

Correlation between the Degree of Esophageal Varices and Liver Stiffness in Liver Cirrhosis Patients

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ABSTRACT

Background: Bleeding due to rupture of esophageal varices is one of main cause of death in liver cirrhosis, that endoscopy screening is recommended. However endoscopy is invasive and frequently cannot be performed due to contraindication, high-cost or uncomfortable effect to the patients, particularly on patients have not had any bleeding before. Consequently, it is necessary to find other assessment which can predict the presence of esophageal varices. Recent studies found liver stiffness measurement by the liver transient-elastography is one of non invasive measurement to evaluate liver fibrosis. This study was designed to know the correlation between degree of the esophageal varices and the degree of liver stiffness.

Method: This was cross sectional study. Liver cirrhosis patients were consecutively enrolled in this study. They underwent endoscopy to determine esophageal varices and subsequently the liver transient-elastography by Fibroscan technique to determine liver stiffness. Degree of the esophageal varices based on OMED criteria. Liver stiffness are expressed in kilopascal (kPa). Correlation analysis was done to assess this study.

Result: There were 13 subjects. Most subjects were male, age > 50 years and Child-Pugh A or B. The mean value of liver stiffness was 35.55 ± 23.60 kPa and mean OMED was 5.61 ± 2.14 . The coefficient correlation between degree esophageal varices and degree liver stiffness was 0.492, $p = 0.087$.

Conclusion: There is moderate correlation but not statistically significant between the degree of liver stiffness and the degree of esophageal varices. Larger sample size is necessary to find the correlation between the degree of liver stiffness and esophageal varices.

Keywords: liver cirrhosis, degree of esophageal varices, liver stiffness

INTRODUCTION

Esophageal Varices (EV) rupture bleeding is one of liver cirrhosis complication that becomes major cause of death in liver cirrhosis patients. Prevention of EV rupture bleeding rely on pharmacological treatments, banding varices or sclerotherapy, is widely

considered effective and may reduce mortality.¹ Risk of EV rupture is related to degree and size of varices. Esophagogastroduodenoscopy (EGD) screening is recommended to evaluate degree and size of EV.² However endoscopy is invasive and frequently cannot be performed due to contraindication, high-cost or uncomfortable effect to the patients, particularly on patients have not had any bleeding before.³ For these reasons selection of patients with a high probability of EV, especially large EV has been proposed with various non-invasive criteria as ratio right liver lobe

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and albumin serum, platelet count, or ratio platelet count and spleen size. Although these criteria of selection are simple but poorly discriminated, hardly use in clinical practice.⁴ Consequently, it is necessary to find other assessment which can predict the presence of esophageal varices. Recent studies found liver stiffness measurement by the liver transient-elastography using FibroScan[®] is one of promising non invasive measurement to evaluate liver fibrosis. Transient Elastography is a sonography-based and rapid bedside method has been designed to quantify liver fibrosis by means of elastography, which is based on changes of the physical properties of the liver during chronic liver injury. Tissue elasticity is acquired through pulse-echo ultrasound, measuring the speed of the low-frequency elastic shear wave, the S-wave. The wave travels faster means the elasticity more loss or stiffness more increase. The results of liver elasticity or stiffness are expressed in kilopascals (kPa). This examination can be performed easily, inexpensive, and no side effects although obesity, ascites and narrow intercostals spaces are physiological boundaries that hamper the accuracy of the test and may be virtually impossible to take measurements in such patients.^{5,6}

The amount of fibrosis can be quantified very easy, reliable, and feasible in more than 95% of the patients. In cirrhotic patients, liver stiffness measurements range from 12.5 to 75.5 kPa. Cut-off values were 7.1 kPa for $F \geq 2$, 9.5 kPa for $F \geq 3$ and 12.5 kPa for $F = 4$ (defined according to the METAVIR classification system).⁷

Many studies showed that liver transient elastography could predict the degree of esophageal varices (EV).⁸ Nguyen et al found that the cut off value of liver stiffness measurement (LSM) was 27.5 kPa in grade II-III EV and 62.7 kPa in esophageal ruptur bleeding with positif predictive value (PPV) > 90%.⁹ Vizzutti et al showed there is a significant correlation between degree of hepatic vein or hepatic venous pressure gradient (HPVG) and degree of liver stiffness. This study also showed the correlation between liver stiffness and the presence EV ($p = 0.002$) although NPV and PPV only 66% and 77%. Prevalency of varices was 64% with cut off value of liver stiffness was 17.6 kPa and sensitivity 90%. But there is no correlation between degree of liver stiffness and degree of esophageal varices. Therefore the liver transient elastography cannot replace EGD especially to evaluate the degree of EV.¹⁰ But Jung et al found that liver stiffness measurement was strongly correlated with the presence of EV. LSM value was 42.7 ± 21.9 kPa ($p < 0.0001$) in patients with EV ($n = 82$) and 19.1 ± 12.6 kPa in patients without EV

($n = 30$), however, there was a weak correlation between LSM and the size of EV.¹¹ Kazemi et al also found liver stiffness measurement ≥ 19 kPa was a predictor the presence of EV grade \geq II.¹²

There is no data about the correlation between degree of liver stiffness and degree of esophageal varices in liver cirrhosis patients in Indonesia. The objective of this study is to know the correlation between degree of liver stiffness and degree of esophageal varices in liver cirrhosis patients. This study can provide data to predict the presence esophageal varices with liver stiffness measurement and it will be prescreening before endoscopy or patients refuse to endoscopy.

METHOD

These was cross sectional study that conducted from September 2008 until March 2009. Liver cirrhosis patients were consecutively enrolled this study. Liver cirrhosis based on clinical, laboratory and abdominal ultrasound. Patients undergone endoscopy by gastroscope GF Olympus[®] GIF J30 to determine esophageal varices in Tarakan hospital, subsequently the liver transient-elastography by *Fibroscan* technique to determine liver stiffness in Division of Hepatology Department of Internal Medicine Cipto Mangunkusumo hospital. Degree of the esophageal varices based on OMED criteria by doing summation between F grading (F0-F3) and the type of red color sign (red wale marking, cherry red spot, hemato cystic spot, diffuse redness), erosion, ground color (blue or white) and location of varices (1/3 inferior, 1/3 middle, 1/3 superior). Liver stiffness is expressed in kilopascal (kPa).

Inclusion criteria were patients liver cirrhosis, age 20-65 years who had esophageal varices. Exclusion criteria were patients had contraindication to undergo endoscopy, could not do liver transient-elastography (massive ascites, obesity), patients on going treatment with beta blocker, banding or sclerotherapy varices before and patients treated with beta blocker, nitrat, diuretic, anti fibrotic, hepato protector, antioxidant, immunomodulator, interferon, pitresin or ocreotide therapy.

This study was evaluated by correlation analyses and linear regression Pearson or Spearman with significance level < 0.05 and 95% confidence interval. Statistical analysis used SPSS version 11.0.

RESULTS

There were 13 subjects. The mean value of liver stiffness was 35.55 ± 23.60 kPa and mean OMED was 5.61 ± 2.14 . Most subjects are male, age > 50 years and child A or B.

Table 1. Characteristic of patients

Characteristic	n (%)	Mean
Sex		
Male	9 (69.2%)	
Female	4 (30.8%)	
Age (years)		50.77
< 50	6 (46.1%)	
≥ 50	7 (53.9%)	
Child		7.69
A	5 (38.5%)	
B	5 (38.5%)	
C	3 (23.0%)	

The coefficient correlation between degree esophageal varices and degree liver stiffness was 0.492, $p = 0.087$. There was a moderate correlation between the degree of liver stiffness and the degree esophageal varices that correlation was not statistically significant.

DISCUSSION

Many studies showed that liver transient elastography could predict the degree of esophagus.⁸ This study also showed a tend to be positive correlation between degree EV and degree of liver stiffness. Mean of liver stiffness measurement was 33.55 ± 23.60 and mean OMED value was 5.61 ± 2.14 that similar with grade II-III of EV. These results are same with Nguyen et al found that the cut off value of liver stiffness in grade II-III EV was 27.5 kPa and 62.7 kPa in esophageal varices bleeding with PPV > 90%.⁹ Jung et al found that liver stiffness measurement was strongly correlated with the presence of EV ($p < 0.0001$): the LSM value was 42.7 ± 21.9 kPa in patients with EV ($n = 82$) and 19.1 ± 12.6 kPa in patients without EV ($n = 30$). The area under the receiver operating characteristic curve (AUROC) was 0.818 (95% CI = 0.732-0.904) for predicting the presence of EV, and an LSM value of 19.7 kPa was predictive of the presence of EV with a sensitivity of 87%, a specificity of 70%, a PPV of 89%, and a NPV of 66%. However, there was a weak correlation between LSM and the size of EV.¹¹ Kazemi also found liver stiffness measurement ≥ 19 kPa was a predictor the presence of EV grade \geq II.¹² Vizzutti et al showed there is a significant correlation between degree of hepatic vein or HPVG and degree of liver stiffness. This study also showed the correlation between liver stiffness and the presence EV ($p = 0.002$) although NPV and PPV only 66% and 77%. But there is no correlation between degree of liver stiffness and degree of esophageal varices although the AUROC

that predict EV was 0.76 and cut off value of liver stiffness was 17.6 kPa with sensitivity 90%.¹⁰ Therefore same with Vizzutti study, this study showed that liver transient elastography still cannot replace EGD especially to evaluate the degree of EV.¹⁰ Limitation of this study is minimal sample size because of time limitation.

CONCLUSION

There is moderate correlation but not statistically significant between the degree of liver stiffness and the degree of esophageal varices. Larger sample size is necessary to find the correlation between the degree of liver stiffness and esophageal varices.

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