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Original Research Article

Liver Elastography as a Predictor of Esophageal Varices in Patients with Chronic Liver Disease

Niraj Kumar Gupta[1], Sudhir Ranjan Prasad[2], Bhaskar Jyoti Sarmah[3], B.D. Goswami[4]

[1]Assistant Professor, Radiology, Sikkim Manipal Medical College
[2]Consultant, Department of Radiology, Dispur Hospital Pvt Ltd
[3]Senior Consultant, Department of Radiology, Dispur Hospital Pvt Ltd
[4]Head of Department Gastroenterology, Dispur Hospitals Pvt Ltd

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Corresponding author: Dr. Sudhir Ranjan Prasad
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Abstract:

Introduction: Chronic liver disease (CLD) is considered as one of the main reason of mortality and morbidity. Esophageal varices (EVs) and their bleeding is an important complication seen in liver cirrhosis. The EVs are detected by esophagogastroduodenoscopy (EGD), which is an invasive produce so the current study aimed to assess liver stiffness (LS) by elastography to detect EV in CLD patients.

Material and methods: The present study was a comparative cross sectional hospital based study carried on 140 CLD patients visiting Dispur Hospitals Pvt Ltd, Guwahati, Assam. Upper endoscopy was done on all the participants and they were additionally assessed for liver stiffness with Acoustic Radiation Force Impulse (ARFI) elastography. Valid ARFI values could be taken only in 138 patients. Spearman correlation coefficient and receiver operating characteristics (ROC) curve for LS were analyzed and "p value <0.05 was considered as significant."

Result: The study recruited 140 CLD patients with age mean age of 48.6±12.4years and male dominance. The chief sign and symptom observed in our study was fatigue followed by loss of appetite. The leading etiology of CLD found in present study was alcohol trailed by hepatitis B. The mean liver stiffness was found to be significantly higher in patients with high risk EVs and a significant linear correlation among them was seen. AUROC analysis of liver stiffness by elastography had good predictive values, specificity and sensitivity for high risk EVs.

Conclusion: The present study found LS to be good predictor and significantly correlated with EVs. Therefore we suggest liver elastography as a helpful non-invasive tool as substitute to EGD in predicting high risk EVs in CLD patients. This will help clinicians in early detection along with timely and apt management of the EVs.

Keywords: CLD, Liver stiffness, EVs, Endoscopy, ARFI, Elastography etc.

Introduction

Chronic liver disease (CLD) is the condition of progressive decline in functions of liver due to replacement of liver tissue by regenerative nodules and fibrotic scar tissue. [1] Globally, CLD is considered as one of the main reason of mortality and morbidity. In recent years, a multicentric study documented that 12% of the patients visiting hospitals in India were CLD patients and one fourth of them were newly diagnosed. [2] CLD has many causes; alcoholism being the commonest trailed by hepatitis B & C. The slow progression of CLD over the years leads to the final stage of disease i.e. cirrhosis. In liver cirrhosis, development of portosystemic collateral circulation in the form of esophageal varices (EVs) is an important complication. [3] Every year 3 to 12 percent of cirrhotic patients develop EVs which slowly progresses in size in almost 8 to 12 percent of the cases. Based on class of CTP (Child Turcotte Pugh), EVs are seen in 40-85 percent of cirrhotic cases; these EVs may bleed and are cause of mortality in 20% to 35% of the patients. Clinically, the assessment of EV size is used to evaluate the risk of bleeding and at present esophagogastroduodenoscopy (EGD) is considered as the gold standard to spot and estimate the size of EV. According to the "American Association for the Study of Liver Diseases (AASLD)", esophagogastroduodenoscopy (EGD) must be done in every newly diagnosed liver cirrhosis patient. However EGD is an invasive, uncomfortable and costly procedure along with some risks associated with it. [4] So researches proposed some non-invasive parameters like few serum analysis and radiological analysis to identify EV but these parameters have shown partial correlation with the

occurrence of EV. Liver stiffness has been related with an upraised risk of EVs and can be helpful as a non-invasive parameter to predict EV. Many techniques have been used till date to assess liver stiffness. Few previous studies have documented that assessment of liver stiffness by Transient elastography (TE) of <20kPa along with platelet count >150000/µl shows significantly reduced rate of EV. However accurate assessment by TE is difficult if patient has ascites, more body fat & restricted intercostal spaces. [5] This limitation of TE has been partially overruled by ultrasound (US) based noval & promising technique i.e. Acoustic radiation force impulse (ARFI), which estimates tissue stiffness by evaluating wave propagation speed. Very few studies have been carried out yet to identify the relevance of assessing liver stiffness to predict EVs. Therefore our study aimed to assess liver stiffness by ARFI to detect EV in CLD patients so that by performing this additional non-invasive test, clinicians can easily detect the probability of EVs which will help them in appropriate decision making and apt treatment of the patients.

Material and Method

The present study was a comparative cross sectional hospital based study carried on CLD patients by the Department of Radio-diagnosis in collaboration with the Department of Gastroenterology at Dispur Hospitals Pvt Ltd, Guwahati, Assam from September 2018 to September 2019.

The study was done on 140 CLD patients of both sexes with age above 18years after having approval from ethics committee. Patients were consecutively selected for the study and written informed consent was obtained from the willing participants. Patients having clinical, radiological, biochemical, serological and histopathological diagnosis suggestive of CLD were included. CLD patients having portal hypertension (PH) due to extra or post hepatic reason, pregnant females, patients with inconclusive elastographic assessment and patients contraindicated to endoscopy were excluded from the study. Upper endoscopy by flexible Olympus S170 series UGI endoscope was done on all the participants and then they were additionally assessed for liver stiffness with ARFI elastography by an Acuson S2000 ultrasound system outfitted with a convex transducer. When ARFI was done, out of 140 patients, valid values could be taken in only 138 patients. Participants were asked to be in supine position with maximum abduction of the right arm (behind the head). Ascites was ruled by standard B-mode sonography. In the mid clavicular line, sagittal approach was used to determine the space from the skin to liver capsule & liver size. Afterward by using ARFI mode, region of interest (ROI) box was positioned to upper limit of 7cm from the skin surface avoiding vessels, around 2-3cm below the liver capsule and whenever possible, the ROI angle was kept at right angles. Patient was asked to hold breath during ARFI elastography measurement to avoid interference by breathing motion. Stiffness measurements were assessed from 2 different locus on the right lobe of liver in segments 7 or 8 and the median of 10 suitable values were taken as the measurement. The right lobe was chosen over left lobe as right lobe has been reported potentially superior for the diagnosis of liver fibrosis. The mean hepatic measurement was recorded in m/sec and the stiffness values were assessed using receiver operating characteristics (ROC) curve, illustrated for the finding of significant EV. Area under ROC curve (AUROC) was calculated using trapezoidal rule. Cut-off values for liver stiffness predicting high risk varices were obtained using Youden index. Spearman correlation coefficient was analyzed to assess correlation between different parameters and "p value <0.05 was considered as significant."

Result

The study recruited 140 CLD patients with age above 18 years and mean age of 48.6±12.4years. The patients were further divided into age groups. Figure 1 shows age distribution of the patients in age group 30-40,41-50,51-60,61-70 and 71-80 years with 16(11.00%), 38(27.00%), 52(37.00%), 32(22.00%) and 2(1.40%) patients respectively.

Present study was comprised of maximum males 129(92.00%) compared to females 11(8.00%). Table 1 depicts the sign and symptoms shown by CLD patients varying from jaundice, ascites, loss of appetite, fatigue, weight loss, itching, muscle loss, easy bruising, spider-like veins in the skin, oedema to abdominal distension with 122(87.14%), 128(91.14%), 138(98.57%), 140(100.00%), 136 (97.14%), 50(35.71%), 90(64.42%), 40 (28.57%), 55(39.28%), 60 (42.85%) and 59 (42.14%) patients consecutively. Thus the most common symptom was fatigue followed by loss of appetite and weight loss. As clearly seen from figure 2, etiology of CLD in present study was noted to be alcohol, hepatitis B, hepatitis C, NAFLD/cryptogenic and autoimmune causes with 90(64.28%), 24(17.10%), 8(5.70%),16(11.40%) and 2(1.40%) patients respectively.

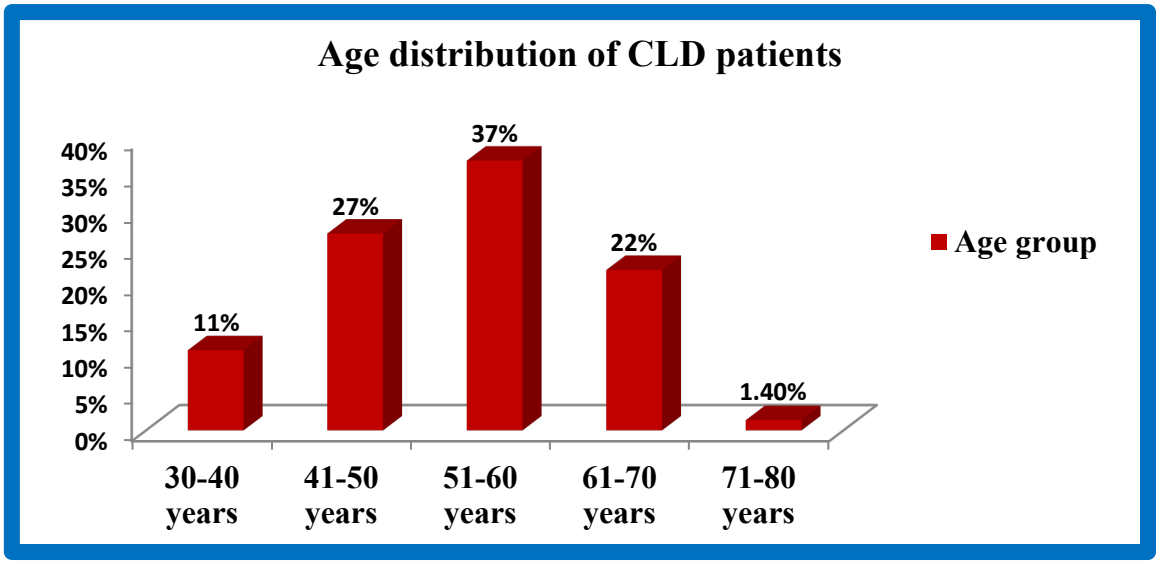

Figure 1: Age distribution of CLD patients

Table 1: Distribution of patients based on demographic variables

Variable		No. of patients n (%)	p-value
Sex	Male	129(92.00%)	
	Female	11(8.00%)	
Sign and symptoms	Jaundice	122(87.14%)	
	Ascites	128(91.14%)	
	Loss of appetite	138(98.57%)	
	Low energy and weakness (fatigue)	140(100.00%)	
	Weight loss	136(97.14%)	
	Itching	50(35.71%)	
	Muscle loss	90(64.42%)	
	Easy bruising	40(28.57%)	
	Spider-like veins in the skin	55(39.28%)	
	Oedema	60(42.85%)	
	Abdominal distension	59(42.14%)	

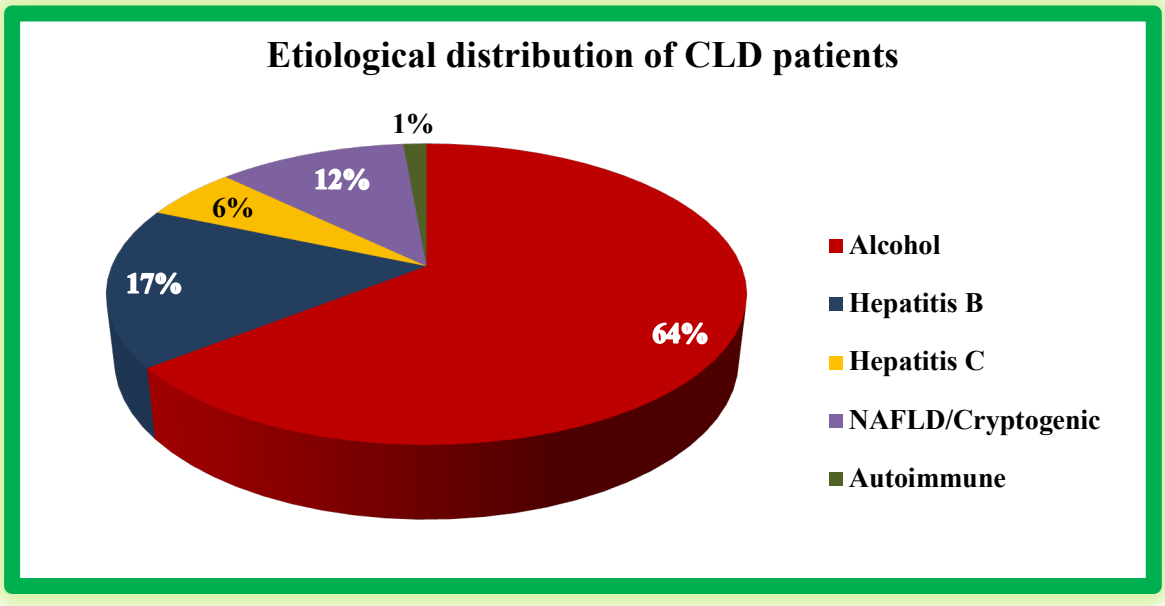

Figure 2: Etiological distribution of CLD patients

Out of 140 patients, valid ARFI measurements could be taken in 138 patients (98.5%). Table 2 shows that in endoscopy, maximum patients i.e. 73(52.89%) in present study were observed to have large varices (>5mm) considered as positive result and 65(47.10%) had small varices with RCS regarded as negative result.

Table 2: Findings in Upper GI endoscopy

Grade of esophageal varices	No. of patients n (%)
Large varices (>5mm) – Positive result	73(52.89%)
Small varices with RCS- Negative result	65(47.10%)

***Large varices taken as positive & small as negative results**

Table 3 shows that in current study mean liver stiffness was significantly increased in high risk patients with large varices (>5mm) i.e. 3.0600±0 .58 than patients with small varices with RCS i.e. 2.7712±0 .46.

A significant linear correlation (Spearmanρ= 0.374, p<0.01) was found between liver stiffness and the high risk EV. This states that LS increases parallely with the increase in grade of EVs. Further figure 3 and table 4 depicts the diagnostic ability and accuracy of liver stiffness as a predictor of EVs in CLD patients. AUC for liver stiffness was assessed to be 0.716. AUROC analysis showed that liver stiffness measured by ARFI had good predictive values for high risk EV. The optimal cut-off values were 3.11m/sec for high risk varices with sensitivity of 58.9% and specificity of 86.2%).

Table 3: Showing mean liver stiffness in high risk EVs

Parameter	Large varices (>5mm) – Positive result 73(52.89%)	Small varices with RCS- Negative result 65(47.10%)	p-value
Liver stiffness in m/sec (mean ±SD)	3.0600±0 .58	2.7712±0 .46	<0.01

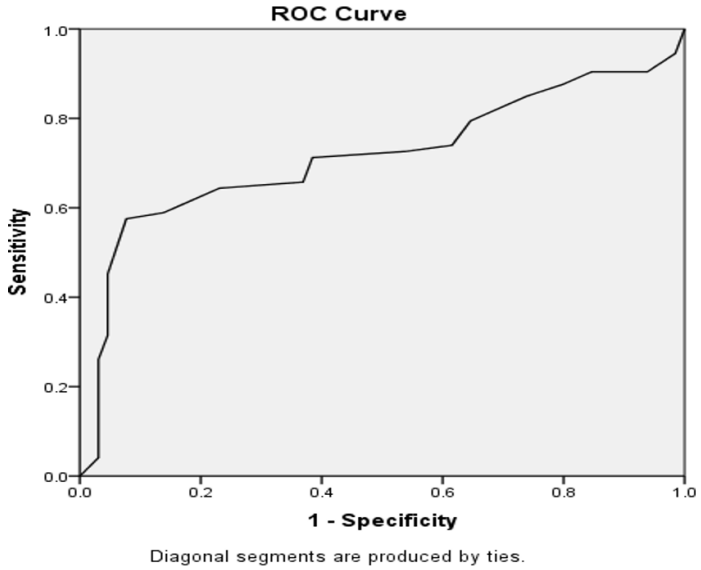

Figure 3: ROC of liver stiffness measured by ARFI elastography for predicting the presence of high risk EV

Table 4: Showing AUC for liver stiffness

Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% ConfidenceInterval	
			Lower Bound	Upper Bound
0.716	0.045	0.000	0.627	0.805

Discussion

The present study was conducted on CLD patients attending Dispur Hospitals Pvt Ltd, Guwahati, Assam. Generally when CLD patients are screened for EVs by endoscopy and it has been seen that many patients do not need any intervention as varices observed are mild or not present at all. Endoscopy is a invasive procedure so to decrease the load of endoscopy in low risk EV patients, there is a need for a noninvasive measure. So, current study was planned to assess the efficacy of LS as non-invasive predictor of EVs in CLD. The participants of the study were from 30-80years with mean age of 48.6±12.4years. Maximum patients were falling into

the age of 51-60years (37.14%) followed by 41-50years (27.14 %) with predominance of male population. A study by AS N et al. [6] also found maximum patient distribution in the same age group. Multicentric study by Mukherjee PS et al. [2] supported our findings as they also had nearby mean age (42.8±14.4years) of cirrhotic patients in their study. The outcome of male dominance was in harmony with study by Danish M et al. [7] and AS N et al. [6] The sign and symptom in our study was combination of the symptoms and the most commonly observed in our participants was fatigue followed by loss of appetite and the least seen was easy bruising trailed and itching. The leading etiology of CLD found in present study was alcohol (64.28%) followed by hepatitis (17.1%). Our finding is in agreement with Sarangapani A et al. [8] and in contrast with Kim HY et al. [9] and Hye Young Sun et al. [10] as they observed hepatitis (63%) as major etiology of Cirrhosis followed by alcohol (41%).

Bulk of the CLD patients in present research had large varices which are in disagreement to the study by Shivam D et al. [11] and El Lehleh et al. [12] as their majority patients had small varices. The mean liver stiffness in our study was significantly high in patients with large varices than with small varices and a significant linear correlation between liver stiffness and the high risk EV was seen. This finding is in harmony with Shivam D et al. [11] and Horia et al. [13], with varying cutoff values. In contrast to our result, Xiao-Ping Ye et al. [14] found no significant correlation between liver stiffness and grade of EV.

AUROC analysis of present study showed that liver stiffness measured by ARFI had good predictive values for high risk EV with optimal cutoff value as 3.11m/sec for high risk varices and AUC to be 0.716 with sensitivity of 58.9% and specificity of 86.2%. These findings were comparable to the research by Zaki et al. [15] and Hashim et al. [16] as they also revealed association among LS and CLD, predicting the presence of EVs. Study by Danish M et al. [7] strongly supported our study as they documented liver elastography as an apt tool to predict EVs in CLD with sensitivity and specificity of 44.90% and 51.90%, respectively. A study by Morishita et al. [17] found results consistent with our study but with lower cut-off value of 2.39 m/s. They also found good sensitivity (81%) and specificity (82%) and the sensitivity observed was better than us. Another study by Bota S et al. [18] also supported our study as they also found mean Liver stiffness as >2.25 m/s to predict significant presence of EVs in newly diagnosed cirrhotic patients. They assessed higher sensitivity than our study although AUROC and specificity for LS in their research was much lesser than our study. Several other studies by Saad et al. [19], Adriana et al. [20], Hu Z et al [21], Sharma et al. [22], Sporea et al. [23] and Yasmin et al. [24], also concluded LS elastography as a good marker for indication of EVs with different cut off values for large varices and with varying but good sensitivity, specificity & AUROC results for LS.

Conclusion

The presence of EVs in CLD patients is detected by EGD, which is an invasive and costly procedure. Hence it is not possible to undergo EGD in every suspected case so clinicians must be able to detect the risk of EVs by some non-invasive tools. So our study was focused on to check efficacy of LS by elastography as non-invasive parameter to predict EVs.

The present study found LS to be good predictor and significantly correlated with EVs detected in CLD patients. Therefore we suggest liver elastography as a helpful non-invasive tool to predict high risk EV in CLD patients so that EGD can only be performed on fewer patients avoiding unnecessary financial burden and discomfort. This will help clinicians in early detection along with timely and apt management of the EV patients. We suggest several such studies targeting different non-invasive parameters to see their impact in predicting EV and their risk of bleeding.

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