively enrolled in the study. Eligible patients were cirrhotics of all etiology and severity who were admitted at department of gastroenterology, NIMS medical college, Jaipur between August 2016 and July 2017. The variables were prospectively collected .Inclusion criteria were age between 18 to 80 years old and cirrhosis confirmed by either radiological imaging (ultrasound or cross- sectional imaging showing lobulated liver, irregular margins or dilated portal vein) or transient elastography (defined as liver stiffness ≥ 14 kPa) or complications of portal hypertension (ascites, varices or variceal bleeding or hepatic encephalopathy) . We excluded patients with active malignancy or end stage renal diseases In all patients we performed LS measurement by TE using a FibroScan device (Echosens, Paris). 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.

The tip of the transducer probe was covered with coupling gel and placed on the skin, between the rib bones at the level of the right lobe of the liver. The operator, assisted by an ultrasonic time-motion image, located a liver portion of at least 6 cm thick, free of large vascular structures. Once the measurement area had been located, the operator pressed the probe button to start an acquisition. Measurement depth was between 25 mm and 65 mm below the skin surface. Measurements which did not had a correct vibration shape or a correct follow up of the vibration propagation were automatically rejected by the software. Ten successful measurements were performed on each patient. The success rate (SR) was calculated as the ratio of the number of successful measurements over the total number of acquisitions. The results are expressed in kilopascal (kPa). The median value of the successful measurements was kept as representative of LS. Only LS measurements obtained with at least 10 successful measurements, with a SR of at least 60% and an IQR < 30% (IQR,

the interquartile range interval, is the difference between the 75th and the 25th percentile, essentially the range of middle 50% of the data) were considered reliable.

Using Olympus GIF- 190 (EXERA II), to evaluate the presence and degree of varices in addition to any relevant upper GIT lesions. Classification of oesophageal varices was done according to Thakeb classification (1988):

Grade 1: Small straight cords of varices confined to the lower third of esophagus.

Grade 2: Moderate sized clubbed varices, with well defined areas of normal mucosa between them, forming several distinct variceal cords and confined to the lower half of the esophagus.

Grade 3: Gross varices extending into the proximal half of the esophagus, normal mucosa might not be visible in between them unless the esophagus is fully distended with air.

Grade 4: Varices like those of grade 3 but with dilated capillaries on top or in between them and encroaching on esophageal lumen We selected only those cases with EV and we divided them into groups on basis of size of esophageal varices (No large oesophageal varices (no LOV) and patients with large esophageal varices (LOV) and on presence of gi bleeding (No upper GI Bleeding and upper GI bleeding)

Statistical analysis: Data were statistically described in terms of mean ± standard deviation (± SD). Continuous variables were compared using Student's t or Mann-Whitney tests as appropriate .Statistical significance was defined as P=0.05

RESULTS:

Patients were mainly men (81.7 %), with mean age of 44 ± 13.5 (Range 13-79 years). The origin of liver disease were alcohol (69.5%), HBV related (16.2%), HCV (1.5%), cryptogenic (9.9%) and autoimmune (4.6%). Patients with sarcopenia had more advanced liver disease as compare to no sarcopenia (Mean child-Pugh score 9.7 ± 1.7 vs. 6.0 ± 1.1 and MELD score 19.8 ± 6.1 vs. 11.1 ± 3.4).

Out of 100 cirrhotic fibroscan values were available in 82 patients. Mean fibroscan value was 43.07± 22.8 Kpa. The mean LS values in the 43 patients with no esophageal varices or small esophageal varices (grade 1 EV) were higher than in the 39 patients with large esophageal varices but was no statistically significant (44.97 ± 3.62 kPa *vs.*40.97 ± 3.52 kPa, *P* =0.432) (Table 2, Figure 2). The mean LS values in the group with a history of variceal bleeding (49 patients) were statistically significantly higher than in the group with no bleeding history (33 patients): 47.28 ± 23.05 kPa *vs.* 36.81 ± 21.47 kPa, *P* < 0.042) (Table 2, Figure 3). Liver stiffness values significantly higher in patients with sarcopenia (Diagnosed by MRI L3 SMI index) as compare to patients with no sarcopenia (49.03±2.64 vs. 20.29±2.78, P=0.00, Table 2). Liver stiffness values does not predicts the presence or absence of large oesophageal varices (40.97±3.52 vs. 44.97±3.62, P=0.43, Table 2) . Liver stiffness significantly higher in patients with history of GI bleeding than patients with no bleeding (47.28±3.29 vs. 36.81± 3.73, P=0.04, Table 2).

DISCUSSION:

Bleeding from esophago-gastric varices is the most important complication of cirrhosis [13].The first crucial step in prevention is to identify the patients at risk for bleeding by endoscopic screening, in order to select them for prophylactic treatment [14]. Predicting the presence of esophageal varices by non –invasive means would permit to restrict the performance of endoscopy to those patients with a high probability of having varices [15]

In previous studies, LS values < 19 kPa were highly predictive of the absence of significant EV (grade 2), the cut off values for the presence of grade 2 and 3 EV ranging from 27.5 to 35 kPa, and the cut off value for esophageal bleeding being 62.7 kPa [16-18]. In other studies, LS measurement by TE was not accurate for the prediction of EV, with AUROC ranging from 0.76 to 0.84. Although sensitivity was good (71%-96%), specificity and PPV were low (60%-80% and48%-54%, respectively)[19]. Foucher*et al*[20] assessed the accuracy of TE for the detection of large EV and the risk of variceal bleeding in patients with chronic liver disease. Klibansky*et al* [21] was more successful in describing a useful application of TE to predict clinical outcomes in cirrhosis. Clinical endpoints were defined as the development of ascites or encephalopathy, variceal bleeding, development of hepatocellular carcinoma, or liver transplantation.

In 2009, Castéra *et al* [22] showed that TE could be a valuable tool for the diagnosis of cirrhosis but cannot replace endoscopy for variceal screening.

The results of our study showed that TE is a useful technique for evaluating the presence of EV and hemorrhage prediction in cirrhotic patients. In our study mean LS values in the group with a history of variceal bleeding (49 patients) were statistically significantly higher than in the group with no bleeding history (33 patients): 47.28 ± 23.05 kPa *vs.* 36.81 ± 21.47 kPa, *P* < 0.042). Liver stiffness values significantly higher in patients with sarcopenia (Diagnosed by MRI L3 SMI index) as compare to patients with no sarcopenia (49.03±2.64 vs. 20.29±2.78, P=0.00). Liver stiffness values does not predicts the presence or absence of large oesophageal varices (40.97±3.52 vs. 44.97±3.62, P=0.43)

Summary Box

What is already known:

- TE may be used to predict the presence of portal hypertension
- LS measurement could predict the presence of large EV in patients with cirrhosis

What the new findings are:

- LS measurement by means of TE is accurate for assessing the risk of variceal hemorrhage in cirrhotic patients
- But its doesn't predicts the presence of large oesophageal varices
- Liver stiffness values significantly higher in patients with sarcopenia as compare to no sarcopenia

Abbreviations:

TE ; transient elastography, LOV; Large esophageal varices , EV; Esophageal varices

Table 1: Baseline Characteristics of the Study Population

Parameters	No upper GI Bleeding	Upper GI Bleeding	P values
Age	45.60 ±2.06	43.58±1.41	0.40
BMI	21.23±0.50	21.23±0.37	0.99
HB	8.9±0.27	9.7±0.87	0.50
TLC	7235.52±578.64	8276.25±1014.49	0.43
PLT	49608.21±	37513.18±4100.6	0.06
Bilirubin	5117.91	3	0.26
INR	3.37±0.55	4.35±0.60	0.64
Creatinine	2.00±0.06	1.95±0.07	0.33
Na	1.25±0.09	1.37±0.08	0.33
Ammonia levels	135.92±2.44	137.86±0.44	0.42
Testosterone	37.83±7.55	31.06±4.74	0.11
MELD	215.88±20.44	173.20±15.78	0.07
MELD-Na	17.00±0.86	19.16±0.77	0.01
MAMC	16.88±0.86	19.96±0.75	0.05
Handgrip	21.11±0.37	20.07±0.36	0.45
Subjective global	31.48±1.23	30.33±0.94	0.00
assessment (SGA)	4.35±0.18	3.47±0.14	
MRI –SMI Index	32.82±1.15	30.48±1.01	0.13

Table-2: Comparisons of mean stiffness (Kpa) as a Function of the Complications of Portal Hypertension

Parameters	Patients		P values
	Without	With	
Spontaneous bacteria peritonitis (SBP)	42.49 ± 2.70	47.77±7.32	0.51
Subclinical HE	40.85±2.86	54.84±7.75	0.04
AKI	41.90±2.98	46.94± 4.60	0.43
Malnutrition by MAMC	35.65±3.38	49.47±3.44	0.00
Sarcopenia by MRI	20.29±2.78	49.03±2.64	0.00
Large oesophageal varices (LOV)	44.97±3.62	40.97±3.52	0.43
Upper GI Bleeding	36.81± 3.73	47.28±3.29	0.04

Fig 1: Fibroscan (Kpa) values according to liver disease severity

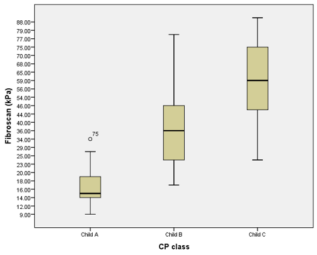


Fig 2: Fibroscan values (Kpa) according to presence of large oesophageal varices (LOV)

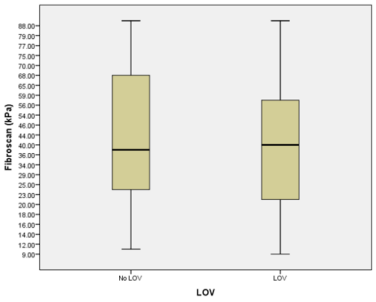
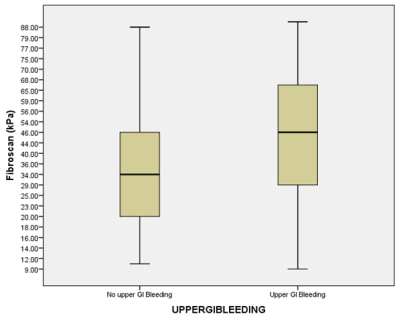


Fig 3: Fibroscan values (Kpa) according to presence of variceal GI bleeding



Predictive value of liver stiffness for upper digestive bleeding due to variceal bleeding. UGIB: Upper GI Bleeding. ROC: Receiver operating characteristic.

Predictive value of liver stiffness for the presence of at least large esophageal varices (LOV). ROC: Receiver operating characteristic.

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