



Transient elastography offers a non-invasive approach for the detection of gastric and esophageal varices in patients with chronic hepatitis B and hepatitis C, serving as an alternative to upper endoscopy

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ABSTRACT

The recent updates in guidelines of Baveno 7, emphasizes on the importance of screening of patients with chronic liver diseases for the identification of esophageal/ gastric varices and further management of the patients accordingly because the surveillance interval and treatment strategies rely on the grade of varices. Lack of early diagnoses of hepatitis Band C, many patients remain untreated till later stages leading to progression of chronic liver disease to decompensation and complications. When there is portal hypertension, it leads to portosystemic shunting by forming collateral vessels. 1 This results in the formation of esophageal and gastric varices which results in complications of decompensation by causing massive hemorrhage. Which can be life threatening and raises the mortality rate up to 14.2 – 14.5%. 2,3 Esophageal and Gastric varices are one of the signs of the progression of chronic liver disease to cirrhosis. This is because of the development of portal hypertension in response to progression of fibrosis and increase stiffness in patients with chronic liver disease secondary to hepatitis B and C.

Many studies have been conducted in the past that have shown that an average of 50% of patients who were initially diagnosed with cirrhosis, do not develop esophageal varices in the period of follow up of 10yr. 4

Keywords: Transient elastography, non-invasive alternative, upper endoscopy, identifying gastric, esophageal varices, chronic hepatitis B and hepatitis C.





INTRODUCTION:

Esophageal and Gastric varices are one of the signs of the progression of chronic liver disease to cirrhosis. This is because of the development of portal hypertension in response to progression of fibrosis and increase stiffness in patients with chronic liver disease secondary to hepatitis B and C. Due to lack of early diagnoses of hepatitis Band C, many patients remain untreated till later stages leading to progression of chronic liver disease to decompensation and complications. When there is portal hypertension, it leads to portosystemic shunting by forming collateral vessels. ¹ This results in the formation of esophageal and gastric varices which results in complications of decompensation by causing massive hemorrhage. Which can be life threatening and raises the mortality rate up to 14.2 – 14.5%. ^{2,3}

The recent updates in guidelines of Baveno ⁷, emphasizes on the importance of screening of patients with chronic liver diseases for the identification of esophageal/ gastric varices and further management of the patients accordingly because the surveillance interval and treatment strategies rely on the grade of varices.

Many studies have been conducted in the past that have shown that an average of 50% of patients who were initially diagnosed with cirrhosis, do not develop esophageal varices in the period of follow up of 10yr. ⁴

Beta blockers and invasive endoscopic procedures like sclerotherapy and band ligation, are used for prophylaxis of esophageal and gastric varices after confirmation of the diagnosis. ¹ Various studies have concluded that the

maximum risk of hemorrhage from varices is not more than 15-25%. Screening endoscopy of majority of patients show either small varices or no varices at all, indicating that they might not be needing any prophylaxis or treatment. ⁵ The current studies are being targeted to find modalities and non-invasive tests that can save patients from avoidable endoscopies, especially patients who are less susceptible for developing varices.

Over the years, several modalities have been studied as means for non-invasive investigations. Transient elastography with Fibroscan has been found to be effective in determining the fibrosis in the liver, which uses ultrasound to measure the stiffness of the liver, which then correlates with the degree of fibrosis (scarring) in liver tissue. ⁶ The device generates a mechanical pulse that creates a shear wave, which travels through the liver. The speed of this wave correlates with the stiffness of the liver. The stiffer the liver, the faster the wave travels.

FibroScan is widely regarded as a rapid, reliable, and non-invasive method for assessing liver fibrosis, making it a valuable tool in managing chronic liver diseases, such as hepatitis B, hepatitis C, and non-alcoholic fatty liver disease (NAFLD). ⁷ ⁸ It can help determine the stage of fibrosis and monitor changes over time, potentially reducing the need for more invasive procedures like liver biopsy. ⁹ Recent studies confirm its efficacy and ease of use in clinical practice. ^{7, 9}

While **FibroScan (Transient Elastography)** is primarily used to measure liver stiffness and assess liver fibrosis,



there is emerging interest in exploring its potential for evaluating **esophageal and gastric varices**—which are complications often associated with advanced liver disease and portal hypertension. 9

AIMS AND OBJECTIVES:

The objective of this study is to determine the correlation and incidence of gastric and esophageal varices in patients with chronic liver disease secondary to hepatitis B and C, who have a transient elastography (FibroScan) score of F3 or F4, and if fibroscan can be used as a predictor of presence or absence of varices in patients in early phases of cirrhosis.

OPERATIONAL DEFINITIONS:

Esophageal varices: Single or multiple columns of dilated vessels seen in lower third of esophagus, seen during Esophagogastroduodenoscopy (EGD).

Grade I Esophageal Varices: Small Straight varices on endoscopy

Grade II Esophageal Varices: Enlarged tortuous varies occupying less than 1/3 of lumen

Grade III Esophageal Varices: Large coil shaped varices occupying more than 1/3 of lumen

Hepatitis B Virus (HBV) related Cirrhotic patients: Patients with HBsAg positive and HBV DNA Quantitative by PCR detected.

Hepatitis C Virus (HCV) related Cirrhotic patients: Patients with anti HCV positive and HCV RNA Qualitative by PCR detected.

Cirrhosis: ultrasound showing coarse parenchymal echotexture of liver.

Fibro scan: This is a non-invasive device that assesses the 'hardness' (or stiffness) of the liver via the technique of shear wave transient elastography. Liver hardness is evaluated by measuring the velocity of a vibration wave (also called a 'shear wave') generated on the skin.

F0-F1: liver stiffness range of 2-7 kPa.

F2: liver stiffness range of 7.5-10 kPa.

F3: liver stiffness range of 10.5-14 kPa.

F4: liver stiffness range of >14 kPa.

MATERIALS & METHODS

STUDY DESIGN:

Cross-sectional study.

SETTING:

Gujranwala liver foundation, Gujranwala, in association with Fatima Memorial Hospital, Lahore.

DURATION OF STUDY:

1st July 2020 to 31st December 2020

SAMPLE SIZE:

75

SAMPLE TECHNIQUE:

Non-probability, consecutive sampling.

SAMPLE SELECTION:

a. Inclusion Criteria:

All patients between 18 to 80 years of any gender diagnosed of chronic viral hepatitis.

Both genders

Patients with Hepatitis C infection

Patients with Hepatitis B infection

b. Exclusion Criteria:

Hepatocellular carcinoma



Chronic liver disease secondary to other causes

Decompensated liver disease

DATA COLLECTION PROCEDURE:

After approval from ethical review committee, a total of 75 patients registered to Gujranwala Liver Foundation, in association with Fatima Memorial Hospital, Lahore, fulfilling the inclusion criteria were selected. Informed consent was taken from each patient and all patients were undergoing the routine screening protocol, clinical examination, laboratory investigations and abdominal ultrasonography, liver stiffness measurement using Fibroscan and upper GI endoscopy as their regular follow up as per devised by the institution. The data was collected from the files by the researcher herself. The selected patients were treated thereafter as per the institution protocol.

DATA ANALYSIS PROCEDURE:

The collected information was analyzed by computer software SPSS version 25.0. Mean and standard deviation were calculated for quantitative variables i.e. ALT and Platelet. Frequency and percentage were calculated for qualitative variables i.e. esophageal and gastric varices and fibroscan results.

Effect modifiers like age, gender, BMI, duration of cirrhosis and type of hepatitis (B/C) were controlled through stratification to calculate test performance including spearman correlation was applied and p-value ≤ 0.05 was considered as significant.

STATISTICAL ANALYSIS:

According to the data analysis, patients were initially categorized into grades of fibroscan score, F1, F2, F3 and F4, non cirrhotic as 0 and Child Pugh Score A, B, C. The patients with fibroscan score of F1 were 9.3%, F2 were 10.7%, F3 were 26.7% and F4 were 53.3%. While the patient categorized according to non-cirrhotic and cirrhotic based on Child Pugh Score were as 16% non-cirrhotic, 32% were CTP A, 50.6% were CTP B and 1.4% were CTP C.

After observing the cross tabulation of fibroscan score and Esophageal varices, we found that assumptions of chi square: more than 80% cells have expected frequency above 5, was not met. So, we used maximum likelihood chi square test which showed statistically significant results with p value < 0.001 .

Fibroscan score * Esophageal varices cross tabulation %

Fibroscan Score	No	Small	Moderate/Large	Total
F1	8%	1%	0%	9%
F2	4%	5%	1%	10%
F3	4%	12%	11%	27%
F4	0%	14%	40%	54%
	16%	32%	52%	100%

Chi-Square Tests

	Value	df	Asymptotic Significance (sided)
Pearson Chi-Square	43.815 ^a	6	<.001
Likelihood Ratio	42.947	6	<.001
Linear-by-Linear Association	35.206	1	<.001



N of Valid Cases	75
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a. 4 cells (50.0%) have expected count less than 5. The minimum expected

a. 7 cells (58.3%) have expected count less than 5. The minimum expected count is .47.

1.12.

In relation to fibroscan and gastric varices, patients with fibroscan score F1 had 0% gastric varices. In patients with fibroscan score F2 out of 10.7% only 1.3% had gastric varices. In patients with fibroscan score F3, out of 26.7% only 2.7% had gastric varices. In patients with fibroscan score F4 out of 53.3% only 2.7% had gastric varices. After observing the cross tabulation, we found that assumptions of chi square:

Fibroscan * Gastric varices cross tabulation %

Fibroscan Score	No	Yes	Total
F1	9.3%	0%	9.3%
F2	9.3%	1.3%	10.6%
F3	24%	2.6%	26.6%
F4	50.6%	2.6%	52.6%
	93.2%	6.5%	100

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	1.473 ^a	3	.688
Likelihood Ratio	1.827	3	.609
Linear-by-Linear Association	.009	1	.925
N of Valid Cases	75		

Patients who had presence of gastric and esophageal varices both were 6.6%, out of which 1.3% had small esophageal varices and 5.3 % had moderate/large varices.

Child Pugh Score and Esophageal Varices

Child Pugh Score	No	Small	Moderate/Large	Total
Non Cirrhotic	9.4%	5.3%	1.4%	16%
CTP A	4%	17.4%	10.6%	32%
CTP B	2.6%	9.3%	38.6%	50.6%
CTP C	0%	0%	1.4%	1.4%
	16%	32%	52%	100%

Child Pugh Score and Gastric Varices

	No	Yes	Total
Non Cirrhotic	13%	0%	13.4%
Child Pugh Score A	32%	2.6%	34.6%
Child Pugh Score B	46.6%	4%	50.6%
Child Pugh Score C	1.4%	0%	1.4%



			100%
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The platelet counts in these patients ranged from 59000 -294000 with a mean of 170 000 and std deviation of 45.3. The ALT values ranged from 7- 200 IU/ml, with a mean value of 57.89, with a standard deviation of 33.6IU/ml. The AST values ranged from 15-205IU/ml with a mean value of 59.8IU/ml, with a standard deviation of 45.2IU/ml. It was observed that the patients who had higher fibroscan score had higher ALT and AST levels while lower platelet count indicating that there is correlation of cirrhosis with low platelet and higher ALT and AST levels.

INTERPRETATION:

The results produced from this data shows that there is an association between fibroscan score and esophageal varices. Fibroscan is a non-invasive method of detection of liver stiffness and it can be a better non-invasive option for screening of esophageal varices in patients with chronic hepatitis B and C.

The strength of this study was that we evaluated the diagnostic accuracy of Liver Stiffness Measure with Fibroscan Score for the detection of Esophageal Varices in different cirrhotic patients and etiological characteristics, to achieve more real assessment of the test performance.

In the future, prospective, well-designed studies for use of noninvasive methods such as TE, which may be a benchmark for diagnostic performance due to its elegant

technique, inexpensive cost and wide availability, are needed to improve accuracy.

DISCUSSION

Esophageal varices are one of the most significant and life-threatening complication of cirrhosis causing massive hemorrhage if ruptured. These are present in 90% of patients with advanced cirrhosis. 11 Chronic liver diseases, regardless of the underlying disease, often progress to cirrhosis. Chronic hepatitis C usually remains undiagnosed till later stages and presents with signs of cirrhosis in 10-20% of patients. 10

The risk of hemorrhage from the varices depends on the size of the varices and it varies from 5% in small to 15% in large varices. This hemorrhaging markedly increases the risk of mortality and averages between 10-20%. 12 Due to the high mortality rates, more emphasis has been placed on frequent screening EGD in every cirrhotic patient. 13 The duration between EGDs resides on the absence/presence of varices in the initial screening, and if present then depends upon the size of the varices. According to recommendations, if the patient lacks varices in initial screening, then follow up EGD should be 2-3yr while in the presence of small varices 1-2yr. Since EGD is an invasive procedure, there has been growing interest in research to illuminate patients at increased risk for larger varices and hemorrhage. Some of the non-invasive techniques recognized so far are based on transient elastography, ultrasonography, clinical assessment and laboratory parameters. 14

This study was conducted to examine the correlation between the grades of esophageal and gastric varices and



the FibroScan score (F0 to F4) in cirrhotic patients. The findings revealed that 25 patients (16.67%) had Grade I esophageal varices (EV), 69 patients (46.0%) had Grade II EV, and 56 patients (37.33%) had Grade III EV. When analyzing the FibroScan scores relative to the severity of esophageal varices, the mean scores were 6.63 ± 2.49 kPa for Grade I EV, 10.56 ± 3.04 kPa for Grade II EV, and 14.03 ± 2.58 kPa for Grade III EV. This resulted in a correlation coefficient (r) of 0.682 and a p -value of 0.0001, indicating a statistically significant relationship.

Jain et al. reported a similar finding, showing a significant positive correlation between liver stiffness (kPa) and varices grading ($r = 0.514$, $p < 0.001$), suggesting that as liver stiffness increases, the grading of varices also tends to increase.

Beom Kyung Kim (2017) conducted a study that demonstrated Transient Elastography (TE) effectively mirrors hepatic venous pressure gradient (HVPG) measurements, making it a valuable tool for assessing portal hypertension and complications of cirrhosis. ¹⁶ The study found that TE values below 13 kPa reliably rule out elevated HVPG, while values above 21 kPa are as accurate as an HVPG of 10 mmHg or higher. Similarly, a study by Sebastian Mueller et al. (2010) found a strong correlation between liver stiffness and portal pressure, indicating that esophageal varices are likely when TE values exceed 20 kPa. ¹⁷

Large research done by Sporea et al. was done in cirrhotic patients and cut off values were investigated for transient elastography which showed minimum of 31kPa to at least detect varices. ¹⁸ The cutoff of TE for forecasting the tendency of bleeding from varices was 50.7kPa. ¹⁹ This

cut off for hemorrhage was also an indication of presence of large varices. ⁶² This was also supported by a study of Lebrec et al. ¹⁹ Another study by Yasmin et al. favored a higher value (29.7kPa) for liver stiffness measurement. ²⁰ These findings are like the findings of our study. An Egyptian study by Tag-aden et al. reported LSM of more than 17kPa to be a profound predictor of varices in esophagus in chronic hepatitis C patients with a sensitivity of 93.6% and specificity of 95%. ²¹ However, another study by Vizzuti et al. concluded a lower cut off value for TE of 17.6 kPa, which can be ascribed to many factors such as clinical, laboratory and regional parameters. ²² Castera et al. reported that even though TE is an emerging tool to estimate cirrhosis, endoscopic screening of varices should not be undermined. ¹⁷

Numerous research works on the application of Transient Elastography (TE) to forecast esophageal varices and portal hypertension have proposed a wide variety of cut-off values. ²³ The recommended cut-offs fluctuate between 13.9 and 21.3 kPa for minor esophageal varices ($\geq F1$) and between 19 and 30 kPa for big varices ($\geq F2$). ²³ There not always seen when liver stiffness (LS) values were less than 19 kPa. However, cut-off values have been proposed to range from 27.5 to 35 kPa for the presence of substantial varices ($\geq F2$), where a value of 62.7 kPa indicates the presence of higher grade of varices with increased tendency to bleed. ²⁴

Many other studies including Kezmi et al., Jang et al. and Mele et al, all supported the predictive nature of transient elastography as a tool for liver stiffness and presence of varices above 19-21kPa, which is resembles



our findings. ²⁵ ²⁶ ²⁷ A value higher than 42.7kPa is a predictor of presence of larger varices. ²⁵ Another study indicated that transient elastography not only precisely predicts the presence and absence of varices, but it also predicts the presence and absence of significant portal hypertension. ²⁸

However there were some limitations in our study, which included smaller study group and shorter interval. Larger studies are required to better understand the correlation of varices with fibroscan score and to recommend that fibroscan score can be used as a non invasive tool for predicting esophageal and gastric varices.

CONCLUSION:

Transient elastography (Fibroscan) is an advanced noninvasive modality that has become popular in accurately predicting the existence of Esophageal and gastric Varices in patients with cirrhosis. This modality can change the existing criteria of endoscopic screening of the patients. It can provide the patients with relief from unnecessary endoscopic screenings in selective patients. It can pave the way for early initiation of pharmacological treatment and in the prevention of complications due to undiagnosed varices. The higher the score for transient elastography, the higher will be the risk of esophageal and gastric varices

The study concludes indicating that there is a positive correlation between different grades of esophageal and gastric varices and fibroscan score (F0 to F4) measured with transient elastography, in cirrhotic patients. So, it is highly recommended that fibroscan score can be used as a reliable screening method to detect early esophageal

varices in our settings, so that the number of unnecessary endoscopies can be reduced.

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