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# Ultrasonic Hepatic Venous Waveform Pattern and its Association with Disease Severity and Related Complications in Patients with Cirrhosis

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## ABSTRACT

*Advanced imaging modalities such as Color Doppler Ultrasound (CDUS) are widely used for the clinical evaluation of liver cirrhosis and port hypertension using assessment of ultrasonic hepatic venous waveform patterns. The present study aimed to assess the usefulness of CDUS in evaluating patients with cirrhosis and also for predicting portal hypertension and esophageal varices as important life threatening consequences of cirrhosis. This cross-sectional study was performed on 31 consecutive patients with cirrhosis. Ultrasonic hepatic venous waveform pattern were determined and categorized as monophasic, biphasic and triphasic. The Damping and Splenoportal indices were also measured. There was no association of ultrasonic hepatic venous waveform pattern with cirrhosis-related complications including liver encephalopathy (p = 0.817), esophageal varices (p = 0.372), and ascites (p = 0.471). We showed also no association between hepatic venous waveform pattern and liver disease severity based on the Child's classification (p = 0.331). The mean of Damping index was similar in the patients with and without each cirrhosis-related complications including liver encephalopathy (p = 0.134), esophageal varices, and ascites. Similar findings were revealed between Splenoportal index and the presence or absence on each complication. We found no difference in the mean of two Damping and Splenoportal indices across the different categorizes of liver disease severity. The record of the monophasic and biphasic patterns is predictable in most patients with cirrhosis and in a small number of healthy subjects without cirrhotic disorders. Also, recording these patterns together with the increase in two Damping and Splenoportal indices does not predict the severity of cirrhosis or its complications.*

**Key words:** Cirrhosis, Portal Hypertension, Color Doppler Ultrasound, Waveform

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## INTRODUCTION

Cirrhosis of the liver is an important cause of mortality and morbidity and is currently the fourth leading cause of death in the world [1]. The initial diagnosis of cirrhosis effectively plays a role in early predicting its consequences, such as variceal hemorrhage, liver encephalopathy and portal vein thrombosis [2]. Staging cirrhosis of the liver also provides prognostic information and allows achieving the most optimal treatment protocol. Parenchymal changes observed in

patients with cirrhosis and other diffuse liver diseases mainly include superficial nodularity, increased echogenicity, and an increase in the ratio of caudate to right lobe ratio [3]. Secondary symptoms of the disease, such as splenomegaly and varices can also be described as the results of portal hypertension in patients with cirrhosis [4].

Advanced imaging modalities include ultrasonography, endoscopic ultrasound, computed tomography, or MRI widely used for the clinical evaluation of cirrhosis of the liver and port hypertension [5]. Among these modalities, ultrasonography including real time ultrasound (RTUS), Color Doppler Ultrasound (CDUS), and Doppler Duplex Ultrasonography (DDU) are the best and most cost-benefit of these modalities [6]. These modalities have high sensitivity as well as high specificity but are similar in assessing liver parenchyma and changes [7]. Spectral and Doppler ultrasonography exhibit many characteristics of flow patterns in vascular bed in patients with cirrhosis with or without portal hypertension [8]. On the other hand, different types of liver associated varieties can easily be identified with the CDUS [9]. On the other hand, this technique has high accuracy in detecting portal vein thrombosis caused by advanced portal venous hypertension [10]. Moreover, DDU has been used to measure portal vein flow and velocity to detect port vein hypertension in cirrhotic patients [11]. But studies have shown a significant difference in the diagnostic accuracy of this method in various researches [12-14].

Given the increasing prevalence of hepatitis B and C in developing countries as the main cause of cirrhosis, access to a comprehensive, high-reliability, and low-cost method for evaluating patients with cirrhosis is felt more than before [15-17]. On the other hand, aggressive methods, in addition to spending a lot of time, are associated with life-threatening hazards [18]. The present study aimed to assess the usefulness of CDUS in evaluating patients with cirrhosis and also for predicting portal hypertension and esophageal varices as important life threatening consequences of cirrhosis.

## MATERIALS AND METHODS

This cross-sectional study was performed on 31 consecutive patients with cirrhosis hospitalized in Besat clinic or Afzalipour hospital in Kerman, Iran. The study subjects were cirrhosis patients aged higher than 18 years regardless of the cause of cirrhosis who were willing to enter the study. The exclusion criteria were dissatisfaction of the patient to enter the study, history of using vasoactive medications, or history of sclerotherapy. The features of the gray scale ultrasonography of the patients such as ascites, splenomegaly, and also parameters of Doppler ultrasonography were evaluated using an ultrasound sonography device (Philips affinity 50G, diagnostic ultrasound system: GMDN 40761,USA,22100 Bothell Everett highway ,WA98021-8431) and with a convex 2-5 MHZ probe using the right intercostal approach. The Doppler sonola model recorded the wave pattern of the hepatic vein and splenoportal as well as the tipping and splenoportal indices in the right hepatic vein. Ultrasonic hepatic venous waveform pattern were determined and categorized as 1) triphasic, which is the normal hepatic waveform pattern, 2) biphasic, which is characterized by the lack of an inverted wave that can or may not be accompanied by a decrease in the amplitude of the phase oscillators, or 3) monophasic that characterized by a flat and smooth waveform. In this study, the Damping index was defined by dividing minimum to maximum hepatic venous velocity that the values higher than 0.6 was considered significant for portal hypertension. Splenoportal index was calculated in cm/second with the following formula: SPI= SI/ PVV mean (where SI denotes the splenic index, which is a product of maximum transverse and vertical diameter of spleen in centimeters and PVV mean is the mean portal vein velocity. Ultrasonography and endoscopy of all patients were performed by one person in order to reduce the error. Endoscopy was performed by the PENTAX machine and the existence of esophageal varices and their size and shape were categorized as straight (F1), enlarged, tortuous (F2), or very large varices (F3). The Child classification system was used to determine the severity of liver disease based on clinical features such as ascites and splenomegaly, as well as laboratory characteristics including serum levels of bilirubin, albumin and prothrombin time.

Results were presented as mean ± standard deviation (SD) for quantitative variables and were summarized by absolute frequencies and percentages for categorical variables. Normality of data was analyzed using the Kolmogorov-Smirnoff test. Categorical variables were compared using chi-square test or Fisher's exact test when more than 20% of cells with expected count of less than

5 were observed. Quantitative variables were also compared with t test or Mann- Whitney U test. For the statistical analysis, the statistical software SPSS version 16.0 for windows (SPSS Inc., Chicago, IL) was used. P values of 0.05 or less were considered statistically significant.

## RESULTS

Of 31 included patients, 77.4% were male and 22.6% were female with overall mean age of 56.74 ± 12.72 years ranged 20 to 83 years. Regarding causes of cirrhosis, the etiology was hepatitis B in 29.0%, hepatitis C in 22.6%, cryptogen in 22.6%, autoimmune in 3.2% and unknown in 22.6%. Regarding severity of liver disease, 41.9% were graded as the Child A, 35.5% as the Child B, and 22.6% as the Child C (Table 1). With respect to cirrhosis-related complications, liver encephalopathy was found in 6.5%, esophageal varices in 77.4%, and ascites in 58.1%. In those with esophageal varices, this finding was categorized as F1 in 33.3%, F2 in 25.0% and F3 in 41.7%. Assessing ultrasonic hepatic venous waveform pattern showed triphasic pattern in 12.9%, biphasic pattern in 51.6%, and monophasic pattern in 35.5%. The mean Damping index was 0.53 ± 0.15 and the mean Splenoportal index was 10.87 ± 4.24. As shown in Table 2, there was no association of ultrasonic hepatic venous waveform pattern with cirrhosis-related complications including liver encephalopathy (p = 0.817), esophageal varices (p = 0.372), and ascites (p = 0.471). we showed also no association between hepatic venous waveform pattern and liver disease severity that the rate of monophasic, biphasic, and triphasic patterns in Child A category was 46.2%, 38.5%, and 15.4%, in Child B category was 36.4%, 45.5%, and 18.2%, and in Child C category was 14.3%, 85.7% and 0.0% (p = 0.331). As shown in Table 3, the mean of Damping index was similar in the patients with and without each cirrhosis-related complications including liver encephalopathy (p = 0.134), esophageal varices (p = 0.969), and ascites (p = 0.206). Similar findings were revealed between Splenoportal index and the presence or absence on each complication (Table 3). We found no difference in the mean of two Damping and Splenoportal indices across the different categorizes of liver disease severity according to the Child grading system (Table 3).

## DISCUSSION

In first step, we showed the two monophasic and biphasic patterns indicating portal hypertension in 87.1% of patients with liver cirrhosis, however unexpectedly, 12.9% of them had triphasic pattern as normal pattern of hepatic venous waveform. In other word, triphasic pattern is not expected in all normal condition and thus a percentage of patients with cirrhosis suffering portal hypertension may also have a triphasic wave pattern. In other words, the existence of a monophasic or biphasic pattern will not always be associated with the occurrence of cirrhosis. In Zang et al study [19], the Doppler flow waveforms in the middle hepatic vein were triphasic in 31.6%, biphasic in 46.7%, and monophasic in 21.6% of subjects. These figures were 86.7%, 10.0%, and 3.3%, respectively, in healthy subjects. In Colli et al observation [20], abnormal hepatic vein waveforms were detected in 75.0% of patients with cirrhosis and in 22.2% of patients without cirrhosis. Also, von Herbay et al [21] also indicated triphasic pattern in 100% of healthy group, also shown in 40% of those with cirrhosis. Besides, biphasic pattern was revealed in none of the healthy individuals, while in 16% of those with cirrhosis. Also, monophasic pattern was not found in healthy group, but in 43% of cirrhotic group. In fact, in their study, monophasic and biphasic patterns were pathognomonic for liver diseases while the lack of these patterns is expected in healthy ones. Overall, it does not appear that the record of biphasic or monophasic patterns is specific for hepatic cirrhosis. The reason for changing the Doppler wave pattern associated with portal hypertension is unknown. Some researchers believe that the reason for this change is the parenchymal fibrosis, as well as infiltration of fat around the portal vein wall, thereby reducing the compliance of this vein [22]. Some also believe that the pathogenic mechanism leading interohepatic shunting is responsible for changing the hepatic venous waveform pattern [23-25].

Contrary to our initial hypothesis, a significant relationship was not found between ultrasonic Doppler wave pattern in portal vein and the severity of liver disease according to Child category, and also with the occurrence of each of the cirrhosis complications, such as liver encephalopathy, ascites and varices. Also, there was no significant relationship between the two indexes related to the portal vein of the portal vein including the Damping and Splenoportal indices with the severity of liver disease or related complications. In fact, the portal vein Doppler pattern as monophasic or biphasic and also the change in flow velocity in the portal vein cannot predict the severity of cirrhosis or the incidence of

**Table 1. Baseline characteristics of the study population**

| | |
|---|---|
| Gender | |
| Male | 24 (77.4) |
| Female | 7 (22.6) |
| Mean age, year | 56.74 ± 12.72 |
| Etiology of cirrhosis | |
| Hepatitis B infection | 9 (29.0) |
| Hepatitis C infection | 7 (22.6) |
| Cryptogenic | 7 (22.6) |
| Autoimmune | 1 (3.2) |
| Unknown | 7 (22.6) |
| Disease severity (Child's score) | |
| Score A | 13 (41.9) |
| Score B | 11 (35.5) |
| Score C | 7 (22.6) |
| Mean serum albumin level | 3.38 ± 0.84 |
| Mean INR | 1.78 ± 1.01 |
| Cirrhosis complications | |
| Liver encephalopathy | 2 (6.5) |
| Esophageal varices | 24 (77.4) |
| Ascites | 18 (58.1) |
| Hepatic venous waveform pattern | |
| Monophasic | 11 (35.5) |
| Biphasic | 16 (51.6) |
| Triphasic | 4 (12.9) |
| Mean Damping score | 0.53 ± 0.15 |
| Mean Splenoportal score | 10.87 ± 4.24 |

**Table 2. The association between hepatic venous waveform pattern and cirrhosis severity and complications**

| Item | Monophasic | Biphasic | Triphasic | P-value |
|---|---|---|---|---|
| Liver encephalopathy | | | | 0.817 |
| Presence | 50.0% | 50.0% | 0.0% | |
| Absence | 34.5% | 51.7% | 13.8% | |
| Esophageal varices | | | | 0.372 |
| Presence | 37.5% | 45.8% | 16.7% | |
| Absence | 28.6% | 71.4% | 0.0% | |
| Ascites | | | | 0.471 |
| Presence | 44.4% | 44.4% | 11.2% | |
| Absence | 23.1% | 61.5% | 15.4% | |
| Disease severity | | | | 0.331 |
| Child A | 46.2% | 38.5% | 15.4% | |
| Child B | 36.4% | 45.5% | 18.2% | |
| Child C | 14.3% | 85.7% | 0.0% | |

**Table 3. The association of Damping and Splenoportal scores with cirrhosis severity and complications**

| Item | Damping score | Splenoportal score |
|---|---|---|
| Liver encephalopathy | | |
| Presence | 0.72 ± 0.08 | 13.65 ± 3.75 |
| Absence | 0.52 ± 0.14 | 10.67 ± 4.26 |
| p-value | 0.134 | 0.453 |
| Esophageal varices | | |
| Presence | 0.53 ± 0.15 | 11.33 ± 3.82 |
| Absence | 0.53 ± 0.14 | 9.27 ± 5.50 |
| p-value | 0.969 | 0.382 |
| Ascites | | |
| Presence | 0.56 ± 0.15 | 11.57 ± 4.87 |
| Absence | 0.49 ± 0.13 | 9.89 ± 3.11 |
| p-value | 0.206 | 0.249 |
| Disease severity | | |
| Child A | 0.53 ± 0.14 | 10.36 ± 2.92 |
| Child B | 0.53 ± 0.14 | 10.39 ± 4.71 |
| Child C | 0.56 ± 0.16 | 12.54 ± 5.63 |
| p-value | 0.672 | 0.508 |

its-related complications. In this regard, some evidence has been found contrary to our study. As shown by Joseph et al [26], the sensitivity of loss of the triphasic wave pattern in detecting significant varices was very high (95.23%) and negative predictive value was also high (75%). However, similar to our study, they found that the severity of liver disease as indicated by Child-Pugh score did not correlate with changes in hepatic venous waveforms. In Bhutto et al survey [27], the relationship of waveforms had significant relation with hepatic dysfunction, while insignificant with grading of esophageal varices. In Antil et al survey [28], there was a positive correlation between Child score and Dam ping index, while, there was weak positive correlation between Splenoportal index a nd Child score. Of the evaluations obtained from the review of studies, there is still a controversy regarding the sensitivity and specificity of biphasic or monophasic patterns in determining the severity of cirrhosis or predicting its complications. But what can be interpreted is that the presence of a triphasic pattern in patients with cirrhosis, especially severe cirrhosis, is less likely, but not specific.

## CONCLUSION

In conclusion, the record of the monophasic and biphasic patterns is predictable in most patients with cirrhosis and in a small number of healthy subjects without cirrhotic disorders. Also, recording these patterns together with the increase in two Damping and Splenoportal indices does not predict the severity of cirrhosis or its complications, such as liver encephalopathy, esophageal varices or ascites.

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