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Hemodynamic Changes of the Hepatic Veins in Liver Cirrhosis evaluated with Pulsed Doppler Sonography

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Abstract To study intrahepatic hemodynamics in liver cirrhosis, diameter, mean velocity, pulsatility index and waveform of the right, middle and left hepatic veins were analyzed in the normal and cirrhotic liver with pulsed Doppler ultrasound equipment. Thirty-three patients with histologically proven liver cirrhosis were studied. Forty-two patients with no history of liver disease were also studied as a control group. The right and left hepatic veins of the cirrhotic liver showed significantly smaller diameter, higher mean velocity and lower value of pulsatility index. Compared with the normal liver, the cirrhotic liver showed a low incidence of triphasic wave as well as a high incidence of biphasic wave in the right and left hepatic veins. In the middle hepatic vein, however, no difference in the waveform was noted between the normal and the cirrhotic liver. Pulsed Doppler ultrasound examination of the right and left hepatic veins is useful for evaluating hemodynamic changes in liver cirrhosis.

Key words: Doppler studies, Hepatic veins, Liver cirrhosis, Ultrasound
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Introduction

Doppler waveforms of the hepatic veins were evaluated in the normal liver in previous reports concerning tricuspid regurgitation. In these reports, Doppler flow measurements of the hepatic veins were taken in the middle hepatic vein only or right superior heptic vein only(1-3). Changes of Doppler waveform in hepatic veins of patients with liver cirrhosis were initially reported by Bolondi et al.(4). However, in that report, measurements were taken at the middle hepatic vein only. There have been no previous investigations, to our knowledge, reporting the hemodynamic balance of all three hepatic veins ; right hepatic vein (RHV), middle hepatic vein (MHV) and left hepatic vein (LHV). The right lobe atrophies while the left lobe enlarges in patients with liver cirrhosis relative to the severity of liver cirrhosis(5). As a consequence, the vascular bed in the right lobe decreases and that in the left lobe increases, so that heterogeneity developes in the regional hepatic blood flow between the right lobe and the left lobe (6,7). This hemodynamic change in liver cirrhosis might cause changes in the flow balance among the three hepatic veins. In this study hemodynamics in liver cirrhosis was analyzed by Doppler ultrasound examination of each of the hepatic veins.

Patients and Methods

Thirty-three patients, 27 males and 6 females, from 46 to 68 years of age (mean ± SD: 58.3 years ± 7.3 years), with histologically proven liver cirrhosis with no history of gastrointestinal bleeding or consumption of drugs that might alter portal hemodynamics, were studied. All subjects (the patients with liver disease and the control subjects) had no clinical, radiologic, or sonographic evidence of heart failure, especially tricuspid regurgitation, and ECGs showed sinus rhythm. Liver cirrhosis was classificated by the etiology. The presence or absence of oesophageal varices was demonstrated by endoscopy. Forty-two patients with no history of liver disease, 16 males and 26 females, from 21 to 82 years (mean ± SD: 51.5 years ± 17.1 years), were also examined as a control group. Causes of cirrhosis and clinical characteristics are summarized in Table 1.

1) Doppler ultrasound recording

Ultrasound(US) examination was performed in RHV, MHV and LHV by pulsed Doppler US equipment(Aloka SSD680) with a convex probe of 3.5MHz provided by a pulsed Doppler device operating at a frequency of 2.5 MHz. Each subject was examined in a supine position after overnight fasting to avoid any influence of meal and posture on splanchnic hemodynamics(8-10). Simultaneous monitoring by ECG was performed. Subjects were asked to hold their breath on expiration during the Doppler examination to avoid modifications caused by deep breathing. All patients were studied conventionally with B scan to assess liver morphology, and in particular, the size of the hepatic veins. Doppler flow measurements were made at the level of the right, middle and left hepatic veins, 2-3 cm proximal to their junction with the inferior vena cava. Our equipment is able to display the angle between the ultrasonic beam and the longitudinal axis of the vessel and this angle was estimated below 45 degrees, since large angles affect the accuracy of flow velocity calculation. The spectrum analysis was recorded for at least 4-5 seconds with a filter of 50 Hz.

2) Analysis of flow waveform and velocity

The spectral Doppler waveform of the hepatic veins was analyzed for maximum velocity(Vmax) and minimum velocity (Vmin). The mean velocity was calculated as the time-average during one cardiac cycle and the pulsatility index(PI) was evaluated with the formula PI =Vmax-Vmin/Vmean.

Table 1 Clinical characteristics of patients studied

	Control group	Liver cirrhosis group
Number of patients	42	33
Sex (M/F)	16 / 26	27 / 6
Age (years)		
Mean±SD	51.5±17.1	58.3±7.3
Range	21−82	46−68
Etiology (no. of patients)		
AC/VC/IC/CC[a]		2/28/1/2
Child-Pugh score		
A		26
B		7
C		0
Ascites present (no. of patients)		5
Varices present (no. of patients)		17

[a]AC=alcoholic cirrhosis; VC=viral cirrhosis; IC=immunological cirrhosis; CC=cryptogenic cirrhosis

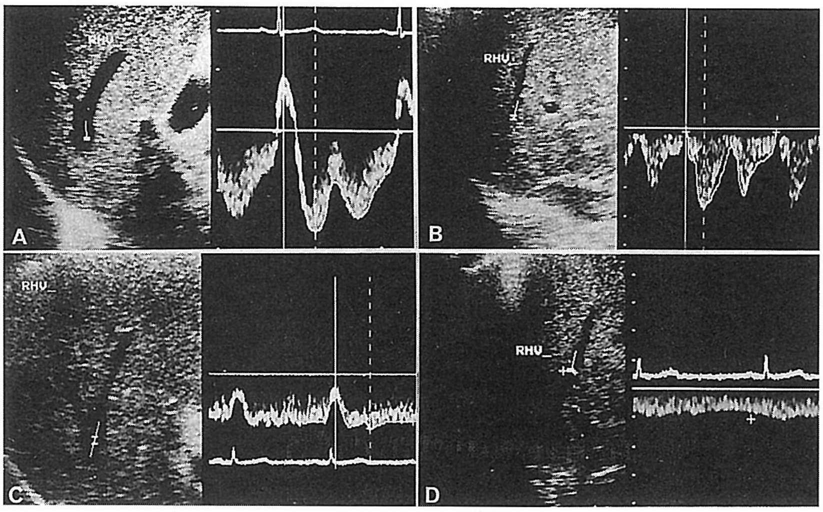

Figure 1. Hepatic waveform patterns of Doppler ultrasound study. (A) Triphasic waveform (TW): A small positive wave correlated with the ECG P wave is followed by two negative waves. (B) Biphasic waveform (BW): The hepatic waveform consists of two negative waves with no positive wave (the Doppler pattern is always below the zero line). (C) Monophasic waveform (MW): The hepatic vein waveform shows a monophasic negative wave observed during ventricular systole and diastole in a broad spectrum of frequencies. (D) Continuous flow (CF): The hepatic vein waveform shows a continuous negative flow with a reduction in the size of the spectrum.

In addition, the diameter of each vessel was measured at the same level at which the Doppler sample was taken. Then the Doppler velocity profile was classified to one of the four groups according to the number of pulsed waves ; (a)TW, triphasic waveform (a small positive wave correlating with the ECG P wave followed by 2 negative waves); (b) BW, biphasic waveform (2 negative waves , with no positive wave); (c) MW, monophasic negative wave (occurring during ventricular systole and diastole.); (d) CF, continuous flow (Figure 1).

The severity of liver cirrhosis was estimated by Child-Pugh score(11) and present or absent of esophageal varices.

The results were expressed as a mean ± standard deviation (SD). Statistical analysis of the results was performed using unpaired t-test, one-way analysis of variance (ANOVA) and χ^2 test. Significance was considered at $P < 0.05$.

Results

Mean velocity of hepatic venous blood flow in liver cirrhosis was significantly higher than that in normal livers in RHV and LHV ($P<0.005$,Table 2). Vessel diameters of the three hepatic veins in patients with liver cirrhosis were significantly smaller than those in controls. There was a significant difference in the pulsatility index of RHV and LHV between the two groups ($P<0.005$), but no difference was found in MHV. We were unable to detect RHV and LHV by B-mode and their waveforms by Doppler mode in one case and 4 cases in the control groups, respectively, and RHV, MHV and LHV in 3, 4 and 9 cases in the liver cirrhosis group respectively. The incidences of TW in the normal liver group were 76% in RHV ,64% in MHV and 87% in LHV (Table 3). Waveform patterns other than TW frequently appeared in the normal liver group in each hepatic vein. Especially, the incidence of BW was high in MHV of normal liver group. The incidence of TW in the normal liver group was significantly higher than that in the liver cirrhosis patients in RHV and LHV ($P<0.01$, Table 3). In addition, in cirrhotic patients, the incidence of BW was signifi-

Table 2 Mean values of Vmean, diameter and pulsatility index in the three hepatic veins in the control and liver cirrhosis groups

	Vmean (cm/s)		Diameter (mm)		Pulsatility index	
	Control	Liver cirrhosis	Control	Liver cirrhosis	Control	Liver cirrhosis
RHV (number)	11.5±5.3 (41)	16.7±7.2* (30)	5.9±1.8 (41)	4.6±1.7* (30)	3.50±2.0 (41)	1.97±1.2* (30)
MHV (number)	14.7±7.2 (42)	16.6±7.2 (29)	5.8±1.7 (42)	4.1±1.5* (29)	2.55±1.7 (42)	1.98±1.1 (29)
LHV (number)	10.2±5.7 (38)	17.3±11.3* (24)	4.6±1.8 (38)	3.5±1.6** (24)	3.98±2.4 (38)	2.07±1.5* (24)

RHV=right hepatic vein, MHV=middle hepatic vein, LHV=left hepatic vein
Vmean=mean velocity
*, $P<0.005$, vs. control group.
**, $P<0.05$, vs. control group.

Table 3 Distribution of hepatic venous waveform types in the control and liver cirrhosis groups

	Control group				Liver cirrhosis group			
	CF	MW	BW	TW	CF	MW	BW	TW
RHV	4(10)	3(7)	3(7) [ab]	31(76) [ac]	3(10)	0(0)	17(57) [b]	10(33) [c]
MHV	2(5)	2(5)	11(26)	27(64)	2(7)	2(7)	13(45)	12(41)
LHV	3(8)	1(2.5)	1(2.5) [de]	33(87) [df]	3(13)	0(0)	14(58) [e]	7(29) [f]

RHV=right hepatic vein;MHV=middle hepatic vein; LHV=left hepatic vein
CF=continuous flow;MW=monophasic wave;BW=biphasic wave;TW=triphasic wave
Number (percent)
Superscripts indicate significance of difference between pairs of values having the same letter. For a ,b, c,d,e, and f, $P<0.01$.

cantly higher than that in the normal liver group in RHV and in LHV ($P<0.01$). There was no difference between the two groups concerning the incidence of each waveform pattern in MHV.

Discussion

Previously, estimation of the hepatic venous flow was reported in studies concerning tricuspid regurgitation (2,13) and congestive heart failure (1) in subjects with normal livers. The pulsed Doppler spectral waveform of the normal hepatic vein is triphasic which consists of large antegrade systolic and diastolic waves and a small retrograde wave of flow towards the transducer related to the right auricular systole and correlating with the ECG P wave (Fig.1A). In the previous studies, the incidences of TW in subjects with normal livers were variable. For example, Bolondi (4) described it as 100 % in MHV , Alvarez (1) as 66 % in MHV, Pennestri (2) as 66% in the superior right hepatic vein, and Appleton (3) as 100% during all phases of respiration in the superior right hepatic vein. In our study, it was 64 % in MHV, slightly less than previous studies. Therefore, Doppler waveforms in MHV may be unreliable to estimate overall hepatic venous flow. In normal livers, the incidence of BW is significantly higher in MHV than in RHV and LHV. The reason for this is not clearly understood, but it may reflect the anatomical situation that the flow of the middle hepatic vein consists of inflowing blood to both the right and left hepatic lobe.

Kashiwagi reported intrahepatic hemodynamic changes in patients with liver cirrhosis on scintiphotosplenoportography (14). In his study, it was demonstrated that the right lobar flow significantly decreased in patients with liver cirrhosis compared with that in patients without liver disease or with chronic hepatitis.

Doppler investigations of liver cirrhosis has been performed (8-10,12),but to date, the use of this technique has been directed mostly, toward the hemodynamics of the main portal vein and its tributaries and collaterals. Tanabe reported that the ratio of the portal blood flow in the left branch to that in the right branch is higher in patients with liver cirrhoisis than in control subjects (6). As the first study of intrahepatic portal circulation using pulsed Doppler examinations, Nishihara indicated that an inverse correlation existed between the flow volume of the right anterior portal branch and the retention of indocyanine green (ICGR15) and that the progression of liver cirrhosis caused a decrease in the flow volume in the right hepatic lobe (5). It was suggested that the change in the intrahepatic portal hemodynamics would affect venous flow as the outflow pathway of hepatic circulation. Accordingly, the blood flow of each of the three hepatic veins has respective significance. The present study indicates that Doppler imaging of the hepatic veins can clarify the intrahepatic hemodynamics of liver cirrhosis; i.e., when a small positive wave is not recognized in RHV and LHV, this finding suggests liver cirrohsis.

Bolondi et al. (4) investigated hepatic venous waveforms in patients with liver cirrhosis, but in that study, the blood flow was measured only in the middle hepatic vein. In this study, the pulsed wave without a small reversed wave appeared more frequently in RHV and LHV in patients with liver cirrhosis than in subjects with normal livers; 67% and 71% in patients with liver cirrhosis and 24% and 13% in subjects with normal livers respectively. Especially, the incidence of BW was significantly higher in patients with liver cirrhosis compared to that in subjects with normal livers ($P<0.01$). Therefore, it was suggested that the pulsed wave without a small reversed phase, especially BW in RHV and LHV implies liver cirrhosis.

Orrego et al. (15) demonstrated that hypertrophy of the hepatic cells might compress the hepatic vein because of the low elasticity of the liver capsule. Therefore, the underlying mechanism of changes in the hepatic venous waveform could be related to the extent of liver fibrosis, which progressively reduces phasic oscillations in hepatic veins subsequent to a lack of compliance in the tissue.

Nishihara et al. reported that the portal flow volume in liver cirrhosis was lower in the right anterior branch and higher in the left umbilical branch than in the normal liver (5). The portal hemodynamics of liver cirrhosis reflect the morphological changes in liver cirrhosis; i.e.,the right hepatic lobe is progressively atrophied and the left hepatic lobe enlarged. In this study, we presumed that the intrahepatic portal flow volume of the liver cirrhosis group would behave as reported.

Therefore, we expected that in the liver cirrhosis group, the vessel diameters of the hepatic veins would become smaller and their mean velocities slower than in the normal group. However, in this study, the diameters became smaller, whereas the mean velocities increased in RHV and LHV as the outflow pathway of hepatic circulation. This phenomenon may indicate that the volume of the hepatic venous flow does not decrease markedly in liver cirrhosis.

We presented the changes of intrahepatic hemodynamics in liver cirrhosis by the pulsed Doppler examination.

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