Can hepatic vein waveforms predict the presence of esophageal varices?

Ebtsam Elsayed Abdelmonem Abdallah, Salama Shaaban Alghonaimy, Amira Mohammad Soliman, Mohamed Ibrahim Amin

1 M.B.B.CH.- Ain Shams University, Tropical Resident Doctor, Zagazig Hospital for Fever, Gastroenterology and Hepatology

2 Professor of Tropical Medicine Department, Faculty of Medicine, Zagazig university

3 Professor of Tropical Medicine Department, Faculty of Medicine, Zagazig university

4 Associate Professor of Radiodiagnosis Department, Faculty of Medicine, Zagazig university

Corresponding Author: Ebtsam Elsayed Abdelmonem Abdallah

Email: bosbos141987@gmail.com

Abstract

Background: Portal hypertension often leads to the development of unsightly varices. Presence of non invasive method for their prediction will improve patients life quality and increase their adherence to follow up.

Aim: To evaluate the value of hepatic vein waveforms in prediction of esophageal varices in cirrhotic patients as a non-invasive tool to discriminate the patients who need upper endoscopy from those who don't need.

Subjects and Methods: This cross-sectional trial included 48 cirrhotic patients (as evidenced with history, clinical examination, biochemical data and pelviabdominal ultrasound) which were divided into 2 groups according to presence of esophageal varices. Group (1): 26 patients with esophageal varices. Group (2): 22 patients without esophageal varices.

Results: HVW distributed as 68.7% monophasic, 12.5% biphasic, and 18.8% triphasic. 96.2% (25/ 26) of patients with esophageal varices had monophasic waveform and 90% of patients in Child Pugh class C also had monophasic waveform. There is no significant relation between severity of ascites and HVW.

Conclusion: Monophasic hepatic vein waveform is a good non-invasive indicator for presence of esophageal varices and advanced cirrhosis.

Keywords: Hepatic Vein Waveform, Esophageal Varices, Cirrhotic Patients

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1. Introduction

Cirrhosis of the liver is a major contributor to worldwide mortality and morbidity. It's the eleventh leading killer and fifteenth leading cause of disability worldwide. (1). Portal hypertension is the most significant and life-threatening consequence of liver cirrhosis. Varices of the esophagus and stomach, as well as a condition called portal hypertensive gastropathy, are symptoms of portal hypertension.(2).

Portal hypertension causes varices, and up to 30% of cirrhotic patients experience variceal bleeding, a life-threatening condition. If the portal pressure in the body increases by more than 12 mm Hg, the esophagus can develop varices. Esophageal varices can be classified as minor, moderate, or severe. Two percent to nine percent of esophageal and gastric bleeding can be attributed to them. (3).

Acute variceal haemorrhage has a fatality rate of up to 20%, despite advances in detection and treatment. Furthermore, it is the second leading cause of death among those with cirrhosis.(4 ,5). Although upper gastrointestinal endoscopy is a reliable method for diagnosing esophageal varices, it is not always accessible or practical for many patients because of its high price tag, limited availability, and intrusive nature.(6).

The detection of esophageal varices has progressed from invasive procedures to a variety of noninvasive options. Clinically significant portal hypertension (CSPH) in patients with compensated advanced chronic liver disease is a unique situation in which non-invasive techniques play an important role. (7).

In order to detect portal hypertension and foretell oesophageal varices, colour Doppler ultrasound of the hepatic veins has evolved as a non-invasive approach. There are three distinct categories of hepatic vein waveform (HVW): The triphasic structure consists of three phases: No reversal of flow, with or without reduced phasic oscillation, defines a biphasic waveform, while a monophasic waveform defines a flat waveform. Severe portal hypertension is linked to both biphasic and monophasic HVW.(8; 9).

It was the goal of this study to evaluate the value of hepatic vein waveforms in prediction of esophageal varices in cirrhotic patients as a non-invasive tool to discriminate the patients who need upper endoscopy from those who don't need.

2. Subjects and Methods

We did this study at Tropical Medicine and Radiodiagnosis Departments Zagazig University hospital, forty-eight patients, with liver cirrhosis either with or without esophageal varices were studied in cross sectional research. Research ethics council at Zagazig University approved the study (ZU-IRB #8092) as long as all participants provided informed consent forms. Ethics guidelines for human experimentation were adhered to by the World Medical Association's Helsinki Declaration.

- **Inclusion criteria:** Liver cirrhosis either with or without esophageal varices. Diagnosis of cirrhosis is based on clinical, laboratory and ultrasonographic assessment.
- **Exclusion Criteria:**

- Esophageal varices due to causes other than liver cirrhosis.
- Patients with history of organ failure other than liver failure.
- Any chest or heart diseases that affect the blood flow in the right side of the heart.

- Patients presented with acute variceal bleeding or any case of hypo or hypervolemia.
- Currents treatment with beta blockers or any other medications that could affect portal pressure.
- Portal vein thrombosis
- Hepatic encephalopathy grades 3 or 4 or any condition interfering with endoscopy.
- Patients with hepatocellular carcinoma (HCC).
- Patients who don't sign in consent.

II. Operational Design:

Type of Study: cross sectional study

Methods: From each patient the following data had been collected upon admission.

I. Full history taking and thorough clinical examination with stress on presence of general signs of chronic liver disease and presence of ascites and splenomegaly.

1. Laboratory assessment of:

- Complete blood count
- Liver function tests (serum bilirubin, serum total protein, serum albumin, liver enzymes)
- Kidney function tests
- Coagulation profile

2. Calculation of Child-Pugh Score

The Child classification system was used to determine the severity of liver disease based on clinical features such as ascites and encephalopathy, as well as laboratory characteristics including serum levels of bilirubin, albumin and INR.

Table (1): Child-Pugh Score (Pugh et al., 1973):

Factor	1 point	2 points	3 points
Total bilirubin (umol/L)	<34	34-50	>50
Serum albumin (g/L)	>35	28-35	<28
PT INR	<1.7	1.7-2.30	>2.30
Ascites	None	Mild	Moderate to Severe
Hepatic encephalopathy	None	Grade I-II (or suppressed with medication)	Grade III-IV (or refractory)
	Class A	Class B	Class C
Total points	5-6	7-9	10-15
1 year survival	100%	80%	45%

3. Imaging evaluation:

Abdominal Ultrasonography:

(Mindary, diagnostic ultrasound system, Model: DC-N2) to show cirrhosis, patency of portal vein, ascites, size of spleen and exclusion of HCC.

Colored Doppler Studies:

- Colored Doppler ultrasound for assessment of hepatic vein waveform and calculation of damping index.
- Doppler ultrasonography were evaluated using an ultrasound sonography device (Canon applio I 500 tm Japan and with 3.5 Mhz curvilinear probe) using the right intercostal approach or subcostal.

The Doppler recorded the wave pattern and velocity of the right hepatic vein. HV waveforms were recorded from three repeated measurements. After the HV was depicted intercostally along its longitudinal axis with colour Doppler flow mapping, Doppler shift signals were obtained in the right HV at a distance of 3–6 cm from the junction of the HV and the inferior vena cava

Doppler HV waveforms were recorded for at least 5 s with end-expiration breath holding.

Ultrasonic hepatic venous waveform pattern were determined and categorized as:

1. The typical waveform in the liver is triphasic. The reserved flow is in at least one phase of this pattern.
2. When the phase oscillators exhibit biphasic behaviour, there is no inverted wave and there may or may not be a reduction in amplitude.
3. Monophasic that characterized by a flat and smooth waveform with or without flickering.

4. Upper endoscopy with grading of esophageal varices.

Upper GI Endoscopy was done by Pentax endoscope 3000 to look for and grading of esophageal varices if present. Patients were informed and consent was taken before the procedure.

Esophageal varices were graded according to (9) to:

- **Grade (1):** elevated varices at the mucosal layer.
- **Grade (2):** Varices that extend beyond the liminal diameter by a third and cannot be compressed with insufflation of air.
- **Grade (3):** Esophageal varices grow huge and coil, taking up more than a third of the oesophagus' interior.

After endoscopy, the patients were divided into two groups:

- **Group (1):** Included 26 Patients with esophageal varices.
- **Group (2):** Included 22 Patients without esophageal varices.

Statistical Analysis:

Data was collected, then presented and statistically analysed on a computer using SPSS version 20. The chi-square and Fisher exact tests were used to analyse the data. When (P value < 0.05 %) was used to determine the significance of the result treated with THR using direct anterior approach under regional or general anesthesia.

3. Results

The waveform in the hepatic vein does not significantly change from the baseline characteristics of the study population. p>0.05, Except there is significant relation between hepatic vein waveform and esophageal varices , Child Pugh class p<0.0001, present of esophageal varices mainly associated with monophasic wave p=0.0001. Almost monophasic or biphasic hepatic vein waveform were found in child Pugh class C patients versus triphasic wave represented mainly in Child Pugh class B, p=0.0001. **(Table 1).**

There is significant relation between Child Pugh class and hepatic vein waveform of the studied patients, almost monophasic and biphasic hepatic waveform were found in Child Pugh class C patients, while triphasic waveform represented mainly in Child Pugh class B. There is no significant relation between damping index and patients' Child Pugh class are shown in **(Table 2)**

Table 1: Relation between Hepatic vein waveform and basic characters of studied group (n.48):

Variables	Hepatic vein waveform						χ^2	P
	Monophasic n.33		Biphasic n.6		Triphasic n.9			
	No.	%	No	%	No.	%		
sex								
Males	23	69.7	4	66.7	5	55.6	0.64	0.73
Females	10	30.3	2	33.3	4	44.4		
Age per years								
≤50	11	33.3	3	50.0	6	66.7	3.4	0.18
>50	22	66.7	3	50.0	3	33.3		
Bilirubin <2 mg/dl	33	100.0	6	100.0	9	100.0		
Albumin (g/dl)								
>3.5	2	6.1	1	16.7	3	33.3	8.4	0.077
2.8-3.5	5	15.2	2	33.3	3	33.3		
<2.8	26	78.8	3	50.0	3	33.3		
INR								
≤1.1	1	3.0	1	16.7	2	22.2	4.03	0.13
>1.1	32	97.0	5	83.3	7	77.8		
Ascites								
Mild ascites	3	9.1	2	33.3	2	22.2	3.04	0.55
Moderate ascites	20	60.6	3	50.0	5	55.6		
Tense ascites	10	30.3	1	16.7	2	22.2		
Esophageal varices								
Present	25	75.8	1	16.7	0	.0	20.2	0.0001*
Absent	8	24.2	5	83.3	9	100.0		
Esophageal varices								
Grade2	17	51.5	0	.0	-	-	f	0.35
Grade3	8	24.2	1	16.7	-	-		
Child pugh								
Child pugh class B	3	9.1	1	16.7	7	77.8	19	0.0001*
Child pugh class C	30	90.9	5	83.3	2	22.2		

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Table (2): Relation between presence of esophageal varices and ultrasonographic parameters and Child Pugh class.

	Esophageal varices		χ^2	p-value
	Present n= 26 n (%)	Absent n= 22 n (%)		
Ascites grade • Mild ascites (n= 7) • Moderate ascites (n= 28) • Tense ascites (n= 13)	0 (0.0) 15 (57.7) 11 (42.3)	7 (31.8) 13 (59.1) 2 (9.1)	13.1	0.001
Child Pugh class • Class B (n= 11) • Class C (n= 37)	1 (3.4) 25 (96.6)	10 (45.5) 12 (54.5)	11.6	0.001
Hepatic vein waveform • Monophasic (n= 33) • Biphasic (n= 6) • Triphasic (n= 9)	25 (96.2) 1 (3.8) 0.0 (0.0)	8 (36.4) 5 (22.7) 9 (40.9)	22.2	P (0.0001) P1(0.0004) P2 (0.12) P3 (0.0005)

4. Discussion

In terms of worldwide mortality and morbidity, liver cirrhosis is by and away the most common cause. The World Health Organization ranks it as the 11th leading cause of mortality and the 15th greatest cause of disability.**(1)** Portal hypertension is the most significant and life-threatening consequence of liver cirrhosis. Esophageal varices, gastric varices, and portal hypertensive gastropathy are vascular symptoms of portal hypertension.**(2).**

Colour One of the non-invasive methods for diagnosing portal hypertension is Doppler ultrasound of the hepatic veins. Among its many benefits, patients like that it poses no risk of radiation exposure, causes no discomfort, costs very little, and can be performed repeatedly. Doppler sonography is able to identify changes in the hemodynamics of the liver due to liver cirrhosis at the tissue level. Many Doppler observations correspond with clinical characteristics and the Child Pugh score, including direction flow, velocity of the major portal vein, and child Pugh index. **(7,10)**.

Hepatic vein waveform (HVW) is one of the Doppler qualitative assessments that reflects the cardiac cycle on hepatic veins and affected by liver cirrhosis. Normal (Triphasic), biphasic (no reversal of flow with or without diminished phasic oscillation), and monophasic (flat waveform) are the three categories into which they fall. When it comes to portal hypertension, both biphasic and monophasic HVW are linked to very serious consequences.**(11).**

In this study, about 23% of patients presented in Child-Pugh class B and 77% in class C. This is because the patients were recruited from the inpatient wards which receive the advanced cases while the early cases were managed at the

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outpatient clinic. This result agrees with that of **(12).**

Patients with esophageal varices have a much higher prevalence of Child Pugh class C. The increased portal pressure associated with advanced cirrhosis has been cited by numerous studies as a risk factor for the development of esophageal varices.**(13 ,14)**. About half of cirrhotic people have varices, and the prevalence of varices increases with the severity of liver disease: only 40% of cirrhotic in Child-Pugh A have varices, while 85% of cirrhotic in Child-Pugh C do.**(15).**

This research shows that esophageal varices are associated with a certain type of hepatic vein waveform in patients with cirrhosis. Almost all patients with esophageal varices had monophasic hepatic wave (96.2%), while patients without esophageal varices had the three forms of waves with the highest percentage for triphasic waveform (40.9%). Study by **Joseph et al., (16)** stated that, The absence of the triphasic pattern in the hepatic venous tracing was highly predictive of the existence of large esophageal varices, whereas the presence of the triphasic pattern in a patient with cirrhosis was highly predictive of the absence of such varices. Moreover, **Baik et al. (8)** demonstrated that a high degree of sensitivity and specificity had been demonstrated between HVPG and hepatic venous waveforms; a monophasic waveform was related with severe portal hypertension (HVPG > 15 mmHg)..

On the other hand, **Bhutto et al., (11)** did not discover this correlation but did find that the connection between these waveforms and esophageal varices grading was substantial. In spite of the fact that 85% of their patients were in Child Pugh class A and only 5% in class C, 60% of their patients had extensive varices.

In this study, there is significant relation between Child Pugh class and hepatic vein waveform. Almost monophasic or biphasic hepatic wave were found in Child Pugh class C patients versus triphasic wave represented mainly in Child Pugh class B. Normal triphasic waveform changed to biphasic and then monophasic when Child Pugh score ascended. **(12, 17).**

These results agree with those of **Bolondi et al. (18)** and **Yasmin et al. (19)** who concluded that monophasic and biphasic waveforms had significant relation with advancing grade of cirrhosis. This could be because of the increasing architectural distortion of liver parenchyma with increasing portal pressure, resulting in loss of normal transmission of normal triphasic heart cycle to hepatic veins.

Even while **Sudhamshu et al. (20)** and **Joseph et al. (16)** were unable to find a connection between the severity of liver disease and the hepatic venous waveform, our study finds a significant association between the two. **Sudhamshu et al., (20)** explained their results by the statement of **Abu-Yousef (21)**; Hepatic vein wave phases are thought to originate in the heart; nevertheless, right atrial pressure and respiratory motion can significantly modify HV waveforms and their components, and flat waveforms are observed in roughly 9% of normal persons without liver or cardiac disease.**(22)**. They also noted that flat waveforms could be the result of careless Doppler measurements taken from the inferior right hepatic vein or the larger marginal vein.

5. Conclusion

Monophasic hepatic vein waveform is a good non-invasive indicator for esophageal varices presence and advancement of cirrhosis.

Conflict of Interest: None

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