Research Article

Role of right liver lobe diameter /albumin ratio in the assessment of esophageal varices in Egyptian patients with liver cirrhosis

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Abstract
Background and Study Aims: Portal hypertension is a frequent complication of liver cirrhosis, and plays a crucial role in the transition from the pre clinical to the clinical phase of the disease, Bleeding from ruptured oesophagogastric varices is the most severe complication of cirrhosis, and is the cause of death in about one third of cirrhotic patients. Cirrhotic patients frequently undergo screening endoscopy for the presence of varices. In the future, this social and medical burden will increase due to the greater number of patients with chronic liver disease and their improved survival. In this study, our aim was to determine the predictive value of noninvasive parameters (Rt. lobe diameter/ albumin ratio) in the prediction of esophageal varices. **Patients and Methods:** ١٥٠ patients with liver cirrhosis with no history of variceal haemorrhage were subjected to clinical examination; laboratory investigations (CBC, Liver function tests, prothrombin time and concentration), modified Child-Pugh score and Abdominal ultrasonography (studying the right lobe and left lobe diameter, the presence of periportal thickening, the splenic longest axis and the presence of ascites and Portal vein vein diameter, Right liver lobe diameter/albumin ratio were calculated for all patients. Upper endoscopy was done for detection and grading of esophageal varices. **Results:** This study revealed that ١٣٠ (٨٦.٦٪) of patients had oesophageal varices ٨٠, The predictors that showed statistically significantly associated with the presence of varices were splenomegaly, thrombocytopenia, shrunken Rt. hepatic lobe, and the Increased right lobe diameter/Albumin. **Conclusion:** Right lobe diameter/Albumin ratio is good predictor for the presence of esophageal varices.
Key Words: albumin ratio, liver**,** hypertension**,** Liver function tests

Introduction
Cirrhosis is a pathologic condition characterized by fibrosis of the liver parenchyma and evidence of regenerative activity, resulting in portal hypertension (Neil Rajoriya and David Gorard, ٢٠١٣).

Esophageal varices is related to portal hypertension which commonly accompanies the presence of liver cirrhosis, with a prevalence that can range from ٤٠ to ٨٠٪ in patients with cirrhosis (Garcia-Tsao and Bosch, ٢٠١٠).

The yearly rate of development of ‘‘new” varices is about ٥–١٠٪ per year in patients with cirrhosis, and the progression from small to large varices occur in ١٠٪ to ٢٠٪ of cases after ١ year. In the ٢ years following the first detection of esophageal varices, the risk of variceal bleeding ranges between ٢٠٪ to ٣٠٪ and results in ٢٥٪ to ٥٠٪ mortality within a week of the first bleeding episode (Garcia-Tsao et al., ٢٠١٠).
The current recommendations are that all cirrhotic patients should be screened for the presence of varices at the time of initial diagnosis of cirrhosis. Follow-up endoscopy should be performed at ٢-٣ years intervals

in compensated patients with no varices, and at ١-٢ years intervals in compensated patients with small varices (de Franchis, ٢٠١٠).
Although all patients with cirrhosis will eventually develop esophagogastric varices at a given point in time, a variable proportion of un selected cirrhotic patients will not have varices. Therefore, performing endoscopy in all patients to detect varices implies a number of unnecessary endoscopies (D'Amico et al., ٢٠٠١)

These recommendations imply a considerable burden of endoscopies and related costs; they require that patients repeatedly undergo an unpleasant invasive procedure, even though up to ٥٠٪ of them may still not have developed esophageal varices ١٠ years after the diagnosis of cirrhosis. Therefore, these guidelines might not be ideal for clinical practice (D'Amico and Morabito, ٢٠٠٤)

It would be impossible to perform endoscopic examinations at regular interval for all patients with chronic liver disease and it may be more cost-effective to routine screening of varices, On the other hand, many patients refuse repeated endoscopies because of discomfort and fear of transmission of infection (Thomopoulos et al., ٢٠٠٣).

Endoscopic examination is considered an invasive procedure. Moreover, sedation of a cirrhotic patient to perform endoscopy may be hazardous (Mc Guire, ٢٠٠١). Also, diagnostic upper gastrointestinal endoscopy may contribute to bacterial infections in patients with liver cirrhosis due to associated disruption of the natural barriers (Almeida et al., ٢٠٠١).

As a consequence, several non-invasive tools have been evaluated as an alternatives to endoscopy, to avoid unnecessary endoscopy in low-risk patients, and to identify noninvasive factors that may predict the presence of esophageal varices (Kim et al., ٢٠١٠, Sebastiani et al., ٢٠١٠ and Angelo Zambam et al., ٢٠١٣)

As far as the clinical/laboratory parameters are concerned, some of them have been found to correlate with the presence of esophageal varices. However, none of these parameters (or combination of them) has been proven precise enough to make endoscopy unnecessary (D'Amico et al, ٢٠٠١).

Patient and methods

١٥٠ patients with liver cirrhosis with no history of variceal haemorrhage were subjected to clinical examination; laboratory investigations (CBC, Liver function tests, prothrombin time and concentration), modified Child-Pugh score and Abdominal ultrasonography (studying the right lobe and left lobe diameter, the presence of periportal thickening, the splenic longest axis and the presence of ascites and Portal vein vein diameter. Right liver lobe diameter/albumin ratio were calculated for all patients. Upper endoscopy was done for detection and grading of esophageal varices. The patients were grouped according to the results of the upper GIT endoscopy, into Patient with oesophageal varices (١٣٠patients) and Patients without oesophageal varices (٢٠ patients).
All collected data were analyzed Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS, version ٢٠.٠).

Results

Esophageal varices were present in ١٣٠ patients (٨٦.٦٪),In the current study, the presence of varices was significantly higher in Child C patients and Child B patients compared to Child A patients (٤٥٪, ٣٥٪, ٢١٪) respectively with p value =٠.٠٠٠٣.

In univariate analysis for the presence of varices between patients with and without varices, statistical significance were present for splenomegaly (p=<٠.٠٠١), hypoalbuminaemia (p=<٠.٠٢), thrombocytopenia (p= <٠.٠٠١), Right lobe diameter (p=<٠.٠٢) and Increased right lobe diameter/Albumin ratio (p=<٠.٠٠٢). The multivariate analysis (by logistic regression stepwise method) of the significant variables (by univariate analysis); splenomegaly, thrombocytopenia,

shrunken Rt. hepatic lobe and the Increased right lobe diameter/Albumin independent risk factors for the presence of varices.

Discussion

In our study ٨٦.٦٪ of patients had esophageal varices, the prevalence of esophageal varices was estimate in multiple studies, this results are in agreement with that obtained by Pagliaro et al., ١٩٩٥ who reported prevalence of ٧٦٪ in cirrhotic patients with ascites, Recently; Hesham et al., ٢٠١٠, Serag and Dalia, ٢٠١١, Ghada et al., ٢٠١١ and in studies done on Egyptian patients reported prevalence of ٩١.٧٪, ٨٢٪ and ٨٣.٢٪ respectively. But Emad et al., ٢٠٠٩ reported lower prevalence (٦٤.٣٪) in Egyptian cirrhotic patients and that was due to choosing of compensated child class A patients only in their study.

An enlarged spleen was detected clinically and by ultrasonography in the studied patients, and was significantly prevalent in patients with varices {٥٨ (٤٤.٦٪) P=٠.٠١}, the same finding was reported in many studies, Thomopoulos et al. (٢٠٠٣) in a study done on ١٨٤ patients with liver cirrhosis they found that splenomegaly were independent predictor for the presence of esophageal varices , Sharma and Aggarwal (٢٠٠٧) reported the same finding. Serag and Dalia ٢٠١١ on their study which conducted on ١٠٠ Egyptian cirrhotic patients, for noninvasive prediction of esophageal varices, they found that enlarged spleen gave high accuracy for prediction of esophageal varices.

Sherlock and Dooley ٢٠١١, reported that an enlarged spleen is the most important clinical sign of portal hypertension and found in almost all patients. It has been reported that portal venous congestion leads to splenomegaly.

Analysis of data in our study showed that low level of serum albumin was significantly prevalent in patients with varices {٣.١٥±٠.٧٧ versus ٣.٥٧±٠.٨٤ and (p=٠.٠٢)}, Hypoalbuminemia in cirrhosis is multifactorial and may be due to reduced production (liver parenchyma replaced by fibrous tissue), or increased loss through gut (portal gastropathy/enteropathy) all related to portal hypertension (Torres et al., ١٩٩٨). Similar result had been reported in several studies; Schepis et al. (٢٠٠١), on their study conducted on {One hundred forty-three consecutive cirrhotic patients} for prediction of esophageal varices found that low serum albumin was more prevalent with patients with esophageal varices (p=٠.٠٠٨).

Madhotra et al., (٢٠٠٢), found that low serum albumin was significantly associated with the presence of esophageal varices with (P value =٠.٠٠١).

Hossain et al,. ٢٠١١, in a study which was done on ١٠٠ cirrhotic patients for estimation of hypoalbuminemia and its correlation with development of esophageal varices, concluded that hypoalbuminemia is a good surrogate marker for the presence of esophageal varices.

Ayman et al., ٢٠٠٩ in their study on ١٢٠ Egyptian cirrhotic patients found that low serum albumin is significantly associated with presence of varices (P value = ٠.٠٠٩) , same results was found on a study by Adel and George ٢٠١١.

A low platelet count has been constantly found to be related to the presence of varices (Burton et al., ٢٠٠٧), in our study the mean platelets count was significantly lower in the patients with varices, {١٠٧.١٨±٤٣ versus ١٤٠.١٥±٢٨.١٥ (P value= ٠.٠٠١)}.

This result is agreed by the results of Hesham et al., ٢٠١٠ and Serag et al., ٢٠١٢ Serag et al., ٢٠١٢ found that platelet count at cut off value ١٣١ x١٠٣ is a good predictor and showed significant correlation for presence of esophageal varices.

Hesham et al., ٢٠١٠ concluded that thrombocytopenia can be used to stratify risk for occurrence of esophageal varices in cirrhotic patients and gastroscopy will have a high yield for varices when platelet count is ≤١٣٠,٠٠٠/mm³.

Schepis et al., (٢٠٠١) reported a mean platelets count of < ١٠٠ x١٠٣/ mm for prediction of esophageal varices in cirrhotic patients. While Zaman et al., (٢٠٠١) reported a mean platelets count of < ٩٠ x١٠٣/ mm in patients with varices versus ١٢٨.٥ x١٠٣/mm for patients without varices, and platelet count of <٩٠ x١٠٣/ mm increased the risk of having esophageal varices by nearly ٢.٥ fold.
Hong et al., ٢٠٠٩ stated that the discriminating threshold for the presence of varices varies widely ranging between (٦٨ x١٠٣/ mm) and (١٦٠ x١٠٣/ mm) , These results could be explained by variation among studies regarding etiology and stage of liver cirrhosis.

The lower mean platelets count in these studies may be attributed to the high percentage of patients with alcoholic cirrhosis included in these studies, because alcohol has a myelotoxic effect on the bone marrow (Peck-Radosavlijevic, ٢٠٠٠).

Thrombopoietin production depends on functional liver cell mass and it is reduced when liver cell mass is severely damaged. This leads to a further decrease in peripheral platelets in patients with advanced liver disease while thrombopoietin production is restored after liver transplantation. This means that, platelet count in cirrhotic patients is considered as an indirect marker of both portal hypertension and impaired liver synthetic capacity (Thomopoulos et al., ٢٠٠٣).

In our study we found that the more advanced the liver disease (according to child class scoring of the patients), the more likely the presence of varices, as expected, esophageal varices were significantly more in Child-class C patients and Child-class B patients compared to Child-class A patients ٥٨(٤٥٪), ٤٥(٣٥٪) and ٢٧(٢١٪) respect-tively with P value = ٠.٠٠٠٣.

Burton et al., ٢٠٠٧ showed that the incidence of esophageal varices increases with worsening Child-Pugh class and raised a predictive model relying on thrombo-cytopenia and Child-Pugh class. Burton's model revealed that patients with platelet count less than ٩٠,٠٠٠/mm will have a probability of ٠.٥٧, ٠.٨١ and ٠.٨٢ of having any varices, if they are in Child A, B, or C classes, respectively.

Serag et al., ٢٠١٢ found that advanced Child class (Child class B&C) showed statistically significant correlation with the presence of esophageal varices, Ayman et al., ٢٠٠٩ reported that patients with Child class B and C had higher incidence of esophageal varices compared to Child A patients (٣٩.٨٪,٤٣.٤٪,١٦.٨٪) respectively with p value=٠.٠٠٤.

In our study we found that patients with shrunken right lobe of the liver had significantly high incidence of varices (P = ٠.٠٠٠١).

Sharma and Aggarwal (٢٠٠٧), found that shrunken liver correlated significantly with the presence of varices (P=٠.٠٢), Same result reported by Serag et al., ٢٠١٢ who found significant difference in the live size between the patient with varices and those without varices (P=٠.٠٣).

The application of the right liver lobe diameter/albumin ratio as a predictor of esophageal varices was first proposed by Alempijevic et al., ٢٠٠٧ in a study of ٩٤ cirrhotic patients, he found that Right liver lobe/albumin ratio correlated with presence of esophageal varices, We found statistical significant difference between the right liver lobe diameter/albumin ratio in the patient with varices and those without varices ٤٧.٥±١٧.٤ versus ٣٥.٩±١٣.٥ (p value= ٠.٠٠٥), the same results were obtained by Hesham et al, (٢٠١٠), Serag and Dalia, (٢٠١١) and Adel and George (٢٠١١).

In multivariate logistic regression analysis of the parameters which showed significant difference between patients with varices and those without varices we found that enlarged spleen, thrombocytopenia decr-eased right lobe diameter, and right liver lobe diameter/albumin ratio were the parameter which associated with the presence of esophageal varices.

A receiver operator characteristic (ROC) curve was constructed and the area under the ROC curve (AUROC) was calculated. The cutoff value of the right lobe diameter/ Albumin ration was determined at the point of highest sensitivity and specificity, cut off value were (٣٢.٨) where sensitivity and specificity were ٨٣.١٪ and ٦٥٪ respect-tively, the area under curve (AUC) is ٠.٨٠٪ (p=٠.٠٠٢) which has good prediction power for presence of esophageal varices.

Conclusion

Thrombocytopenia, splenomegaly, advan-ced liver disease (worsen child score) and decreased right lobe diameter, were significantly associated with the presence of varices. The right liver lobe diameter/ albumin ratio might be considered a significant predictor for the presence of esophageal varices.

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