Hepatic venous waveform and Damping index in liver cirrhosis: Correlation with Child Pugh's Score

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Abstract— Clinical assessment of chronic liver disease is done by Modified Child Pugh's and Model for end-stage liver disease scoring system. Measurement of hepatic venous pressure gradient (HVPG) and Upper GI Endoscopy are considered the gold standards for measurement of portal hypertension in cirrhotics. There is a need for non-invasive evaluation of portal hypertension. Ultrasonography with colour and spectral Doppler evaluation may be an effective, rapid and inexpensive alternative.To evaluate hepatic venous waveform, damping index, in patients of cirrhosis on Colour Doppler ultrasound, also predict severity of portal hypertension Twenty patients of chronic liver disease were included in the study. Ultrasound and colour Doppler was done to look for hepatic venous waveform pattern and Damping Index (DI).Fifteen (75%) patients had monophasic waveform. Biphasic and triphasic waveforms were seen in 3 (15%) and 2 (10%) cases respectively. Fifteen patients (75%) had monophasic waveforms and majority of them were in class C. This distribution of hepatic vein waveform was statistically significantly with the Child Pugh's class ($p<0.05$). Fourteen patients (70%) had value of Damping index more than >0.6 where majority of patients (12) belonged to class C and 2 in class B. There was a positive correlation between Child Pugh's total score and Damping index.Change in triphasic to monophasic waveform and DI >0.6 suggests severe liver dysfunction and is associated with severe portal hypertension.

Index Terms— Colour Doppler ultrasound, Hepatic vein wave form, Monophasic wavefoem, Biphasic waveform,Triphasic Waveform, Damping index, Child Pugh's score.

INTRODUCTION

Cirrhosis, is defined as an abnormal liver pathology in which there is diffuse irreversible scarring of the liver parenchyma and replacement by structurally abnormal nodules" [1]. The scoring system used for predicting the cirrhosis was first introduced by Child and Turcotte in 1964 and later revised by Pugh in 1974 [2–5]. Cirrhosis is by far the most common cause of intrahepatic portal hypertension. Portal venous pressure is the blood pressure in the hepatic portal vein and the normal portal vein pressure is 5-10 mmHg. Portal hypertension is defined by HVPG more than 5mmHg, splenic vein pressure greater than 15mmHg, or portal vein pressure (measured surgically) greater than 10mmHg (30 cm water) [2,5]. Portal hypertension can lead to the development of oesophageal varices that are at risk of rupture.

Clinical assessment of chronic liver disease is done by Modified Child Pugh's [Table/Fig-1] and Model for end-stage liver disease (MELD) Scoring system [Table/Fig-2]. Portal hypertension is evaluated by invasive and non-invasive methods. Invasive methods are direct portal vein pressure and HVPG measurement. Non-invasive methods are Ultrasonography, colour and spectral Doppler evaluation, Computed Tomography (CT) scan and Magnetic Resonance Imaging (MRI). HVPG is considered the gold standard for diagnosis of portal hypertension. Currently, the most commonly used parameter for portal pressure is the HVPG. HVPG is the difference between the wedged (WHVP) and the free hepatic venous pressures (FHVP). The normal HVPG is 1-5 mmHg. Portal hypertension is pressure more than 5mmHg. HVPG ≤ 10 mmHg is clinically significant and is predictive of the development of complications of cirrhosis. HVPG above 12 mmHg is a risk factor for variceal rupture. The main advantages of HVPG are its simplicity, reproducibility, and safety. However, HVPG measurement is an invasive procedure. Thus there is a need for non invasive methods to accurately diagnose and predict portal hypertension and oesophageal varices.

[Table/Fig-1]:

Child-Turcotte Pugh's Scoring System.

	1 points	**2 points**	**3 points**
Encephalopathy	None	Grade 1-2	Grade 3-4
Ascites	None	Easily Controlled	Poorly Controlled

	1 points	2 points	3 points
Bilirubin (mg/dl)	< 2.0	2-3	> 3
Albumin (g/dl)	> 3.5	2.8-3.5	< 2.8
Prothrombin Time (sec)	< 4	4-6	> 6

Child Pugh's scoring classes: Class A: 5-6 points; Class B: 7-9 points; Class C: 10-15 points

[Table/Fig-2]:

Model for end-stage liver disease (MELD).

Serum bilirubin (mg/dL)
Serum creatinine (mg/dL)
International Normalized Ratio (INR) for prothrombin time (secs)
MELD equation: 9.57x loge (creatinine mg/dL)+3.78x loge (bilirubin mg/dL)+11.2x loge (INR)+6.43

Colour Doppler ultrasound of the hepatic veins has emerged as a non-invasive technique for the diagnosis of portal hypertension and to predict oesophageal varices. The normal hepatic vein waveform is triphasic-retrograde A wave and antegrade S and D waves [Table/Fig-3]. Hepatic vein waveform (HVW) is classified into 3 types - Triphasic: normal pattern, Biphasic: no reversed flow and with or without decreased phasic oscillation and Monophasic: flat waveform. Biphasic and monophasic HVW are associated with severe portal hypertension. Damping of the hepatic veins is indicative of cirrhosis.

Aim

The aim of the study was to evaluate hepatic venous waveform, damping index, in patients of cirrhosis on Doppler ultrasound, also predict severity of portal hypertension

Materials and Methods

This was a prospective study conducted in the Department of Radiodiagnosis , between August 2019 to December 2019.Thirty patients of chronic liver disease were included in the study after obtaining an informed consent.

Patients with co-existent cardiac or respiratory disease, hepatocellular carcinoma, non cirrhotic portal fibrosis, acute variceal haemorrhage, past history of endoscopic variceal ligation/sclerotherapy were excluded from the study.

The patients then underwent gray-scale and colour Doppler Ultrasound examination.

Based on the clinical (ascites and hepatic encephalopathy) and laboratory parameters (serum bilirubin, serum albumin, and prothrombin time) the patients were divided into three classes namely Child Pugh's A,B and C according to Child Pugh's classification [4,5].

Gray scale and Colour Doppler Ultrasound: Ultrasound examination was performed on Mindray ultrasound machine using both convex 2-5 and linear 3-12MHz transducers. Patients were sonographically evaluated on gray scale ultrasound for hepatic echotexture, nodularity, hypertrophied caudate lobe, ascites and splenomegaly. Colour Doppler of hepatic veins was done. To trace the hepatic veins, the 2-5 MHz convex probe was placed in the right intercostal space. Hepatic venous blood flows was recorded for more than 5 seconds at the end of normal expiration or in quiet respiration by using a 2-5 MHz transducer with Doppler capability. Doppler waveforms were taken from the right hepatic vein. Middle hepatic vein readings were taken when the right hepatic vein was not well-visualized. Minimum of three recordings were taken and the data considered for analysis was the mean of the readings. The hepatic vein Doppler waveform was classified as triphasic, biphasic or monophasic depending upon the phasicity observed. Damping index (DI) was calculated as

minimum velocity/maximum velocity of hepatic venous waveform. Damping index > 0.6 was considered significant for portal hypertension.

Statistical Analysis

Descriptive statistics was used to quantitatively describe the frequency of various features observed in our study population. Chi-square and Pearson correlation test was used to study the significant difference and correlation between the variables.

Results

A total of 20 patients (15 males and 5 females) were enrolled in the study. The age group and severity of cirrhosis is summarized in [Table/Fig-4]. Fifteen patients were found in class C,Four patients were in class B and only one patient was in class A.

[Table/Fig-4]:

Age wise distribution of patients with severity of cirrhosis (N = 20).

Age Group	Statistics	Child Pugh's Class			Total
		A	B	C	
26-35 years	n	0	1	6	7
	%	0%	25%	40%	45%
36-45 years	n	0	1	8	9
	%	0%	25%	53.3%	45%
46-56 years	n	1	2	1	4
	%	100%	50.%	6.67%	20.0%
Total	n	1	4	15	20

n=number of patients

Eighteen patients presented with ascites, out of which 9 (50%) had poorly controlled ascites. All these patients were noted majorly in class Child Pugh's class C. Only two (10%) patients with cirrhosis had hepatic encephalopathy and all were in class C. Nine patients with cirrhosis had S. bilirubin more than 3 mg/dl whereas 7 (35%) patients with cirrhosis were found with S. bilirubin less than 2 mg/dl. 13 (65%) patients had serum albumin less than 3 g/dl and all patients were in class C. Five (25 %) patients were found with serum albumin between 3 to 3.5 g/dl, where 4 patients were in class B and 4 patients were in class C. Only 2 (10%) patients had serum albumin levels more than 3.5 g/dl, two patients were in class B and one patient was in class A. 18 (90.0%) patients had prothrombin time >6 sec. Out of these 18 patients, 14 patients were in class C and 3 patients were in class B. Two (10.0%) patients had prothrombin time of 4-6 sec.

Among 20 patients, 15 (75 %) patients had monophasic waveform. Biphasic and triphasic waveforms were seen in 3 (15 %) and 2 cases respectively. Fifteen patients (75%) had monophasic waveforms and majority of them were in class C. Three patients (15%) had biphasic waveform in which two were from class B and one were from class C. Remaining 2 patients had triphasic waveforms where one belonged to class B and one was in Class C. So, as the severity of the liver dysfunction increases, as evidenced clinically by Child Pugh's scoring system, change in the hepatic vein waveform was observed from normal pattern of triphasic to biphasic and/or monophasic. This distribution of hepatic vein waveform was statistically significantly with the Child Pugh's class ($p<0.05$). The same has been illustrated in [Table/Fig-5]. Fourteen patients (70%) had value of Damping

index more than >0.6 where majority of patients (12) belonged to class C and 2 in class B. Six patients (30%) had Damping index ≤0.6; 3 were from class C, 2 were from class B and 1 was from class A. There was a positive correlation between Child Pugh's total score and Damping index [Table/Fig-5]:

Hepatic venous waveforms according to Child Pugh's class.

HVD Findings	Statistics	Child Pugh's Class			Total
		A	B	C	
Monophasic	n	0	2	13	15
	%	0%	40%	86.7%	75%
Biphasic	n	0	2	1	3
	%	0%	40%	6.7%	15%
Triphasic	n	0	1	1	2
	%	0%	20%	6.7%	10%
Total	n	0	5	15	20

[Table/Fig-9]:

Damping Index in various Child Pugh class

Damping index	Child Pugh's Class			Total
	A	B	C	
>0.6	0	2	12	14
0.6 or <0.6	1	2	3	6
Total	1	4	15	20

DISCUSSION

Cirrhosis is an end stage liver disease and it is the most common cause of portal hypertension. HVPG measurement is invasive as well as expensive with potential for complications in cirrhotics with coagulopathy. Colour Doppler Ultrasound is safe radiation-free, painless, inexpensive and repeatable method which is well accepted by the patients. In our study of 20 patients (male=15; female=5), most of the patients were in third to fourth decade of life with age ranging from 26-56 years (39.53±7.32). Our series had 15 cases in Child Pugh's class C, 4 in class B and 1 in class A. In a study by Bhutto et al., there were 32 (49.2%) patients in Child-Pugh Class A, 23 (35.4%) were in Class B and 10 (15.4%) patients were in Class C. Compared to studies done by previous authors, our study had more number of patients in Child Pugh's class C. This may be due to late presentation to the hospital in advanced stage of the disease, being a referral hospital. Twenty eight patients had ascites and majority of them were in class C (76.6%). Mittal et al., in their study of 50 patients found similar association that severity of ascites correlated with the increasing Child Pugh's score ($p<0.0001$) [2]. Our study also shows similar findings. Three patients with cirrhosis had hepatic encephalopathy and all were in class C. Mittal et al., showed that higher trends of hepatic encephalopathy was observed in patients with hepatofugal flow in portal vein ($p<0.01$) and also the Child Pugh's score was significantly higher in patients with a reversed flow in portal vein. Our study showed similar findings to Mittal

et al in relation to serum bilirubin, albumin and prothrombin time.

We did colour Doppler evaluation of hepatic veins in all our patients and found monophasic pattern in 15(75%) patients, biphasic in 3(15%) and triphasic in 2(10%) patients. On correlating this hepatic venous waveform pattern with Child Pugh's scoring system we found out of 15 patients in class C, Thirteen (87%) had monophasic waveform, two (8.7%) had biphasic waveform. In class B, two patients each had monophasic, biphasic and one tirphasic waveform. Whereas the only patient in class A had one triphasic waveform. As the Child Pugh's score increased, there was conversion of normal triphasic waveform into biphasic to finally monophasic. Hence the relationship of these waveforms had a significant correlation with the Child Pugh's class ($p<0.05$). Similar results were observed by Bhutto et al., in their research involving 65 patients. They concluded that relationship of these waveforms had significant relation with hepatic dysfunction ($p < 0.012$) whereas was insignificant in grading oesophageal varices (p 0.29). Baik et al., in their study on 78 patients found abnormal hepatic vein waveforms in 72 patients [9]. Forty four patients had biphasic, 28 had monophasic and 6 had normal triphasic waveform. They concluded mean HVPG of 14.6±4.3mmHg is suggestive of severe portal hypertension, which was observed in 35(45%) of their patients. They also concluded that monophasic venous flow was associated with severe portal hypertension (HVPG > 15mmHg) and was statistically significant ($p<.01$). Results of our study and Baik et al., are comparable. In our study, we used Child Pugh's scoring system to correlate severity of liver disease with hepatic venous waveform whereas Baik et al., used both non-invasive and invasive methods to show correlation between the abnormal hepatic vein waveform and increase in HVPG. Studies by Sudhamshu et al., and Joseph et al., could not establish any correlation between severity of liver disease and hepatic venous waveform. Their studies showed that the flat waveforms have no diagnostic value and suggested that role of hepatic blood flow seems to be important suggesting haemodynamic changes rather than liver dysfunction as a plausible cause of change in waveforms. However, Joseph et al concluded that loss of triphasic hepatic venous waveform is highly sensitive in predicting significant varices in patients with cirrhosis.

Damping index (DI) is the ratio between the minimum velocity and maximum velocity of the hepatic venous flow. DI > 0.6 was suggestive of portal hypertension. Higher DI values tend to give flat hepatic venous waveforms. In our study DI was 0.02-0.90 (0.702± 0.21). Positive correlation was found between Child Pugh's total score and DI, therefore higher the Child Pugh's score, higher was the Damping index value ($r = 0.614$; $p<0.05$). Kim et al., in their study of 76 patients found abnormal hepatic venous waveforms in 66 patients (86.8%). They also found that DI significantly correlated with the grade of HVPG, i.e. with higher HVPG increased DI was observed ($p<0.01$). They concluded that Damping index of the HV waveform by Doppler ultrasonography is a non-invasive supplementary tool in evaluating the severity of portal hypertension.

Joseph et al., showed that sensitivity of loss of the normal triphasic waveform in detecting large varices is high (95.23%). The negative predictive value is high (75%) although the positive predictive value (42.6%) and specificity (10%) are low. In class B. one patient had collaterals at splenic hilum and other patient had paraumbilical collateral. In class C, 14 patients had no other collaterals, 5 had collaterals at splenic hilum and three patients had paraumbilical collateral. This distribution of patient with other collaterals was not significantly associated with Child Pugh's score.

Limitations and Future Prospects

The study population was small in our study. Upper GI endoscopy was not done in all cases to identify varices in our study. Also, HVPG was not done in all cases because of resource constraint and lack of expertise in our institute. Sick patients could not be transferred to higher centre for these investigations. Future studies with damping index ratio (DI ratio= DI expiration/DI inspiration), and difference (ΔDI = DI inspiration – DI expiation) can be done to look for the sensitivity and specificity in predicting portal hypertension.

Conclusion

At present, the gold standard for the measurement of portal pressure is HVPG, which is an invasive procedure with several other drawbacks. So there is need to replace invasive procedure by noninvasive methods, which have maximum accuracy, with none or minimal side effects. Hepatic venous waveform pressure changes and DI have significant relation with the severity of hepatic dysfunction which is measured by Child Pugh's scoring system. We would like to conclude by saying that Doppler ultrasound may be an excellent non-invasive modality for the assessment of severity of liver disease.

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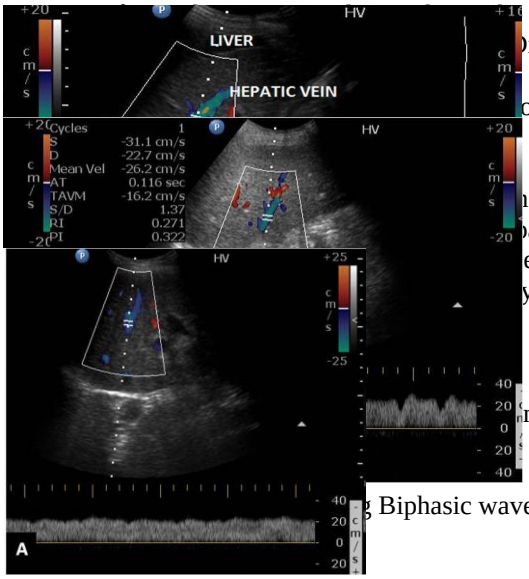

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g Biphasic waveform

[1] Figure 3c colour doppler showing monophasic waveform