Hepatic Vein Doppler Waveform Changes in Nonalcoholic Fatty Liver Disease with Hepatomegaly

Hepatomegali ile Birlikte Seyreden Alkolik Olmayan Hepatosteatozda Hepatic Ven Akım Formu Değişiklikleri

Hepatomegalide Karaciğer Doppler Bulguları / Liver Doppler Findings in Hepatomegaly

Ozum Tuncyurek[1], Sule Akin[2,3], Sibel Taskend Aydin[4], Pars Tuncyurek[5], Hakan Erpek[5]
[1]Ataturk Goverment Hospital, Department of Radiology, [2]Ataturk Goverment Hospital, Department of Internal Medicine,
[3]Adnan Menderes University School of Medicine, Department of Internal Medicine,
[4]Ataturk Goverment Hospital, Department of Biochemistry,
[5]Adnan Menderes University School of Medicine, Department of Surgery, Aydin, Turkey

30. Ulusal Türk Radyoloji Kongresi-Antalya poster sunum olarak sunulmuştur.

Özet

Amaç: Doppler Ultrason (DUS) karaciğer damarlarının değerlendirilmesinde güvenir bir yöntem olduğu bilinmektedir. Karaciğer yağlanması sirozda olduğu gibi organ kanlanmasında değişiklik meydana getirmektedir. Alkolik olmayan diffüz karaciğer yağlanması (DKY) rutin ultrason uygulamasında sık karşılaşılan bir bulgudur. Kronik karaciğer hastalıklarında küçük karaciğer boyutları ile birlikte hepatik venlerde dalga form değişiklikleri izlenir. DKY olgularında hepatomegalinin varlığı bu değişimi etkilemekte midir, bu çalışmada değerlendirilmiştir. Gereç ve Yöntem: Yağlanma derecelerine göre sınıflanan olgular, (Grade I: 35 (%19.3); Grade II: 129 (%71.3); Grade III: 17 (%9.4)) hepatomegali 107 (%59.1) olguya eşlik etmekteydi. 74 olguda ise, (%40.9) hepatomegali yoktu. 35 erkek, 72 kadın olgunun yaş ortalaması 53.5 (± 11.1; 27-83) idi. Hepatik ven dalga formları Doppler ile incelendi. Trifazik, bifazik ve monofazik olarak gruplandı. Etyolojik faktörler arasında diyabet, hipertrigliseridemi ve kolesterolemi vardı. 119 olguda anormal dalga boyu saptandı (%65). DKY derecesi ile Hepatik ven Doppler ultrasonografik dalga boyu arasında korelasyon bulundu (p=0.03). Hepatomegali ile DKY derecesi arasında ilişki yokrtu (p=0.5). Bulgular: Sonuç olarak, hepatosteatoz derecesi ile Doppler ultrasonografik dalga boyu değişiklikleri arasındaki ilişki bilinmektedir ancak hepatomegalinin eşlik etmesi bulgularda anlamlı değişikliğe yol açmamaktadır.

Anahtar Kelimeler

Karaciğer Yağlanması; Doppler Us; Hepatomegali

Abstract

Aim: Doppler Ultrasonography (DUS) has become an important diagnostic technique in the hepatic vasculature evaluation. Fatty infiltration of the liver can also change the Doppler findings -like cirrhosis- of hepatic veins. Diffuse fatty liver (DFL) is the most common finding in liver with the method of ultrasonography. Most literature reports mention the effect of chronic liver disease with a small-size liver on the waveform alterations. The objective of the study was to evaluate the hepatic vein (HV) Doppler waveforms in cases with hepatomegaly and diffuse fatty infiltration of the liver. Material and Method: Steatosis was present in all cases (Grade I: 35 (19.3%); Grade II: 129 (71.3%); and Grade III: 17 (9.4%)). Steatosis was accompanied by hepatomegaly in 107 (59.1%) cases. However, steatosis was accompanied by nonhepatomegaly in 74 (40.9%) cases. Results: Of the cases that were detected to have hepatomegaly, 35 (33%) were male and 72 (67%) were female. Their ages ranged from 27 to 83 years (mean: 53.5 ± 11.1). Hepatic vein waveforms were examined in all cases. HV waveforms were divided into 3 groups, namely regular triphasic form, biphasic form, and monophasic form. Etiologic factors were diabetes, hypertriglyceridemia, and hypercholesterolemia. An abnormal HV Doppler waveform was present in 119 (65%) of 181 cases. A correlation was detected between DFL grade and HV Doppler waveforms (p=0.03), whereas no correlation was detected between DFL grade and hepatomegaly (p=0.5). It is known that there is an association between the grade of steatosis and a change in the hepatic vein waveform. Discussion: Nevertheless, hepatomegaly that is observed with steatosis does not cause any significant change in HV flow, which can be detected with a Doppler apparatus.

Keywords

Fatty Infiltration of the Liver; Doppler Us; Hepatomegaly

DOI: 10.4328/JCAM.1423 Received: 25.11.2012 Accepted: 31.01.2013 Printed: 01.11.2014 J Clin Anal Med 2014;5(6): 485-488
Corresponding Author: Ozum Tuncyurek, Ataturk Devlet Hastanesi Radyoloji, Ultrason Bölümü 09010 Aydin, Turkey.
T.: +905363253831 F.: +902562252505 E-Mail: ozum.tuncyurek@gmail.com

Introduction

Liver fatty infiltration is a process of morphological changes. This process may cause hepatomegaly, obtuse edge, and fuzzy superficial veins [1,2]. Thin-walled vein pulsatility drains blood from the hepatic sinusoids towards the inferior vena cava. Doppler ultrasonography (DUS) has become an essential diagnostic method in hepatic vasculature and some hepatic parenchymal diseases, such as cirrhosis, fibrosis, hepatitis, rejection of transplantation, and fatty infiltration. These parenchymal diseases may cause an alteration of the waveform in a hepatic vein [3-5]. However, these chronic liver diseases are always associated with small liver sizes.

To our knowledge, no prior study has focused on the effect of hepatomegaly on the hepatic vein. Thus, we investigated the effect of hepatomegaly on the hepatic vein Doppler waveform in patients with diffuse fatty liver (DFL).

Material and Method

Patients were screened using B-mode US for DFL. DFL was detected in 181 patients. Of 181 patients, hepatomegaly was detected in 35 males and 72 females (27-83; 53.3 ± 11.2). Nonhepatomegaly patients (37 male, 37 female (31-78; 53.7 ± 11.1)) with DFL were recorded as the control group. Diabetes mellitus (DM) and hyperlipidemia were etiologic factors for DFL. Liver biopsy was not carried out for healthy subjects and patients with DFL. Those patients who had chronic liver and heart diseases were excluded from the study. These cases may have caused changes in the hepatic vein (HV) waveform.

After an overnight fast on supine position, all patients were examined with B-mode and duplex Doppler US using a 3.5 MHz convex array transducer (Xario XG; Toshiba, Japan). For patients, hepatomegaly was defined as the (mid clavicular) long axis of the liver being longer than 155 mm [6]. The presence or absence and severity of fatty infiltration were graded using a scale from 0 to 3 corresponding to increasing degrees of hepatic echogenicity.

All eight segments of the liver were carefully scanned and vascular malformations and space-occupying lesions were excluded. After the HV had been depicted intercostally along its longitudinal axis with color 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. The patients were asked to stop breathing at the slight inspiration; a spectral analysis of hepatic venous flow was recorded for at least 2-3 cycles; and the Doppler angle was set at less than 60°. The waveforms of a HV were divided into three groups, namely regular triphasic waveform, biphasic waveform without a reverse flow, and monophasic or flat waveform (Figure 1A-B-C).

Statistical analysis

The data were expressed in mean ± standard deviation for numerical variables and in percentage (%) for categorical variables. Chi-square was used to analyze categorical variables, and the Student's t-test was used to analyze continuous variables. The Kruskal-Wallis correlation test was used to show the relationship between the fat infiltration of the liver and the presence of an abnormal hepatic vein Doppler waveform. A P value of less than 0.05 was considered statistically significant.

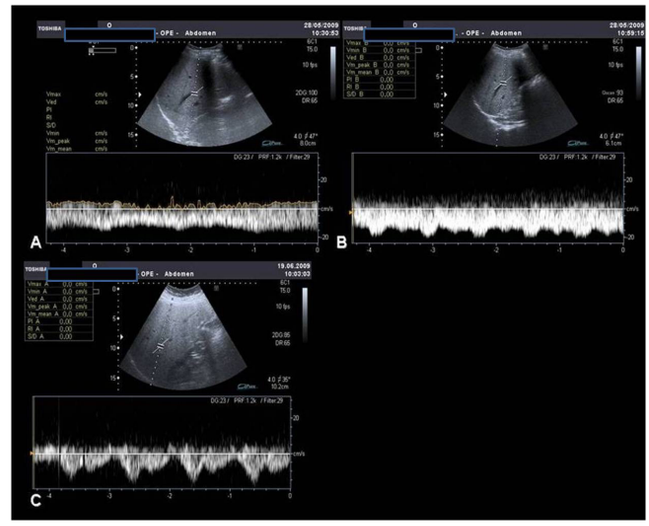


Figure 1. The waveforms of a HV were divided into three groups, namely monophasic or flat waveform, biphasic waveform without a reverse flow, and triphasic waveform (A,B,C).

Results

The Doppler flow pattern in the right hepatic vein was abnormal in 70 (65.4%) cases of the hepatomegaly group, monophasic in 29 (27.1%) and biphasic in 41 (38.3%). The DUS finding was abnormal in 49 (66.2%) cases of the nonhepatomegaly group, monophasic in 22 (29.7%) and biphasic in 27 (36.5%) (Tables 1 and 2).

Table 1. Demographic and sonographic features

	Hepatomegaly (n=107)	Control (n=74)
Age (year, mean±SD)	53.3±11.2	53.7±11.1
Sex (male/female)	35/72	37/37
DFI grades		
Grade 1	21 (19.6%)	14 (18.9%)
Grade 2	74 (69.2%)	55 (74.3%)
Grade 3	12 (11.2%)	5 (6.8%)
Hepatic vein waveforms		
Monophasic	29 (27.1%)	22 (29.7%)
Biphasic	41 (38.3%)	27 (36.5%)
Triphasic	37 (34.6%)	25 (33.8%)

Table 2. Distribution of HV flow pattern by DFL grade (HM: Hepatomegaly positive /NHM: Hepatomegaly negative)

Hepatic vein waveforms	Grade 1 (HM/NHM)	Grade 2 (HM/NHM)	Grade 3 (HM/NHM)
Monophasic	3/3	23 /18	3/1
Biphasic	6/3	28/24	7/0
Triphasic	12/8	23/13	2/4

DFL was grade 1 in 21 (19.6%), grade 2 in 74 (69.2%) and grade 3 in 12 (11.2%) cases of the hepatomegaly group. In the nonhepatomegaly group, DFL was grade 1 in 14 (18.9%), grade 2 in 55 (74.3%) and grade 3 in 5 (6.8%).

There was no statistically significant difference in the phasicity of the hepatic venous flow between the hepatomegaly and nonhepatomegaly subjects (p > 0.05)

Discussion

The normal triphasic Doppler waveform of the HVs is composed of two antegrade flow peaks towards the heart during atrial and ventricular diastole, followed by a short interval of a reversed flow peak towards the liver during atrial contraction. Pressure in the right atrium, compliance of the hepatic parenchyma, and modification of the intrathoracic and intraabdominal pressures influence this flow pattern [7].

It has been demonstrated that a monophasic waveform is associated with cirrhosis, fibrosis, hepatitis, transplant rejection, vein stenosis, and fatty liver [4, 8, 9].

In previous studies, there was a difference in hepatic vein waveforms between cases with and without diffuse fatty infiltration of the liver [5, 10]. Hepatomegaly is a common physical finding in most patients with DFL. A hyperechogenic (bright) liver indicates steatosis, with sensitivity and specificity rates being as high as 95% in ultrasonography [11].

In a study by Millener P et al., hepatic venous flows were observed to be normal in 12 of 20 cases with hepatomegaly (60%) [12]. Our study showed normal hepatic venous flows in 37 of 107 cases with hepatomegaly (34.6%). Only the effect of hepatomegaly on venous blood flow has not been clarified in literature yet. Therefore, we intended to put forward the effect of hepatomegaly, which frequently accompanied steatosis, on the venous flow. However, we detected that except for steatosis, hepatomegaly did not create any additional change.

The hepatic vein pulsatility decreases clearly with steatosis. In addition, this is intended to be explained by the compressive effect of fat deposition on hepatic veins. This is also observed in the nonhepatomegaly cases. Hepatomegaly has little effect on the physiopathology of the hepatic venous flow. This might be because the primary circulation of the liver is provided with the portal system. Thus, the venous drainage flow of the liver is more stable even if the dimension of the liver increases in comparison with organs that increase in dimension over time, such as the spleen and the heart.

Fatty accumulation in the hepatocytes leads to a reduction in the size of hepatic sinusoid space as the cell volume increases. As a result, hepatic microcirculation decreases, which leads to ischemia. Ischemia is a process that enhances fibrosis. In the long term, the liver progresses to fibrosis [10].

In their study on children, Uzun et al. suggested that hepatic vein pulsatility decreased in correlation with the grade of hepatosteatosis. This finding might also be evaluated as a consequence of fat deposition in the hepatocytes, which was previously detected in adults [10]. Ueno et al. reported that diet and exercise contributed to the change in the liver histology before the progression of fibrosis [13].

Some 50–73% of patients with cirrhosis were found to have an abnormal HV Doppler waveform [14-16]. In a previous study, a positive correlation was detected between Child-Pugh score and flat waveform [15]. This waveform in cirrhosis might be due to some decrease in resistance as a result of fibrosis in the liver parenchyma.

In a study on rabbits, a phase shift was detected. According to this study, the phasic oscillation curve shifted to the left in cirrhotic cases and to the right in fatty liver cases [9]. Because fibrosis was present in cirrhotic cases, vascular compliance decreased as a result of fibrotic changes. However, in fatty liver cases, this finding was detected as a result of increased vascular compliance.

Hepatocyte volume, which increases after fatty accumulation, causes hepatic veins to be compressed under the capsule. This leads to abnormal flows in hepatic veins. This suggestion was based on a study which revealed the elevation of intrahepatic pressure upon hypertrophy of the hepatic cells [17].

Limitation of this study included the lack of definitive proof of the absence of liver disease in addition to fatty liver, for we did not perform liver biopsies in all patients.

The results of this study confirmed that an abnormal HV Doppler waveform could be seen in patients with DFL.

Hepatomegaly was seen in glycogen storage disease, Budd-Chiari syndrome, cardiac failure, infections, and hepatosteatosis. Unlike other diseases, the accompanying hepatomegaly in cases with the DFL problem did not lead to any additional change in HV waveforms.

When hepatomegaly appears in hypertriglyceridemia patients upon physical examination, Doppler examination with B-mode US should be used. Nevertheless, we know that in the literature there is no relationship between the etiologic factors for DFL and abnormal hepatic vein Doppler findings [5].

Like B-mode US in parenchymal evaluation, DUS examination is an indispensable technique in hypertriglyceridemia cases that are detected to have hepatomegaly upon physical examination.

In conclusion, the results of this study confirm that an abnormal DUS finding

(biphasic and monophasic forms) can be seen in patients with DFL. Hepatic veins are the only drainage system of the liver. The waveform changes in veins are not affected by hepatic cell enlargement. In diseases developing with hepatomegaly, this does not lead to any additional impairment of the waveform in liver drainage problems.

Competing interests

The authors declare that they have no competing interests.

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