

Doppler Waveform Abnormalities of Hepatic Veins with Histological Changes in Chronic Hepatitis - C Infection

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Abstract

Background : To study the diagnostic accuracy of the abnormalities in Doppler waveform of hepatic veins by comparing with histological changes in chronic liver disease (HCV infection).

Methods: In this cross sectional study 150 patients with chronic hepatitis C infection were included. Patients were subjected to real time Ultrasound and Doppler scanner, Using a 3.75 MHZ sector transducer through a trans-abdominal approach . The sample volume, as large as at least one third of the vessel's diameter, was positioned within the middle hepatic vein at a distance of 3-6 cm from the outlet into the inferior vena cava. Histopathology results were taken as gold standard. The New Inuyama scoring system was used to assess the fibrosis stage. The sensitivity, specificity, positive predictive value (PPV) and negative predictive values (NPV) were calculated for Doppler US. Data was analyzed by SPSS version 14.

Results: In our study the diagnostic accuracy of the abnormalities in Doppler waveform of hepatic veins by comparing with histological changes (gold standard) in chronic liver disease (HCV infection) was calculated in 79%, sensitivity 86%, specificity 61%, PPV 83% and NPV 67%

Conclusion: The study concludes that Doppler ultrasound is equally a very reliable and dependable technique for the validation of Doppler ultrasonography of hepatic veins in diagnosis of chronic liver disease due to HCV infection as histopathological grading.

Key Words: Viral Hepatitis, Cirrhosis, Diagnostic accuracy, Histopathological Grading.

Introduction

Hepatitis C infection is a major cause of chronic liver disease. It has affected an estimated 170 million persons worldwide and is a viral pandemic. In Pakistan more than 10 million people are infected with HCV with high morbidity and mortality.^{1,2} It progresses to chronic disease in majority of patients.

The prevalence of cirrhosis in chronic liver disease is 50%. The diagnosis of cirrhosis requires histological proof of diffuse fibrosis associated with architecturally abnormal regenerative nodules. Liver biopsy is considered gold standard for diagnosing the liver damage. Although relatively safe, it is still associated with a risk of complications and patient discomfort and is not cost effective^{1, 3}

Doppler ultrasonography is a non-invasive, inexpensive and repeatable modality .It can be used for diagnosis and follow up of patients with chronic liver disease. The sensitivity and specificity of abnormal hepatic vein waveform abnormalities in detection of cirrhosis is 75% and 78% respectively.^{4,5}

Normal HV waveform is triphasic reflecting the variations in central venous pressure due to the cardiac cycle.⁵ There are two hepatofugal peaks due to atrial filling in the systolic and diastolic phases and two retrograde valleys due to the atrial and ventricular contractions.⁶

Liver parenchymal disease can impair the HV wall compliance decreasing phasic oscillations.¹ In patients with well-compensated liver disease, flattening of the Doppler hepatic vein waveform is suggestive of cirrhosis¹. Abnormal hepatic vein waveforms are positively related to the hepatic fibrosis on Histopathology¹. The New Inuyama scoring system is widely used to assess fibrosis stage.⁷ According to it Score 0 is no fibrosis, Score 1 is fibrous portal expansion, score 2 is bridging fibrosis, score 3 is bridging fibrosis with lobular degeneration and score 4 is cirrhosis.⁷

Patients and Methods

In this cross sectional study 150 patients with chronic hepatitis C infection were included. Duration of study was 6 months i.e. from April to October 2012. After 12 hours of fasting patient was subjected to real time Ultrasound and Doppler scanner, Using a 3.75 MHZ sector transducer through a trans-abdominal approach. The sample volume, as large as at least one third of the vessel's diameter, was positioned within

the middle hepatic vein at a distance of 3-6 cm from the outlet into the inferior vena cava. Measurements were done during mid inspiration and normal breathing in supine or 30 degree left lateral position. Histo-pathological results were considered as gold standard. The New Inuyama scoring system was used to assess the fibrosis stage. Inclusion criteria was patients of both genders between 13-50 years of age with evidence of HCV infection as detected by the positive HCV RNA by PCR study. Patient with any clinical signs of decompensated liver disease (ascites, jaundice, porto systemic encephalopathy, malnutrition, portal hypertension, patients with history of substance or alcohol abuse ,patients subjected to liver biopsy before, pregnant women and patients with history of hypertensive / ischemic heart disease were excluded. The sensitivity, specificity, positive predictive value (PPV) and negative predictive values (NPV) were calculated for Doppler US. Data was analyzed by SPSS version 14.

Results

In the current study we had 66 male(56%) and 84(44%) female,from 13 years to 50 years Mean age of population of study was 33.86(Table 1). On Doppler ultrasound waveform changes 90 patients had fibrosis stage 4 against 28 with no fibrosis . Abnormal hepatic wave form was seen in 72 %(Table 2; Figure 1-3). Results of histopathological grading (score 0 - 4) confirmed that 104 patients had cirrhosis against 28 with no fibrosis (Table 3).Findings on Doppler ultrasound were compared with histopathological findings of liver biopsy specimen (Table 4;Figure 4&5). Overall diagnostic accuracy of doppler ultrasound of hepatic veins as 79% is comparable with gold standard biopsy. Sensitivity was 86% and specificity 61%. PPV was 83% and NPV was 67% (Table 5 &6).

Table.1:Age distribution (n=150)

Age in years	No (%)
13-20	24 (16)
21-30	30 (20)
31-40	45 (30)
41-50	51 (34)

Table 2:Cirrhosis on doppler-hepatic vein waveform

	No (%)
Normal hepatic vein waveform	42 (28)
Abnormal hepatic vein waveform	108 (72)

Table 3:Chronic hepatitis C infection - Histo-pathological grading (0-4)

	No (%)
Absence of fibrosis=0	28 (18.7)
Fibrosis portal expansion=1	4(2.7)
Bridging fibrosis=2	6 (4.0)
Bridging fibrosis with lobular degeneration=3	8(5.3)
Cirrhosis=4	104 (69.3)

Table 4:Patients having cirrhosis detected on doppler ultrasound and histopathology (n=150)

	Ultrasound	Histopathology
Cirrhosis present	108 (72)	104 (69.3)
Cirrhosis absent	42 (28)	46 (30.7)

Table 5:Diagnostic accuracy of doppler ultrasound in cirrhosis using histopathology as gold standard

		Histopathology		
		+	-	
Doppler Ultrasound	+	True Positive (a)=90	False Positive (b)=18	A+b=108
	-	False Negative (c)=14	True Negative (d)=28	c+d=42
		a+c=104	b+d=46	150

Table 6 : Accuracy of Doppler Ultrasound in diagnosis of cirrhosis

Index	Percentage
Sensitivity	86%
Specificity	61%
Positive Predictive Value	83%
Negative Predictive Value	67%



Fig 1:HV Triphasic waveform with both positive and negative oscillations



Fig 2:HV biphasic waveform.No negative oscillations.

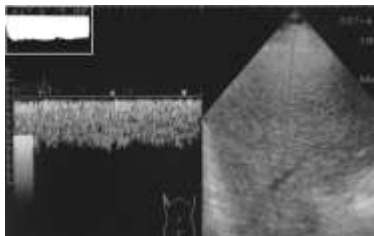


Fig 3:HV flat waveform .No oscillation.



Fig 4: Portal tract (left) and central vein (right) without substantial fibrosis (Trichrome stain).

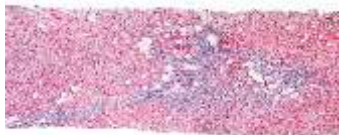


Fig 5:Portal fibrous expansion with periportal fibrosis (trichrome stain).

Discussion

HCV Hepatitis is endemic disease in Pakistan.¹ Morphologic alterations in the liver parenchyma may impair hepatic veins wall compliance . Damped waveforms is attributed to the stiffness of the liver parenchyma in various liver diseases.⁸

In our study the relationship of type of flow in hepatic veins (type 0, type 1, and type 2) and degree of fibrosis (mild, moderate and severe) was studied. Greater the amount of fibrosis present more was the abnormality in hepatic vein waveform.

. Mean age of the patients was 33.86years .Thus taking 34 years as mean age, 67 patients were between 13 and 33years while 79 patients above 34 years but below 50. On the average, 44.67% patients were below the mean age and 52.67% above the mean age adding up to 96%. Patients with mean age of 34 years represented 2.6% of the total sample populationThe study conducted by T Nishiura et.al reported mean age of the patients being 51 years which is comparatively older age sampled population against 34 years as mean age in current study. ⁹ These results reflect HCV affects people in developing countries like Pakistan in comparatively younger age group than elsewhere as also supported by Umar M et al.¹⁰ Yoshida et al revealed that annual incidence of hepatocellular carcinoma has increased from 0.5% among patients with the stage F0 or F1 fibrosis to 7.9%

among the patients with stage F4 fibrosis.¹¹ So it is apparent that fibrosis stage is a key factor in determining the prognosis and management of HCV chronic liver diseases.

The relationship between fibrosis and abnormalities of Doppler HV waveform in our study was consistent with the results shown by the Colli A et al who detected abnormal waveforms in 12 of 16 patients with cirrhosis and 8 of 36 patients without cirrhosis.⁴

Bolandi et al classified the hepatic veins waveforms into three patterns, i.e., HV0, a normal waveform; HV1, lower oscillations without the reversed phase, and HV2, completely flat waveform. ¹² The waveform of HV in all healthy people corresponded to the HV0 pattern. Among cirrhotic patients HV2 was the major waveform observed, which correlates strongly with the results shown in our study. Zheng et al also proved that ultrasonography and serology have their own advantages and disadvantages for the evaluation of liver fibrosis. ¹³⁻¹⁷ Haktanir et al concluded in their study that Doppler sonography is sensitive to hemodynamic alterations resulting from fibrosis, and is modality of choice to follow the progression of hepatitis. ¹⁴

Conclusion

Doppler sonography of hepatic vein is useful for studying liver disease associated with fibrosis. This non invasive technique is helpful for the diagnosis and follows up of patients with HCV infection. It has the advantage of being cost effective, non invasive and repeatable. However its combination with serological and histological markers remain the gold standard.

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