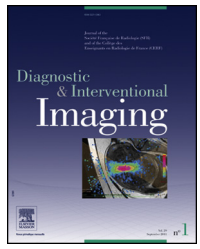
Diagnostic and Interventional Imaging (2015) xxx, xxx—xxx



ORIGINAL ARTICLE /*Digestive*

Doppler ultrasonography helps discriminate between cirrhotic and non-cirrhotic patients with viral B and C hepatitis

G. Soker[a,*], A. Bahadir Ozturk[b], B. Gulek[a], F. Kuscu[c], U. Bilge Doğan[d], C. Yilmaz[a]

[a] *Department of Radiology, Numune Teaching and Research Hospital, Adana, Turkey*
[b] *Department of Family Medicine, Adiyaman University School of Medicine, Adiyaman, Turkey*
[c] *Department of Infectious Disease and Microbiology, Numune Teaching and Research Hospital, Adana, Turkey*
[d] *Department of Gastroenterology, Mustafa Kemal University School of Medicine, Adana, Turkey*

KEYWORDS
Cirrhosis;
Doppler ultrasonography;
Portal flow;
Hepatic artery;
Hepatic veins

Abstract
Objective: The aim of this study was to define the cutoff values between compensated cirrhosis and non-cirrhotic patients with viral hepatitis B and C, using the criteria of the Doppler parameters of liver vascularity.
Materials and methods: Seventy non-cirrhotic patients with viral hepatitis B and C and 30 cirrhotic patients were included in this prospective study. The diagnostic decisiveness properties of the Doppler values in the pre-determination of liver cirrhosis were evaluated using receiver operating characteristics curve analysis.
Results: Taking the cutoff value for hepatic vein waveform index as 0.605, a sensitivity of 80% and a specificity of 77.1% were obtained. The sensitivity was 80%, and the specificity was 68.6% for a mean max portal velocity cutoff value of 18.25 cm/s. When the hepatic artery resistivity index cutoff value was taken as 0.705 for the diagnosis of cirrhosis, the sensitivity was 82.5% and the specificity 72.1%. For a hepatic artery pulsatility index cutoff value of 1.295, a sensitivity of 82.5% and a specificity of 72.1% were found.

* Corresponding author. Yurt Mah. Ahmet Sapmaz Bulvari Gizerler Plaza B Blok Kat: 13 Daire: 26 PK: 01160 Çukurova/Adana, Turkey.
E-mail address: gsoker@hotmail.com (G. Soker).

http://dx.doi.org/10.1016/j.diii.2015.05.014

Please cite this article in press as: Soker G, et al. Doppler ultrasonography helps discriminate between cirrhotic and non-cirrhotic patients with viral B and C hepatitis. Diagnostic and Interventional Imaging (2015), http://dx.doi.org/10.1016/j.diii.2015.05.014

Conclusion: It is not possible to diagnose cirrhosis with only hemodynamic changes. However, the cutoff values may be helpful in the selection of patients to undergo the procedure of liver biopsy.

The prognosis of chronic liver disease is primarily dependent on the stage of fibrosis. The distinction of cirrhotic from non-cirrhotic patients with viral hepatitis B and C is of crucial importance in the determination of therapy for chronic liver disease due to viral hepatitis. The current method of choice for the diagnosis and staging of hepatic fibrosis is the histologic evaluation of the liver tissue. This necessitates liver biopsy, which has some limitations such as invasiveness, complications, and sample error [1—6]. A non-invasive method to help decide which patients should undergo liver biopsy would be useful [4—6].

The aim of this study was to define the cutoff values between compensated cirrhosis and non-cirrhotic patients with viral hepatitis B and C, in terms of the criteria of the Doppler parameters of liver vascularity. In this study, Doppler parameters from the hepatic artery, hepatic vein, and portal vein were evaluated in patients belonging to two groups, one consisting of patients with compensated cirrhosis and the other consisting of non-cirrhotic patients with viral hepatitis B and C. Differences between these two groups were investigated in terms of hepatic artery resistivity index (HARI), hepatic artery pulsatility index (HAPI), mean of the max portal velocity (MMPV), and hepatic vein waveform index (HVWI). Hepatic venous flow was also qualitatively evaluated in terms of phase characteristics. As a unique characteristic of the study, it aimed to achieve a cutoff value between these two groups in terms of all Doppler parameters studied. The changes in hepatic venous flow were quantitatively investigated.

Materials and methods

Patients

The study was approved by our institutional review board and was carried out in accordance with the provisions of the Declaration of Helsinki and Good Clinical Practice guidelines. Informed consent was obtained from all individuals in both non-cirrhotic and cirrhosis groups. A total of 100 patients were included in this controlled prospective study. The patients were categorized into two groups, one consisting of patients with chronic viral hepatitis, and the other consisting of patients with cirrhosis. The diagnosis was based on persistent or fluctuating high serum aminotransferase levels for more than six months, the presence of hepatitis B surface antigen with hepatitis B virus DNA or hepatitis C antibodies and hepatitis C virus RNA in the serum, and chronic hepatitis with or without cirrhosis at liver biopsy. All patients had undergone a liver biopsy within six months of entry into the study. Liver histology was graded using the histological activity index (HAI) according to the criteria of Ishak et al. [7]. According to the staging table developed by Ishak et al., those patients with stages 1—4 fibrosis were evaluated as non-cirrhotic patients with viral hepatitis B and C, while those with stages 5—6 fibrosis were classified with cirrhosis. The following groups of patients were excluded from the study: those with chronic liver disease due to etiologies other than viral hepatitis, those with cardiac and pulmonary diseases that can affect liver hemodynamics, those on prescriptions that may alter hepatic blood flow, those with habitual alcohol intake of over 20 gm/day, those having stage 2 or 3 hepatic steatosis, those presenting with a history of decompensated liver disease, those with liver tumors, and those who did not accept to be included in the study.

Methods

All patients from the three groups were examined by three radiologists with 7, 10, and 12 years' experience, who did not have any information about the liver biopsy results. These examinations were performed on a Mindray DC-7 ultrasonography device (Medical International Limited, Shenzhen, China), and a 3.5 MHz abdominal transducer was utilized for this purpose. US examinations were performed following a fasting period of a minimum of six hours, and a resting period of 20 minutes, prior to the examination. Initially, a B-mode abdominal US examination was performed. This was followed by three successive Doppler examinations by each radiologist, in which quantitative measurements were made and their averages were obtained. Then, recordings were made, concerning the liver function tests and patients' ages and genders. Liver biopsy results were recorded and held in the gastroenterology department, and they were drafted after the decision to terminate the study. Hepatic artery peak systolic velocity (HAPSV), hepatic artery end-diastolic velocity (HAEDV), HARI, and HAPI measurements were obtained from the subcostal regions during breath holding sessions, with Doppler angles between 30°—60°. Hepatic artery Doppler measurements were performed at the distal end of the hepatic artery, near the bifurcation site, and preferably from the right or left intrahepatic branch. After obtaining the HAPSV and HAEDV values, the HARI and HAPI values were extracted automatically from the manually drawn spectral wave forms, according to the following formulas, respectively: HAPSV-HAEDV/HAPSV, and HAPSV-HAEDV/mean velocity of

Please cite this article in press as: Soker G, et al. Doppler ultrasonography helps discriminate between cirrhotic and non-cirrhotic patients with viral B and C hepatitis. Diagnostic and Interventional Imaging (2015), http://dx.doi.org/10.1016/j.diii.2015.05.014

HA [8,9]. Hepatic artery flow measurements could not be obtained in three patients whose hepatic arteries were not visible at the bifurcation sites or more distally.

Portal vein diameter and mean of the MMPV measurements were performed at the crossing point with the hepatic artery. These portal vein samplings, too, were obtained from the subcostal regions during breath holding sessions, again utilizing Doppler angles ranging between 30° and 60°.

The evaluation of the hepatic vein was performed at a site about 4—5 cm away from the confluence of the right hepatic vein with the inferior vena cava (IVC), during a slight inspiration, and through the subcostal plane. Because of the risk of influence by cardiac pulsatility, the middle and left hepatic veins were not sampled. The spectral wave forms were evaluated as triphasic, biphasic, or monophasic; then, the maximum and minimum flow velocity values were recorded, with Doppler angles ranging between 30° and 60°. Flow patterns were evaluated as triphasic in the presence of a retrograde flow, biphasic in its absence, and monophasic if there was an ondulation of an amount of under 10% in the velocity of the flow [3]. The HVWI value was measured using the following formula: maximum negative velocity—minimum negative velocity (positive flow velocity in the presence of triphasic flow)/maximum negative velocity [10].

Statistics

The statistical analyses were performed by the 20.0 version of SPSS (SPSS Inc., Chicago, Illinois, USA). Descriptive analyses were made by using the mean values and standard deviations for normally distributed variants. The one-way Anova test was used to compare the normally distributed variants. Post-hoc comparisons of two-member groups were performed by the Tukey test, in case a statistically significant difference was found between the groups. The Kruskal-Wallis test was administered for the comparison of the variants, which did not demonstrate a normal distribution. If a statistically significant result was obtained, then two-member comparisons were performed using the Mann-Whitney U-test. The results were evaluated following the Bonferroni correction. The probability of the presence of a difference in the phase between the non-cirrhotic and cirrhotic groups was investigated by using the chi square test, and the measurements were made as odds ratio values. The diagnostic decisiveness properties of the HARI, HAPI, MMPV, and HVWI values in the pre-determination of liver cirrhosis were evaluated by the receiver operating characteristics (ROC) curve analysis. The sensitivity, specificity, and the positive and negative predictive values were measured, in case of the presence of significant border values. In all tests, a P value less than 0.05 was accepted as statistically significant. The weighted kappa statistic was employed to evaluate inter-observer variability.

Results

Seventy patients were included in the non-cirrhotic group, of whom 42 (60%) were males and 28 (40%) were females. The mean age of the patients was 51.4 ± 13.44 years. Fifty-eight patients (82.9%) had hepatitis B, and 12 patients (17.1%) had hepatitis C. The cirrhosis group consisted of 30 patients. Nineteen (63.3%) of these were males, whereas 11 (36.7%) were females. The mean age in this group was 52.6 ± 9.4 years. Sixteen (53.3%) patients had chronic hepatitis B, and 14 (46.7%) had hepatitis C. Demographic characteristics of the patients are shown at Table 1. According to Ishak scoring, 12, 30, 20, 8, 5, and 25 patients had score 1, score 2, score 3, score 4, score 5, and score 6, respectively. The mean interval between liver biopsy and US exam was three months.

Table 1 Demographic characteristics of the patients.

	Chronic hepatitis without cirrhosis group (n = 70)	Cirrhosis group (n = 30)	P value
Male	42 (60%)	19 (63.3%)	> 0,05
Female	28 (40%)	11 (36.7%)	> 0,05
Age	51.4 ± 13.4	52.6 ± 9.4	> 0,05

The flow patterns detected in the patient groups are shown at Table 2. When the flow patterns of the cirrhotic and non-cirrhotic groups were compared, and the monophasic and triphasic flow patterns were significantly different between the two groups (P = 0.031 and P < 0.001, respectively). There was no statistically difference in terms of biphasic flow patterns between the two groups (P = 0.72).

HVWI values were 0.45 ± 0.40 in the cirrhosis group, while it was 0.87 ± 0.38 in the non-cirrhotic group. Statistically significant differences were found between the cirrhosis and non-cirrhotic patients groups in terms of HVWI values (P < 0.0001). The receiver operating characteristics (ROC) curve analysis was administered in order to determine a cutoff value between the non-cirrhotic patients and cirrhosis patient groups. The area under curve (AUC) value for HVWI was 0.827 (P < 0.0001; 95% confidence interval: 0.718—0.936). With an HVWI cutoff value of 0.605 for the diagnosis of cirrhosis, the following statistical values were obtained: sensitivity 80%, specificity 77.1%, positive predictive value (PPV) 60%, and negative predictive value (NPV) 90% (Fig. 1).

The MMPV was 15.9 ± 6.1 cm/s in the cirrhotic group, while it was 21.8 ± 5.9 cm/s in the non-cirrhotic patient group. Statistically significant differences were found between the two groups (P < 0.0001). The AUC value for

Table 2 Hepatic vein flow patterns seen in the patients groups.

Hepatic vein trace phasicity (n = 100)			
Phasicity of hepatic veins	Cirrhosis (n = 30)	Chronic hepatitis without cirrhosis (n = 70)	P value*
Triphasic	3	21	0.031
Biphasic	22	49	0.72
Monophasic	5	0	< 0.001

* Z test was calculated for comparing two proportions with cirrhosis and non-cirrhosis groups.

Please cite this article in press as: Soker G, et al. Doppler ultrasonography helps discriminate between cirrhotic and non-cirrhotic patients with viral B and C hepatitis. Diagnostic and Interventional Imaging (2015), http://dx.doi.org/10.1016/j.diii.2015.05.014

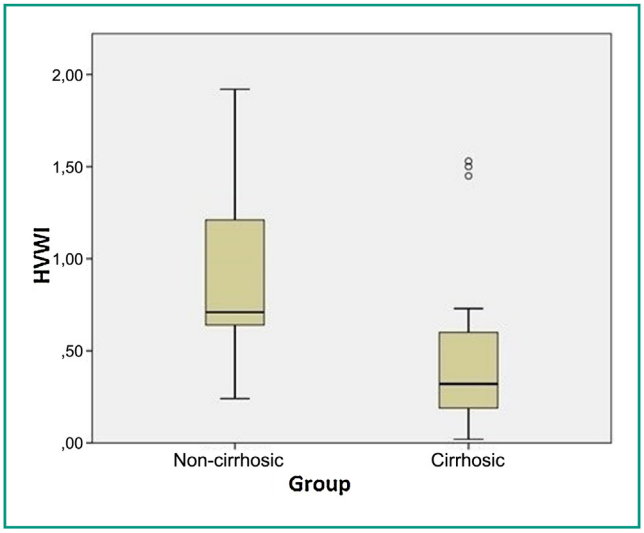


Figure 1. Box plot showing the distribution of HVWI values of the two groups (hepatic vein waveform index [HVWI]).

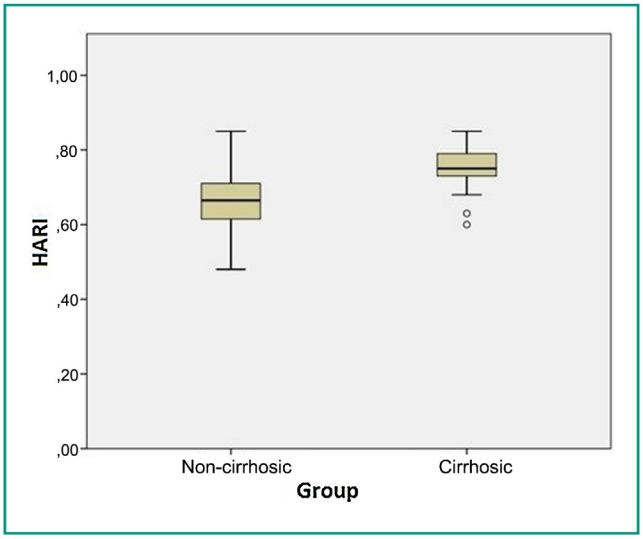


Figure 3. The box plots to illustrate the distribution of HARI values of the two groups (hepatic artery resistivity index [HARI]).

MMPV was 0.813 ($P < 0.0001$; 95% CI: 0.705—0.921). The cutoff value for MMPV was 18.25 cm/s, with 80% sensitivity, 68.6% specificity, 52.2% PPV, and 88.9% NPV (Fig. 2).

A statistically significant difference was detected in the HARI values, between the cirrhotic and non-cirrhotic groups ($P < 0.0001$). In regard to the HAPI values, a statistically significant difference was noted between the cirrhotic and non-cirrhotic groups ($P < 0.0001$). The HARI value was 0.75 ± 0.06, and the HAPI value was 1.56 ± 0.34 in the cirrhosis group. The same values were 0.66 ± 0.70 and 1.20 ± 0.32 for the non-cirrhotic group. The AUC value for HARI was 0.834 ($P < 0.0001$; 95% CI: 0.746—0.923). When the cutoff value was determined as 0.705 for HARI, the sensitivity was 82.5%, specificity was 72.1%, PPV was 55.8%, and the NPV was 90.7%. The AUC value for HAPI was 0.813 ($P < 0.0001$; 95% CI: 0.705—0.896) (Figs. 3 and 4). On the other hand, a sensitivity of 82.5%, a specificity of 72.1%, a PPV of 55.8%, and an NPV of 90.7% were found when the cutoff value for HAPI was set at 1.295 (Fig. 5).

Doppler values of cirrhotic and non-cirrhotic groups are summarized in Table 3.

No significant inter-observer variation occurred in measuring these indices (Kappa value = 0.91). The Kappa value was calculated 0.93, 0.90, 0.94, and 0.85 for HARI, HAPI, MMPV, and HVWI, respectively.

Discussion

The prognosis of chronic liver disease is primarily dependent on the stage of fibrosis [3]. This necessitates liver biopsy, which is an invasive procedure that bears in itself the risk of various complications. A non-invasive method to aid in

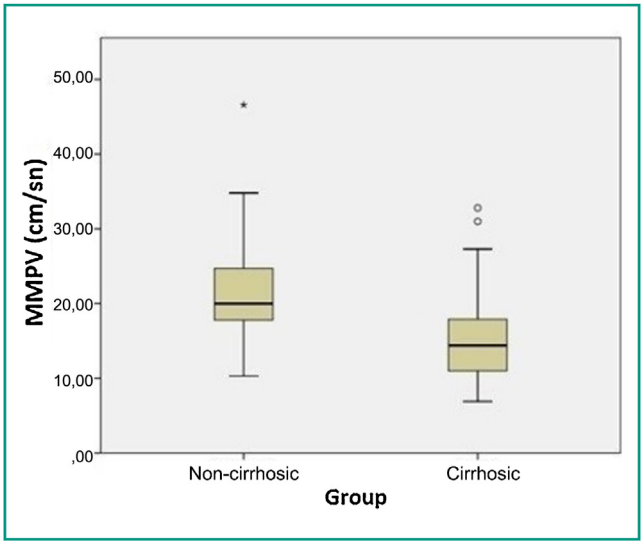


Figure 2. Box plot showing the distribution of MMPV values of the two groups (mean of the max portal velocity [MMPV]).

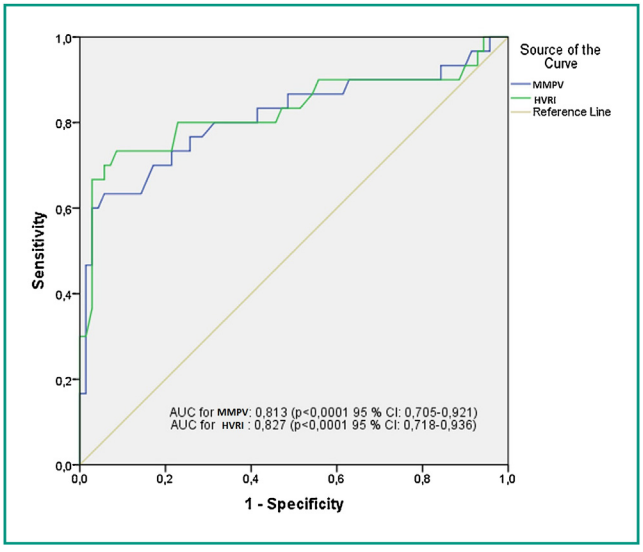


Figure 4. The ROC diagram for the HVWI and MMPV values in the chronic hepatitis and cirrhosis groups (hepatic vein waveform index [HVWI], mean of the max portal velocity [MMPV]).

Please cite this article in press as: Soker G, et al. Doppler ultrasonography helps discriminate between cirrhotic and non-cirrhotic patients with viral B and C hepatitis. Diagnostic and Interventional Imaging (2015), http://dx.doi.org/10.1016/j.diii.2015.05.014

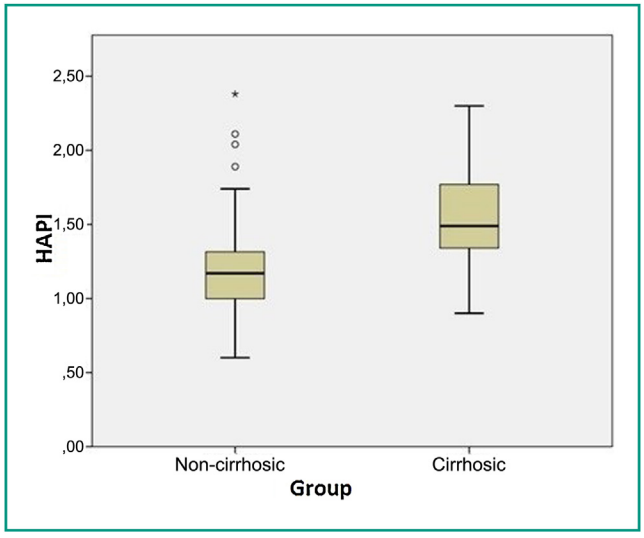


Figure 5. Box plots representing HAPI values of the two groups (hepatic artery pulsatility index [HAPI]).

determining which patients must undergo biopsy would be useful.

During the process in which the chronic liver disease progresses to cirrhosis, some alterations in the hemodynamic circulation of the liver occur. Inflammatory cytokines and anatomic repair affect hepatic circulation by dilatation or constriction [4,11]. It has also been stated that increased fibrous tissue in the liver and hepatic sinusoidal endothelial proliferation can change liver hemodynamics by causing increased vascular resistance [12].

Hepatic arterial and portal vein Doppler indices are affected by many factors including some physiological factors. Steatosis and peripheral collateral shunts cause an increased RI value, whereas advanced patient age leads to a reduction in the post-prandial term HARI value [13]. Portal flow may be affected by many factors such as patient positioning, meal times, exercise, and cardiac output [11]. As hepatic veins can be affected by cardiac pathologies and respiratory phase, hepatosteatosis may also deteriorate hepatic venous flow by affecting compliance [14].

Various studies have shown that an increase in the hepatic artery PI and RI values occur in chronic liver disease patients [4,15—19]. Our study showed compatibility with these results, the HARI and HAPI values showed statistically significant differences between the non-cirrhotic and cirrhotic patients. HARI and HAPI scores over the calculated cutoff values (0.705 for HARI and 1.295 for HAPI) in chronic hepatitis patients may indicate stage 5 or 6 fibrosis and thus necessitate a biopsy.

Table 3 Doppler values of cirrhotic and non-cirrhotic groups.

	Chronic hepatitis without cirrhosis group ($n = 70$)	Cirrhosis group ($n = 30$)	P value
HVRI	0.87 ± 0.38	0.45 ± 0.40	< 0.05
MMPV (cm/s)	21.8 ± 5.9	15.9 ± 6.1	< 0.05
HARI	0.66 ± 0.70	0.75 ± 0.06	< 0.05
HAPI	1.20 ± 0.32	1.56 ± 0.34	< 0.05

The flow pattern in the hepatic veins is usually pulsatile and triphasic, due to right-side cardiac activity during the cardiac cycle, and the intrathoracic and intra-abdominal pressure [20,21]. The hepatic parenchyma becomes less compliant in pathologic conditions that directly affect it, and this, in turn, impairs the normally triphasic flow pattern [20]. A relationship between hepatic vein flow patterns and liver fibrosis has been reported in previous studies [22,23].

In the current study, the monophasic and triphasic flow patterns are significantly different between cirrhotic and non-cirrhotic groups. In accordance with previous studies, an impairment of the hepatic vein waveform was detected in patients with diffuse parenchymal disorders that impaired the compliance of the liver tissue. As a novelty of this study, which differentiates it from other studies conducted, the flow patterns in the hepatic veins of all the patients were quantitatively assessed by HVWI measurements. The HVWI values demonstrated statistically significant differences between the non-cirrhotic and cirrhotic groups. The value that showed the highest sensitivity and specificity values was stated as the cutoff- value. When the cutoff value was set at 0.605 for HVWI, a sensitivity of 80% and a specificity of 77.1% were found.

The study of Koda et al. reported that MMPV is more sensitive than portal vein flow volume in determining grade of hepatic fibrosis [24]. On the other hand, another study conducted on 47 patients with chronic viral hepatitis by Piscaglia et al. revealed that no significant correlation was found between MMPV and the grade of hepatic fibrosis [16]. In our study, which was compatible with the study of Koda et al., statistically significantly differences were found between the MMPV values of both groups. However, it must be noted that the MMPV may show differences due to the alterations of portosystemic collaterals, in the presence of similar portal pressures.

In recent years, other techniques such as elastography and MR elastography have been used to estimate liver fibrosis. Elastography measures the grade of liver fibrosis by various techniques. Ultrasound elastography is used in the diagnosis of cirrhosis due to various etiologies. One study reported that ultrasound elastography has 83% sensitivity and 89% specificity in the diagnosis of cirrhosis due to hepatitis B, hepatitis C, and other factors [25]. In hepatic C infections, 6.8—7.6 kPa and 11—13.6 kPa threshold values are recommended for stage 2 and stage 4 fibrosis, respectively. The threshold values for hepatitis B infections are 7 and 11 kPa, respectively. MR elastography also measures liver fibrosis as US elastography. In the literature, various threshold values for liver fibrosis are recommended [26—29]. Liver fibrosis and cirrhosis changes the micro-architecture and consequently leads to increased vascular resistance and reduced portal blood flow. Based on these changes, a limited number of MRI perfusion studies have been conducted to evaluate liver fibrosis [30].

Our study has some limitations. Measurements were obtained during breath holding. Breath holding could be a limitation for portal flow, because if the breath is held after a deep inspiration, this can decrease the portal flow. In this study, viral activity was not evaluated. Varying viral

Please cite this article in press as: Soker G, et al. Doppler ultrasonography helps discriminate between cirrhotic and non-cirrhotic patients with viral B and C hepatitis. Diagnostic and Interventional Imaging (2015), http://dx.doi.org/10.1016/j.diii.2015.05.014

activity may change the hemodynamics in the patients with the same fibrotic score. However, it has not been designed in our study, hemodynamic changes due to alcohol and hepatosteatosis can be compared to hemodynamic changes due to viral hepatitis.

The previous studies on the Doppler indices of hepatic and portal veins in parenchymal liver diseases demonstrated wide inter-observer variability. The study of Sacerdoti et al. revealed that Doppler indices of hepatic, splenic, and renal arteries demonstrate a statistically significantly difference in inter-observer variability [9]. In another study, Fisher et al. reported minimal inter-observer variability in Doppler indices of portal and hepatic arteries [31]. We encountered a lower inter-observer variability in our study. We concluded that this fact is associated with strict compliance to the designed method, as well as the experience of the specialist radiologists in our study.

Conclusion

It is not possible to diagnose cirrhosis with only hemodynamic changes, and the dispersion of the Doppler values make this tool difficult to use in clinical practice. However, hemodynamic modifications are a part of the ultrasound signs that are part of the diagnosis of cirrhosis. Hepatic vasculature must be evaluated by Doppler US, in addition to the evaluation of the hepatic parenchyma by B-mode US, during the routine examinations of chronic hepatitis patients. Those patients who show an increase in HARI and HAPI, and a decrease in the MMPV and HVWI values, together with patients who demonstrate impairment of their hepatic vein flow patterns, must undergo liver biopsy in order to be evaluated in terms of stage 5 or 6 hepatic fibrosis. The cutoff values may be of serious help in the selection of patients to undergo the liver biopsy.

Disclosure of interest

The authors declare that they have no competing interest.

References

[1] Frulio N, Trillaud H. Ultrasound elastography in liver. Diagn Interv Imaging 2013;94:515—34.
[2] Goyal N, Jain N, Rachapalli V, Cochlin DL, Robinson M. Non-invasive evaluation of liver cirrhosis using ultrasound. Clin Radiol 2009;64:1056—66.
[3] Bernatik T, Strobel D, Hahn EG, Becker D. Doppler measurements: a surrogate marker of liver fibrosis? Eur J Gastroenterol Hepatol 2002;14:383—7.
[4] Colli A, Fraquelli M, Andreoletti M, Marino B, Zuccoli E, Conte D. Severe liver fibrosis or cirrhosis: accuracy of US for detection — analysis of 300 cases. Radiology 2003;227:89—94.
[5] Lim AK, Patel N, Eckersley RJ, Kuo YT, Goldin RD, Thomas HC, et al. Can Doppler sonography grade the severity of hepatitis C-related liver disease? AJR Am J Roentgenol 2005;184:1848—53.
[6] Aubé C, Winkfield B, Oberti F, Vuillemin E, Rousselet MC, Caron C, et al. New Doppler ultrasound signs improve the non-invasive diagnosis of cirrhosis or severe liver fibrosis. Eur J Gastroenterol Hepatol 2004;16:743—51.
[7] Ishak K, Baptista A, Bianchi L, Callea F, De Groote J, Gudat F, et al. Histological grading and staging of chronic hepatitis. J Hepatol 1995;22:696—9.
[8] Numata K, Tanaka K, Kiba T, Morita K, Saito S, Fujii T, et al. Hepatic arterial resistance after mixed-meal ingestion in healthy subjects and patients with chronic liver disease. J Clin Ultrasound 1999;27:239—48.
[9] Sacerdoti D, Gaiani S, Buonamico P, Merkel C, Zoli M, Bolondi L, et al. Inter-observer and inter-equipment variability of hepatic, splenic, and renal arterial Doppler resistance indices in normal subjects and patients with cirrhosis. J Hepatol 1997;27:986—92.
[10] Pedersen JF, Madsen LG, Larsen VA, Hamberg O, Horn T, Federspiel B, et al. Doppler waveform index to characterize hepatic vein velocity pattern and evaluate hepatic fibrosis. J Clin Ultrasound 2008;36:208—11.
[11] Kok T, van der Jagt EJ, Haagsma EB, Bijleveld CM, Jansen PL, Boeve VJ. The value of Doppler ultrasound in cirrhosis and portal hypertension. Scand J Gastroenterol Suppl 1999;230:82—8.
[12] Yang YL, Di L, Duan YY, Liu X, Liu J, Yang RJ, et al. A prospective experimental study of liver fibrosis with ultrasound and its correlation with hepatic reservefunction and hemodynamics. BMC Gastroenterol 2012;12:168.
[13] Mcnaughton DA, Abu-yousef MM. Doppler US of the liver made simple. Radiographics 2011;3:161—88.
[14] Scheinfeld MH, Bilali A, Koenigsberg M. Understanding the spectral Doppler waveform of the hepatic veins in health and disease. Radiographics 2009;29:2081—98.
[15] Zeinab AE, Hamza RT, Hakim AS, Tawfik LM. Thyroid and hepatic haemodynamic alterations among Egyptian children with liver cirrhosis. ISRN Gastroenterology 2012;2012:595734.
[16] Piscaglia F, Gaiani S, Calderoni D, Donati G, Celli N, Gramantieri L, et al. Influence of liver fibrosis on hepatic artery Doppler resistance index in chronic hepatitis of viral origin. Scand J Gastroenterol 2001;36:647—52.
[17] Walsh KM, Leen E, MacSween RN, Morris AJ. Hepatic blood flow changes in chronic hepatitis C measured by duplex Doppler color sonography: relationship to histological features. Dig Dis Sci 1998;43:2584—90.
[18] Schneider AW, Kalk JF, Klein CP. Hepatic arterial pulsatility index in cirrhosis: correlation with portal pressure. J Hepatol 1999;30:876—81.
[19] Salvatore V, Borghi A, Peri E, Colecchia A, Li Bassi S, Montrone L, et al. Relationship between hepatic haemodynamics assessed by Doppler ultrasound and liver stiffness. Dig Liver Dis 2012;44:154—9.
[20] Murat A, Akarsu S, Cihangiroglu M, Yildirim H, Serhatlioglu S, Kalender O. Assessment of Doppler waveform patterns and flow velocities of hepatic veins in children with acute viral hepatitis. Diagn Interv Radiol 2006;12:85—9.
[21] Jequier S, Jequier JC, Hanquinet S, Gong J, Le Coultre C, Belli DC. Doppler waveform of hepatic veins in healthy children. AJR Am J Roentgenol 2000;175:85—90.
[22] Sudhamshu KC, Sharma D, Chataut SP. Hepatic vein waveforms in liver cirrhosis re-evaluated. Hepatol Int 2011;5:581—5.
[23] Dietrich CF, Lee JH, Gottschalk R, Herrmann G, Sarrazin C, Caspary WF, et al. Hepatic and portal vein flow pattern in correlation with intrahepatic fat deposition and liver histology in patients with chronic hepatitis C. AJR Am J Roentgenol 1998;171:437—43.
[24] Koda M, Murawaki Y, Kawasaki H, Ikawa S. Portal blood velocity and portal blood flow in patients with chronic viral hepatitis: relation to histological liver fibrosis. Hepatogastroenterology 1996;43:199—202.
[25] Sharma S, Khalili K, Nguyen GC. Non-invasive diagnosis of advanced fibrosis and cirrhosis. World J Gastroenterol 2014;20:16820—30.

Please cite this article in press as: Soker G, et al. Doppler ultrasonography helps discriminate between cirrhotic and non-cirrhotic patients with viral B and C hepatitis. Diagnostic and Interventional Imaging (2015), http://dx.doi.org/10.1016/j.diii.2015.05.014

[26] Soresi M, Giannitrapani L, Cervello M, Licata A, Montalto G. Non invasive tools for the diagnosis of liver cirrhosis. World J Gastroenterol 2014;20:18131—50.
[27] Venkatesh SK, Yin M, Ehman RL. Magnetic resonance elastography of liver: clinical applications. J Comput Assist Tomogr 2013;37:887—96.
[28] Valasek M, Lin G, Brenner D, Gamst A, Ehman R, Sirlin C. Magnetic resonance elastography predicts advanced fibrosis in patients with nonalcoholic fatty liver disease: a prospective study. Hepatology 2014;60:1920—8.
[29] Bonekamp S, Kamel I, Solga S, Clark J. Can imaging modalities diagnose and stage hepatic fibrosis and cirrhosis accurately? J Hepatol 2009;50:17—35.
[30] Ronot M, Lambert S, Daire JL, Lagadec M, Doblas S, Garteiser P, et al. Can we justify not doing liver perfusion imaging in 2013? Diagn Interv Imaging 2013;94:1323—36.
[31] Fisher AJ, Paulson EK, Kliewer MA, DeLong DM, Nelson RC. Doppler sonography of the portal vein and hepatic artery: measurement of a prandial effect in healthy subjects. Radiology 1998;207:711—5.

Please cite this article in press as: Soker G, et al. Doppler ultrasonography helps discriminate between cirrhotic and non-cirrhotic patients with viral B and C hepatitis. Diagnostic and Interventional Imaging (2015), http://dx.doi.org/10.1016/j.diii.2015.05.014