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RESEARCH ARTICLE

VARICEAL INDEX: SCORING SYSTEM FOR PREDICTION OF ESOPHAGEAL VARICES USING NON-INVASIVE PARAMETERS

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ABSTRACT

Background: Endoscopic examination is the gold standard for diagnosing esophageal varices (EV). However, endoscopy is invasive, painful and costly.The aim of this study was to find a noninvasive method to predict the presence of varices.

Methods: The study included 50 cirrhotic subjects. Clinical, laboratory, ultrasonographic, endoscopic data were obtained. A new noninvasive scoring system was postulated and a novel index included 7parameters namely platelet count, serum albumin, prothrombin concentration, right lobe of the liver diameter, portal vein diameter, splenic diameter and ascites was obtained. The scoring system was obtained by giving points to each variable.

Results: The relationship between the presence of esophageal varices and the parameters representing the variceal index was established. It was detected that at the cutoff value (score 12) specificity was 100% and sensitivity was 70% in prediction of esophageal varices.

Conclusion: The proposed variceal index could be a reliable tool to predict the presence of varices instead of a single parameter.

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INTRODUCTION

The prevalence of esophageal varices (EV) in patients with liver cirrhosis ranges from 60% to 80% and the reported mortality ranges from 17% to 57% (Zardi *et al*., 2007; Giannini *et al*., 2006). The American Association for the Study of Liver Diseaseand the Baveno IV Consensus Conference on portal hypertension recommended that all cirrhotic patients should be screened for the presence of EV when liver cirrhosis is diagnosed (Grace *et al*., 1998; Amico *et al*., 2001). However, Fewer than 50% of cirrhotic patients have varices at screening endoscopy and most have small-sized variceswith low bleeding risk. (Bințințan *et al*., 2013) furthermore, endoscopyis invasive, painful and costly, especially to those in developing countries, which ultimately limits the frequency of examinations. Previous studies have shown that biochemical, clinical and ultrasonographic parameters alone or together have a good predictive power for noninvasively assessing the presence of EV. (Wang *et al*., 2014; Abu El Makarem *et al*., 2011) Overall, the most common result of these studies was that parameters such as splenomegaly, thrombocytopenia, Childs score, ascites, portal flow patterns, and platelet count/splenic size ratio were predictors of the presence of EV. (Manohar *et al*., 2014) The aim of the present study is to overcome the obstacle offrequent endoscopies and to develop a safe, non-invasive and affordable index to better predict the presence ofvarices in liver cirrhosis.

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PATIENTS AND METHODS

After obtaining the approval of the ethical committee of faculty of medicine, CairoUniversity, the current study was conducted in Kasr Al-AinyHospital, Internal Medicine department over 12 months. Fifty subjects were included in this cross sectional study. All of them underwent a detailed clinical evaluation (from August 2011 till July 2013). The study included 50 patients with liver cirrhosis who presented to the emergency unitbecause of hematemesis, hepatic encephalopathy or spontaneous bacterialperitonitis (SBP). The included patients are those with liver cirrhosis, Child A, B. or Cwith age more than 18years. Patients with evidence of hepatocellular carcinoma onultrasonography, or previous or current treatment with beta-blockers, nitrates anddiuretics were excluded from the study. Patients who have received endoscopic orsurgical intervention for portal hypertension previously were also excluded from thestudy. Relevant history and physical characteristics including symptoms and signs ofliver failure, disturbed conscious level, liver size, and splenic

size were recorded. Asciteswas graded as none, mild (detectable only on ultrasound), moderate (visible moderateabdominal distension) or severe (marked abdominal distension). Diagnosisof cirrhosis was based on clinical, biochemical, and ultrasonographic findings.

Blood tests

Laboratory workup included measurement of hemoglobin, total leukocyte count, platelet count, prothrombin concentration (PC) and INR, serum concentrations ofbilirubin (total and conjugated), protein, and albumin, alanine aminotransferase (ALT) and aspartate aminotransferase (AST).

Abdominal Ultrasonography

All patients underwent ultrasonography after fasting overnight and the following data were recorded: diameter of the right lobeof the liver; nodularity of liver surface; spleen size (length of its longest axis); diameter of the portal and splenic veins; presence of portal-systemic collaterals; and confirmation of the presence or absence of ascites.

Endoscopic evaluation

All patients underwent upper gastrointestinal endoscopy for assessment of esophageal and gastric varices to detect sites of varices, grades of varices according to Paquetscoring system (Paquet and Oberhammer, 1978). Control of bleeding was done either with injection sclerotherapy orband ligation.

Variceal index:

Data has been collected to develop a scoring system as non-invasive index includingclinical, biochemical and sonographic parameters for predicting the presence ofesophagealvarices.We graded each parameter to 1,2,3,4 grades and then correlate withesophageal varices. Platelet :(100,000-150,000 grade 1), (75000-100000 grade 2), (50000-75000 grade3), (<50000 grade 4) Albumin :(3-3.5g/dl grade 1), (2.5-3g/dl grade 2), (<2.5g/dl grade 3) PC: (60-75% grade 1), (50-60% grade 2), (<50% grade 3) Right liver lobe: :(13cm -14cm grade 1), (12cm -13cm grade 2), (<12cm grade 3)Portal vein :(1.2cm - 1.29cm grade 1), (1.3cm -1.39cm grade 2), (>1.4cm grade 3) Spleen : (up to 15cm grade 1), (15-18cm grade 2), (>18cm grade 3) Ascites :(No grade 1), (minimal grade 2), (moderate grade 3), (marked grade 4)

Statistical analysis

Data were statistically described as mean± standard deviation (± SD), median andrange, or frequencies (number of cases) and percentages when appropriate. Comparison of the numerical variables between the study groups was done using Mann Whitney U test for independent samples when comparing 2 groups and Kruskal Wallis test when comparing more than 2 groups. For comparing categorical data, Chi square ($\chi 2$) test was performed. Exact test was used instead when the expected frequency is less than 5. Accuracy was represented using the terms of sensitivity and specificity. Receiver Operator Characteristic (ROC) analysis was used to determine the optimum cut offvalue of the total score in diagnosing OV. p values less than 0.05 was considered statistically significant. All statistical calculations were done using SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) software, version 15 for Microsoft Windows.

RESULTS

The present study enrolled 50 patients with a mean age of 51.78 ± 8.41 years. They were 14 females (28%) and 36 males (72%) with liver cirrhosis .Patients were presented byeither hematemesis (40 patients; 80%), spontaneous bacterial peritonitis (SBP) (4 patients; 8%), or hepatic encephalopathy (6 patients; 12%). Clinical, laboratory, ultrasonographicand endoscopic findings of all patients are illustrated in Tables (1,2).

Table 1. Patients characteristics regarding clinical, laboratory and sonographic data

Variable	Mean	Std. Deviation
Age	51.78	8.406
TLC(10^3/uL)	5.986	3.4426
PLT(10^3/uL)	125.74	80.365
HB(g/dl)	8.323	2.2927
AST(IU/l)	65.36	47.812
ALT(IU/l)	55.66	94.226
BIL(T)(mg/dl)	2.08	1.705
BIL(D)(mg/dl)	1.015	1.0760
T.P(g/dl)	6.408	0.6492
Alb.(g/dl)	2.472	0.5976
PC (%)	57.02	16.722
INR	1.701	0.7669
Rt.Lobe(cm)	13.309	1.7500
PV(mm)	1.6804	2.07237
SV(mm)	0.956	0.2727
Spleen(cm)	15.737	2.6085
Ascites: No	12	28
Mild	7	14
Moderate	17	34
Severe	14	24

TLC: total leukocytic count, Hb:haemoglobin, PLT: platelet count, AST: aspartate transaminase, ALT: alanine transaminase, BIL: bilirubin total & direct, ALB: albumin, T.P: total proteins, PC: prothrombin concentration, INR: international normalized ratioRt.Lobe: right lobe of the liver V: portal Vein diameter, SV:splenic vein diameter

Table 2. Upper Endoscopic findings in the studied patients

Grade	Percent (%)
No	6%
I	22%
I,II	14%
II	22%
II,III	18%
III	12%
III,IV	6%

Comparison between patients with and without EVs showed that higher percentage of patients with EVs had lower platelet count, serum albumin and PC levels than those without varices, but the difference did not assume statistical significance. All the patients with PC <50%, splenic diameter >15cm and massive ascites had EVs (Table 3). In order to put a scoring system, the 7 studied parameters wereused by giving points to each variable. An ROC analysis demonstrated that none of theselected parameter alone is sufficient in providing diagnostic accuracy for EVprediction. However, a significant diagnostic accuracy was achieved when these 7parameters were combined as one index. By establishing the above cutoff value, acorrect prediction for EV was possible. According to

the ROC curve of the total score for diagnosing OV, we detected that at the cutoff value (score 12) had 100% specificity and 70% sensitivity in prediction of EV. Figure (1)

Table 3. The relation between the studied parameters and the presence of esophageal varices

	Esophageal varices:N (%)				P value
Parameter	NO		YES		
	N	%	N	%	
Albumin: 3 or more	1	33.3%	6	12.8%	0.0607
2.5-3	1	33.3%	19	40.4%	
<2.5	1	33.3%	22	46.8%	
PC: 60 or more	2	66.7%	23	48.9%	0.570
50-60	1	33.3%	11	23.4%	
<50	0	0.0%	13	27.7%	
PLT: 100 or more	3	100%	29	61.7%	0.616
75-100	0	0.0%	5	10.6%	
50-75	0	0.0%	8	17.0%	
<50	0	0%.0	5	10.6%	
Right lobe: 13 or more	1	33.3%	29	61.7%	0.623
12-13	1	33.3	9	19.1	
<12	1	33.3	9	19.1%	
Spleen :Up to 15	3	100%	19	40.4%	0.131
15-18	0	0.0%	17	36.2%	
>18	0	0.0%	11	23.4%	
PV: <1.29	1	33.3%	10	23.3%	0.749
1.29-1.39	1	33.3%	9	20.9%	
1.4 or more	1	33.3%	24	55.8%	
Ascites: NO	2	66.7%	12	25.5%	0.405
Minimal	0	0.0%	7	14.9%	
Moderate	1	33.3%	16	34.0%	
Massive	0	0.0%	12	25.5%	

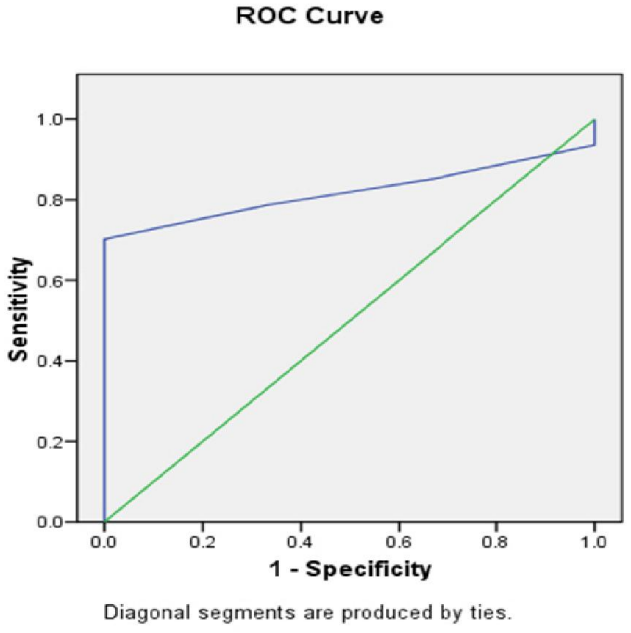

Figure 1. According to the ROC curve for total score in diagnosing OV at cutoff value 12 (70% sensitivity and 100% specificity). Receiver operator characteristic (ROC) analysis was used to determine the optimum cut off value of the total score in diagnosing OV. *p* values less than 0.05 was considered statistically significant

DISCUSSION

The population in Egypt has a heavy burden of liver disease, mostly due to chronic infection with hepatitis C virus (HCV). (Cuadros *et al*., 2014) EVs present in 40% of Child A patients, andin 85% of Child C of patients with cirrhosis per yearand its presence correlates with the severity of liver disease. (Grace, 1997) Compared with many previous studies of non-invasive screening tools, the current study has a unique feature which is proposing a scoring system for prediction of EVscollecting the most important parameters that might predict and correlate with the presence of EVs. Our study included seven parameters (platelet count, albumin, PC, right lobe of the liver, portal vein diameter, splenic diameter, and ascites). We found that none of these parameters alone was restrictedto patients with EVs.In our sitting, about 40% of patients with EVs had platelet count below 100.000/mm^3 while patients without varies had higher count. Thrombocytopenia is frequent in patients with cirrhosis. (Qamar *et al*., 2008) Several studies suggested that platelet count maypredict the presence and the size of EVs; however the discriminating threshold for the presence of varices varies widely. (Berzigotti *et al*., 2013; Cherian *et al*., 2011) Many factors contribute to Thrombocytopenia in patients with chronic liver disease other than portal hypertension including auto antibodies against platelets, and direct effect of HCV. (Giannini *et al*., 2006) Some previous studies found no association between hypoalbuminemia and the presence of EVs. (Grace, 1997; Lopamudra *et al*., 2011) However, other studies showed its value inEVs prediction. (Arulprakash *et al*., 2010; Min *et al*., 2012) like prothrombinconcentration, serum albumin reflects the synthetic function of the liver.In agreement with previous result, PC alone was not related to presence of EVs. (Lopamudra *et al*., 2011) However, PT was associated with the size of EVs in other studies. (Hong *et al*., 2011) The relation between the sonographic findings and the presence of EVs has been previously searched. (Jeon *et al*., 2006; Adel and George, 2011) Liver size was found to be poorly correlated with the portal pressure although high pressure has been found more often with small, contracted and fibrotic liver (Sherlock and Dooley, 2002), Contradictory to our results, Dragoni *et al*. reported that patients with EVs have significantly higher hepatic longitudinal diameter, splenic longitudinaldiameter, PV diameter than the remaining HCV patients. (Kashani *et al*., 2015) An enlarged spleen is the single most important clinical sign of portal hypertension and found in almost all patients. It is larger in young people withmacronodular rather than micronodular cirrhosis. (Sherlock and Dooley, 2002) Moreover, splenomegaly is found more frequently in posthepatitic cirrhosis than in alcoholic cirrhosis. (Kashani *et al*., 2015)

Similar to other series (Dragoni *et al*., 2005; Chawla *et al*., 2012), our study foundall patients with EVs had splenic diameter more than 15 cm. although there was no statistically significant difference between patients with and with EVs.These differences may be due to the variations among different studies regarding the etiology and the stage of liver cirrhosis. Most of patients with EVs in our study had ascites.Various studies found that the presence of ascites was predictor of EVs. (Cherian *et al*., 2011) In hepatitis C cirrhosis, portal pressure ispresumably relatively stable whereas in alcohol-related liver disease, portal pressure may vary with consumption and abstinence. (Bolognesi *et al*., 2014) In our study, More than half of patients with variceshad PV diameter > 1.4 cm. Although PV diameter has been reported as a significant predictor of EVs, (Manohar *et al*., 2014) it lacks the accuracy owing to intra- and interobserver variation (Baik, 2010) None of aforementioned clinical, biochemical, and radiological parameters is sufficiently accurate toprevent screening endoscopy. Thus, the current study was trying to find a scoring system that collects the most important parameters in

order to put an index to predict the presence of EVs in patients with liver cirrhosis. Seven parameters were used which constitute the variceal index and points were given to each variable according to the ROC curve at the cutoff (score 12) specificity was 100% and sensitivity was 70% in predicting EVs. This index provides higher specificity for EVs prediction than previously given by any single parameter. (Arulprakash *et al*., 2010; Min *et al*., 2012; Hong *et al*., 2011) It's worth to mention that our study has severallimitations; it was a cross-sectional study that needs to be further examined in a longitudinal study. The study covered only a small sample size 50 patients due to the exclusion criteria and the difficulties that we faced to follow patients during admission.

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