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Doppler Analysis of Hepatic Venous Waveforms: A Reliable Way to Diagnose and Guess the Size of Esophageal Varices in People with Cirrhosis of the Liver

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ABSTRACT

Objective: To determine the diagnostic accuracy of Doppler assessment of hepatic venous waveforms for predicting large esophageal varices in patients with cirrhosis, keeping esophagogastroduodenoscopy as a gold standard.
Study Design: Cross-sectional study.
Place and Duration of Study: Armed Forces Institute of Radiology & Imaging, Rawalpindi Pakistan, from Jan 2021 to Jan 2022.
Methodology: According to the Child-Pugh classification, 157 cases of liver cirrhosis were included in this study. With a convex probe operating at 3.5 to 5 MHz, a Doppler ultrasound was executed. If quiet breathing wasn't an option, the spectral waveform was captured at the end of the inhalation phase while holding your breath. This was roughly 3–6 cm from where it connects to the inferior vena cava. All patients underwent an esophagogastroduodenoscopy.
Results: In Doppler USG-positive patients, 84 (true positive) developed significant esophageal varices on endoscopy, while 4 (false positive) did not. Among 69 individuals with negative Doppler USG results, six (false negative) had significant esophageal varices on endoscopy, whereas 63 (true negative) did not (p=0.0001). We found that the overall sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy of Doppler evaluation of hepatic venous waveforms were 93.33%, 94.0%, 95.45%, 91.30%, and 93.6% for finding large esophageal varices in cirrhotic patients using esophagogastroduodenoscopy as the gold standard.
Conclusion: This study proved that using Doppler to look at hepatic vein waveforms is a very sensitive and accurate noninvasive way to tell if someone with cirrhosis will get big esophageal varices.

Keywords: Esophageal varices, Hepatic vein waveforms, Liver cirrhosis

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INTRODUCTION

Chronic liver disease is a major disease burden in Pakistan. In 2017, 10.6 million cases of decompensated cirrhosis and 112 million cases of compensated cirrhosis were prevalent worldwide. [1]. Chronic liver disease, also known as liver cirrhosis, is a condition where normal hepatocytes are replaced by damaged tissue, leading to architectural distortion, scarring, and fibrosis. Its complications include ascites, varices, hepatic encephalopathy, HCC (hepatocellular carcinoma), and spontaneous bacterial peritonitis[2]. The major cause of death in individuals suffering from liver cirrhosis is esophageal varices, which constitute one of the major complications of the disease. The development of varices is mostly influenced by portal hypertension. Portal hypertension occurs when the intrahepatic vessels' resistance to the portal vein flow increases.[3] Hyperdynamic circulation further exacerbates the problem by expanding the splanchnic vasculature, which in turn increases portal blood flow. Multiple collaterals between the portal and systemic circulation arise when portal vein pressure rises above a critical threshold.[4] Esophageal varices are the most important collaterals, and due to portal hypertension, the possibility of their rupture increases. Variceal rupture as a result of portal hypertension accounts for approximately one percent of deaths in people with liver cirrhosis.[5] In light of this, early detection of esophageal varices and their severity would aid in enhancing the long-term survival of cirrhotic patients[6].

Many parameters evaluated by Doppler ultrasonography have been suggested as noninvasive determinants for the presence of gastroesophageal varices. Several Doppler indices are used to assess the

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degree of portal hypertension and esophageal varices in patients with liver cirrhosis[7].

Typically, hepatic veins exhibit a tri-phasic waveform pattern. In liver cirrhosis, the waveform becomes biphasic and then monophasic due to a decrease in liver compliance (Figure). A strong link exists between cirrhotic individuals not having a normal tri-phasic waveform and the discovery of large esophageal varices.[8,9] The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of monophasic HVW were 96.2%, 63.6%, 75.8%, 93.3%, and 81.3%, respectively[10]. Developing countries like Pakistan, where liver cirrhosis is the major disease burden, have limited health care facilities, with endoscopy being semi-invasive and inaccessible in certain areas. Doppler ultrasound of hepatic veins is an easily available and cost-effective investigation. The goal of this study is to find a link between Doppler ultrasonography analysis of hepatic vein waveforms and the presence of significant esophageal varices in people who have cirrhosis. The findings could lead to its widespread use as a screening tool for significant esophageal varices in cirrhotic patients.

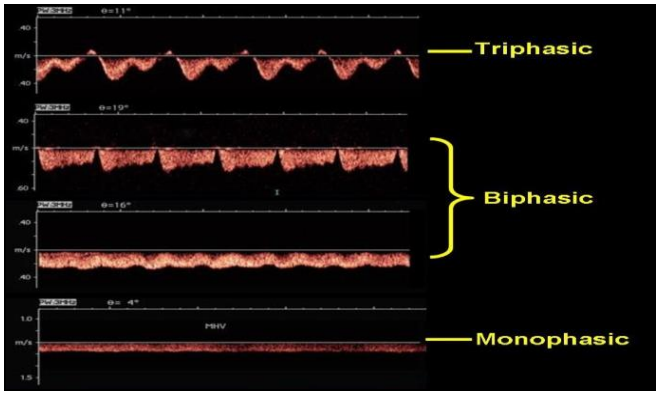

Figure: Hepatic vein waveform patterns (a) Triphasic (b) Biphasic (c) Monophasic

METHODOLOGY

The cross-sectional study was conducted at the Armed Forces Institute of Radiology & Imaging (AFIRI) Rawalpindi Pakistan, from January 2021 to January 2022. The sample size was calculated using the WHO sample size calculator, with 60% reported prevalence.[11] The Hospital Ethical Committee permission was taken (IERB approval certificate number: 012).

Inclusion Criteria: Patients of either gender, aged 20 to 80 years, who had been diagnosed with liver cirrhosis according to the Child Pugh classification were included.

Exclusion Criteria: Patients who had endoscopic variceal ligation or sclerotherapy for esophageal varices, a history of hepatocellular carcinoma or portal vein thrombosis, a history of taking propranolol or vasodilators, a history of heart or lung disease, an acute variceal haemorrhage, or who were taking anticoagulants were excluded.

After explaining the study's purpose and benefits, informed consent was obtained from patients who met the research inclusion criteria. All indoor and outdoor patients who fulfilled the inclusion criteria were studied. We conducted a thorough medical history and physically examined each patient. Patients with cirrhosis of the liver were chosen according to the Child Pugh staging system. After 6–8 hours of fasting, a Doppler ultrasonography scan with a convex probe working at 3.5–5 MHz showed the hepatic venous waveform. During periods of quiet breathing or during the inspiratory phase of a held breath, the spectral waveform of the inferior vena cava was recorded 3–6 cm from its confluence with the inferior vena cava.

Esophagogastroduodenoscopy was performed on all patients by a gastroenterologist in the gastro-enterology department at PEMH/CMH Rawalpindi Pakistan, Small lesions were defined as those with a diameter of less than or equal to 5 mm, as recommended by the American Association for the Study of Liver Disease, while large lesions were defined as those with a diameter of 5 mm or more. Strict exclusion criteria were applied to control for confounding variables and bias in the study's findings (Table-I).

Statistical Package for Social Sciences (SPSS) version 23.0 was used for the data analysis. Quantitative variables were expressed as Mean±SD and qualitative variables were expressed as frequency and percentages. During esophagogastro-duodenoscopy, Doppler ultrasonography variations in the hepatic vein waveform were analyzed for their sensitivity, specificity, positive predictive value, and negative predictive value in identifying the presence of significant esophageal varices (Table-I).

RESULTS

The study included a total of 157 patients who met the inclusion criteria. Among these, 43.95% were females and 56.05% were males. Out of 157 patients,

49(28.66%) were from Child-Pugh class A, 52(33.12%) from Child-Pugh class B, and 60(38.22%) were from Child-Pugh class C. Large esophageal varices were confirmed by Doppler ultrasound in 88 patients (56.05%), while esophageal varices were ruled out in 69 patients (43.95%). Endoscopy showed that 90 patients, or 57.32%, had significant esophageal varices while 67 patients, or 42.68%, did not. The endoscopic results for 84 (true positive) patients who had a positive Doppler USG were compared to 4 (false positive) patients who did not show significant esophageal varices. When compared to esophago-gastroduodenoscopy, Doppler evaluation of hepatic venous waveforms had a 93.33% sensitivity, a 94.0% specificity, a 95.4% positive predictive value, a 91.3% negative predictive value, and a 93.6% diagnostic accuracy in predicting large esophageal varices in cirrhotic patients. Table-II reveals that out of the 69 patients who received negative results from Doppler USG, 6 had significant esophageal varices on endo-scopy, indicating a false negative, and 63 did not, indicating a true negative.

Table-I: Correlation between Hepatic Veins Waveforms and Endoscopic Findings of Esophageal Varices

	Endoscopic findings	
Doppler Ultrasound of hepatic veins waveform	Loss of hepatic veins waveform with large esophageal varices (TP)	Loss of hepatic veins waveform but no esophageal varices (FP)
	Normal hepatic veins waveform with large esophageal varices (FN)	Normal hepatic veins waveform with no esophageal varices (TN)

Table-II: Diagnostic Accuracy of Doppler Assessment of Hepatic Venous Waveforms in Speculating Large Esophageal Varices in Patients with Liver Cirrhosis Keeping Esophagogastroduodenoscopy as a Gold Standard (n=157)

	Positive outcome on Endoscopy	Negative outcome on Endoscopy
Sonologically positive	84(53 %)	04(2.5%)
Sonologically negative	06(3.8%)	63(40%)

*Sensitivity=TP/(TP+FN)=84/(84+6)*100=93.3%*
*Specificity=TN/(TN+FP)=63/(63+4)*100=94.0%*
*Positive Predictive Value=TP/(TP+FP)*100= 84/(84+04)=95.4%*
*Negative Predictive Value=TN/(TN+FN)*100=63/(63+06)=93.6%*
*Diagnostic Accuracy=(TP+TN)/All patients*100=(84+63)/157=93%*

DISCUSSION

In patients with chronic liver disease, imaging modalities such as ultrasonography, endoscopic ultrasound, computed tomography, and magnetic resonance imaging (MRI) play a crucial role in the timely detection and mitigation of complications. [11] Ultrasound is an important screening method in patients with suspicion of varices and portal vein thrombosis, whereas contrast-enhanced computed tomography (CT) is highly accurate and reliable for evaluating its complications, including varices. [12,13] In everyday practice, liver cirrhosis is diagnosed using clinical findings, laboratory testing, and corresponding imaging examinations. [14] Doppler ultrasound, which incorporates color and pulse wave imaging Doppler shows the dynamics of the portal vein, hepatic artery, and hepatic veins, which in turn depict liver function status [15]. Colour Doppler Ultrasound is considered a safe, radiation-free, and inexpensive method that is well-accepted by atients. [16] Doppler US is a very useful investigation for assessing the hemodynamic changes observed in a cirrhotic patient's liver. [17] The hepatic vascular index, which is found by dividing the speed of the portal veins by the pulsatility of the hepatic arteries, has long been thought to be a very accurate way to diagnose liver cirrhosis and portal hyper-tension. [18]

Changes in hepatic vein waveforms are a function of the hepatic vein pressure gradient. Large varices could be predicted with significant sensitivity when hepatic veins' tri-phasic waveforms were lost. In contrast, it has been demonstrated that the absence of major esophageal varices in cirrhotic patients is strongly predicted by the presence of a normal triphasic hepatic vein pattern. Hepatic venous waveforms and the hepatic vein pressure gradient were not correlated, according to earlier research by Sun *et al*. [18] and Shabestari *et al*.[19] Furthermore, Halpern *et al*. recommended Doppler ultrasonography to be a reliable, non-invasive method for determining the presence of esophageal varices in relation to a variety of factors.[20] Most reliable Doppler measure-ments for finding esophageal varices were the portal vascular resistance, the hemodynamic liver index, and the splenoportal index. These had sensitivity values of 76%, 65%, and 63%, and specificities of 92%, 92%, and 92%, respectively[22]. The existence of significant esophageal varices was not, however, correctly predicted by the above-mentioned characteristics. Liver elastography, on the other hand, was more accurate than any Doppler marker at detecting varices, with a sensitivity of 95% and a specificity of 100%. The Splenoportal Index has been shown to be a valid predictor of the presence of varices in a number of

different studies, with a sensitivity that can reach as high as 96% and a specificity that is quite low.

In addition to other widely investigated Doppler indices, the portal vein congestion index calculates the ratio of the PV's cross-sectional area to the blood flow rate in centimetres per second. This index greatly aided in the detection of substantial varices and red spots, despite the fact that a few previous studies failed to show superior predictive values for indices like PV velocity.[21]

CONCLUSION

Another study discovered that non-invasive Doppler waveforms of hepatic veins are a very good way to tell if a person with cirrhosis will develop large esophageal varices. This method has also significantly improved patient care by allowing for earlier diagnosis and treatment. As a result, we recommend that Doppler evaluation of hepatic venous waveforms be used regularly as the main method for predicting large esophageal varices in people with cirrhosis. This will enable prompt and appropriate therapy, thereby lowering these individuals' morbidity and mortality.

Conflict of Interest: None.

Authors Contribution

Following authors have made substantial contributions to the manuscript as under:

SA & RA: Conception, study design, drafting the manuscript, approval of the final version to be published.

SIZ & IM: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

HS & SF: Data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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