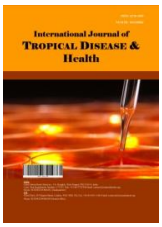

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Assessment of Spleen Stiffness for Prediction of Varices in Patients with Hepatitis C Related Cirrhosis Using Transient Elastography

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Authors' contributions

This work was carried out in collaboration among all authors. Author NETRET designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors SEAH and RAM managed the analyses of the study. Author MAK managed the literature searches. Author BAA also shared in design of the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. All authors read and approved the final manuscript.

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ABSTRACT

Background and Study Aims: Portal hypertension is one of the most important complications of liver cirrhosis. The prevalence of varices among cirrhotic patients is variable. Therefore, endoscopic screening of all patients with liver cirrhosis would result in a large number of unnecessary additional burdens to endoscopic units. Our aim was to assess the diagnostic accuracy of spleen stiffness measured by transient elastography (Fibroscan) for prediction of the presence of varices in patients with hepatitis C related cirrhosis.
Patients and Methods: The study was carried out on 100 patients with HCV-induced cirrhosis and were divided into 2 groups according to presence or absence of varices by Esophago-gastro-duodenoscopy: Group I: patients with HCV-induced cirrhosis with varices; Group II: patients with HCV-induced cirrhosis without varices. Clinical and laboratory parameters, andominal

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ultrasonography, Upper gastrointestinal endoscopy and transient elastography to assess the liver and spleen stiffness were carried out to all studied persons.
Results: Spleen stiffness had significant diagnostic value to differentiate between cirrhotic patients with varices and cirrhotic patients without varices , it had significant diagnostic value in presence of esophageal varices at cut-off (≥46.4 K Pascal) the sensitivity for detection of esophageal varices was 93%, specificity 100%, positive predictive value (PPV) was 80%, negative predictive value (NPV) was 100%; accuracy was 95% and area under the curve was 0.98 denoting that spleen stiffness is a good predictor of esophageal varices.
Conclusion: Spleen stiffness was considered as an excellent predictor of esophageal varices and better than liver stiffness in prediction of esophageal varices presence and had significant diagnostic value to differentiate between the patients with varices and patients without varices at cut off (≥46.4 K Pascal) and it may have a role in variceal grading.

Keywords: Spleen stiffness; fibroscan; esophageal varices.

1. INTRODUCTION

Liver cirrhosis is the final stage of any chronic liver disease and associated with a relevant increase of intra-hepatic resistance to portal blood flow and, as a consequence, portal hypertension. A major complication of portal hypertension is the development of oesophageal varices which may occur in up to 90% of patients with liver cirrhosis. Gastro-oesophageal variceal bleeding is a life-threatening complication of cirrhosis related to portal hypertension [1].

Hepatitis C virus has a high prevalence in Egypt (14.7%) and has many serious effects such as liver cirrhosis [2].

Splenomegaly is a common finding in portal hypertension that should determine changes in the density of spleen because of portal and splenic congestion and/or because of tissue hyperplasia and fibrosis [3].

Recommendations suggest that the presence and degree of portal hypertension must be evaluated in all patients with cirrhosis, but unfortunately, clinical investigation of portal hypertension is mainly invasive and implies either hepatic vein catheterization and hepatic vein pressure gradient (HVPG) measurement or endoscopy for esophageal varices (EV) screening and grading [4].

Transient elastography (fibroscan) is validated for the diagnosis of significant fibrosis and cirrhosis in chronic hepatitis, recurrence of hepatitis after liver transplantation, chronic cholestatic diseases, alcoholic disease and nonalcoholic fatty liver disease. Fibroscan is an excellent tool for the early detection of cirrhosis and for the evaluation of portal hypertension [5].

Spleen elasticity should be closely related to portal venous pressure because histologic changes in the spleen would be directly caused by portal hypertension. These changes might be quantified by elastography, so spleen stiffness can be assessed using transient elastography as its value increasing in the liver disease progresses and portal hypertension [6].The aim of this study was to assess the diagnostic accuracy of spleen stiffness measured by transient elastography (Fibroscan) for prediction of the presence of varices in patients with hepatitis C related cirrhosis.

2. PATIENTS AND METHODS

- This case - control study was carried out on 100 patients with HCV-induced cirrhosis attended the clinics of Hepatology, Gastroenterology and Infectious Diseases, and Internal medicine in Benha University Hospitals, within the period between September 2018 to September 2019 and were divided according to presence or absence of varices by Esophago-gastro-duodenoscopy into group I: patients with HCV-induced cirrhosis with varices and group II: patients with HCV-induced cirrhosis without varices.
- Liver cirrhosis was diagnosed by clinical, laboratory and abdominal ultrasonography.
- Patients bellow 18 years and Patients with BMI > 35, history of upper endoscopy intervention, marked ascites, HCC or other malignancy, other causes of liver disease and liver transplantation were excluded from the study.

2.1 Methodology

- The enrolled patients were subjected to full history taking and thorough clinical examination.
- Severity of liver disease was assessed by MELD score (Model for End Stage Liver Disease) and Child-Pugh scores.
- Laboratory investigations included: complete blood count (CBC), liver and kidney profile tests Hepatitis C Virus (HCV) and Hepatitis B Virus (HBV)) markers.

2.2 Blood Sampling and Biochemical Assays

- Fasting venous blood samples (5ml) were collected by well-trained laboratory technicians under complete aseptic conditions then distributed as follows:

a- 1 mL of whole blood was collected in an EDTA vacutainer and mixed gently for complete blood count measurement that was performed by automated hematology system (Sysmex XE 5000; Sysmex America, Inc., Mundelein, IL, USA).
b- 4 mL of venous blood samples were collected in plain test tubes containing no anticoagulant, allowed to clot for 30 mins at room temperature, then centrifuged for 15 mins at 1000× g. The serum was removed, aliquoted then stored at ≤−20°C until assayed and thawed immediately before the measurement, the separated serum was used for the following assays:

- Biochemical tests using Beckman CX4 chemistry analyzer (NY, USA, supplied by the Eastern Co. For Eng, Egypt), these tests including:

• Fasting blood glucose level.
• Liver function tests: Serum albumin, total and direct bilirubin, Liver enzymes including aspartate aminotransferase (AST), alanine aminotransferase (ALT) and gamma-glutamyl transpeptidase (GGT).
• Kidney function tests: including serum creatinine.
- Viral infection status (HCV-Ab and HBsAg) were assayed using an enzyme immunoassay (EIA) Kit (Abbott, Axyam USA).
-Quantitative PCR for HCV RNA.

2.3 Calculation of Results

The duplicate readings for standard and samples was averaged and subtracted the average zero standard optical density. A standard curve was created by plotting the mean OD value on the Yaxis against the concentration on the X- axis and a fit curve was drawn by some professional software and a best fitting equation of standard curve was calculated using OD values and concentrations of standard samples.

- Radiological assessment by abdominal ultrasonography.
- Transient Elastography (Fibroscan®) on liver and spleen:

Fibroscan® (Echosens, Paris, France) was used for liver stiffness and spleen stiffness measurements. Fibroscan® consists of a castor-mounted frame, 135 cm high by 68 cm wide and 61 cm deep. It equipped with a screen and a shelf supporting a keyboard with a built-in mouse. The entire unit weighs approximately 46 kg. It also has a CD drive and a USB type connection.

-The probe connected to the frame by a 1.5 m long cable equipped with a specific connector. It equipped with a measurement activation button (On side of the handle).
- The unit controlled by a software program that was used to conduct the stiffness measurement examinations and manage patient data. This software was loaded automatically when the unit switched on. The patient placed on an examination bed in the supine position, with his right arm at maximum abduction for liver examination and his left arm at maximum abduction for spleen examination.
- When a suitable measurement zone had been found, the probe was held perpendicular to the skin surface and the pressure applied increased progressively until the pressure indicator was in the green zone. The measurement was activated by pressing the button of the probe. Ten successful acquisitions were performed on each patient. Success rate was calculated as the ratio of the number of successful acquisitions over the total number of acquisitions.

- Endoscopic evaluation: All included patients were underwent Esophago-gastro-duodenoscopy (EGD): using fiberoptic endoscope (EG 530 WR, Fujinon).

Endoscopy was used to assess the presence and degree of esophageal varices according to Reiberger, et al., 2017 [7].

Esophageal varices (EV) should be graded as absent, small (<5mm of diameter), or large (≥5 mm). The presence of red spots should be indicated for risk stratification.

• Gastric varices (GV) according to Sarin classification (Neil and David, 2013) [8].and portal hypertensive gastropathy (PHG).

2.4 Statistical Analysis

The data were coded, entered and processed on computer using SPSS (version 18). The results were represented in tabular and diagrammatic forms then interpreted. Mean, standard deviation, range, frequency, and percentage were use as descriptive statistics. The following test was done: Chi-Square testX^2 was used to test the association variables for categorical data. Student'st-test was used to assess the statistical significance of the difference between two population means in a study involving independent samples. Also non parametric tests were used for abnormaly distributed data.

ROC curve was used to determine cut off value, The following statistics can be defined: Sensitivity: probability that a test result will be positive when the disease is present (true positive rate, expressed as a percentage), Specificity: probability that a test result will be negative when the disease is not present (true negative rate, expressed as a percentage).

3. RESULTS

In the present work, the mean age was 47.71 ± 6.850 in patients with esophageal varices compared to 46.10 ± 9.830 in patients without esophageal varices with no significant difference. In the eighty (80) patients with varices, 44 (55.0%) were male while in the twenty (20) patients without varices, 12 (60.0 %) were male with no statistically significant relation between gender and esophageal varices presence, demographic characteristics Table 1.

Regarding the laboratory investigations hemoglobin, platelets and s. albumin were lower in group I than in group II, while INR and s. bilirubin were higher in group I than in group II with statistical significant difference Table 2.

Cirrhosis was present in 100% in both groups; but ascites, spleen size and portal vein diameter were higher in group I and this was statisticaly significant between the two groups. Table 3.

Fibroscan result including liver and spleen stiffness was higher in Group I than Group II with statistical significance. P<0.001 in both, Table 4. Portal hypertensive gastropathy was more predominant in group I than group II with significant difference, while esophageal and gastric varices were present only in group I Table 5. Most of patients with varices in Group I had advanced grades of varices, 43.75% of them had OV grade III, 38.75% had OV grade II and only 17.5% of them had OV grade I Table 6.

Table 1. Demographic characteristics of the studied patients

Variables	Group I (patients with varices) N = 80(80%)		Group II (Patients without varices) N= 20(20%)		P-value
Age Range	33 - 66		25- 65		
Mean±SD(years)	47.71 ± 6.850		46.10 ± 9.830		0.393
BMI Range	22-34		24-33		
Mean±SD	28.80 ± 2.901		28.50 ± 2.351		0.669
Gender	**N**	**%**	**N**	**%**	**P-value**
Male	44	55.0	12	60.0	0.687
Female	36	45.0	8	40.0	
Residence					
Urban	28	35.0	6	30.0	0.654
Rural	52	65.0	14	70.0	
Occupation					
Farmer	52	65.0	14	70.0	0.654
Non-farmer	28	35.0	6	30.0	
Smoking	28	35.0	11	55.0	0.160
Alcohol intake	0	0.0	0	0.0	

Table 2. Laboratory investigations among studied patients

Variable	Group I (patients with varices) N = 80(80%)	Group II (Patients without varices) N= 20(20%)	P value
	Mean ±SD	Mean ±SD	
Hb (13-17 g/dl)	9.735 ±1.1115	11.655 ± 1.3461	0.000*
WBCs (4 -11x10^3 cell/cmm)	5.219±1.5341	5.045± 1.3213	0.643
Platelets (150 – 450x10^3cell/cmm)	77.050± 14.4291	139.700±28.9266	0.000*
ALT (12-33U/L)	38.40±22.49	43.80±27.2486	0.360
AST (12-33U/L)	59.96±21.49	51.40±37.80	0.291
INR (1)	2.61±0.839	1.45±0.601	0.000*
Creatinine(0.7-1.2mg/dl)	1.177±0.356	1.200±0.238	0. 790
Total Bilirubin(<1mg/dl)	3.08 ± 1.758	1.98 ± 1.717	0.013*
Serum Albumin Level (3.5-5g/dl)	2.98 ± .527	3.32 ± .611	0.017*

**= significant Hb: hemoglobin; WBCs: white blood cells; * = significant; ALT: alanine transaminase; AST: aspartate transaminase; PT: prothrombin time; INR: international normalization ratio*

Table 3. Ultrasonographic findings of the studied patients

Variable	Group I (patients with varices) N = 80(80%)		Group II (Patients without varices) N= 20(20%)		P value
	Mean ±SD		Mean ±SD		
Spleen size(<13cm)	18.463±1.50		14.325± 1.1787		0.000*
Portal vein diameter(<13mm)	16.90± 1.5476		12.947±1.87		0.000*
Cirrhosis	80	100.0%	20	100.0%	
Ascites	37	46.3%	4	20.0%	0.033*

** = significant*

Table 4. Liver stiffness and spleen stiffness by fibroscan of the studied patients

Variable	Group I (patients with varices) N = 80(80%)	Group II (Patients without varices) N= 20(20%)	P value
	Mean ±SD	Mean ±SD	
liver stiffness (kpa)	27.18 ±4.968	19.75 ± 3.024	<0.001*
spleen stiffness (kPa)	56.03±6.119	32.70±4.68	<0.001*

** = significant; kPa: kilopascals*

Table 5. Endoscopic findings of the studied patients

Variable		Group I (patients with varices) N = 80(80%)		Group II (Patients without varices) N= 20(20%)		P value
		N	%	N	%	
EGD (Esophageal varices)	present	80	100.0	0	0	0.000*
EGD (Gastric varices)	present	17	21.2	0	0	0.024*
PHG	present	59	73.8	12	60	0.04*

** = significant; EGD: Esophago-gastro-duodenoscopy; PHG: Portal hypertensive gastropathy*

Table 6. Oesophageal varices grades in group I

	Group I (patients with Varices) N = 80	
	N	**%**
Grade I	14	17.5
Grade II	31	38.75
Grade III	35	43.75

Table 7. Diagnostic performance of spleen stiffness and liver stiffness as markers for esophageal varices

Test	Cutoff	Sensitivit	Specificity %	PPV%	NPV%	AUC	P value
Spleen stiffness (kp a)	46.4	93.8	100	80	100	.98	0.000*
Liver stiffness (kpa)	28	63.8	100	100	71.8	.90	0.000

Table 8. Association between spleen stiffness and presence of GV in group I

	Present GV N =17	Absent GV N = 63	P value
	Mean ±SD	Mean ±SD	
Fibroscan(Spleen Stiffness) (kPa)	60.76 ± 5.618	54.75± 5.634	0.000*

** = significant; kPa: kilopascals*

Table 9. The degree of agreement between spleen stiffness, liver stiffness and varices

Variables		Group I (patients with varices) N = 80(80%)	Group II (Patients without varices) N= 20(20%)	P - value	Kappa coefficient
Spleen Stiffness (46.4 kPa)	Patients with varices	75	0		
	Patients without varices	5	20	0.000	0.85
Liver Stiffness (28 kPa)	Patients with varices	34	0		
	Patients without varices	46	20	0.000	0.22

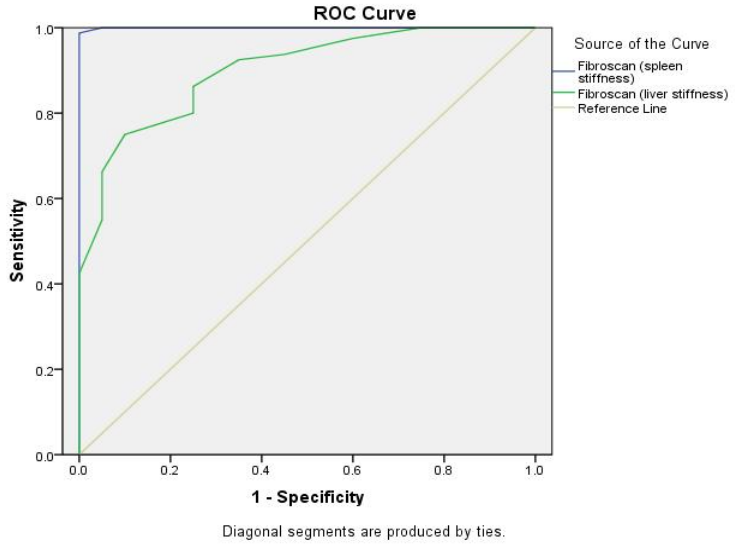

Fig. 1. Receiver operative curve analysis of spleen stiffness and liver stiffness

For spleen stiffness, at cutoff value of 46.4 kPa; the sensitivity for detection of esophageal varices was 93%, specificity 100%, positive predictive value (PPV) was 80%, negative predictive value (NPV) was 100% and area under the curve was 0.98 denoting that spleen stiffness is an excellent predictor of esophageal varices. For liver stiffness, at cutoff value of 28 kPa; the sensitivity for detection of esophageal varices was 63.8%, specificity 100%, positive predictive value (PPV) was 71.8%, negative predictive value (NPV) was 100% and area under the curve was 0.90 denoting that liver stiffness is a good predictor of esophageal varices. However, Spleen stiffness was considered as an excellent predictor of esophageal varices and better than liver stiffness Table 7 and Fig. 1.

Agreement between the different studied test methods was measured by the kappa coefficient. The value of kappa was interpreted as follows: Kappa < 0.2 = poor agreement; Kappa (0.21-0.4) = fair agreement; Kappa (0.41-0.6) = moderate agreement; Kappa (0.61-0.8) = good agreement; kappa (0.81-0.99) = excellent agreement. There was an excellent agreement between spleen stiffness and varices while poor agreement btween liver stiffness and varices Table 9.

4. DISCUSSION

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. As portal hypertension increases spleen stiffness [9] so, this study aimed to assess the measurements of spleen stiffness by transient elastography (Fibroscan®) as a noninvasive tool for prediction of the presence of esophageal varices in patients with liver cirrhosis.

As regard spleen size, the current study disclosed that it was statistically significantly higher in patients with varices (18.463±1.50) than those without varices (14.325± 1.1787). This result was matched with the results of Kazemi et al., who found that splenomegaly was more in patients with varices than patients without varices [10].

The current study showed a higher portal vein diameter in patients with varices (16.90± 1.5476) than those without varices (12.947±1.87). These results agreed with the study of Schepis et al., who showed statistical significant difference as regard portal vein diameter between patients with varices (13.82 + 2.11 mm) than those without varices (12.32+ 2.04 mm) (p value=0.0002) with cut off value >13mm for prediction of varices presence [11].

In the present study, ascites was predominant in cases with varices (46.3%) when compared to cases without varices (20%) (P value=0.033). These results were in agreement with Sarangapani et al., who reported that; ascites was significantly increased in cases with varices when compared to cases without varices (60.5% vs 25.5% respectively) [12].

In the present study, portal hypertensive gastropathy was predominant in cases with varices(73.8%) when compared to cases without varices(60%) (P value=0.04). These results are comparable to those reported by Matei et al., who reported that, there was significant increase of portal hypertensive gastropathy in cases with varices (52.3%) when compared to cases without varices (19.7%) [13].

In the current study, the liver stiffness measurement was significantly higher in patients with gastro- esophageal varices than those with no varices; at cut off (≥28 K Pascal) the diagnostic value of liver stiffness was found in prediction of esophageal varices presence with sensitivity (63.4%), specificity (100%), positive predictive value (PPV: 71.8%), negative predictive value (NPV: 100%).

This came in agreement with Saad et at., who reported that liver stiffness measurement was significantly higher in patients with gastro-esophageal varices and at the best cut off value 29.7 K Pascal, LSM sensitivity was 95% and 67% specificity [14].

In the current study, the spleen stiffness measurement was significantly higher in patients with esophageal varices than those with no varices.

In agreement with these results, Colecchia et al., measured spleen stiffness in 100 consecutive patients with hepatitis C virus-induced cirrhosis and found that the spleen stiffness can be used for noninvasive assessment and monitoring of portal hypertension and to detect esophageal varices in cirrhotic patients with HCV [6].

In the present study, ROC curve analysis of spleen stiffness for prediction of esophageal varices presence revealed that, at a cut off value

of (≥46.4 K Pascal); the sensitivity for detection of varices was (93.8%), specificity (100%), positive predictive value (PPV: 80%), negative predictive value (NPV: 100%) and area under curve was 98 denoting excellent predictive value of spleen stiffness in prediction of varices. Also, the spleen stiffness measurement was found higher in patients with advanced grades of varices with relatively high diagnostic value in prediction the grades of esophageal varices.

This finding was nearly similar to the study of 200 patients done by Sharma et al., who found the spleen stiffness at cut off (≥40.8 K Pascal) with sensitivity (94%), specificity (76%), positive predictive value (PPV:91%), negative predictive value (NPV:84%), area under cure 91 and diagnostic accuracy of (86%) in prediction of esophageal varices. Also, it was significantly higher in patients who had large varices [15].

In agreement with these results, Stefanescu et al., found a higher spleen stiffness value in patients with esophageal varices, as compared with those without. The best cut-off to discriminate between them was (47.4 kPa), which showed a good accuracy and a high PPV (93.4%) [3].

Also, Liu et al., found that the fibroscan appeared to be a clinically valuable non-invasive method to assess portal hypertension in cirrhotic patients. Spleen stiffness measurements correlated with portal hypertension with optimal cut-off level of spleen stiffness (44.5 kPa) (sensitivity: 88%; specificity: 68%) estimated prevalence of esophageal varices [16].

This result was not similar to Singh et al., who found (based on a meta-analysis study) the current techniques for measuring spleen stiffness are limited in their accuracy of esophageal varices diagnosis with pooled sensitivity for detection of any esophageal varices and pooled specificity. Based on these data, spleen stiffness is not yet accurate enough to replace upper endoscopy for esophageal varices assessment [17].

This contradiction to these results may be explained by the size of the sample tested being of more patients in their study with differences in elastography techniques (including transient elastography, acoustic radiation force impulse imaging, magnetic resonance elastography, real-time tissue elastography and virtual touch tissue quantification), study locations (Asian and Western countries) and the etiology of the liver disease (due to hepatitis B and C viruses and other causes).

In this study, ROC curve analysis of SS has a high NPV (100%), PPV (80%), AUC (98) and sensitivity (93.8%) for prediction of OV presence, this was compared to liver stiffness which had NPV (100%), PPV (71.8%), AUC (90) and sensitivity (63.8%). So SS was more sensitive, accurate and specific than LS and that was in accordance with Takuma et al., [18].

5. CONCLUSION

The spleen stiffness and liver stiffness measured by fibroscan were increased in patients which had esophageal varices than those without esophageal varices, but spleen stiffness is superior to liver stiffness for the prediction of esophageal varices in patients with liver cirrhosis. The spleen stiffness can predict the presence of esophageal varices at cut off (≥46.4 K Pascal). The spleen stiffness had a highly significant correlation with different noninvasive tools (negative correlation with Platelets count/Spleen size ratio and positive correlation with spleen size, portal vein diameter) used in diagnosis of esophageal varices.

CONSENT

All authors declared that written informed consent was obtained from the patients for publication of this paper.

ETHICAL APPROVAL

Ethical clearance was obtained from Beni-seuf general Hospital's ethics committee.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Bosch J, Abraldes JG, Fernández M, García-Pagán JC. Hepatic endothelial dysfunction and abnormal angiogenesis: New targets in the treatment of portal hypertension. J Hepatol. 2010;53(3):558–67.
2. Elgharably A, Gomaa AI, Crossey MME, Norsworthy PJ, Waked I, Taylor-Robinson

SD. Hepatitis C in Egypt–past, present, and future. Int J Gen Med. 2017;10:1.

3. Stefanescu H, Grigorescu M, Lupsor M, Maniu A, Crisan D, Procopet B, et al. A new and simple algorithm for the noninvasive assessment of esophageal varices in cirrhotic patients using serum fibrosis markers and transient elastography. J Gastrointest Liver Dis. 2011;20(1).
4. Thabut D, D'Amico G, Tan P, De Franchis R, Fabricius S, Lebrec D, et al. Diagnostic performance of Baveno II/III and Baveno IV criteria in cirrhotic patients with gastrointestinal bleeding. Analysis of the F7 liver-1288 study population. In: AASLD meeting. 2008;625A-625A.
5. De LéDinghen V, Vergniol J. Transient elastography for the diagnosis of liver fibrosis. Expert Rev Med Devices. 2010;7(6):811–23.
6. Colecchia A, Montrone L, Scaioli E, Bacchi–Reggiani ML, Colli A, Casazza G, et al. Measurement of spleen stiffness to evaluate portal hypertension and the presence of esophageal varices in patients with HCV-related cirrhosis. Gastroenterology. 2012;143(3): 646–54.
7. Reiberger T, Püspök A, Schoder M, Baumann-Durchschein F, Bucsics T, Datz C. Austrian consensus guidelines on the management and treatment of portal hypertension (Billroth III). Wien Klin Wochenschr. 2017;129: 135–158.
8. Rajoriya N, David A Gorard. Endoscopic management of oesophageal and gastric varices, endoscopy of GI tract, somchai amornyotin, IntechOpen; 2013.

   DOI: 10.5772/52524

   Available:https://www.intechopen.com/books/endoscopy-of-gi-tract/endoscopic-management-of-oesophageal-and-gastric-varices
9. Calvaruso V, Bronte F, Conte E, Simone F, Craxì A, Di Marco V. Modified spleen stiffness measurement by transient elastography is associated with presence of large oesophageal varices in patients with compensated hepatitis C virus cirrhosis. J Viral Hepat. 2013;20(12): 867–74.
10. Kazemi F, Kettaneh A, N'kontchou G, Pinto E, Ganne-Carrie N, Trinchet J-C, et al. Liver stiffness measurement selects patients with cirrhosis at risk of bearing large oesophageal varices. J Hepatol. 2006;45(2):230–5.
11. Schepis F, Cammà C, Niceforo D, Magnano A, Pallio S, Cinquegrani M, et al. Which patients with cirrhosis should undergo endoscopic screening for esophageal varices detection? Hepatology. 2001;33(2):333–8.
12. Sarangapani A, Shanmugam C, Kalyanasundaram M, Rangachari B, Thangavelu P, Subbarayan JK. Noninvasive prediction of large esophageal varices in chronic liver disease patients. Saudi J Gastroenterol Off J Saudi Gastroenterol Assoc. 2010;16(1):38.
13. Matei D, Groza I, Furnea B, Puie L, Levi C, Chiru A, et al. Predictors of variceal or nonvariceal source of upper gastrointestinal bleeding. An etiology predictive score established and validated in a tertiary referral center. J Gastrointest Liver Dis. 2013;22(4).
14. Saad Y, Said M, Idris MO, Rabee A, Zakaria S. Liver stiffness measurement by fibroscan predicts the presence and size of esophageal varices in egyptian patients with HCV related liver cirrhosis. J Clin diagnostic Res JCDR. 2013;7(10):2253.
15. Sharma P, Kirnake V, Tyagi P, Bansal N, Singla V, Kumar A, et al. Spleen stiffness in patients with cirrhosis in predicting esophageal varices. Am J Gastroenterol. 2013;108(7):1101.
16. Liu F, Li TH, Han T, Xiang HL, Zhang HS. Non-invasive assessment of portal hypertension in patients with liver cirrhosis using FibroScan transient elastography. Zhonghua gan zang bing za zhi= Zhonghua ganzangbing zazhi= Chinese J Hepatol. 2013;21(11):840–4.
17. Singh S, Eaton JE, Murad MH, Tanaka H, Iijima H, Talwalkar JA. Accuracy of spleen stiffness measurement in detection of esophageal varices in patients with chronic liver disease: systematic review and meta-

analysis. Clin Gastroenterol Hepatol. 2014;12(6):935–45.

18. Takuma Y, Nouso K, Morimoto Y, Tomokuni J, Sahara A, Toshikuni N, et al. Measurement of spleen stiffness by acoustic radiation force impulse imaging identifies cirrhotic patients with esophageal varices. Gastroenterology. 2013;144(1): 92–101.

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