

Original Research Article

Transient Elastography (Fibroscan) for the prediction of Esophageal Varices in Egyptian Cirrhotic Patients

ABSTRACT

Background: Esophageal varices (EVs) are atypically dilated submucosal veins, which occurs consequently to portal hypertension. Liver stiffness measurement (LSM), obtained by transient elastography (Fibroscan), strongly correlates with portal hypertension.

Aim: is to predict the presence and grading of esophageal varices in Egyptian patients with liver cirrhosis using Fibroscan and other noninvasive tests.

Methods: 101 cirrhotic patients sorted into Group I (36 patients with EVs and portal hypertensive gastropathy (PHG)), Group II (34 patients with EVs), Group III (15 patients with PHG), and Group 4 (16 patients with neither EVs nor PHG). Upper endoscopy, ultrasonography, routine lab. and Fibroscan assessment were done to all patients.

Results: LSM correlated directly and significantly with the presence ($p < 0.001$), and grading of EVs ($p = 0.001$). A LSM cut off value of 18.55 kPa had an AUC of 0.726, sensitivity of 74.3%, specificity of 54.8%, PPV of 78.79%, and a NPV of 48.57% for predicting the presence of EVs. Platelet count/spleen diameter ratio (PSR) inversely correlated with the EVs presence ($p = 0.002$), and grading ($p < 0.001$). PSR had a cut off value of 742.17, an AUC of 0.695, sensitivity of 71% and a specificity of 58.6% (PPV of 82%, NPV of 43.14%) for EVs presence. Right lobe diameter/Albumin ratio (RLAR) correlated directly with EVs presence ($p = 0.001$), and grading ($p = 0.012$). RLAR cut off value of 3.62 had AUC, sensitivity, specificity, PPV, and NPV of 0.7, 64.3%, 67.7%, 81.8%, and 45.7%, respectively for the prediction of EVs presence.

Conclusion: LSM, PSR, RLAR are noninvasive methods for predicting the presence and grading of EVs at a low cost.

Keywords: Transient elastography, Liver stiffness measurement, Esophageal varices, Liver cirrhosis.

1. INTRODUCTION

Liver cirrhosis is the diffuse scarring of the liver parenchyma with formation of regenerating nodules. Cirrhosis is considered the final phase of various liver diseases. Portal hypertension (PH) is the rise of portal venous pressure > 10 mmHg or hepatic venous pressure gradient (HVPG) > 5 mmHg.^[1,2]

Esophageal varices are aberrantly dilated submucosal veins that occur as a consequence of PH at a HVPG of > 10 mmHg with annual progress rate of 10 – 12% from small to large varices, while bleeding esophageal varices occur at a HVPG of > 12 mmHg with annual risk of variceal hemorrhage of 5% and 15% for small and large varices, respectively. ^[3, 4]

Patients at higher risk of variceal bleeding are identified by variceal size, red wale marks on EVs and decompensated liver disease. Without endoscopic intervention, the risk of rebleeding reaches 60% and mortality rate near 33%. ^[5]

The Baveno IV and V consensus graded EVs into small (minimally elevated EVs), medium (EVs occupying less than one third of esophageal lumen) and large (EVs occupy > one third of esophageal lumen). ^[6, 7] Also, The Japanese Research Society for Portal Hypertension classification graded EVs based on variceal location, form, color, presence of red color signs (red wale marks, Cherry red spots), bleeding signs, and mucosal findings. ^[8]

Esophagogastroduodenoscopy (EGD) remains the gold standard for diagnosing, screening and treatment of EVs. Owing to the invasive nature and expenses of EGD, the search for noninvasive predictors for detecting EVs were sought. ^[9, 10]

Transient elastography (TE; Fibroscan) is an ultrasonic based imaging technique that measures the liver stiffness (LSM), which is a representative of liver fibrosis. LSM was found to have a high diagnostic accuracy for presence of cirrhosis. Also, LSM can predict the presence of PH in cirrhotic patients. Therefore, this study aimed at evaluating the role of Fibroscan and other noninvasive tests for prediction of the presence and grading of EVs. ^[11, 12]

2. PATIENTS AND METHODS

Our cross-sectional study incorporated 101 adult cirrhotic patients presenting to Tropical Medicine Department's endoscopy unit, Tanta University Hospital from June 2019 to June 2021. The Ethics Committee of the faculty of medicine, Tanta University approved the study protocol in April 2019 with the code 33090/04/19. Written consent had been taken from all participating patients.

Our patients were sorted into two groups: Group I (70 patients with EVs) and Group II (31 patients without EVs).

Patients with narrow intercostal space, hepatocellular carcinoma or the presence of severe ascites that preclude TE examination, severe cardiopulmonary diseases, renal failure, patients treated with non-selective beta-blockers, variceal eradication, or with portosystemic shunt and patients with unmeasurable spleen diameter or undergone splenectomy were excluded from our study.

A full history taking, clinical examination, laboratory tests (Complete Blood Count, hepatic functions, kidney functions), Child-Pugh score, ultrasonography, EGD, and LSM using Fibroscan echosens 502 were performed to all the patients.

EVs were classified using the Japanese classification (the Locus, Form, Color, Red Color, bleeding, and mucosal signs) and Baveno classification for grading of EVs into small, medium, and large.

Statistical analysis: Data were processed using IBM SPSS version 22 for Microsoft Windows (Armonk, NY). The independent samples T test was employed for mean comparisons. Chi square test was employed for categorical values.

Associations between different variables was done with Spearman's rank correlation test. Receiver operating characteristic (ROC) curves identified the “cutoffs” for variables associated with EVs. Statistical significance was set at P values < 0.05.

3. RESULTS

The mean age of our patients was 58.24 ± 8.54 years in group I, containing 36 (51.4%) males and 34 (48.57%). While the mean age in group II was 54.87 ± 10.41 years with 18 (58.06%) males and 13 (41.93%). There was no significant difference between the two groups.

Table (1): Patients baseline characteristics

parameter	Group I (no. = 70)	Group II (no. =31)	P value
Age (years): Mean \pm SD.	58.24 \pm 8.54	54.87 \pm 10.41	0.76
Sex: male no. (%)	36 (51.4)	18 (58.06)	0.537
Etiology of cirrhosis: no. (%)			0.196
HCV	63 (90)	27 (78.1)	
HBV	2 (2.86)	0	
Wilson's disease	1(1.43)	1 (3.2)	
NAFLD	0	2 (6.5)	
others	4 (5.71)	1 (3.2)	
Jaundice: no. (%)	9 (12.86)	2 (6.45)	0.341
Ascites: no. (%)	17 (24.29)	2 (6.45)	0.034*
Lower limb edema: no. (%)	25 (35.71)	6 (19.35)	0.100
Child Class: no. (%)			0.055
A	39 (55.7)	25 (80.6)	
B	27 (38.6)	5 (16.1)	
C	4 (5.7)	1 (3.2)	
History of blood transfusion: no. (%)	34 (48.57)	13 (41.94)	0.537
History of hematemesis and melena: no. (%)	10 (14.29)	5 (16.13)	0.810
History of DAAs: no. (%)	34 (48.57)	18 (58.06)	0.379
History of hepatic encephalopathy: no. (%)	7 (10)	2 (6.45)	0.564

HCV: Hepatitis C virus, HBV: Hepatitis B virus, NAFLD: non-alcoholic fatty liver disease, DAAs: Direct acting antivirals, * statistically significant at P <0.05

HCV was the main etiology of cirrhosis in 63 (90%) patients in group I and in 27 (78.1%) patients in group II whereas other etiologies as HBV was found in 2 patients in group I, NAFLD in 1 patient in group I and 1 patient in group II

II, Wilson's disease in 2 patients in group II, and unknown etiology in 4 patients in group I and 1 patient in group II with no significant difference between the groups. (Table 1)

There was no significant difference amongst the groups regarding the clinical data as presence of jaundice and lower limb edema. Although a significant difference were detected between the EVs group and non EVs group regarding the presence of ascites clinically ($P = 0.034$). Child-Pugh class A was found in 39 (55.7%) patients class B in 27 (38.6%) patients, and class C in 4 (5.7%) patients in group I, while group II had 25 (80.6%), 5 (16.1%), and 1 (3.2%) patients with classes A, B, and C, respectively with no significant difference between the two groups. (Table 1)

Table (2): Laboratory findings.

parameter	Group I (no. = 70)	Group II (no. =31)	P value
Hb (gm/dl): Mean \pm SD.	10.13 \pm 2.00	10.91 \pm 2.04	0.081
WBCs $\times 10^3$ /(mm3): Mean \pm SD.	4.92 \pm 2.19	5.54 \pm 2.52	0.241
Platelets $\times 10^3$ /(mm3): Mean \pm SD.	117.37 \pm 49.26	146.81 \pm 49.02	0.007*
T. Bilirubin (mg/dl): Mean \pm SD.	1.42 \pm 1.03	1.24 \pm 0.68	0.311
AST (U/L): Mean \pm SD.	50.2 \pm 22.89	44.56 \pm 18.41	0.193
ALT (U/L): Mean \pm SD.	36.11 \pm 18.39	33.7 \pm 11.01	0.417
S. Albumin (gm/dl): Mean \pm SD.	3.21 \pm 0.61	3.64 \pm 0.54	0.001*
Prothrombin activity (%) : Mean \pm SD.	74.7 \pm 17.3	85.05 \pm 16.68	0.006*
INR : Mean \pm SD.	1.36 \pm 0.29	1.23 \pm 0.28	0.037*
S. Creatinine (mg/dl): Mean \pm SD.	0.94 \pm 0.42	0.93 \pm 0.3	0.924
Fasting blood sugar (mg/dl): Mean \pm SD.	142.68 \pm 60.26	119.68 \pm 45.56	0.061

Hb: hemoglobin, WBCs: white blood cells, AST: aspartate aminotransferase, ALT: alanine aminotransferase, INR: international normalized ratio, * statistically significant at $P < 0.05$

Full blood count demonstrated no significant differences between the two groups concerning the hemoglobin level ($P = 0.081$) and the white blood cells ($P = 0.241$). The platelet count was significantly lower in group I than group II ($P = 0.007$). (Table 2)

Serum bilirubin, ALT, and AST demonstrated no significant difference among the studied groups ($P > 0.05$). Serum albumin was significantly lower in group I with EVs than group II without EVs ($P = 0.001$). A significant difference between the two groups was demonstrated concerning the prothrombin activity ($P = 0.006$) and INR ($P = 0.037$). (Table 2)

No significant difference was detected among the studied groups concerning serum urea, creatinine ($P = 0.924$) and

fasting blood sugar (P =0.061). (Table 2)

Table (3): Radiological and endoscopic Findings

parameter	Group I (no. = 70)	Group II (no. =31)	P value
Ultrasonographic findings: Mean \pm SD.			
Right lobe diameter (cm)	12.52 \pm 1.29	12.19 \pm 1.28	0.239
Spleen diameter (cm)	16.4 \pm 2.48	15.36 \pm 2.21	0.038*
Ascites: no. (%)	19 (27.14)	3 (9.68)	0.0498*
PSR: Mean \pm SD.	749.21 \pm 380.2	988.46 \pm 375.39	0.005*
RLAR: Mean \pm SD.	4.04 \pm 0.897	3.44 \pm 0.712	0.001*
LSM med. (kPa): Mean \pm SD.	29.26 \pm 14.8	19.46 \pm 4.84	<0.001*
CAP med. (dB/m): Mean \pm SD.	200.21 \pm 69.55	202.77 \pm 81.46	0.880
Grading of EVs: no. (%)			
Small	28 (40)		
Medium	24 (34.3)		
Large	18 (25.7)		
PHG: no. (%)	36 (51.4)	15 (48.6)	0.778

LSM: liver stiffness measurement, CAP: controlled attenuation parameter, EVs: esophageal varices, PSR: platelet count/spleen diameter ratio, RLAR: right liver lobe diameter/albumin ratio, * statistically significant at P <0.05

Platelet count/ spleen diameter ratio (PSR) was significantly reduced in group I than group II (P =0.005). Right lobe/ albumin ratio (RLAR) was significantly elevated in group I than in group II (P =0.001). (Table 3)

The Fibroscan results detected that LSM median was significantly higher in group I than in group II (P <0.001). The controlled attenuation parameter (CAP) median demonstrated no significant difference amongst the groups (P =0.880). (Table 3)

The endoscopic findings demonstrated that EVs was identified in 70 (96.3%) of our patients (small EVs in 28 (40%) patients, medium sized varices in 24 (34.3%) patients, and large EVs in 18 (25.7%) patients). (Table 3)

Table (4): Correlations between the laboratory, radiologic, and endoscopic findings and EVs presence and grading.

	EVs presence		EVs grading	
	r	P value	r	P value
Hb	-0.159	0.112	-0.213	0.032*
WBCs	-0.109	0.279	-0.091	0.363
Platelets	-0.286	0.004*	-0.369	<0.001*

T. Bilirubin	0.022	0.826	0.086	0.390
AST	0.097	0.331	0.038	0.706
ALT	-0.008	0.936	-0.087	0.385
S. Albumin	-0.311	0.002*	-0.245	0.014*
Prothrombin time	0.269	0.0067*	0.295	0.0029*
Prothrombin activity	-0.287	0.0037*	-0.275	0.0054*
INR	0.264	0.0078*	0.250	0.0117*
Child class	0.221	0.027*	0.279	0.0048*
Child score	0.286	0.0039*	0.259	0.009*
Ultrasonographic findings				
Right lobe diameter	0.0810	0.420	0.0122	0.904
Spleen diameter	0.172	0.085	0.210	0.035*
Ascites	0.195	0.0506	0.191	0.0563
PSR	-0.311	0.002*	-0.384	<0.001*
RLAR	0.319	0.001*	0.248	0.012*
LSM median	0.361	<0.001*	0.314	0.001*
CAP median	-0.0575	0.567	-0.0289	0.773

PHG: portal hypertensive gastropathy, Hb: hemoglobin, WBCs: white blood cells, AST: aspartate aminotransferase, ALT: alanine aminotransferase, INR: international normalized ratio, PSR: platelet count/spleen diameter ratio, RLAR: right liver lobe diameter/albumin ratio, LSM: liver stiffness measurement, CAP: controlled attenuation parameter, * statistically significant at P <0.05

Table (5): Cut off values for detection of EVs presence

	Cut off value	AUC	P value	Sensitivity	Specificity	PPV	NPV	LR+	LR-
platelets× 10³/mm³	122.5	0.679	0.004*	64.5	60	79.25	41.67	1.6125	0.888
Albumin (gm/dl)	3.45	0.694	0.002*	64.5	71.4	81.97	50	2.255	0.497
PSR	742.17	0.659	0.002*	71	58.6	82	43.14	1.715	0.495
RLAR	3.62	0.700	0.001*	64.3	67.7	81.8	45.7	1.99	0.527
LSM (kPa)	18.55	0.726	< 0.001*	74.3	54.8	78.79	48.57	1.644	0.469

PHG: portal hypertensive gastropathy, PSR: platelet count/spleen diameter ratio, RLAR: right liver lobe diameter/albumin ratio, AUC: area under the curve, PPV: positive predictive value, NPV: negative predictive value, LR: likelihood ratio, * statistically significant at P <0.05

The hemoglobin level showed a significant inverse correlation with EVs grading (p = 0.032). The white blood cells and their differentiation showed insignificant correlation with the presence and grading of EVs. The platelet count had a significant correlation with the presence (p = 0.004), and grading of EVs (p <0.001) (Table 4). A platelet cut off value of 122.5 × 10³/mm³ had an AUC of 0.679, sensitivity of 64.5%, specificity of 60%, a PPV of 79.25% and a NPV of 41.67% for detecting the presence of EVs. (Table 5) (Figure 1)

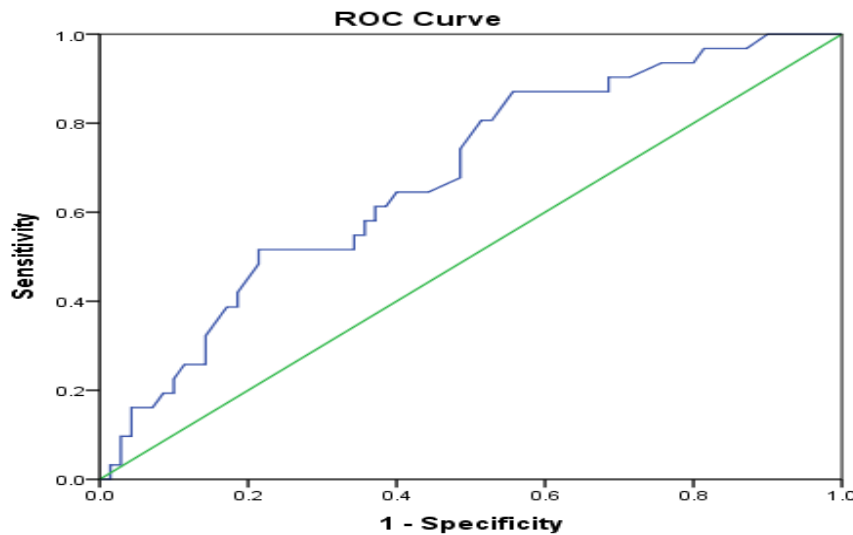


Figure (1): ROC curve of platelet count for detection of EVs presence (AUC= 0.679, $p= 0.004$, 95% CI (0.570 - 0.789)). AUC: Area under the curve, EV: esophageal varices, CI: Confidence interval

No significant correlation was found between the presence and grading of EV and bilirubin or transaminases. Serum albumin had significant inverse correlations with the presence ($p = 0.002$) and grading of EVs ($p = 0.014$) (Table 4). Serum albumin cut off value of 3.45 gm/dl had a sensitivity of 64.5%, specificity of 71.4%, PPV of 81.97%, and a NPV of 50% for detection of the presence of EVs. (Table 5) (Figure 2)

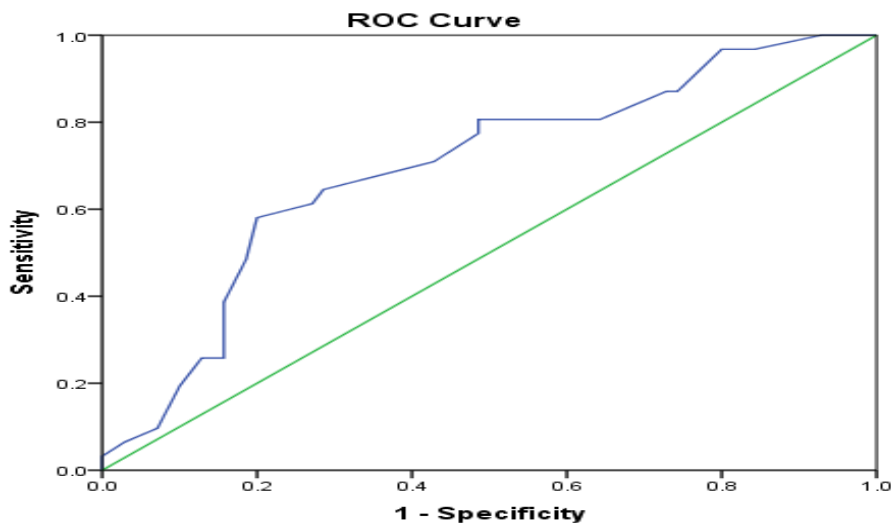


Figure (2): ROC curve of serum albumin for detection of EVs presence EV (AUC= 0.694, $p= 0.002$, 95% CI (0.583 - 0.806)). AUC: Area under the curve, EV: esophageal varices, CI: Confidence interval

The prothrombin time had direct correlations with the EVs presence ($p = 0.0067$), and EVs grading ($p = 0.0029$). The prothrombin activity had inverse correlations with the EVs presence ($p = 0.0037$), and EVs grading ($r = -0.275$, $p = 0.0054$). The INR had direct correlations with EVs presence ($p = 0.0078$) and EV grading ($p = 0.0117$). (Table 4)

The Child-Pugh score showed significant direct correlations with the EVs presence ($p = 0.027$) and grading ($p = 0.0048$). The Child-Pugh class showed significant direct correlations with the EVs presence ($p = 0.0039$) and grading ($p =$

0.009). The spleen diameter by ultrasound correlated significantly and positively with EVs grading ($p = 0.035$) but it showed insignificant correlations with the presence of EVs. (Table 4)

The PSR had significant inverse correlations with the presence ($p = 0.002$), and grading of EVs ($p < 0.001$) (Table 4). PSR cut off value of 742.17 had an AUC of 0.695, sensitivity of 71%, a specificity of 58.6%, PPV of 82%, and NPV of 43.14% for the presence of EVs. (Table 5) (Figure 3)

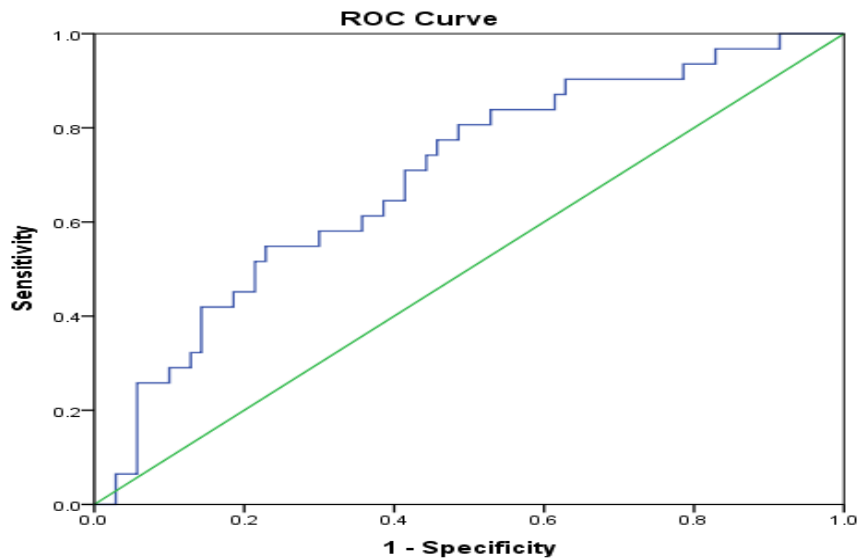


Figure (3): ROC curve of PSR for detection of EVs presence (AUC= 0.695, $p= 0.002$, 95% CI (0.585 - 0.804)). PSR: Platelet count/ spleen diameter ratio, AUC: Area under the curve, EV: esophageal varices, CI: Confidence interval

The RLAR had significant direct correlations with the presence ($p = 0.001$), and grading of EVs ($p = 0.012$) (Table 4). RLAR had a sensitivity, specificity, PPV, NPV, and AUC of 64.3%, 67.7%, 81.8, 45.7%, and 0.700, respectively for a cut off value of 3.62 to detect the presence of esophageal varices. (Table 5) (Figure 4)

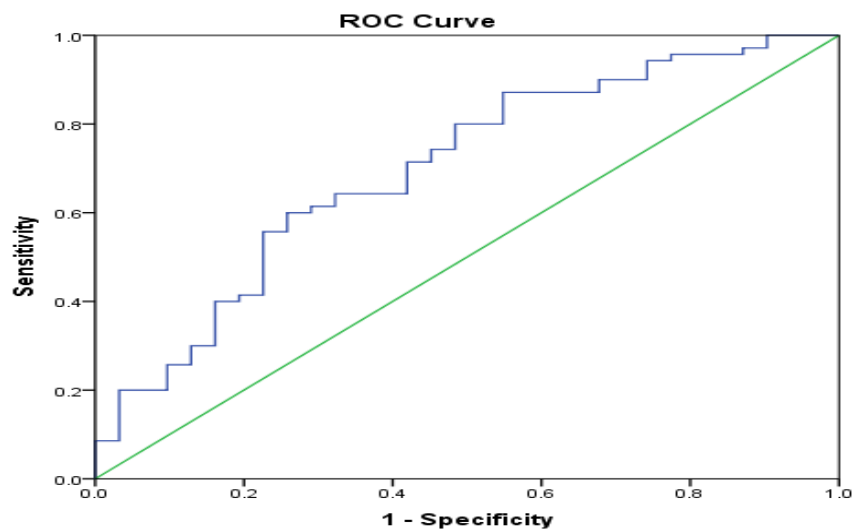


Figure (4): ROC curve of RLAR for detection of EVs presence (AUC= 0.700, $p= 0.001$, 95% CI (0.587 - 0.812)). RLAR: Right liver lobe/Albumin ratio, AUC: Area under the curve, EV: esophageal varices, CI: Confidence interval

LSM correlated directly and significantly with EVs presence ($p < 0.001$), and grading ($p = 0.001$) (Table 4). A LSM

cut off value of 18.55 kPa had a sensitivity, specificity, PPV, NPV, and AUC of 74.3%, 54.8%, 78.79%, 48.57%, and 0.726 for the prediction of the presence of EVs (Table 5) (Figure 5).

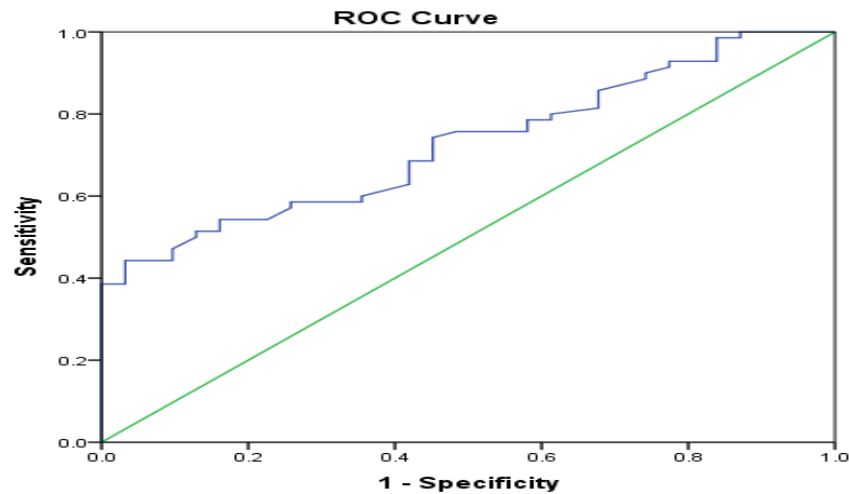


Figure (5): ROC curve of LSM for detection of EVs presence (AUC= 0.726, $p < 0.001$, 95% CI (0.628 - 0.823)). AUC: Area under the curve, EV: esophageal varices, CI: Confidence interval

4. DISCUSSION

Esophageal varices pose an important health sequel of portal hypertension giving the risks of morbidity and mortality associated with variceal hemorrhage having 15 – 25% six weeks mortality rate. Owing to the expenses and invasiveness of endoscopy, several noninvasive predictors of EVs were proposed. ^[13]

Transient Elastography is a technique that uses ultrasonic shear waves to measure liver stiffness as a substitute of liver fibrosis. The Baveno VII consensus set a criteria of LSM ≥ 20 kPa and platelet count $\leq 150,000/\text{mm}^3$ to predict the presence of EVs and the need for endoscopic variceal screening. ^[14] The aim of our study was to evaluate the accuracy of TE and other markers for the non-invasive prediction of EVs in Egyptian cirrhotic patients.

Concerning the hematological tests in this study, The Hb level and the WBC count showed no significant difference between the studied groups. The platelet count showed significant difference between the two groups agreeing with Tag-Aden et al. 2017 and Kumar et al. 2020. ^[15, 16]

The serum bilirubin, ALT and AST showed no significant difference between the studied groups while the serum albumin was significantly lower in group I than group II agreeing with Kumar et al. 2020 but disagreeing with Rahmani et al. 2021 who found no significant difference regarding serum albumin. ^[16, 17]

Prothrombin activity and INR showed significant difference between the studied groups ($P = 0.006$ and $P = 0.037$) in agreement with Alsebaey et al.2020 and Rahmani et al. 2021. ^[17, 18] This could be explained by progression of portal hypertension and cirrhosis with deterioration of liver synthetic functions.

The ultrasonographic examination demonstrated insignificant difference between the two groups regarding the right liver lobe diameter disagreeing with Kumar et al. 2020. ^[16] However, spleen diameter and presence of ascites were

showed significant differences between the two groups ($P = 0.038$, $P = 0.0498$) agreeing with Kumar et al. 2020 and Alsebaey et al. 2020. ^[16, 18]

PSR was significantly lower in patients with EVs than in patients without ($P = 0.005$). RLAR was significantly elevated in group I than in group II ($P = 0.001$). These results were in agreement with Jamil et al. 2017, Salem et al. 2018, and Elbasiony et al. 2021 ^[19-21]

LSM was significantly elevated in patients with EVs than in patients without ($P < 0.001$) agreeing with Paternostro et al. 2019, Alsebaey et al. 2020, and Fofiu et al. 2021. ^[18, 22, 23]

Concerning the correlations of EVs with the hematological tests, an inverse relationship was detected between Hb level and grading of EVs indicated by the Baveno classification ($P = 0.032$). As the risk of EVs bleeding is about 25 – 35% and larger esophageal varices is associated with increase in esophageal wall tension which increase the risk of bleeding. No correlations between EVs and WBCs and its differentials.

The platelet count showed a significant inverse correlation with the presence ($P = 0.004$) and grading of EVs ($P < 0.001$). Our data was in harmony with the studies of Alsebaey, et al. (2020), Elbasiony, et al. (2021). As both low platelet count and large EVs tend to occur in advanced liver disease. ^[18, 20]

A platelet count cut off value of $122.5 \times 10^3/\text{mm}^3$ had a sensitivity, specificity, PPV, and NPV of 64.5%, 60%, 79.25%, and 41.67% respectively for the detection of the presence of EVs. Baveno VII consensus stated that a platelet count of $> 150 \times 10^3/\text{mm}^3$, LSM < 20 kPa could be used for ruling out the presence of high risk EVs. ^[14]

Colli et al., (2017) in a systematic review stated that a platelet count cut off value of around $150 \times 10^3/\text{mm}^3$ from 10 studies had a sensitivity and a specificity of 71% and 80% respectively for the detection of varices of any size. Elbasiony et al. (2021) found that a cut off value of platelet count of $\geq 112.5 \times 10^3/\text{mm}^3$ had a sensitivity and a specificity of 84% and 87% for ruling out the presence of EVs. ^[20, 24]

The correlations between the liver function tests and the presence and grading of EVs demonstrated insignificant association as regards serum bilirubin, ALT and AST. However, serum albumin was significantly inversely associated with the presence of EVs ($P = 0.002$) and grading ($P = 0.014$). These results agreed with Kumar et al. (2020). This association is explained as large EVs and low serum albumin are associated with advanced liver disease. ^[16]

A cut off value of serum albumin of 3.45 mg/dl had a sensitivity of 64.5%, specificity of 71.4%, PPV of 81.97%, and a NPV of 50% for detecting the presence of EVs. **Wong et al. (2021)** proposed a criteria of serum albumin > 4 mg/dl, serum bilirubin < 2.2 gm/dl, and platelet count $> 114 \times 10^3/\text{mm}^3$ for the exclusion of high risk EVs. ^[25]

A significant correlation was detected between the coagulation profile and the presence and grading of EVs as follows: a significant negative correlation between the prothrombin activity and presence ($P = 0.0037$) and grading of EVs

(P 0.0054) and a direct correlation between the INR and presence (P = 0.0078) and grading of EVs (P 0.01117) were detected in our study. These findings were similar to the findings of Kraja et al. (2017), and Alsebaey et al. (2020).^[18, 26]

A significant positive correlation was found between the Child Pugh score and the presence (P = 0.0039) and grading of EVs (P 0.009). Also, a significant correlation was present between the Child Pugh Class and the presence (P = 0.027) and grading of EVs (P 0.0048). These results were in agreement with Bhattarai S et al. (2017), Kraja et al. (2017), and Krige, et al. (2019).^[26-28]

The ultrasonographic examination in our study demonstrated that the right liver lobe diameter, median spleen diameter and presence of ascites showed no correlation with EVs presence and grading. Although a significant correlation was found between spleen diameter and EVs grading (P = 0.035). These results agreed with Hassan, et al., (2018) and Rahmani, et al., (2021).^[17, 29]

PSR was significantly correlated with the presence (P = 0.002) and grading of EVs (P <0.001). These results agreed with Jamil, et al., (2017), Colli et al., (2017), Mahfuzzaman, et al. (2018), and Rahmani, et al., (2021). In our study, a cut off value of 742.17 for PSR for detection of EVs presence with AUC, sensitivity, specificity, PPV, and NPV of 0.695, 71%, 58.6%, 82%, and 43.14% respectively.^[17, 19, 24, 30]

Jamil, et al., (2017) set a PSR cut off value of ≤ 1077.42 for prediction of EVs with AUC, sensitivity, and specificity of 0.9, 88.75%, and 81.43%. Mahfuzzaman, et al. (2018) used a cut off value for PSR of 908.5 had a sensitivity, specificity, PPV, and NPV of 100%, 55.6%, 85.4%, and 100% respectively. Rahmani, et al., (2021) concluded that a cut off value of <6.95 ($\mu\text{L} / \text{cm}^3$) had an AUC, sensitivity, specificity, PPV, and NPV of 0.794, 76.2%, 71.2%, 68.1%, and 78.7% for the prediction of EVs.^[17, 19, 30]

RLAR was found to correlate significantly with the presence (P = 0.001) and grading of EVs (P = 0.012). Our data were similar to those of Salem, et al., (2018) and Akram, et al., (2019). A RLAR cut off value of >3.62 had an AUC of 0.7, sensitivity 64.3%, specificity 67.7%, PPV 81.8%, and NPV 45.7% for the prediction of EVs. Nouh, et al., (2019) used a RLAR cut off value 3.7 with sensitivity and specificity of 95% and 76.4%. Awad, et al., (2020) set a cut off value of >3.88 with sensitivity and specificity of 86.67 and 73.33. while Kamal, et al., (2020) set a cut off value of >2.8 with sensitivity and specificity of 80% and 53%.^[21, 31-34]

Transient elastography (Fibroscan) results showed insignificant association between fibrosis stage, steatosis stage, and CAP median and the presence and grading of EVs. However, a significant association was detected between LSM and the presence of EVs (P <0.001) and the grading of EVs (P = 0.001). Our results were also similar with Zhu et al., (2018), Sarkar et al., (2018), Fofiu et al., (2021), and Elbasiony et al., (2021).^[20, 23, 35, 36]

The ROC curve yielded a cut off value of 18.55 kPa for the prediction of EVs with AUC 0.726, sensitivity 74.3%, specificity 54.8%, PPV 78.79%, and NPV 48.57%. Sarkar et al., (2018) proposed a cut off value of LSM 18 kPa with a sensitivity and specificity of 88.7% and 75% respectively for the prediction of EVs. A meta-analysis conducted by Cheng

et al., (2018) concluded that LSM is useful for the detection of the presence and severity of EVs. However, a single cut off value couldn't be reached. Elbasiony et al., (2021) set a cut off value of >23.1 kPa for the prediction of EVs with a sensitivity of 94% and specificity of 81%.^[20, 36, 37]

5. CONCLUSION

LSM, PSR, RLAR, serum albumin and platelet counts are valuable easy screening modalities for predicting the presence and grading of EVs.

ETHICAL APPROVAL

THE ETHICS COMMITTEE OF THE FACULTY OF MEDICINE, TANTA UNIVERSITY APPROVED THE STUDY PROTOCOL IN APRIL 2019 WITH THE CODE 33090/04/19.

REFERENCES

- [1] Ginès, P., Krag, A., Abraldes, J. G., Solà, E., Fabrellas, N., & Kamath, P. S. (2021). Liver cirrhosis. *Lancet (London, England)*, 398(10308), 1359–1376.
- [2] Sharma, M., Singh, S., Desai, V., Shah, V. H., Kamath, P. S., Murad, M. H., & Simonetto, D. A. Comparison of Therapies for Primary Prevention of Esophageal Variceal Bleeding: A Systematic Review and Network Meta-analysis. *Hepatology*, 2019; 69(4), 1657–1675.
- [3] Procopet, B., & Berzigotti, A. Diagnosis of cirrhosis and portal hypertension: imaging, non-invasive markers of fibrosis and liver biopsy. *Gastroenterology Report*, 2017; 5(2), 79–89.
- [4] Amitrano, L., Guardascione, M. A., Manguso, F., Bennato, R., Bove, A., Denucci, C., ... Riccio, E. The effectiveness of current acute variceal bleed treatments in unselected cirrhotic patients: Refining short-term prognosis and risk factors. *American Journal of Gastroenterology*, 2012; 107(12), 1872–1878.
- [5] Boregowda, U., Umapathy, C., Halim, N., Desai, M., Nanjappa, A., Arekapudi, S., ... Saligram, S. Update on the management of gastrointestinal varices. *World Journal of Gastrointestinal Pharmacology and Therapeutics*, 2019; 10(1), 1–21.
- [6] De Franchis, R. Evolving Consensus in Portal Hypertension Report of the Baveno IV Consensus Workshop on methodology of diagnosis and therapy in portal hypertension. In *Journal of Hepatology*, 2005; Vol. 43, pp. 167–176.
- [7] De Franchis, R. Revising consensus in portal hypertension: Report of the Baveno v consensus workshop on methodology of diagnosis and therapy in portal hypertension. In *Journal of Hepatology*, 2010 Vol. 53, pp. 762–768.
- [8] Miyaaki, H., Ichikawa, T., Taura, N., Miuma, S., Isomoto, H., & Nakao, K. Endoscopic management of esophagogastric varices in Japan. *Ann Transl Med.*, 2014; 2(5), 42.
- [9] Garcia-Tsao, G., Abraldes, J. G., Berzigotti, A., & Bosch, J. Portal hypertensive bleeding in cirrhosis: Risk

- stratification, diagnosis, and management: 2016 practice guidance by the American Association for the study of liver diseases. *Hepatology*, 2017; 65(1), 310–335.
- [10] Hwang, H. J., Shergill, A. K., Acosta, R. D., Chandrasekhara, V., Chathadi, K. V., Anton Decker, G., ... Cash, B. D. The role of endoscopy in the management of variceal hemorrhage. *Gastrointestinal Endoscopy*, 2014; 80(2), 221–227.
- [11] Bazerbachi, F., Haffar, S., Wang, Z., Cabezas, J., Arias-Loste, M. T., Crespo, J., ... Watt, K. D. Range of Normal Liver Stiffness and Factors Associated With Increased Stiffness Measurements in Apparently Healthy Individuals. *Clinical Gastroenterology and Hepatology*, 2019; 17(1), 54-64.e1.
- [12] Zhang, Y. N., Fowler, K. J., Ozturk, A., Potu, C. K., Louie, A. L., Montes, V., ... Sirlin, C. B. Liver fibrosis imaging: A clinical review of ultrasound and magnetic resonance elastography. *Journal of Magnetic Resonance Imaging*, 2019; 51(1), 25–42.
- [13] Reverter, E., Tandon, P., Augustin, S., Turon, F., Casu, S., Bastiampillai, R., ... Abraldes, J. G. A MELD-Based Model to Determine Risk of Mortality Among Patients With Acute Variceal Bleeding. *Gastroenterology*, 2014; 146(2), 412-419.e3.
- [14] de Franchis, R., Bosch, J., Garcia-Tsao, G., Reiberger, T., Ripoll, C., Abraldes, J. G., ... Yoshiji, H. Baveno VII – Renewing consensus in portal hypertension. *Journal of Hepatology*, 2022; 76(4), 959–974.
- [15] Tag-Adeen, M., Alsenbesy, M., Ghweil, A. A., Abd Elrazek, M. A. H., Elgohary, E. A., Sallam, M. M., ... Nawara, A. Liver stiffness measurement and spleen diameter as predictors for the presence of esophageal varices in chronic hepatitis C patients. *Medicine*, 2017; 96(46), e8621.
- [16] Kumar, P., Singh, K., Joshi, A., Thakur, P., Mahto, S. K., Kumar, B., ... Lamba, B. M. S. Evaluation of non-invasive marker of esophageal varices in cirrhosis of liver. *Journal of Family Medicine and Primary Care*, 2020; 9(2), 992.
- [17] Rahmani, P., Farahmand, F., Heidari, G., & Sayarifard, A. Noninvasive markers for esophageal varices in children with cirrhosis. *Clinical and Experimental Pediatrics*, 2021; 64(1), 31.
- [18] Alsebaey, A., Elmazaly, M. A., & Abougabal, H. M. Prediction of esophageal varices in patients with HCV-related cirrhosis using albumin-bilirubin, platelets-albumin-bilirubin score, albumin-bilirubin-platelets grade, and GAR. *Egyptian Liver Journal*, 2020; 10(1), 22.
- [19] Jamil, Z., Malik, M., & Durrani, A. A. Platelet count to splenic diameter ratio and other noninvasive markers as predictors of esophageal varices in patients with liver cirrhosis. *Turkish Journal of Gastroenterology*, 2017; 28(5), 347–352.
- [20] Elbasiony, M., Abed, H., Alaskalany, H. M., & Saleh, A. Transient elastography and platelet count as noninvasive predictors of gastroesophageal varices in patients with compensated hepatitis C virus–related liver cirrhosis. *Medical Journal Armed Forces India*, 2021.
- [21] Salem, M. N. E., Elhawary, M. A. A., roho, M. G. M. S., Abdallah, S. R., & Khedr, M. A. H. B. Role of Right Liver Lobe Diameter/Serum Albumin Ratio in Esophageal Varices Assessment in Cirrhotic Patients. *The Egyptian Journal of Hospital Medicine*, 2018; 73(7), 7112–7118.
- [22] Paternostro, R., Reiberger, T., & Bucsics, T. Elastography-based screening for esophageal varices in patients with

- advanced chronic liver disease. *World Journal of Gastroenterology*, 2019; 25(3), 308-329.
- [23] Fofiu, R., Bende, F., Popescu, A., Şirli, R., Lupuşoru, R., Ghiuchici, A. M., & Sporea, I. Spleen and Liver Stiffness for Predicting High-Risk Varices in Patients with Compensated Liver Cirrhosis. *Ultrasound in Medicine & Biology*, 2021; 47(1), 76–83.
- [24] Colli, A., Gana, J. C., Yap, J., Adams-Webber, T., Rashkovan, N., Ling, S. C., & Casazza, G. Platelet count, spleen length, and platelet count-to-spleen length ratio for the diagnosis of oesophageal varices in people with chronic liver disease or portal vein thrombosis. *Cochrane Database of Systematic Reviews*, 2017; 26;4(4), CD008759.
- [25] Wong, Y. J., Kew, G. Sen, Tan, P. S., Chen, Z., Putera, M., Yip, W. A., ... Lim, S. G. Novel albumin, bilirubin and platelet criteria for the exclusion of high-risk varices in compensated advanced chronic liver disease: A validation study. *Clinics and Research in Hepatology and Gastroenterology*, 2021; 45(6), 101598.
- [26] Kraja, B., Mone, I., Akshija, I., Koçollari, A., Prifti, S., & Burazeri, G. Predictors of esophageal varices and first variceal bleeding in liver cirrhosis patients. *World Journal of Gastroenterology*, 2017; 23(26), 4806–4814.
- [27] Bhattarai S, KR, D., Shrestha G, & Patowary BS. Non-Invasive Predictors of Gastro-Oesophageal Varices - PubMed. *JNMA J Nepal Med Assoc*, 2017; 65(207), 298–303.
- [28] Krige, J., Spence, R. T., Jonas, E., Hoogerboord, M., & Ellsmere, J. A New Recalibrated Four-Category Child–Pugh Score Performs Better than the Original Child–Pugh and MELD Scores in Predicting In-Hospital Mortality in Decompensated Alcoholic Cirrhotic Patients with Acute Variceal Bleeding: a Real-World Cohort Analysis. *World Journal of Surgery*, 2019; 44:1, 44(1), 241–246.
- [29] Hassan, M. A., Abass, A. M., Mirghani, H. O., Osman, E., & Gadour, M. O. E. Noninvasive Prediction of Esophageal Varices Grade (Size) in Sudanese Patients with Periportal Fibrosis. *International Journal of Gastroenterology*, 2018; 2(2), 28–33.
- [30] Mahfuzzaman, M., Hoque, M. N., Ahmed, S., & Bhuiyan, T. M. Correlation between Platelet Count vs Spleen Bipolar Diameter Ratio and Esophageal Varices in Liver Cirrhosis. *BIRDEM Medical Journal*, 2018; 8(2), 159–166.
- [31] Akram, M., Soomro, M. H., & Magsi, M. The Right Liver Lobe Size/Albumin Concentration Ratio in Identifying Esophageal Varices among Patients with Liver Cirrhosis. *Middle East Journal of Digestive Diseases*, 2019; 11(1), 32–37.
- [32] Nouh, M., El-Hamouly, M., Mohamed, S., & Metwally, A. H. Right liver lobe diameter/serum albumin ratio in the prediction of esophageal varices in cirrhotic patients. *Menoufia Medical Journal*, 2019; 32(3), 1113.
- [33] Awad, E. A., Yousry, W. A., Hasan, H. M., & ElGhandour, A. M. Assessment of Right Liver Lobe Size / Serum Albumin Ratio as a New Non-Invasive Predictor for the Presence of Oesophageal Varices in Egyptian Patients with HCV Related Liver Cirrhosis. *The Egyptian Journal of Hospital Medicine*, 2020; 81(5), 2016–2025.
- [34] Kamal, G. M., Zaghloul, A. M., & El Aref, R. Evaluation of the Sabadell noninvasive hepatitis C-related cirrhosis early detection index and right lobe diameter to albumin ratio in the prediction of presence of varices in Egyptian cirrhotic patients. *The Egyptian Journal of Internal Medicine*, 2020; 31(4), 442–450.
- [35] Zhu, Qingjing, Wang, W., Zhao, J., Al-Asbahi, A. A. M., Huang, Y., Du, F., ... Yang, L. Transient Elastography Identifies the Risk of Esophageal Varices and Bleeding in Patients with Hepatitis B Virus-Related Liver Cirrhosis. *Ultrasound*, 2018; 34(3), 141–147.

- [36] Sarkar, D. K., Azam, G., Haque, M., & Rahman, A. Prediction of esophageal varices in liver cirrhosis by transient elastography and aspartate aminotransferase - to - platelet ratio index (APRI). *Bangladesh Critical Care Journal*, 2018; 6(1), 16–21.
- [37] Cheng, F., Cao, H., Liu, J., Jiang, L., Han, H., Zhang, Y., & Guo, D. Meta-analysis of the accuracy of transient elastography in measuring liver stiffness to diagnose esophageal varices in cirrhosis. *Medicine*, 2018; 97(28).

DEFINITIONS, ACRONYMS, ABBREVIATIONS

EVs: Esophageal varices

PH: portal hypertension

PSR: platelet count/ spleen diameter ratio

RLAR: Right liver lobe diameter/ Albumin ratio

LSM: Liver stiffness measurement

TE: Transient elastography

UNDER PEER REVIEW