Original Article

Hepatic vein waveform in liver cirrhosis: Correlation with Child's class and size of varices

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Abstract

Objective: To determine the correlation of hepatic venous waveform changes with severity of hepatic dysfunction and grading of oesophageal varices.

Methods: A cross-sectional analytical study was conducted at Jinnah Postgraduate Medical Centre, Karachi, Medical Unit-III, Ward-7 from January 2009 to December 2009. Cirrhotic patients with portal hypertension were included in study. Patients presented with acute variceal bleeding, previous treatment with beta blockers or nitrates, sclerotherapy endoscopic band ligation, portal vein thrombosis, severe clotting defects, hepatic encephalopathy grade III or IV and noncirrhotic portal hypertension; were excluded from the study. Upper G I endoscopy was carried out in all patients after informed consent. Oesophageal varices were classified according to Baveno III while hepatic function was assessed and grouped by Child-Pugh classification. Colour Doppler ultrasound was carried out on all patients. Their waveforms were classified as monophasic, biphasic triphasic and the correlation of these hepatic vein waveforms with Child-Pugh class and size of oesophageal varices was evaluated. Statistical significance was defined as P?0.05.

Results: Total of 65 patients who met the inclusion criteria and included in the study with mean age of 47.39±10.91 (range 23-70) years. Among these 51 (78.5%) were males while 14 (21.5%) were females. On the basis of hepatic function 32 (49.2%) patients presented in Child-Pugh Class A, 23 (35.4%) with Class B and 10 (15.4%) patients had Class C. Hepatic venous waveform was triphasic in 5 (7.7%), biphasic in 18(27.7%), and monophasic in 42 (64.6%) cases. The relationship of these waveforms had significant relation with hepatic dysfunction ($p < 0.012$) while insignificant with grading of oesophageal varices (p 0.29). Upper GI endoscopy revealed large grade varices in 37 (56.9%) patients, 17 (26.2%) patients had small grade varices while no varices were found in 11 (16.9%) patients.

Conclusion: Hepatic venous waveform pressure changes have significant relation with severity of hepatic dysfunction but insignificant relation with grading of oesophageal varices. Further studies using a combination of various Doppler parameters are required to create indices with a better predictive value.

Keywords: Hepatic vein waveforms. Oesophageal varices. Child-Pugh Class. (JPMA 62: 794; 2012)

Introduction

Portal hypertension is one of the major complications of chronic liver disease and cirrhosis. The presence of portal hypertension is related to the formation of oesophageal varices, ascites and fluid and electrolyte redistribution, hepatorenal syndrome, and hepatic encephalopathy.[1-3] Portosystemic collaterals develop above a portal pressure gradient of 10mmHg,[4] and bleeding from varices develops when pressure rises above 12 mm Hg[5] Accordingly, in BAVENO III, portal pressure above 10 mm Hg was taken as the cutoff for "clinically significant portal hypertension".[6]

Direct portal pressure measurement requires puncturing the portal vein surgically or percutaneously. These approaches are not feasible in clinical practice and have potential for complications in cirrhotics with coagulopathy. Moreover, there is an additional requirement for hepatic vein catheterization for measurement of PPG.[7]

Currently, doppler ultrasound has emerged as a non invasive technique that can be performed on outpatient basis. Hepatic venous waveform (HVW) is useful in the noninvasive evaluation of severity of portal hypertension; biphasic and monophasic HVW are associated with severe portal hypertension.[8-10] Cirrhosis of the liver results in loss of compliance in hepatic veins and leads to portal hypertension and may reflect as biphasic or monophasic waves which are essentially abnormal and indicate moderate to severe portal hypertension respectively (HVPG 12-15mmHg).[10-12]

The clinical correlations of HVW in several important aspects of CLD still remain to be fully studied.

The relation of findings of monophasic, biphasic and triphasic on Doppler ultrasound to the grade of varices and the severity of liver disease is also not well established. We undertook this study to evaluate the correlation of HVW in cirrhotic patients with Child's status and variceal grade.

Patients and Methods

Patients admitted to the hepatology section of medical unit III between 2002 and 2004 who had presented with signs/symptoms and/or investigations suggestive of chronic liver disease were prospectively included in the present study. A detailed history and a thorough physical examination were done in each patient. Patients presented with acute variceal bleeding, with a previous treatment with beta blockers or nitrates; with portal vein thrombosis; hepatocellular carcinoma (HCC), severe coagulation defects, hepatic encephalopathy grade III or IV, portal hypertension secondary to non cirrhotic causes, previous endoscopic procedures like sclerotherapy and bandligation or transjugular intrahepatic portosystemic shunt (TIPS); and those who did not provide informed consent were excluded from the study.

Doppler ultrasound was conducted after 8 hours fasting on patients by same sonologist using a VOLUSION 730 PRO-V, Kretz Austria Doppler machine with a 3.5 MHz convex probe. After taking rest in supine position recordings were carried out with probe in right intercostal space, patient holding his/her breath in end expiration for at least 5 seconds. The right hepatic vein was identified at a distance of 3-5 cms from the junction of hepatic vein with inferior vena cava and waveforms were obtained. These waveforms were classified as monophasic (flat - without flutter), monophasic to biphasic (flat and with flutter), biphasic (no reversed flow, decreased phasic oscillation), biphasic to triphasic (normal phasic oscillations yet no flow reversal) and triphasic (reversed flow in at least one phase).[13-15] To avoid bias the Doppler evaluation was done first and to keep the sonologist blind the clinical or biochemical data was not shared.

Complete blood count, liver function test, total protein, A/G ratio, serum albumin, HBsAg, anti HCV, ultrasound whole abdomen, were all done. Upper GI endoscopy was carried out in all patients after informed consent. Oesophageal varices were classified according to Baveno III, i.e. into two grades; small and large varices with size of ≤5 mm and >5mm respectively.[6] The hepatic function was assessed and grouped by Child-Pugh classification.

The correlation of these hepatic vein waveforms with Child-Pugh class and size of oesophageal varices were evaluated.

The ethics committee of the hospital approved the protocol, and all patients provided written informed consent to participate in the study.

Quantitative data are expressed as mean ± SD. Correlation between variables was analyzed using the Spearman correlation test. Differences between categorical variables were assessed by using Chi-square test. Statistical analysis was done using SPSS 10.0.5 software package (SPSS Inc., Chicago, IL). Statistical significance was defined as $P \leq 0.05$.

Results

Total of 65 patients who met the inclusion criteria were included in the study with mean age of 47.39±10.91 (range 23-70) years. Among these 51 (78.5%) were males while 14 (21.5%) were females. Forty two (64.6%) patients had Anti HCV reactive, 8 (12.3%) had HBV, 2 (3.1%) had dual infection of HBV and HCV, 1 (1.5%) had HBV and HDV while in 12 (18.5%) patients no known cause of cirrhosis was present. On the basis of hepatic function 32 (49.2%) patients presented in Child-Pugh Class A, 23 (35.4%) with Class B and 10 (15.4%) patients had Class C. Hepatic venous waveform was triphasic in 5 (7.7%), biphasic in 18(27.7%), and monophasic in 42 (64.6%) cases. Upper GI endoscopy revealed large grade varices in 37 (56.9%) patients, 17 (26.2%) patients had small grade varices while no varices

Table: Correlation of hepatic venous waveform with different variables.

Variable	Hepatic venous waveforms			p-value
	Triphasic (n=5)	Biphasic (n=18)	Monophasic (n=42)	
Child-Pugh class				
A	3	13	16	
B	2	4	17	0.012
C	0	1	9	
Ascites				
None	2	15	24	
Slight	3	3	15	0.187
Moderate to severe	0	0	3	
Encephalopathy				
None	4	18	41	
Slight to moderate	1	0	1	0.066
Severe	0	0	0	
Bilirubin (mg/dl)				
<2	4	10	21	
3-Feb	1	6	13	0.674
>3	0	2	8	
Albumin (g/dl)				
>3.5	2	11	12	
2.8-3.5	3	6	23	0.152
<2.8	0	1	7	
Prothrombin time (seconds increased)				
3-Jan	3	13	17	
6-Apr	1	4	22	0.133
>6	1	1	3	
Oesophageal varices				
No varices	0	3	8	
Small varices	3	7	7	0.29
Large varices	2	8	27	

were found in 11 (16.9%) patients. Changes in HV waveforms didn't correlate with grading of oesophageal varices (r = 0.29).On the basis of hepatic dysfunction; 9 (90%) of Child-Pugh Class C, 17 (73.91%) of Class B and 16 (50%) of class A patients had monophasic HV waveform and found that as severity of hepatic dysfunction increased the HV waveforms showed changes from normal pattern of triphasic to biphasic and/or monophasic and this correlation was statistically significant (p 0.012). However, individually the parameters of Child-Pugh scoring system had no significant relationship with hepatic venous waveform pressure changes (Table).

Discussion

While there is an abundance of data on the relevance of a reduction in portal pressure in the primary and secondary prophylaxis of variceal bleeding, the correlation of hepatic vein waveform by Doppler ultrasound with complications of portal hypertension like oesophageal varices, ascites and hepatic function has still not been studied. Upper GI endoscopy is a conventional method for detection of oesophageal varices in cirrhotic patients. However, it is a semi-invasive test and some patients are not comfortable with this modality of diagnosis. Hence, non invasive tests are being tried and Doppler ultrasound is foremost among them as an alternative to endoscopy to predict the varices and also to assess hepatic venous pressure gradient. Baik and colleagues found a positive correlation between waveform and hepatic vein pressure gradient (HVPG) in their study.[10] A normal person showed triphasic waveform of hepatic vein (HV) and in a cirrhotic patient monophasic or biphasic waveform of HV was seen.[11,12] When HVPG increased the waveform became flat. Monophasic waveform in HV was associated with severe portal hypertension HVPG > 15 mmHg with a relatively high sensitivity and specificity.[10]

In our study we tried to use the Doppler parameter to identify the correlation of hepatic venous waveforms with size of oesophageal varices noninvasively and also relationship of those waveforms with other factors like ascites, child-Pugh class. We did not find significant correlation of hepatic vein waveform changes with grading of oesophageal varices. There are more than a few studies which have evaluated the relationship of the degree of portal hypertension as measured by invasive techniques with oesophageal varices[13-16] but to our knowledge there is very limited data on correlation of hepatic venous waveform as depicted by Doppler ultrasound with portal hypertension or its complications like oesophageal varices. A study conducted by Joseph and colleagues[17] on correlations of hepatic venous waveform and oesophageal varices and results of them are consistent with our findings but these results are in disagreement with the findings of studies in which standard invasive method for measurement of portal pressure is used.[14,16]

Our study revealed 90% of Child- Pugh Class C, 73.91% of Class B and 50% of class A patients had monophasic HV waveform and found significant correlation between waveform changes and liver dysfunction (r=-.309, p=0.012). Again, the studies conducted on correlation of severity of portal hypertension measured by invasive technique with hepatic dysfunction supported our findings[14,16] however, the findings of an Indian study using Doppler waveform parameter were not consistent with these results.[17] Further studies evaluating the role of HV waveform in hepatic dysfunction are needed.

A minimum portal pressure gradient of 10-12 mm Hg has also been established for the development of ascites. In fact, the concept of "clinically significant portal hypertension" was recently defined as an increase in the portal pressure gradient to a threshold above 10 mm Hg.[6]

Limitations of this study included, standard technique of portal pressure of measurement was not compared with HV waveform; although studies suggest a relationship between these two techniques. Secondly sample size was small but this was expected because we excluded cirrhotic patients with portal pressure causing acute variceal bleeding, patients on beta blockers/vasodilators and patients with endoscopic therapeutic interventions.

Conclusion

Hepatic venous waveform pressure changes have significant relation with severity of hepatic dysfunction but there pressure changes have insignificant relation with grading of oesophageal varices. Further studies using a combination of various Doppler parameters are required to create indices with a better predictive value.

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