

Liver and Spleen Stiffness as Predictors of Esophageal Varices in Patients with Liver Cirrhosis

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ABSTRACT

Introduction

The risk for the occurrence of esophageal varices in a cirrhotic patient is assessed by two gold standard invasive tests: hepatic venous pressure gradient measurement and esophagogastroduodenoscopy. We aim to find the association between spleen and liver stiffness with the occurrence of esophageal varices in our settings.

Methods

This was a prospective cross-sectional study. In the study duration of one year, 94 cirrhotic patients who met the inclusion and exclusion criteria were included. All patients were subjected to transient elastography for measuring liver and spleen stiffness and endoscopy.

Results

Of 94 patients, only 77 (81.9%) had esophageal varices. The mean liver stiffness in patients with and without varices was 19.46 ± 4.9 SD kPa and 12.92 ± 1.52 SD kPa respectively. The difference was statistically significant, $p < 0.001$. The mean spleen stiffness in patients with and without varices was 22.26 ± 4.6 SD kPa and 14.08 ± 1.20 SD kPa respectively. The difference was statistically significant, $p < 0.001$. The optimal cut-off value of liver and spleen to detect patients with any grade of esophageal varices was 14 and 16.15 kPa respectively.

Conclusion

The stiffness of liver and spleen using transient elastography can be considered an equivalent method for screening cirrhotic patients for esophageal varices in clinical settings.

Keywords

Cirrhosis; esophageal varices; liver stiffness; spleen stiffness

INTRODUCTION

Cirrhosis results from a number of mechanisms of liver injury which leads to necroinflammation and fibrogenesis.¹ The distortion in liver architecture resulting in the development of portal hypertension and its complication leads to majority of deaths in patients with cirrhosis.² Early detection of varices is crucial for prevention of progression and management of varices. Recent guidelines suggest a screening esophagogastroduodenoscopy (EGD) in every cirrhotic patient.³ However, there are concerns regarding this. This is because esophagogastroduodenoscopy is an invasive and expensive procedure with procedural risk.⁴

Various serum and radiological parameters like serum fibrosis markers, platelet count to spleen diameter ratio, liver stiffness (LS) and spleen stiffness (SS) can predict the presence of varices.⁵ Among these, it has been revealed that both spleen and liver stiffness are more sensitive in predicting the occurrence of esophageal varices as compared to other non-invasive parameters.⁶

The Baveno VI criteria: the combination of parameters liver stiffness (LS) < 20 kPa by transient elastography (TE) along with platelet count > 150 × 10⁹ cells/cumm predict the low risk of occurrence of esophageal varices which could essentially omit endoscopy in a patient.⁷ Multiple studies have evaluated measuring liver stiffness by transient elastography and the value of liver stiffness obtained is an easily reproducible non-invasive parameter.⁸

The aim of this study is to evaluate whether the spleen and liver stiffness measured by transient elastography would be an accurate non-invasive method for evaluation of the presence of EV in a patient with liver cirrhosis in our settings.

METHODS

It was a hospital based cross-sectional prospective observational study. The study was done from September 2020 to December 2021 in patients admitted to TUTH. Participants who fulfilled both the inclusion and exclusion criteria were consecutively enrolled for the study and evaluated with upper gastrointestinal endoscopic examination. Spleen and liver stiffness were measured using a transient elastography.

The study was approved by the Institutional

Review Committee of Institute of Medicine, Kathmandu, Nepal. An informed consent was taken. The obtained data was analyzed using SPSS version 20. Continuous variables were analyzed using mean±SD. Categorical variables were described using number and percentage. Data were compared using cut off value from previous studies. A p value of less than 0.05 was considered statistically significant. The performance of spleen and liver stiffness in evaluating the presence as well as severity of esophageal varices were analyzed by area under receiver operating characteristics curves (AUROC).

RESULTS

The mean age of the patients was 51.15 (±11.87) years. There were 61 (64.9%) males and 33 (35.1%) female patients. Of 94 patients, 77 (81.9%) had esophageal varices and 17 had none (18.1 %). Among 77 patients with EV, small EV was present in 29 (30.9%) patients & large EV was present in 48 (51.1%) patients (Figure 1).

The mean stiffness of liver in patients without varices was 12.92±1.52 SD. The mean stiffness of liver in patients with varices was 19.46±4.9SD. The difference was statistically significant (p <0.001) (Table 1).

The mean stiffness of spleen in patients without varices was 14.08±1.20 SD. The mean stiffness of spleen in patients with varices was 22.26±4.6SD. The difference was statistically significant (p <0.001) (Table 1).

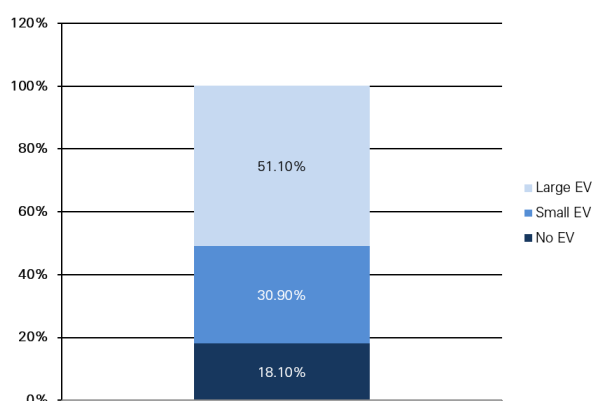


Figure 1. Bland-Altman plot to evaluate the limits of agreement between volumes based and DTPA based differential function

Table 1. Correlation between liver stiffness, splenic stiffness and esophageal varices using 2-tailed t-test

Parameters	Esophageal varices		p-value
	Present (n= 77)	Absent (n= 17)	
Liver stiffness (kPa)	19.46±4.9	12.92±1.52	<0.001
Splenic stiffness (kPa)	22.26±4.6	14.08±1.20	<0.001

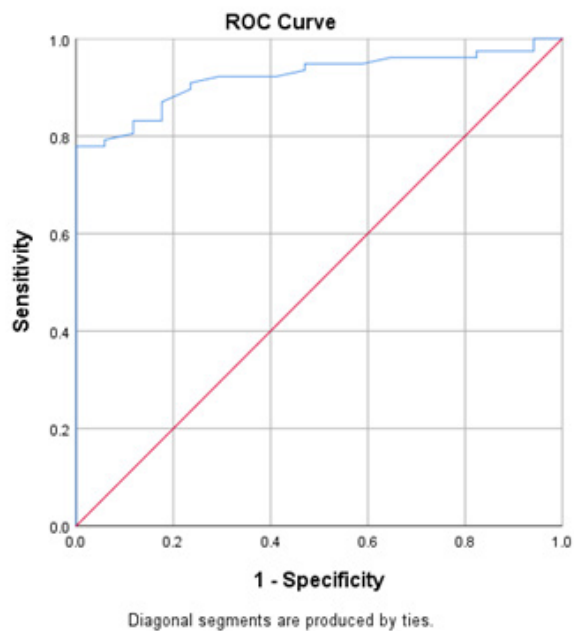


Figure 2. ROC curve for stiffness of liver in predicting the presence of esophageal varices

The optimal cut off of stiffness of liver to detect patients with any grades of EV was 14 kPa with the area under the ROC curve being 0.921 (Figure 2). It had sensitivity SN (87%), specificity SP (82.4% %), +LR (positive likelihood ratio) (4.94), -LR (Negative likelihood ratio) (0.158) in predicting the occurrence of EV.

The optimal cut off of stiffness of spleen was 16.15 kPa to detect patients with any grades of EV with the area under the ROC curve being 0.924 (Figure 3). It had SN (90.9%), SP (94.1%), LR+ (15.45), LR- (0.097) in predicting the occurrence of EV.

DISCUSSION

The onset of clinically significant portal hypertension is an important step in the natural progression of cirrhosis of liver.⁹ It is of utmost importance to evaluate the status of portal hypertension (PH) in every cirrhotic patient for prognosis and risk assessment at the time of initial diagnosis of cirrhosis.

The Baveno VI consensus focused the importance of non-invasive parameters in the screening of EVs. They particularly emphasized on liver stiffness (LS) and came to a conclusion that patients with LS < 20 kPa and platelet count > 150 cells/cumm were highly unlikely to have HRVs (<5%).² These criteria have been validated by various studies thus, confirming that Baveno VI cut-offs could exclude 98–100% of patients who can safely avoid endoscopy.¹⁰ Stiffness of spleen (SS) has been evaluated as a better predictor of PH than liver stiffness. It was thus combined with Baveno VI criteria. Using spleen

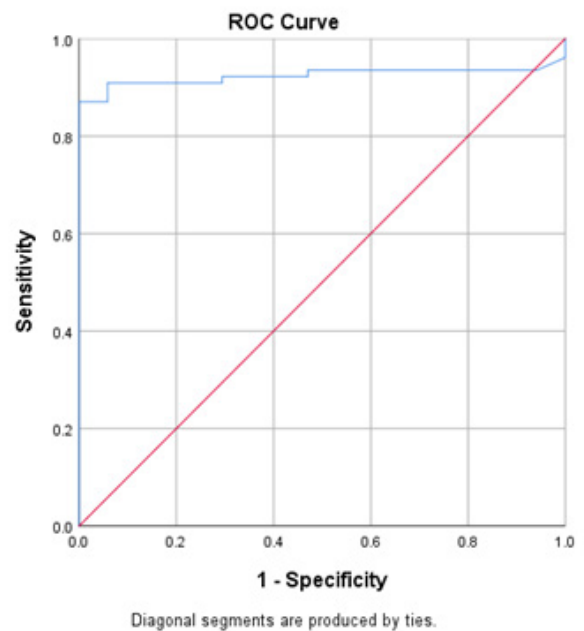


Figure 3. ROC curve for stiffness of spleen in predicting the presence of esophageal varices

stiffness spared EGD in 44% of patients with a rate of missing high risk varices in < 5% patients.¹¹

Liver stiffness well reflects the structural (fibrosis/cirrhosis) component of PH but it lacks the dynamic (vascular) component of PH and it is where SS comes into play.¹² There was a study done in 2011 on 191 patients (135 liver cirrhosis, 39 chronic hepatitis and 17 healthy controls) using transient elastography in Romania which revealed a significant association between spleen and liver stiffness in patients with PH.¹³ Since then, there has been increasing interest to evaluate whether SS could be a potential non-invasive parameter for PH and the presence of EV.

In this study, transient elastography was used to measure spleen and liver stiffness. A total of 94 patients with diagnosis of liver cirrhosis were evaluated. 77(81.91%) had EV and 17 patients (18.1 %) had no varices in EGD. Among patients with EV, small EV was present in 30.9 % (29) patients and large EV was present in 51.1 % (48) patients. This was comparable to a study done in 2011 on 191 patients (135 liver cirrhosis, 39 chronic hepatitis and 17 healthy controls) using transient elastography in Romania; 84.9 % had EV and 15.1 % had no EV.¹³ However, the grading of the varices could not be compared due to variability in the grading methods in that study.

The mean stiffness of liver in patients without varices was 12.92 ± 1.52 SD kPa. The mean stiffness of liver in patients with varices was 19.46 ± 4.9 SD kPa. The difference was statistically significant ($p < 0.001$). Similarly, in a study done in India in 2021 including 100 CLD patients, mean LSM value

increased significantly from no varices (14.60 ± 0.88 kPa) to small esophageal varices (15.51 ± 2.76 kPa) to large esophageal varices (23.80 ± 3.17 kPa).¹⁴

The mean stiffness of spleen in patients without varices was 14.08 ± 1.20 SD kPa. The mean stiffness of spleen in patients with varices was 22.26 ± 4.6 SD kPa. The difference was statistically significant ($p < 0.001$). Similarly, in a study done in 2011 in 191 patients (135 liver cirrhosis, 39 chronic hepatitis and 17 healthy controls) using transient elastography in Romania, the stiffness of spleen was significantly higher in patients with esophageal varices as compared to those without (63.69 vs 47.78 kPa, $p < 0.001$).¹³

The optimal cut off for liver stiffness to detect any grade of EV was 14 kPa with the area under the ROC curve being 0.921. It had SN (87%), SP (82.4%), +LR (4.94), -LR (0.158) in predicting the presence of EV.

The optimal cut off for spleen stiffness to detect any grade of EV was 16.15 kPa with the area under the ROC curve being 0.92. It had SN (90.9%), SP (94.1%), LR+ (15.45), LR- (0.097) in predicting the presence of EV.

Thus, this study was done to establish the role of non-invasive parameters like spleen and liver stiffness in predicting the occurrence of esophageal varices in cirrhotic patients. This could lead to avoidance of unnecessary esophagogastroduodenoscopy.

CONCLUSION

The grading of spleen and liver stiffness can predict the occurrence of esophageal varices in patients with liver cirrhosis, which makes it an optimal method to use for screening cirrhotic patients for esophageal varices in clinical settings. Thus, this study contributes in recognizing SS and LS as novel parameters in screening of cirrhotic population. This may thereby reduce the number of endoscopic evaluation. A prompt endoscopic evaluation for varices is justifiable at spleen and liver stiffness levels at or above the cut-off values revealed in this study for the presence of esophageal varices.

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CONFLICT OF INTEREST

The author(s) declare that they do not have any conflicts of interest with respect to the research, authorship, and/or publication of this article.

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