

## Role of Liver and Spleen Stiffness in Predicting the Degree and Bleeding Risk of Esophageal Varices in Cirrhotic Patients

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**Abstract:**

**Background:** Bleeding esophageal varices (BEV) is a life-threatening complications of liver cirrhosis resulting from portal hypertension. **Aim:** The aim of our study was to investigate the role of spleen and liver stiffness in predicting the degree and bleeding risk of esophageal varices in cirrhotic patients. **Patients and methods:** 50 patients with established liver cirrhosis were enrolled in this study. All patients were assessed by history taking, clinical examination, laboratory investigations, Child-Paugh score calculation, pelvi-abdominal ultrasound, upper gastrointestinal endoscopy, transient elastography for measurement of LS and SS. **Results:** Endoscopic examination revealed that 18 (36%) have no esophageal varices (no EVs), 25 (50%) have small sized EVs (EVs I) and 7 (14%) have medium sized EVs (EVs II). There was a statistical significant difference between groups as regards platelet count, serum bilirubin, serum albumin, INR, Child score, splenomegaly, LS and SS between variceal and non variceal group and among patients with

different grades of varices ( $p < 0.05$ ). Splenic stiffness measurement (SSM) is better than liver stiffness measurement (LSM) for predicting presence and degree of EVs in cirrhotic patients. **Conclusion:** LS and SS are valuable non-invasive parameters for prediction of EVs in patients with liver cirrhosis. SS measurement is considered to be an optimal method to use in clinical practice, for screening of cirrhotic patients for EVs and diagnosing high-risk EVs.

**Key words:** Bleeding ; esophageal varices; Liver stiffness; Spleen stiffness

**Introduction:**

Esophageal varix is one of the serious complications of liver cirrhosis resulting from portal hypertension. Given the high

prevalence of varices and the significant mortality rate associated with variceal hemorrhage, early diagnosis of clinically

significant portal hypertension (10 mmHg) and varices is of paramount importance in the management of compensated cirrhosis and in the prevention of liver related morbidity and mortality (1).

Recent guidelines recommend a screening upper gastrointestinal endoscopy in all cirrhotic patients and call for primary prophylaxis against variceal hemorrhage if indicated. In addition, measurement of hepatic venous pressure gradient (HVPG) is a standard method to evaluate portal hypertension. However, both methods are invasive, Therefore, noninvasive and accurate methods for predicting the presence and severity of varices are further needed (2).

Portal hypertension-related splenomegaly is frequently accompanied by patients with cirrhosis due to portal venous congestion and hyperplasia of splenic tissue, and its usefulness for diagnosis of portal hypertension has been studied. Some studies have focused on ultrasound-based measurement of liver or spleen stiffness (LS or SS); LS reflects the degree of hepatic fibrosis and resultant portal hypertension, and SS is reflective of portal hypertension related changes in the spleen, including splenomegaly (3).

Studies using transient elastography to measure LS have reported acceptable diagnostic performance in grading hepatic fibrosis and in detecting clinically significant portal hypertension. Measurement of SS using transient elastography has also accurately predicted both the presence of varices and the degree of portal hypertension (4).

The aim of our study is to investigate the role of spleen and liver stiffness in predicting the degree and bleeding risk of esophageal varices in cirrhotic patients.

## **Patients and methods**

### **Type of the study:**

This study is a cross-sectional study.

**Patients:** 50 patients with established liver cirrhosis were enrolled in this study, they presented to internal medicine department at Benha University Hospital, and National liver institute, Menoufia University in the period from June 2019 to September 2021. Outpatients or in-patients included in the study gave their written informed consent to participate in the study.

The study was approved by the local ethics committee of faculty of medicine, Benha University in accordance with the declaration of Helsinki. Oral and written

consent were taken from all patients who participated in this study.

They were chosen according to the following inclusion and exclusion criteria.

**Inclusion criteria:** Patients with established liver cirrhosis diagnosed by clinical manifestation, biochemical investigations and ultrasonographic finding.

**Exclusion criteria:** Patients less than 18 years old, patients with ongoing gastrointestinal hemorrhage, patients with hepatocellular carcinoma (HCC) on the basis of ultrasonography, alpha-fetoprotein level  $\geq 400$  microgram /L and confirmed diagnosis by triphasic spiral CT abdomen and lastly patients with previous or current treatment for portal hypertension in the form of (Beta blocker therapy, or Trans jugular intra-hepatic portosystemic shunt ) were excluded.

#### **Methods:**

For all studied cases after giving their informed consent, they were subjected to the following:

#### **I- Proper history taking:**

#### **II- Clinical examination**

#### **III- Laboratory investigations:**

- Complete blood count

- Liver biochemical profile (Aspartate aminotransferase [AST], alanine aminotransferase [ALT], total and direct bilirubin& serum albumin)

- Prothrombin time& INR.

- Viral markers.

- 1- HBs Ag: by using third generation enzyme – linked immunosorbent assay technique (ELISA)

- 2- Anti-HCV Ab: by using third generation enzyme – linked immunosorbent assay technique (ELISA).

- serum  $\alpha$ -feto protein (AFP).

#### **IV- Conventional abdominal U/S:**

Abdominal ultrasonography was done after an overnight fasting for all patients.

**Liver:** was examined for signs of cirrhosis, portal vein patency, hepatic focal lesions.

**Spleen:** was examined for splenomegaly

4. Child-Paugh score was calculated

The Child-Pugh scoring system was designed to predict mortality in cirrhosis patients. Originally conceptualized by Child and Turcotte in 1964 to guide the selection of patients who would benefit from elective surgery for portal decompression, it broke

down patients into three categories: A - good hepatic function, B - moderately impaired hepatic function, and C - advanced hepatic dysfunction. Their original scoring system used five clinical and laboratory criteria to categorize patients: serum bilirubin, serum albumin, ascites, neurological disorder, and clinical nutrition status. (5).

#### 5. Transient Elastography:

For measurement of liver stiffness (LS) and splenic stiffness (SS).

#### 6. Upper gastrointestinal endoscopy:

To assess presence and severity of esophageal varices (EVs), varices were graded according to their size as follow (6);

- **Small sized:** small, straight varices
- **Medium sized:** enlarged tortous varices occupying less than one third of the lumen.
- **Large sized:** large coil shaped varices occupying less than one third of the lumen.

#### Study groups

Patients were divided according to endoscopic examination revealed:

- 18 (36%) have no esophageal varices (no EVs),
- 25 (50%) have small sized EVs (EVs I)

- 7 (14%) have medium sized EVs (EVs II).

#### Data management:

The clinical data were recorded on a report form. These data were tabulated and analyzed using the computer program SPSS (Statistical package for social science) version 25 to obtain descriptive data. Descriptive statistics were calculated for the data in the form of mean and standard deviation ( $SD\pm$ ) for quantitative data, Frequency and distribution for qualitative data. In the statistical comparison between the different groups, the significance of difference was tested using student's t-test, Chi square test, Fisher exact test and Correlation Study. Evaluation of diagnostic performance was done using Diagnostic sensitivity, Diagnostic specificity, Predictive value for a positive test (PPV), Predictive value for a negative test (NPV), Diagnostic efficacy, Receiver-operating characteristic (ROC) curve analysis. The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant as the following: Non-significant: P value > 0.05, significant : P value < 0.05, Highly significant : P value < 0.01.

## Results:

Study had begun by patient evaluation in form of clinical examination and laboratory investigation for 50 patients with liver cirrhosis. Of these 50 patients, 36 (72%) are males and 14 (28%) are females. The mean age ( $\pm$  SD) was  $53.1 \pm 6$  years. Of these 50 patients, 43(86%) were Child-Pugh class A, 7(14%) were child B. The mean  $LS \pm SD$  was  $31.8 \pm 10.3$  kilo pascal (kPa), while the mean  $SS \pm SD$  was  $59.6 \pm 13.5$  kPa. About 46 patients (92%) have splenomegaly. Endoscopic examination revealed that 18 (36%) have no esophageal varices (no EVs), 25 (50%) have small sized EVs (EVs I) and 7 (14%) have medium sized EVs (EVs II).

### Comparison of laboratory data, Child-Pugh Score, Splenomegaly, LS and SS among No EVs, EVs I and EVs II groups:

The age and sex distribution among the studied groups was statistically non-significant (p value  $>0.05$ ).

As regards laboratory data, serum bilirubin, albumin, INR and platelet count were statistically significant among the three groups (p1, p3, p4 values  $< 0.05$ ). The mean  $\pm$  SD serum bilirubin was  $0.7 \pm 0.1$  mg /dl among no EVs group, and  $1 \pm 0.1$  mg /dl among

EVs I, group, and  $1.4 \pm 0.4$  mg/dl among EVs II group, the difference was highly significant (p  $< 0.001$ ). The mean  $\pm$  SD serum albumin was  $4.2 \pm 0.2$  g/dl among no EVs group, and  $3.5 \pm 0.4$  g/dl among EVs I group, and  $2.9 \pm 0.9$  g/dl among EVs II group, the difference was highly significant (p value  $< 0.001$ ). The mean  $\pm$  SD INR was  $1 \pm 0.03$  among no EVs group, and  $1.2 \pm 0.1$  among EVs I group,  $1.4 \pm 0.1$  among EVs II group, the difference was highly significant (p value  $< 0.001$ ). The mean  $\pm$  SD platelet count was  $112.2 \pm 27.9 \times 10^9$  /L among no EVs group and  $100.1 \pm 18.7 \times 10^9$  among EVs I, and  $74.4 \pm 23.9 \times 10^9$  among EVs II group, the difference was statistically significant (p value  $< 0.05$ ). All 18 patients with no EVs (100%) were child A, of these 25 patients with EVs I, 22 (92%) were child A, 3 (8%) were child B, and of these 7 patients with EVs II, 3 (71.4%) were child A, 4 (28.6%) were child B. The difference was statistically significant as (p1, p2, p3, p4 value  $< 0.05$ ). As regard splenomegaly, of these 18 patients with no EVs, 14(77.8%) have splenomegaly, all these 25 patients with EVs I (100%) have splenomegaly, all these 7 patients with EVs II (100%) have splenomegaly. The difference was statistically significant (p1, p2 value  $< 0.05$ ). The mean  $LS \pm SD$  among no EVs group was

22.7±5.3 kPa, while the mean LS±SD among EVs I group was 32.9 ±7.0, kPa and the mean LS±SD among EVs II group was 51.4±7.9 kPa.

The difference was statistically significant (p1, p2, p3, p4 value < 0.05). The mean SS±SD among no EVs group was 45.4±8.1 kPa, the mean SS±SD among EVs I group was 65.5±8.2 kPa and the mean SS±SD among EVs II group was 74.9±0.4 kPa.

The difference was statistically significant (p1, p3, p4 value < 0.05). The mean LS±SD among patients with no splenomegaly was 21.7 ±3.6 kPa, while the mean LS±SD among patients with splenomegaly was 32.7 ±10.3 kPa, the difference was statistically significant (P value < 0.05).

The mean SS±SD among patients with no splenomegaly was 34.4 ±6.8 kPa, while the mean SS±SD among patients with splenomegaly was 61.8±11.5 kPa, the difference was statistically highly significant (P value < 0.01). (p1, comparison between no EVs, EVs I, EVs II; p2, comparison between No EVs and EVs I; p3, comparison between No EVs and EVs II; p4, comparison between EVs I and EVs II). table 1,2 and figure 1

**Validity of liver, spleen stiffness and child score for detecting presence of EVs:** LSM cut-off for predicting EVs was 28.2 KPa with AUC of 0.905, sensitivity of 75%, specificity of 83.3%, PPV of 88.9%, NPV of 65.2% and accuracy of 78% while, SSM cut-off for predicting EVs was 55.5 KPa with AUC of 0.970, sensitivity of 87.5 %, specificity of 94.4%, PPV of 96.5 %, NPV of 80.9% and accuracy of 54%. Child score cut-off for predicting EVs was 6 with AUC of 0.606, sensitivity of 40.6%, specificity of 77.8%, PPV of 76.5%, NPV of 42.4% and accuracy of 54%. (AUC, area under ROC curve; PPV, positive predictive value; NPV, negative predictive value). table 3 and figure 2.

**Validity of liver and spleen stiffness discrimination between cirrhotic patients with EVs I and EVs II:** LSM cut-offs for discrimination between patients with EVs I and EV II was 41.5 KPa with AUC of 0.911, sensitivity of 85.5%, specificity of 80%, PPV of 54.5%, NPV of 95.2% and accuracy of 81.2%. SSM cut-offs for discrimination between patients EVs I and EVs II was 74.5 KPa with AUC of 0.929, sensitivity of 85.7%, specificity of 88%, PPV of 66.7%, NPV of 95.6% and accuracy of 87.5%. Child score cut-off for predicting

EVs was 6 with AUC of 0.634, sensitivity of 57.1%, specificity of 64%, PPV of 30.8%, NPV of 84.2% and accuracy of 62.5%. table 4 and figure 3 Our study demonstrated that SSM is better than LSM and child score for predicting presence of EVs as regard AUC, sensitivity, specificity, PPV, NPV. Logistic regression analysis was conducted for prediction of EVs susceptibility using age, AST, INR, platelet count, Child score, LS, SS as confounders. Lower platelet count, higher (Child score, LS and SS) were associated significantly with EVs susceptibility in Univariable analysis. However, considering significant

confounders into multivariable analysis revealed that only higher Child score, LS and SS were considered as risk predictors for EVs susceptibility.

Ordinal regression analysis was conducted for prediction of higher EVs grade using age, gender, INR, platelet count, Child score, LS, SS as confounders. Lower platelet count, higher Child score, LS and SS were associated significantly with EVs susceptibility in Univariable analysis. However, considering significant confounders into multivariable analysis revealed that only higher Child score, LS, SS were considered as risk predictors for higher risk varices.

**Table 1:** Comparison of laboratory data among No EVs, EVs I and EVs II groups:

|                                      |                      | No EVs<br>n=18 |      | EVs I<br>=small sized<br>N=25 |      | EVs II<br>= medium<br>sized<br>N=7 |      | <i>P1</i>    | <i>p2</i>    | <i>p3</i>    | <i>p4</i>    |
|--------------------------------------|----------------------|----------------|------|-------------------------------|------|------------------------------------|------|--------------|--------------|--------------|--------------|
| <b>Total Bilirubin (mg/dL)</b>       | <b>mean± SD</b>      | 0.7            | 0.1  | 1                             | 0.1  | 1.4                                | 0.4  | <0.001       | <0.001       | <0.001       | <0.001       |
| <b>Direct Bilirubin (mg/dL)</b>      | <b>mean± SD</b>      | 0.3            | 0.1  | 0.5                           | 0.1  | 0.7                                | 0.2  | <0.001       | <0.001       | <0.001       | <0.001       |
| <b>Albumin (g/dL)</b>                | <b>mean± SD</b>      | 4.2            | 0.2  | 3.7                           | 0.3  | 2.9                                | 0.2  | <0.001       | <0.001       | <0.001       | <0.001       |
| <b>AST (U/L)</b>                     | <b>mean± SD</b>      | 59.4           | 16.4 | 66.6                          | 21.1 | 53.9                               | 17.5 | 0.575        | 0.525        | 0.308        | 0.545        |
| <b>ALT (U/L)</b>                     | <b>mean± SD</b>      | 52.1           | 14.1 | 55.4                          | 16.9 | 48.4                               | 15.8 | 0.283        | 0.265        | 0.553        | 0.157        |
| <b>INR</b>                           | <b>mean± SD</b>      | 1.0            | 0.03 | 1.2                           | 0.1  | 1.4                                | 0.1  | <0.001       | <0.001       | <0.001       | <0.001       |
| <b>AFP (ng/mL)</b>                   | <b>median, range</b> | 5.4            | 1.56 | 6                             | 2.31 | 10.5                               | 7.22 | 0.092        | 0.513        | 0.060        | 0.082        |
| <b>HB (g/dL)</b>                     | <b>mean± SD</b>      | 11.6           | 1.0  | 11.4                          | 1.1  | 11.2                               | 1.4  | 0.128        | 0.191        | 0.097        | 0.099        |
| <b>Platelets (X10<sup>9</sup>/L)</b> | <b>mean± SD</b>      | 112.2          | 27.9 | 100.1                         | 18.7 | 74.4                               | 23.9 | <b>0.009</b> | <b>0.042</b> | <b>0.002</b> | <b>0.015</b> |

ALT= alanine aminotransferase; AST= aspartate aminotransferase; INR= international normalized ratio; AFP= alfa feto protein; HB= hemoglobin; EVs= esophageal varices; SD= standard deviation.

**Table (2).** Comparison of Liver and Spleen Stiffness among studied cases:

|                 | No EVs |     | EVs I<br>=small sized |     | EVs II<br>= medium<br>sized |     | <i>P1</i>        | <i>p2</i>        | <i>p3</i>        | <i>p4</i>        |
|-----------------|--------|-----|-----------------------|-----|-----------------------------|-----|------------------|------------------|------------------|------------------|
|                 | N=18   |     | N=25                  |     | N=7                         |     |                  |                  |                  |                  |
|                 | Mean   | SD  | mean                  | SD  | Mean                        | SD  |                  |                  |                  |                  |
| <b>LS (kpa)</b> | 22.7   | 5.3 | 32.9                  | 7.0 | 51.4                        | 7.9 | <b>&lt;0.001</b> | <b>0.001</b>     | <b>&lt;0.001</b> | <b>&lt;0.001</b> |
| <b>SS (kpa)</b> | 45.4   | 8.1 | 65.5                  | 8.2 | 74.9                        | 0.4 | <b>&lt;0.001</b> | <b>&lt;0.001</b> | <b>&lt;0.001</b> | <b>0.006</b>     |

LS: liver stiffness; SS: Spleen stiffness; EVs= esophageal varices; Kpa=kilo pascal; p1, comparison between no EVs, EVs I, EVs II; p2, comparison between No EVs and EVs I; p3, comparison between No EVs and EVs II; p4, comparison between EVs I and EVs II.

**Table (3).** Validity of liver, spleen stiffness and child score for detecting presence of EVs:

|                        | <b>LS</b> | <b>SS</b> | <b>Child score</b> |
|------------------------|-----------|-----------|--------------------|
| <b>AUC</b>             | 0.905     | 0.970     | 0.606              |
| <b>Cut off</b>         | 28.2      | 55.5      | 6                  |
| <b>Sensitivity (%)</b> | 75        | 87.5      | 40.6               |
| <b>Specificity (%)</b> | 83.3      | 94.4      | 77.8               |
| <b>PPV (%)</b>         | 88.9      | 96.5      | 76.5               |
| <b>NPV (%)</b>         | 65.2      | 80.9      | 42.4               |
| <b>Accuracy (%)</b>    | 78        | 90        | 54.0               |

LS= liver stiffness; SS= spleen stiffness; AUC, area under ROC curve; PPV, positive predictive value; NPV, negative predictive value.

**Table(4).** Validity of liver, spleen stiffness and child score for discrimination between cirrhotic patients with EVs I and EVs II:

|                        | <b>LS</b> | <b>SS</b> | <b>Child score</b> |
|------------------------|-----------|-----------|--------------------|
| <b>AUC</b>             | 0.911     | 0.929     | 0.634              |
| <b>Cut off</b>         | 41.5      | 74.5      | 6                  |
| <b>Sensitivity (%)</b> | 85.7      | 85.7      | 57.1               |
| <b>Specificity (%)</b> | 80        | 88        | 64                 |
| <b>PPV (%)</b>         | 54.5      | 66.7      | 30.8               |
| <b>NPV (%)</b>         | 95.2      | 95.6      | 84.2               |
| <b>Accuracy (%)</b>    | 81.2      | 87.5      | 62.5               |

LS= liver stiffness; SS= spleen stiffness; AUC, area under ROC curve; PPV, positive predictive value; NPV, negative predictive value.

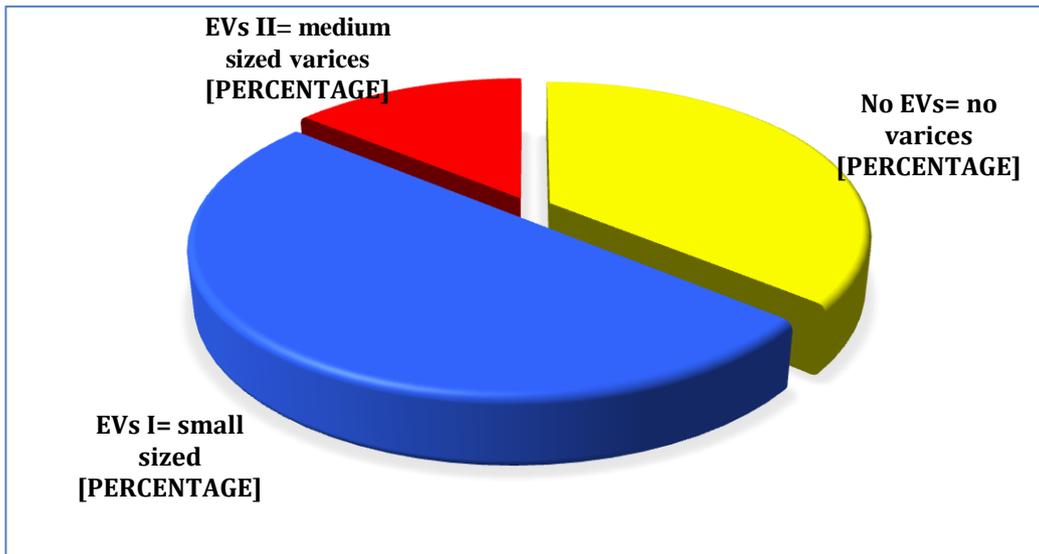


Figure (1). Esophageal varices of studied cases.

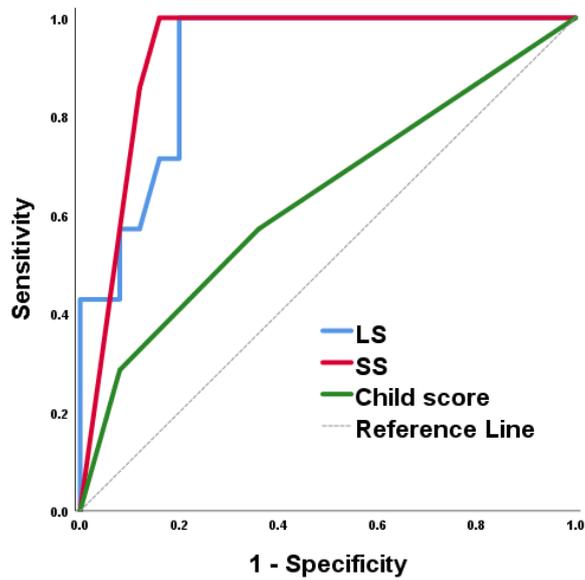
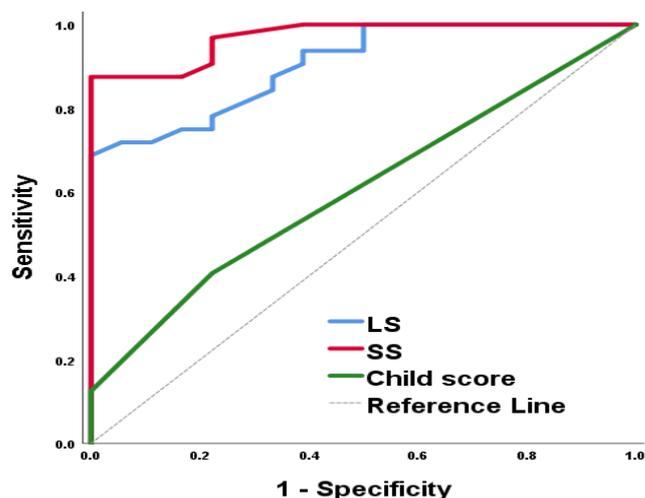


Figure (2). ROC of liver and spleen stiffness validity for detecting EVs



**Figure (3).** ROC of liver and spleen stiffness discrimination between cirrhotic patients with EVs I and without EVs II

### Discussion:

The present study aimed to assess diagnostic performance of LSM and SSM using fibroscan for predicting the presence and degree of EVs.

In this study there was no significant statistical difference between different groups as regards age and gender. As regards laboratory investigations, our study found a significant statistical decrease in serum albumin in the variceal patients and also, lower in patients with large EVs group. In accordance to our results, a previous study (7) reported that serum albumin was lower in patients with EVs than patients without EVs and also lower in patients with large EVs than patients with small EVs and there was a statistically significant difference. Other researchers (8,9) agreed with our results,

they stated that low serum albumin level correlated with the presence of EVs.

In the present study, Platelet count was significantly statistically decreased in patients with EVs and it was lower in patients with large EVs compared to patients with small EVs. That was stated by Other researchers (8,9) who found that platelet count was statistically significantly lower in patients with large EVs compared to patients with small EVs. Our results were also in agreement with the results reported by a previous study (7) who found that low platelets and advanced child-pugh class are predictors of large EVs.

In the current study, significant increase was observed as regards the mean values of serum bilirubin and INR in patients with EVs, also this was agreed by

another study (10), who reported higher bilirubin levels and prolonged INR in variceal group than non variceal group, and in patients with large EVs than small EVs. previous studies (11) found higher bilirubin levels and prolonged INR in patients with EVs than those without EVs. Also Other researchers (8,9) reported a significant increase in the serum bilirubin and INR in patients with EVs.

In the current study, 77.8% of patients with no EVs have splenomegaly, and 100% of patients with EVs have splenomegaly. The difference was statistically significant ( $p$  value  $< 0.05$ ). Also this was agreed by other researchers (8) who reported that splenomegaly was a significant predictor for large EVs. This agrees with results of previous studies (9,12) who reported that splenomegaly alone was a significant predictor for the development of large EVs. Also, another study (13) in a prospective study showed that splenomegaly was the independent predictor for the presence of large EVs.

In the present study there was a highly significant statistical increase in Child score and the Child class between grades of EVs. other researchers (8) who reported that AUC of Child score for predicting the presence of EVs was 0.729, The AUC of Child-Pugh score for

distinguishing medium to large EVs from small EVs or the absence of EVs was 0.683. Child score could be used as a non-invasive predictor of EVs with a cutoff value  $> 5.5$ , with 93.3% sensitivity, 100% specificity, 100% PPV and 93.7% NPV. Another study (9) found that the Child score could be used as a non-invasive predictor of EVs with a cutoff value  $> 5.5$ , with 93.3% sensitivity, 100% specificity, 100% PPV and 93.7% NPV while, child score can be used to discriminate between risky and non-risky EVs at a cutoff level of  $> 8.5$ , with 95% sensitivity, 80% specificity, 82.6% PPV and 94.1% NPV. Another study (12) reported that there was a highly significant statistical increase in Child score and the Child class between different grades of EVs.

Our study detected LSM cut-off for predicting EVs was 28.2 KPa with AUC of 0.905, sensitivity of 75%, specificity of 83.3%, PPV of 88.9%, NPV of 65.2% and accuracy of 78%. other researchers (7), identified 13.9 kPa for any varices (including small varices) and 19.0 kPa for VNT (varices needing treatment) as the suitable cut-offs.

Another study (12) reported that LS was 17.2kPa with 93.3% sensitivity, 76.7% specificity, 80% PPV and 92% NPV and 89.6% diagnostic accuracy for predicting presence of EVs. This is supported by

the study done by other researchers (14) who reported LS cut off: 12.27 kPa for EVs with 100% sensitivity and 66.6% specificity and cut off: 23.87kPa with 73.81% sensitivity and 59.5% specificity.

Our study demonstrated SSM cut-off for predicting EVs was 55.5 KPa with AUC of 0.970, sensitivity of 87.5 %, specificity of 94.4%, PPV of 96.5 %, NPV of 80.9% and accuracy of 54%. SSM cut-offs for discrimination between patients EVs I and EVs II was 74.5 KPa with AUC of 0.929, sensitivity of 85.7%, specificity of 88%, PPV of 66.7%, NPV of 95.6% and accuracy of 87.5%.

Our study demonstrated that SSM is better than LSM and child score for predicting presence and grades of EVs as regards AUC, sensitivity, specificity, PPV, NPV.

Another study (12) detected that SS cut off value was 32kPa with 90% sensitivity, 96.7% specificity, 96.4% PPV and 90.6% NPV and 96.7% diagnostic accuracy for prediction of EVs and >37.12kpa for prediction of large EVs.

On the contrary to our study another researchers (15) observed no significant differences in the mean SS values between patients with and without EVs and between those with different EVs grades. The difference in the results may

be explained by the following possible reasons. The interval between SS measurements and the distribution of patients according to varix grades was unequal and the relative small number of the patients group.

Another study (16) evaluated the performance of TE for detecting EVs in cirrhotic patients, concluded that TE is not suitable for implementation in the clinical practice due to varying cut-of values and different etiologies.

Also, other researchers (8) detected that AUCs of SS, LS for predicting the presence of EVs were 0.785, 0.747, respectively. The AUCs of SS, LS, for distinguishing medium to large from small EVs or the absence of EVs were 0.762, 0.687 respectively. For detecting large EVs, the AUCs of SS, LS, were 0.786, 0.616, respectively.

## **Conclusion:**

LS and SS are valuable non-invasive parameters for prediction of EVs in patients with liver cirrhosis. Both LS and SS were significantly associated with presence of EVs among cirrhotic patients. Moreover, both LS and SS increases with the severity of EVs but, SS correlates better with portal hypertension and the presence of EVs. SS measurement is considered to be an

optimal method to use in the clinical practice, for the screening of cirrhotic patients for EVs and diagnosing high-risk EVs.

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