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• BRIEF REPORTS •

Value of portal hemodynamics and hypersplenism in cirrhosis staging

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Abstract

AIM: To determine the correlation between portal hemodynamics and spleen function among different grades of cirrhosis and verify its significance in cirrhosis staging.

METHODS: The portal and splenic vein hemodynamics and spleen size were investigated by ultrasonography in consecutive 38 cirrhotic patients with cirrhosis (Child's grades A to C) and 20 normal controls. The differences were compared in portal vein diameter and flow velocity between patients with and without ascites and between patients with mild and severe esophageal varices. The correlation between peripheral blood cell counts and Child's grades was also determined.

RESULTS: The portal flow velocity and volume were significantly lower in patients with Child's C (12.25±1.67 cm/s *vs* 788.59±234 mm/min, respectively) cirrhosis compared to controls (19.55±3.28 cm/s *vs* 1254.03±410 mm/min, respectively) and those with Child's A (18.5±3.02 cm/s *vs* 1358.48±384 mm/min, respectively) and Child's B (16.0±3.89 cm/s *vs* 1142.23±390 mm/min, respectively) cirrhosis. Patients with ascites had much lower portal flow velocity and volume (13.0±1.72 cm/s *vs* 1078±533 mm/min) than those without ascites (18.6±2.60 cm/s *vs* 1394±354 mm/min). There was no statistical difference between patients with mild and severe esophageal varices. The portal vein diameter was not significantly different among the above groups. There were significant differences in splenic vein diameter, flow velocity and white blood cell count, but not in spleen size, red blood cell and platelet counts among the various grades of cirrhosis. The spleen size was negatively correlated with red blood cell and platelet counts (r = -0.620 and r = -0.8.34, respectively).

CONCLUSION: An optimal system that includes parameters representing the portal hemodynamics and spleen function should be proposed for cirrhosis staging.

Key words: Liver cirrhosis; Portal vein; Splenic vein; Hemodynamics; Hypersplenism

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INTRODUCTION

Liver cirrhosis due to various causes is a very common and irreversible state. In China, there are hundreds of thousands of new cases annually, most of which are developed from chronic hepatitis[1]. The diagnosis and prognosis in cirrhosis of liver mostly depend upon the Child's grading system or the modified Child-Pugh system, which takes into account the severity of jaundice, ascites, hypoalbuminemia, encephalopathy, and prothrombin time[2]. Other liver function tests and biochemical markers are also reported to correlate with the prognosis and severity of liver cirrhosis[3-5]. However, the most common clinical signs and symptoms of cirrhosis include three aspects: liver dysfunction, portal hypertension and hepersplenism, and the major causes of death for the patients with cirrhosis are hepatic failure, gastrointestinal hemorrhage and secondary infection. The criteria of the Child-Pugh system are all reflections of hepatocyte function, but not of portal hemodynamics and spleen. Therefore, a comprehensive evaluation for the cirrhosis staging should cover hepatocyte function, portal hemodynamics and spleen function. Several studies have shown that portal hemodynamics is closely related to the Child's scores and liver fibrosis[2]. There are also published papers concerning the relationship among spleen size, hemodynamics of splenic vein, esophageal varices and Child's scores[5-9]. To verify the correlation between portal hemodynamics, splenomegaly and various Child's scores and clarify the significance of portal hemodynamics and spleen function in cirrhosis staging, we studied retrospectively a group of patients with cirrhosis.

MATERIALS AND METHODS

Patients

Thirty-eight consecutive patients with cirrhosis (22 Child's grade A, 8 Child's grade B, and 8 Child's grade C) and 20 age- and sex-matched (authors) normal healthy controls were enrolled in this study. The diagnosis of cirrhosis was established by a combination of clinical, biochemical, surgical and pathological investigations. Child's grading was done by the modified Child-Pugh scoring method. All patients with cirrhosis underwent an upper gastrointestinal endoscopy within three months prior to the study, to determine esophageal varices and the varix degree if present, according to the Japanese Classification.

The exclusion criteria were 1, patients with gastrointestinal bleeding in the previous four weeks; 2, those who were taking portal pressure-lowering drugs such as β-blockers; 3, those with encephalopaphy grade II or more; 4, those with portal or splenic vein thrombosis; and 5, those with a previous history of sclerotherapy or banding for esophageal varices.

Methods

A color Doppler US system BK3535 (BK Medical, Copenhagen,

Denmark) was used. All measurements were performed by the same examiner without knowledge of the clinical information of subjects. All patients and controls were kept fasting overnight prior to the sonography. Portal trunk was scanned longitudinally with the sector scanner. The 3 mm sampling marker was shifted to the corner of the lumen at 1.5-2.5 cm before the bifurcation of right and left branches, and the angle of insonation was kept below 60 ℃. The portal vein diameter was measured directly at this point. The portal flow velocity (PFV) in centimeters per second (cm/s) was averaged by Doppler traces of 2-3 cardiac cycles. The portal blood flow rate (PBFR) in milliliters per minute (mL/min) was obtained by the formula: PBFR = PFV×A×60, (A as cross-sectional area of portal vein in square centimeters).

The spleen maximal length, transverse diameter, and thickness at the hilum were measured. These were then multiplied together, and a further factor of 0.6 was included to obtain an approximation of volume. The diameter and flow velocity of the splenic vein were obtained at 1.0-1.5 cm before bifurcation. Peripheral blood routine test was also performed for each patient to evaluate the grade of hepersplenism.

Statistical analysis

All the data were analyzed with SAS10.0 software. Differences in mean values of Doppler US parameters between the normal control subjects and patients with cirrhosis were tested by Student's *t* test and univariate analysis. Correlation among variables was assessed by linear regression analysis. The results were expressed as mean±SD, and the difference was considered statistically significant when $P<0.05$.

RESULTS

Correlation between portal hemodynamics and Child's grade

There was no difference in the portal vein diameter between the controls and the patients with different grades of cirrhosis (Table 1). The portal flow velocity and volume were significantly lower in Child's C cirrhosis compared to controls, and Child's A and B cirrhotics. The portal flow velocity was also lower in Child's B cirrhotics than in Child's A cirrhotics ($P<0.05$). However, there was no difference in the portal blood volume between patients with Child's A and B cirrhosis and the controls (Table 1). With increasing Child's grades of severity, the portal flow velocity and volume decreased significantly.

Table 1 Portal hemodynamics in patients with various grades of Child's cirrhosis (mean±SD)

	Cases	Diameters (cm)	Flow velocity (cm/s)	Flow volume (mL/min)
Control	20	1.17±0.13	19.55±3.28	1 254.03±410
Child A	22	1.23±0.17	18.5±3.02	1 358.48±384
Child B	8	1.24±0.15	16.0±3.89[a]	1 142.23±390
Child C	8	1.16±0.20	12.25±1.67[b]	788.59±234[bc]

[a]$P<0.05$, [b]$P<0.01$ *vs* Child's A; [c]$P<0.05$ *vs* Child's B.

The difference was not significantly in portal vein diameter between patients with and without ascites. However, both portal flow velocity and volume of the patients with ascites were statistically lower than those without ascites (Table 2).

There was no significant difference in portal flow velocity and volume between patients with mild varices and those with severe varices (Table 3).

Table 2 Portal hemodynamics between cirrhotics with and without ascites (mean±SD)

	Number	Diameter (cm)	Velocity (cm/s)	Volume (mL/min)
With ascites	8	1.32±0.17	13.0±1.72	1 078±533
Withour ascites	30	1.20±0.21	18.6±2.60	1 394±354
P		>0.05	<0.01	<0.05

Table 3 Portal hemodynamics between cirrhotics with mild and severe varices (mean±SD)

	Number	Diameter (cm)	Velocity (cm/s)
Mild varices	21	1.20±0.14	18.0±3.92
Severe varices	17	1.26±0.21	19.50±3.93
P		>0.05	>0.05

Splenic hemodynamics and Child's grading

There were significant differences in splenic vein diameter, splenic flow velocity, peripheral white blood cell count among patients with various grades of Child' score. With the development of cirrhosis from Child's A to B and C, the splenic vein diameter increased correspondingly, while splenic flow velocity and white blood cell count decreased significantly. There was no statistical difference in peripheral red blood cell and platelet count among patients with various grades of cirrhosis (Table 4). The spleen volume negatively correlated with red blood ($R = -0.620$, $P<0.05$) and platelet counting ($R = -0.8.34$, $P<0.001$). Peripheral platelet count positively correlated with red blood cell count ($R=0.583$, $P<0.001$).

Table 4 Univariate analysis of parameters for hypersplenism among patients with various Child's grades

Parameters	*F*	*P*
Splenic diameter	4.832	0.014
Splenic velocity	4.873	0.013
Spleen size	4.136	0.024
WBC	5.286	0.010
RBC	1.746	0.189
Platelet	1.935	0.159

DISCUSSION

Cirrhosis is defined as a chronic disease of the liver in which diffuse destruction and regeneration of hepatic parenchymal cells have occurred, and in which a diffuse increase in connective tissues has resulted in disorganization of the lobular and vascular architecture. The principal pathologic features of cirrhosis include hepatic parenchymal necrosis, regeneration, and scarring. Clinically, distortion of the vascular architecture causes the most serious complications, portal hypertension with resulting ascites, variceal hemorrhage and hypersplenism[10].

There are many factors that can cause liver cirrhosis and portal hypertension such as viral hepatitis, alcohol abuse, sclerosing cholangitis, schistosomiasis, and common inborn errors of metabolism including Wilson disease, hemochromatosis and α-antitrypsin deficiency. There are differences both in pathology and in clinical signs and symptoms among individual patients. Even in the same patient, there are different pathological and clinical characteristics at different stages. Accordingly, the treatment is very specific for each patient at different stages. Therefore, a clear and correct staging system for cirrhosis is required[11].

However, there has been no optimal staging system so far to give a comprehensive stage analysis for cirrhosis. Warren *et al*[12] once classified portal hypertension into four stages according to the degree of interference with portal flow to the liver, i.e., stage I (normal or only slightly restricted portal flow, hepatopetal portal flow), stage II (moderate reduction, hepatopetal or bi-directional portal flow), stage III (severe restriction of flow, bi-directional or hepatofugal portal flow), stage IV(lack of opacification of the portal vein by radiographic study), hepatofugal flow. But what they included was only portal flow direction not hepatocyte function. The most commonly used system to assess the severity of cirrhosis is still Child's score or Child-Pugh's score, which takes into account the jaundice, ascites, hypoalbuminemia, encephalopathy and prothrombin time. Biochemical markers are also reported to be helpful for Child's score[13,14]. But all the parameters included are those for the hepatocyte function, but not for portal blood flow and spleen function.

Ultrasonography provides not only liver hemodynamics by color Doppler flow imaging, but also valuable information on the morphological changes of the liver[15-19]. It has been reported that evaluating liver hemodynamics and morphology in patients with cirrhosis and portal hypertension is of immense value for the estimation of severity and prognosis of the disease[20-22]. There also have been reports on the relationship between the hemodynamic changes of portal vein and the histological changes in chronic hepatitis[19,22-24]. Aube *et al*[22] observed that the decrease of portal venous velocity closely correlated with the histological degree of fibrosis. Similar to other studies[2,6-8], our study showed a significant decrease in portal flow velocity and volume with increasing Child's grades of severity. In fact, portal flow velocity is a better parameter to reflect the portal pressure gradient and more useful for the diagnosis of portal hypertension. Therefore, the portal hemodynamics is very helpful in the assessment of the real status of cirrhosis and in finding the choice of the optimal therapy.

In contrast to the portal flow velocity, there was no significant difference in portal vein diameter among various Child's grades suggesting that portal vein diameter does not correlate with the high portal pressure and the severity of cirrhosis.

Our study also demonstrated that cirrhotics with ascites had a significantly lower portal flow velocity and volume compared to those without ascites, which confirms that ascites is a sign of liver function decompensation. However, there was no significant difference in portal flow velocity and volume between patients with mild and severe varices, indicating that the mechanisms of varices in cirrhosis are very complicated. They are not only the consequences of high portal pressure but also of formation of regional collaterals.

Splenomegaly is a cardinal feature of hepatic cirrhosis complicated by portal hypertension. The prevalence of splenomegaly in cirrhosis varies from 36-92%[24,25]. Various mechanisms underlying the development of hypersplenism in portal hypertension have been proposed, including increased pooling and increased destruction of blood cells in the spleen, the dilutional effects of increased blood volume, and humoral factors. Hypersplenism can be regarded as the association of one or more of anemias, leukopenia, and thrombocytopenia with splenomegaly, and a normal or hypercellular bone marrow. Hypersplenism is a vital pathophysiological change in portal hypertension, and should be considered as a parameter in cirrhosis staging. In our study, although the splenic flow velocity and splenic vein diameter correlated with Child's grades as others reported, peripheral red blood cell and platelet count did not correlate with them. Furthermore, thrombocytopenia is the most common manifestation of hypersplenism in cirrhosis and portal hypertension[26,27]. Similar to previous studies[26-28], we also observed a negative correlation between the platelet count and spleen volume. Therefore, peripheral blood cell count represents the severity of hypersplenism, and should also be taken into consideration in cirrhosis staging.

In conclusion, an optimal system that includes parameters representing the portal hemodynamics and spleen function should be proposed for cirrhosis staging.

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