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Non-Invasive Prediction of Gastric Varices in HCV Related Cirrhosis

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ABSTRACT

Background: Gastric varices may bleed severely and are often associated with poor outcomes. The Baveno VII consensus encouraged non-invasive tests (NITs) to identify patients at risk of acute upper GI bleeding (AUGIB) due to ruptured varices and to avoid unnecessary screening upper GI endoscopic examination (UGIE). Recently, various NITs have been demonstrated as simple and non-invasive predictors of the presence of esophageal varices (EVs) and gastric varices (GVs) in patients with liver cirrhosis. **Objectives:** The current work aimed to evaluate the NITs that could predict the presence of GVs in patients with HCV related liver cirrhosis. **Patients and Methods:** 260 adult patients with HCV-related cirrhosis who were admitted for UGIE for either screening for varices or management of AUGIB were enrolled. Various NITs were calculated. **Results:** Liaoning score at a cutoff value > - 0.1635 was a statistically significant predictor of GVs with sensitivity=78.6%, specificity = 60.1%, positive predictive value (PPV) = 27.5 %, false discovery rate (FDR) = 72.5%, negative predictive value (NPV) = 93.6 %, false omission rate (FOR) = 6.4% & accuracy= 63.1%. RLLD at a cutoff ≤ 9.75 cm was a statistically significant predictor of GVs with sensitivity=73.8%, specificity= 54.1%, PPV= 22.3%, FDR= 77.7%, NPV= 90.9 %, FOR= 9.1% & accuracy= 54.2%. On multivariate regression analysis, Liaoning score & RLLD were significant predictors of GVs in patients with HCV related cirrhosis.
Conclusion: Liaoning score & RLLD are significant predictors of GVs in HCV Egyptian cirrhotic patients with very high negative predictive value & very low false omission rate.
Keywords: Liver cirrhosis, Chronic hepatitis C, Gastric varices, Esophageal varices, Non-invasive tests.

INTRODUCTION

In Egypt, liver cirrhosis (LC) has been considered as a main etiology of morbimortality (0.727/1000) [(1)]. It has a mortality of 18% in males aged 45–54 years [(2)]. There are a lot of adverse events of LC which ultimately ends in a decrease in life expectancy such as ascites, spontaneous bacterial peritonitis (SBP), bleeding owing to ruptured varices, hepatorenal syndrome (HRS), hepatic encephalopathy (HE), hepatic failure and hepatocellular carcinoma (HCC) [(3)].

AUGIB due to ruptured EVs accounts for a mortality of 30% within six weeks of the attack, ranging from zero percent for cases with CTP class A to 30% for cases with CTP class C. The possibility of AUGIB is associated with the size of varices, existence of red signs and decompensated cirrhosis [(4)]. Compared to EVs, GVs aren't common, occurring in approximately 20% of cirrhotic cases. On the other hand, GVs have more liability for severe bleeding and are occasionally accompanied by bad prognosis [(5)]. GVs were displayed to bleed at minimal portal pressures compared to EVs, mainly owing to the greater prevalence of gastro-renal shunts which decompress the portal system [(6)].

In recent years, different noninvasive tests (NITs), which include model for MELD, aspartate transferase (AST) to alanine transferase (ALT) ratio (AAR), AST to platelet ratio index (APRI), PLC to spleen diameter (PLC/SD) ratio,fibrosis-4-index (FIB-4),fibrosis index (FI) and King's score are revealed as a simple, noninvasive and simple predictors of EVs in cirrhotic patients [(7)].

However, their clinical utility is indefinite.

Their accuracy varies in various populations and in various causes of LC [(8)]. The present study aimed to evaluate the NITs that could predict the presence of GVs in cases with HCV related LC.

PATIENTS AND METHODS

This was two centers, cross-sectional study included a total of 260 cirrhotic patients, attending at the Department of Internal Medicine, Hepatology & Gastroenterology Unit, Specialized Medical Hospital, Faculty of Medicine, Mansoura University and the Department of Internal Medicine at Mansoura New General Hospital, Mansoura, Ministry of Health, from December 2021 to December 2022.

Sample size: Based on a previous study, total sample size of 260 cirrhotic patients achieves a 90% confidence level for expected prevalence of 60% and an acceptable margin of error of ± 5 and to achieve the rule of thumb of 15 to 50 participants for each predictor variable.

Inclusion criteria: Adult cases whose age more than or equal to 18 years old with HCV related LC who were admitted for UGIE for either screening for varices or for management of AUGIB.

Exclusion criteria: Cases who underwent preceding endoscopic treatment for EVs, GVs or portal hypertensive gastropathy (PHG), cases who underwent previous surgical interference for portal hypertension (PH), patients who underwent splenectomy, patients who were on nonselective beta blockers (NSBB), patients with non-portal hypertensive source of bleeding, patients with combined chronic hepatitis B & C infections, patient with Bilharzial hepatic diseases, patient with other causes of chronic liver disease, patients with malignancy, cases with portal or splenic vein thrombosis, patients with bleeding disorder, patients with organ failure other than the liver, patients who underwent preceding endoscopic or surgical intervention for gastro-esophageal reflux disease and patients who did not provide informed consent, were excluded.

Out of 400 HCV cirrhotic patients, 260 patients were enrolled and 140 patients were excluded (figure 1).

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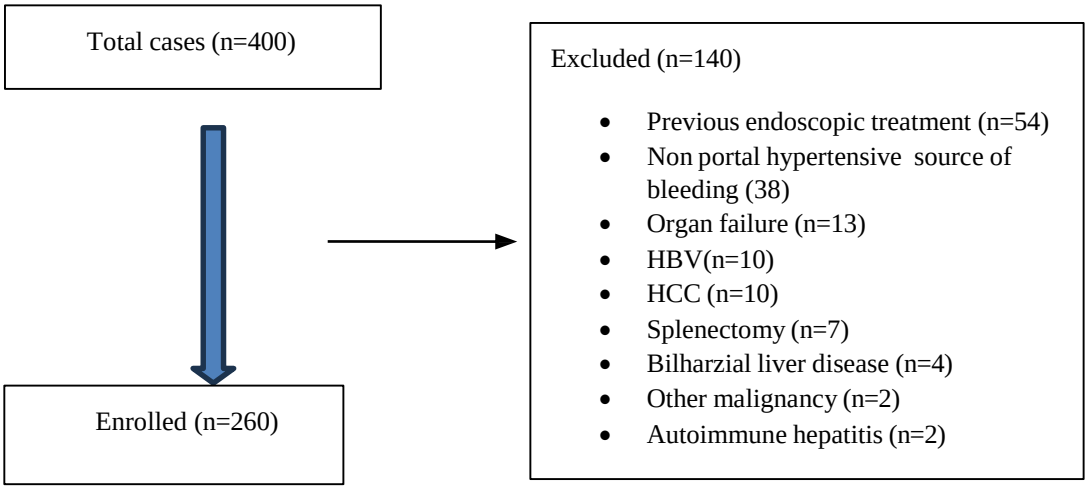

Figure (1): Study flowchart.

All enrolled patients were subjected to a detailed medical history and full clinical evaluation.

The following laboratory investigations were done including complete blood count (CBC) using automated hematology analyzer (Mindray BC-2800), serum creatinine, alanine aminotransferase (ALT), Aspartate transaminase (AST), serum bilirubin, serum albumin (using clinical chemistry analyzer: Cobas C 311), PT (Prothrombin Time) & INR (International Normalized Ratio), Anti HCV antibodies, Anti-HIV antibodies and HBs-Ag (by 4th generation ELISA approach). The serum level of HCV RNA was measured by PCR technique. Abdominal ultrasonography (US), using Logiq E9 US machine (Wisconsin, USA) with a C1–6- VN 2D convex probe was done. US measurement of the right liver lobe diameter (RLLD) in cm was done in the fasting state (for 4 hours before US examination). For a more accurate evaluation, gel was applied to the upper abdomen prior to scanning. RLLD images were acquired with patient positioned in a left anterior oblique position, with the right arm placed above the head and taking a deep breath and holding it for few seconds. The probe was positioned in a longitudinal manner between the mid axillary line (MAL) and anterior axillary line (AAL). Also, the splenic diameter (SD) in cm was measured between the upper and the lower splenic borders, while the patient was in the right lateral decubitus during taking a deep breath and holding it. Contrast- enhanced multi-phasic computed tomography (MPCT) of the abdomen was done when there was suspicion of HCC.

The NITs that were examined in this study and the equations of their calculation were:

1- RLLD in cm / albumin (g/dl) ratio (RLLD/A).
2- Platelet count (PLC) (10^9/L) to spleen diameter (SD) ratio.
3- Lok score = -5.56 –0.0089 ×PLC +1.26 × (AST/ALT) +5.27×INR.
4- APRI score = [(AST/upper limit of normal (ULN)× 100] / PLC (10^9/L). If the score was < .5, it denotes minimal or no fibrosis, .5 to 1.5, denotes significant fibrosis & >1.5, denotes cirrhosis.
5- AST/ALT ratio (AAR).
6- FIB4 score = [age × AST/PLC (10^9/L) × √ALT]. If the score was < 1.45, it denotes minimal or no fibrosis, 1.45 to 3.25, denotes significant fibrosis & >3.25, denotes cirrhosis.
7- Fibrosis index (FI) score = 8 - 0.01× PLC (10^9/L) - albumin. If the score was < 2.1, it denotes minimal or no fibrosis, 2.1 to < 2.3, denotes significant fibrosis & ≥ 2.3, denotes cirrhosis.
8- King score = Age × AST × INR / PLC (10^9/L).
9- MELD score = 9.57 × [s Cr (µmol/L) ×0.011] +3.78 × [T bilirubin (µmol /L) ×11.2+ [0.058× (INR)+ 6.43.
10- Liaoning score = 0.466 + 1.0889 × AUGIB (yes =1; no = 0) + 1.1479 × ascites (yes =1; no = 0) − 0.0129 × PLC (10^9/L) [9].
11- Child -Turcotte-Pugh (CTP) score was measured and it was considered class A if the score was 5-6 points, class B if it was 7-9 points and class C if it was 10-15 points (table1).

Table (1): CTP score calculation

Parameter	1 point	2 points	3 points
Albumin (g/dl)	>3.5	2.8-3.5	<2.8
Bilirubin (mg/dl)	<2	2-3	>3
INR	<1.7	1.7-2.3	>2.3
Ascites	No	Mild	Moderate, severe
Hepatic encephalopathy	No	Grade 1-2	Grade 3-4

UGIE was done using a Pentax gastro-scope with EPKi 5000 processor under conscious sedation. A full endoscopy, followed by retroflexion of the scope for evaluation of GVs, was done. UGIE was done by two experienced endoscopists who were unaware of the results of the studied NITs. GVs were graded according to Sarin classification into gastroesophageal varix type

1 (GOV1)(varices extend over the cardia and lesser curvature of the stomach ending in gastric fundus), gastroesophageal varix type 2 (GOV2) (varices extend over the cardia and the greater curvature of the stomach ending in gastric fundus), Isolated gastric varix type 1 (IGV1) (varices which exist in the gastric fundus and they do not extend into the esophagus or the cardia) or Isolated gastric varix type 2 (IGV2)**(**ectopic varices that occur in other parts of the stomach) [(10)].

EVs were graded according to modified Paquet classification [(11)] into grade 1 (varices extending just above the mucosal level), grade 2 (varices projecting to one- third of the luminal diameter and cannot be compressed with air insufflation) and grade 3 (varices projecting up to 50% of the luminal diameter and in contact with each other).

PHG was graded according to Baveno III [(12)] into mild (mosaic-like pattern of mild degree without redness of the areola) and severe (mosaic-like pattern with red signs or brown-black spot).

Ethical considerations:

Study design was approved by the ethics committee of Faculty of Medicine in Mansoura University (Code number: MS.22.01.1815). All participants had given an informed written consent after assuring confidentiality. The Helsinki Declaration was followed throughout the study's conduct.

Statistical analysis

Data analysis was performed by SPSS software, version 25.0. Qualitative data were described using number and percent. Quantitative data were described using median for non-normally distributed data and Mean ± SD for normally distributed data after testing normality using Kolmogrov-Smirnov test. Significance of the obtained results was judged at the (≤ .05) level. Receiver operating characteristics curve (ROC curve) was used to calculate validity (sensitivity & specificity) of continuous variables with calculation of best cut off value. The positive predictive value (PPV), the negative predictive value (NPV) & overall accuracy, were calculated. The complement of the PPV is the false discovery rate (FDR) & was calculated as 1-PPV. The complement of the NPV is the false omission rate (FOR) & was calculated as 1-NPV.

RESULTS

Table (2) shows that the mean age of the enrolled patients was 62.6 year, 61.5% of them were males & 38.5% were females. It shows that 50% of the enrolled patients presented for their first UGIE due to AUGIB and 50% of them presented for their first UGIE for screening for varices. The mean RLLD as measured by abdominal US was 9.48 cm, the mean SD was 15.48 cm & ascites was present in 28.1% of the enrolled patients. The mean PLC was 125.17×10^9/L, 73.1% of the patients had thrombocytopenia and 26.9% had normal PLC. The mean values of serum albumin, serum bilirubin, INR, ALT & AST were 2.77 g /dl, 1.68 mg/dl, 1.42, 30.7 IU /l and 38.7 IU/l, respectively. The mean CTP score was 7.2 points with 16.5% of the patients had CTP class A, 71.2 % had CTP class B & 12.3% had CTP class C. The mean value of MELD score was 8.2 points and that of FIB 4 score was 4.94 points. According to FIB 4 score, 30.8% of the patients had significant fibrosis, 63.8% had cirrhosis, while 5.4% had insignificant fibrosis. The mean value of APRI score was 1.14 points.

According to APRI score, 69.2 % of the patients had significant fibrosis, 14.6 % had cirrhosis, while

16.2 % had insignificant fibrosis. The mean value of FI score was 3.98 points. According to FI score, 14% of the patients had significant fibrosis, 82% had cirrhosis, while 4 % had insignificant fibrosis. The mean values of AAR, PLC/SD ratio, RLLD /Albumin ratio, King's score, Lok score & Liaoning score were 0.846, 8.41, 3.49, 39.31, 13.62 and -0.29 points, respectively.

Table (2): Clinical, laboratory& radiologic data as well as the tested NITs

Variable	Mean ± SD (Min-Max)
Age (years)	62.61±8.09 (48-80)
Male (No., %) Female (No., %)	160 (61.5%) 100 (38.5%)
AUGIB: Yes/No	50/50%
RLLD (cm)	9.48±0.82 (8-11)
SD (cm)	15.48±1.86 (12.5-20)
Ascites: Yes/No	28.1/71.9%
PLC (10^9/L)	125.17±66.81 (25-335)
PLC < 150 / ≥ 150 (10^9/L)	73.1% / 26.9%
Serum albumin (g/dl)	2.77±0.41
Bilirubin (mg/dl)	1.68±0.41
INR	1.42±0.28
ALT (IU/L)	30.73±7.50
AST (IU/L)	38.71±9.38
CTP score (points)	7.2±1.62 (6-14)
CTP class: A/B/C	16.5/71.2/12.3%
MELD score (points)	8.20±1.75 (4.86-12.83)
FIB4 score (points)	4.94±5.26 (1.14-39)
FIB4:< 1.45/1.45-3.25/>3.25	5.3/30.8/63.8%
APRI score (points)	1.14±1.01 (0.23-6.78)
APRI score: < .5 /.5 - 1.5 / >1.5	16.2 /69.2/14.6%
FI score (points)	3.98±0.84 (1.95-5.62)
FI: < 2.1/ > 2.1 < 2.3 / ≥ 2.3	4/14/82%
AAR	0.846±0.25 (0.22-1.33)
PLC (10^9/L) / SD(cm) ratio	8.41±4.89 (1.39-23.93)
RLLD /Albumin ratio	3.49±0.61 2.5-5.25
King's score (points)	39.31±43.90 (7.6-299.24)
Lok score (points)	13.62±2.04 (10.36-20.6)
Liaoning score (points)	-0.29±1.21 (-3.86- 2.21)

Table (3) and figure 2 show that EVs were present in 98.5% of cases, grade 1varices were present in 20.4%, grade 2 varices in 39.2% and grade 3 varices in 38.8% of enrolled patients. GVs were present in 16.2% of HCV cirrhotic patients.

GOV1 was present in 10.4% of enrolled patients, representing 64.28% of patients with GVs. GOV2 was present in 4.2% of enrolled patients, representing 26.19% of patients with GVs. IGV1 was present in 1.5% of enrolled patients, representing 9.52% of patients with GVs (figure 2). PHG was present in 86.2 % of enrolled patients.

Mild PHG was present in 48.8 % of enrolled patients, representing 56.6% of patients with PHG. Severe PHG was present in 37.3% of enrolled patients, representing 43.3% of patients with PHG.

Table (3): Prevalence of EVs, GVs and PHG in HCV cirrhotic patients

Variable	Number	Percent
EVs: Yes/No	256/4	98.5/1.5%
Grade 1	53	20.4%
Grade 2	102	39.2%
Grade 3	101	38.8%
GVs: Yes/No	42/218	16.2/83.8%
GOV1	27(64.28%)	10.4%
GOV2	11(26.19%)	4.2%
IGV1	4 (9.52%)	1.5%
PHG:Yes/No	224/36	86.2/13.8%
Mild	127(56.6%)	48.8%
Severe	97(43.3%)	37.3%

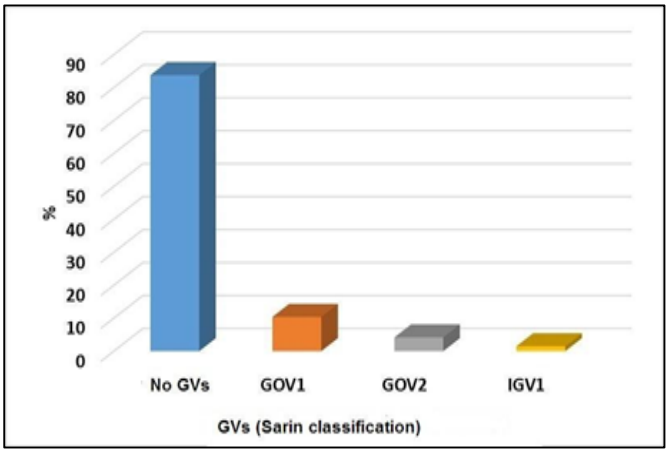

Figure (2): Prevalence and types of gastric varices in HCV cirrhotic patients.

Table (4) illustrates that CTP score, MELD score, FIB4 index, APRI score, FI index, AAR, PLC/SD, RLLD/SD, Lok score and Kings score were insignificant predictors of the presence of GVs in HCV cirrhotic patients.

Table (4): Validity of CTP score, MELD score, FIB4 index, APRI score, FI index, AAR, PLC/SD, RLLD/ Albumin ratio, Lok score and Kings score in prediction of GVs in HCV related cirrhosis.

Variable	AUC	Std. Error	p-value	Asymptotic 95% CI	
				Lower Bound	Upper Bound
CTP score	0.419	0.048	0.096	0.325	0.513
MELD score	0.533	0.038	0.494	0.459	0.607
FIB4 index	0.541	0.046	0.402	0.451	0.631
APRI score	0.527	0.044	0.573	0.441	0.614
FI index	0.523	0.048	0.635	0.429	0.618
AAR	0.497	0.042	0.955	0.415	0.579
PLC/SD	0.454	0.052	0.344	0.352	0.556
RLLD/ Albumin ratio	0.441	0.047	0.230	0.349	0.534
Lok score	0.451	0.049	0.317	0.355	0.547
Kings score	0.521	0.046	0.660	0.431	0.612

Table (5) & figure (3) show that Liaoning score at a cutoff value > -0.1635 was a statistically significant predictor of GVs in HCV related cirrhosis (AUC = 0.640, p = 0.004). Its sensitivity and specificity were 78.6%, and 60.1%, respectively. The PPV was 27.5 %, the FDR was 72.5%, NPV was 93.6 % & FOR was 6.4%. The overall accuracy was 63.1%.

Table (5): Liaoning score in prediction of GVs in HCV related cirrhosis

Variable	AUC	S.E.	P	Asymptotic 95% CI		Cut off point	Sen.	Spe.	PPV	FDR	NPV	FOR	Accuracy
				Lower Bound	Upper Bound								
Liaoning score	.640	.044	.004	.554	.726	-0.1635	78.6 %	60.1 %	27.5%	72.5%	93.6%	6.4%	63.1 %

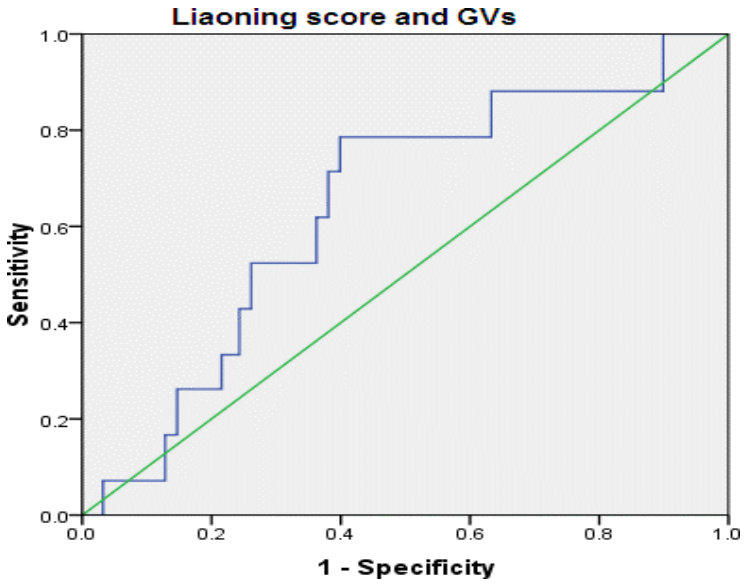

Figure (3): ROC curve for Liaoning score in prediction of GVs in HCV related cirrhosis

Table (6) & figure (4) show that RLLD at a cutoff value of less than 9.75 cm was a statistically significant predictor of GVs in HCV related cirrhosis (AUC = 0.656, p = 0.001). Its sensitivity and specificity were 73.8% and 54.1%, respectively. The PPV was 22.3 %, FDR was 77.7%, NPV was 90.9 % & FOR was 9.1%. The overall accuracy was 54.2%.

Table (6): RLLD in prediction of GVs in HCV related cirrhosis

Variable	AUC	S.E	P	Asymptotic 95% C. I		Cut off point	Sen.	Spe.	PPV	FDR	NPV	FOR	Accuracy
				Lower Bound	Upper Bound								
RLLD	.656	.042	.001	.575	.737	9.75 cm	73.8 %	54.1%	22.3%	77.7%	90.9 %	9.1%	54.2 %

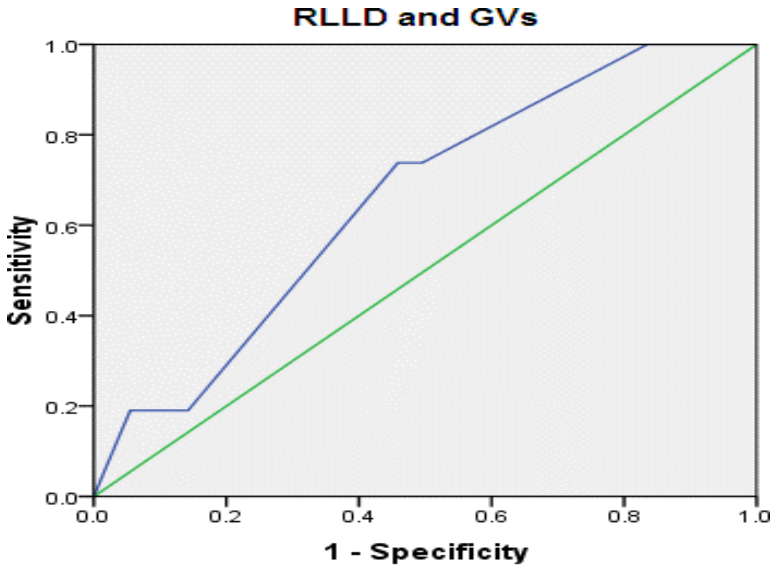

Figure (4): ROC curve for RLLD in prediction of GVs in HCV related cirrhosis

Table (7) shows that the univariate analysis denotes that SD, RLLD, RLLD/serum albumin ratio &Liaoning score, were significant predictors; while age, INR, serum albumin, FI score & LOK score were insignificant predictors of GVs in HCV related cirrhosis. On multivariate analysis, Liaoning score & RLLD were significant predictors of GVs in HCV related cirrhosis.

Table (7): Univariate & multivariate regression analysis for predictors of GVs in HCV related cirrhosis

	Univariate analysis		**Multivariate analysis**		
Variable	**p-value**	**COR (95% CI)**	**β**	**p-value**	**AOR (95% CI)**
Age (years)	0.555	1.01 (0.972-1.05)			
INR	0.074	0.241 (0.051-1.15)			
Serum albumin (g/dl)	0.888	0.943 (0.418-2.13)			
SD (cm)	0.013	1.24 (1.05-1.46)	-0.163	0.293	0.85 (0.627-2.15)
FI index	0.639	1.1 (0.738-1.64)			
RLLD Albumin ratio	0.04	0.504 (.262-.970)	-0.475	0.209	0.621 (0.296-1.31)
LOK score	0.147	0.869 (.719-1.05)			
Liaoning score	0.02	1.43 (1.06-1.93)	1.281	0.04	1.33 (1.09-2.1)
RLLD (cm)	0.001	0.451 (0.287-0.709)	-0.818	0.03	0.44 (0.21-0.925)

DISCUSSION

Portal hypertension (PH) is usually associated with varices development. AUGIB due to ruptured varices could be accompanied by death in 1/3 of affected subjects at six weeks. GVs represent 20% of variceal bleeds and it tends to bleed more severely than EVs with worse outcomes. Hepatic venous pressure gradient (HVPG) measurement determines the risk of bleeding of EVs. Regarding GVs, the bleeding risk isn't totally dependent on PH severity, on the other hand it also dependent GVs size, their wall tension, and presence of red color signs [13-14].

UGIE confirms the presence of GVs in patients with LC; unfortunately, it isn't gaining much more popularity owing to its invasive nature. Endoscopic ultrasound (EUS) has better diagnostic performance of GVs, but is invasive, costly and not available at all centers. CT is used to screen for GVs, but has suboptimal specificity [15].

Capsule endoscopy is an expensive method for diagnosis of GVs & difficult to be used, especially in developing countries. The Baveno VII consensus encouraged NITs to recognize patients at risk of gastroesophageal varices (GOV) and to avoid unnecessary screening UGIE. Accordingly, liver stiffness < 15 Kilo Pascal (Kpa), measured by transient elastography (TE), along with platelet count of > 150 × 10^9/L is accompanied by < 5% chance of having risky varices. On the other hand, such recommendation isn't confirmed in the context of GVs [16].

Primary prophylaxis of GVs includes non-selective Beta Blockers (NSBB) for all types. EBL or glue injection can be used for GOV1, glue injection for GOV2 (using a 3.7mm width channel endoscope for ease in glue administration) & EUS guided glue injection plus coiling (using a 19-G access needle), for all types. Transjugular intrahepatic portosystemic shunt (TIPS) isn't suitable for primary prophylaxis. Balloon-retrograde transvenous occlusion (BRTO), coil-assisted retrograde transvenous occlusion (CARTO), plug-assisted retrograde transvenous occlusion (PARTO), and direct coil-assisted antegrade transvenous occlusion (CAATO) cannot be suggested as a primary prophylactic measure [17].

The diagnosis and management of GVs require special scopes, needles, glues, coils and well equipped interventional radiology units, which are not available in every hospital, especially in developing countries. In this context, we aimed to assess the NITs that could predict GVs in HCV cirrhotic patients. In this study, the mean age of HCV cirrhotic patients was 62.61 year and males represented 61.5 %, while females represented 38.5% of them. Similarly, **Ghada *et al.*** [18] found that 62.4% of cirrhotic patients were males. Also, **Abdel-Gawad *et al.*** [19] showed that HCV RNA positivity was significantly higher in males than females. The mean PLC was 125.17×10^9/L and 73.1% of the patients had thrombocytopenia. Low PLC may be attributed to hypersplenism secondary to PH in LC [20].

Also, decreased secretion of thrombopoietin, resulting from impaired synthetic function of the cirrhotic liver, may be a cause. Low PLC was accompanied by the existence of EVs, on the other hand, the accuracy of PLC alone for predicting EVs was moderate [21]. The present study revealed that EVs were present in 98.5% of enrolled patients. Previous studies had shown that the prevalence of varices in cirrhotic patients was 40% in patients with CTP class A and up to 85% in those with CTP class C [22]. The present study revealed that; 82% of enrolled patients had LC according to FI score. The present study displayed that GVs were present in 16.2% of patients with HCV related cirrhosis. Previous studies had reported that GVs were less common than EVs with an incidence approximately 20% [23]. The present study showed that GOV1 was present in 64.28%, GOV2 in 26.19% & IGV1 in 9.52% of patients with GVs. This finding was similar to that previously reported by Sarin who reported that the most common type of GVs was GOV1, representing 70%, followed by GOV2 in 21% & IGV1 in 6.7% of patients with GVs.

The current study displayed that FIB4 score, APRI

score, FI score, which are well known indirect serum markers of hepatic fibrosis, were insignificant predictors of GVs in HCV related cirrhosis. This may be explained by the fact that these NITs had moderate (FI score) to poor (APRI and FIB4 scores) agreement with Metavir score in staging of hepatic fibrosis among chronic HCV cases, as confirmed in a previous Egyptian study [24]. The present study showed also that CTP score, MELD score, PLC/SD, AAR, RLLD/ Albumin ratio, Lok score and Kings score were insignificant predictors of GVs in HCV related cirrhosis. Similarly, a meta-analysis comparing ability of NITs to predict varices showed that FIB-4, APRI, AAR, and Lok scores had low to moderate diagnostic accuracy in prediction of varices development in LC [25]. Also, another study showed that PLC/SD ratio may not be accurate in predicting the presence of varices [26].

This finding can be explained by the information that these NITs were initially explored in patients with CTP class A and their diagnostic performance was poor in cirrhotic patients with AUGIB [27]. In the present study, 83.5% of the enrolled patients had CTP class B or C and AUGIB was present in 50% of them. On the other hand, a meta-analysis had found that FIB-4, APRI, AAR, King, and Lok scores predicted EVs [25].

Liaoning score was calculated using simple clinical, radiologic and laboratory data (AUGIB, ascites & PLC) which reflects both the vascular and cellular hepatic decompensation. Our study demonstrated that Liaoning score was a significant predictor of GVs in HCV related cirrhosis at cut off value of more than -0.1635 with a sensitivity of 78.6%, a specificity of 60.1% and AUC of 0.640. Its PPV was 27.5 %, the FDR was 72.5%, NPV was 93.6 % & FOR was 6.4%. The overall accuracy was 63.1%. On performing multivariate regression analysis, Liaoning score was statistically significant predictor of GVs in HCV related cirrhosis. Lioaning score was reported to be a significant predictor of EVs at cut-off value 0.477 with a sensitivity of 81.96% and a specificity of 65.22% with AUC of 0.737 [28]. In that study, only patients with AUGIB were enrolled and multiple etiologies of LC as HBV (51.3%), alcohol abuse (26, 1%), drug induced liver injury (9.6%), autoimmune liver disease (5.6%) and HCV patients (6%), were enrolled. They also enrolled patients with HCC (14.7%).

Amer *et al.* [29] showed that Liaoning score at a cut-off > 0.483 was able to predict PHG with a sensitivity of 78%. To the best of our knowledge, our study was the first one to show the ability of the Lioaning score to predict GVs in HCV related cirrhosis. The present study also showed that RLLD, as measured by abdominal US, at a cutoff value of less than 9.75 cm was a statistically significant predictor of GVs. Its sensitivity and specificity were 73.8%, and 54.1%, correspondingly. The PPV was 22.3 %, FDR was 77.7%, NPV was 90.9 % & FOR was 9.1%. The overall accuracy was 54.2%. This was confirmed by univariate & multivariate regression analysis. The RLLD ranged from 8 to 11 cm, denoting a shrunken right hepatic lobe, which is a sure sign of liver cirrhosis. It was reported that the total liver volume reduced with the progression of virus-related cirrhosis due to atrophy of right lobe resulting from significant reduction of its blood perfusion compared to the caudate & left lobes [30]. Although the RLLD could be measured by palpation and percussion, radiological studies demonstrated that clinical examination underestimates RLLD [31].

In agreement with our study, it was reported that liver volume, as measured by CT or MRI, was a potential predictor of GOVs and variceal bleeding among cases with hepatic cirrhosis [22]. Also a recent study found that the rough hepatic surface, splenic thickness and hepatic stiffness could be considered as independent predictors of GOV [32]. The strong NPP and the very low FOR of Lioaning score & RLLD in prediction of GVs in HCV related cirrhosis promote the use of these cheap, easily collected, and applicable NITs for exclusion of GVs in HCV cirrhosis; especially at hospitals where the facilities to manage GVs like special scopes, needles, glues, hemospray, EUS, coils and experts in GVs management, are lacking. This will enable the healthcare provider to take a decision regarding the referral of patients to a well-equipped secondary or tertiary care hospitals. Also, at well-equipped hospitals, the prediction of the presence of GVs either during AUGIB or during screening for varices, allows the staff at the endoscopy unit to be ready for the management of such serious cause of AUGIB.

The limitations of our study were that its results could not be generalized to all causes of LC. Also, the severity of GVs was not mentioned, and the cut-off points were used to confirm the presence or absence of GVs, but they did not differentiate risky from non-risky GVs. Lastly, these NITs, especially Liaoning score, depend on modifiable variables which can be affected by ongoing treatments like salt restriction and diuretics for ascites. It is recommended to test the accuracy of these NITs in prediction of GVs in different populations with different causes of LC.

CONCLUSION

Liaoning score & RLLD as measured by abdominal US, are significant predictors of GVs in Egyptian patients with HCV related cirrhosis. In this context, they had very high negative predictive value & very low false omission rate.

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