Value of portal hemodynamics and hypersplenism in cirrhosis staging

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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) compared to controls (15.5±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.

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

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[3,4]. However, the most common clinical signs and symptoms of cirrhosis include three aspects: liver dysfunction, portal hypertension and hypersplenism, 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[5]. There are also published papers concerning the relationship among spleen size, hemodynamics of splenic vein, esophageal varices and Child’s scores[6-9]. 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 encephalopathy 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,
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   | 1.17±0.13      | 19.55±3.28           | 1254.03±410          |
| Child A   | 1.23±0.17      | 18.5±3.02            | 1358.48±384          |
| Child B   | 1.24±0.15      | 16.0±3.89            | 1142.23±390          |
| Child C   | 1.16±0.20      | 12.25±1.67           | 788.59±234           |

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.[12-15] 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), 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.[14,15-19]. 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.[20-23]. There also have been reports on the relationship between the hemodynamic changes of portal vein and the histological changes in chronic hepatitis[20,22-24]. Aube et al.[22] observed that the decrease of portal venous velocity closely correlated with the histological degree of fibrosis. Similar to other studies[20,25-41], 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.

REFERENCES

1. Zhang CP, Tian ZB, Liu XS, Zhao QX, Wu J, Liang YX. Effects of Zhaoyangwan on chronic hepatitis B and posthepatic cirrhosis. World J Gastroenterol 2004; 10: 295-298
2. Chawla Y, Santa N, Dhiman RK, Dilawari JB. Portal hemodynamics by duplex Doppler sonography in different grades of cirrhosis. Dig Dis Sci 1998; 43: 354-357
3. Herold C, Heinz R, Radespiel-Troger M, Schneider HT, Schumann D, Hahn EG. Quantitative testing of liver function in patients with cirrhosis due to chronic hepatitis C to assess disease severity. Liver 2001; 21: 26-30
4. Herold C, Heinz R, Niedobitek G, Schneider T, Hahn EG, Schumann D. Quantitative testing of liver function in relation to fibrosis in patients with chronic hepatitis B and C. Liver 2001; 21: 260-263
5. Wehler M, Kokoska J, Reulbach U, Hahn EG, Strauss R. Short-term prognosis in critically ill patients with cirrhosis assessed by prognostic scoring systems. Hepatology 2001; 34: 255-261
6. Nakano R, Iwao T, Oho K, Toyonaga A, Tanikawa K. Splanchnic hemodynamic pattern and liver function in patients with cirrhosis and esophageal or gastric varices. Am J Gastroenterol 1997; 92: 2085-2089
7. Iwao T, Toyonaga A, Oho K, Tayama C, Masumoto H, Sakai T, Sato M, Tanikawa K. Value of Doppler ultrasound parameters of portal vein and hepatic artery in the diagnosis of cirrhosis and portal hypertension. Am J Gastroenterol 1997; 92: 1012-1017
8. Shah SH, Hayes PC, Allan PL, Nicoll J, Finlayson ND. Measurement of spleen size and its relation to hypersplenism and portal hemodynamics in portal hypertension due to hepatic cirrhosis. Am J Gastroenterol 1996; 91: 2580-2583
9. Angermayr B, Cejna M, Karnel F, Gschwantler M, Koenig F, Piclich J, Mondel H, Pichler L, Wichlas M, Kreil A, Schmid M, Felrissil A, Lipinski E, Brunner H, Lammer J, Ferenci P, Gang A, Peck-Radosavljevic M. Child-Pugh versus MELD score in predicting survival in patients undergoing transjugular intrahepatic portosystemic shunt. Gut 2003; 52: 879-885
10. Nakaji M, Hayashi Y, Ninomiya T, Yano Y, Yoon S, Seo Y, Nagano H, Komori H, Hashimoto K, Orino A, Shirane H, Yokozaki H, Kasuga M. Histological grading and staging in chronic hepatitis: its practical correlation. Pathol Int 2002; 52: 683-690
11. Zhou GW, Tao ZY, Peng CH, Li HW. Reasonable choice of surgical procedures for patients with portal hypertension. Hepatobiliary Pancreat Dis Int 2003; 2: 330-333
12. Warren WD, Fomon JJ, Viamonte M, Zeppa R. Preoperative assessment of portal hypertension. Ann Surg 1967; 165: 999-1012
13. Korner T, Kroop J, Kosche B, Kristahl H, Jaspersen D, Gressner AM. Improvement of prognostic power of the Child-Pugh classification of liver cirrhosis by hyaluronan. J Hepatol 2003; 39: 947-953
14. Myers RP, De Torres M, Imbert-Bismut F, Ratziu V, Charlotte F, Poynard T. Biochemical markers of fibrosis in patients with chronic hepatitis C: a comparison with prothrombin time, platelet count, and age-platelet index. Dig Dis Sci 2003; 48: 146-153
15. Tchlepi H, Ralls PW, Radin R, Grant E. Sonography of diffuse liver disease. J Ultrasound Med 2002; 21: 1023-1032; quiz 1033-1034
16. Martinez-Noguera A, Montserrat E, Torrubia S, Villalba J. Doppler in hepatic cirrhosis and chronic hepatitis. Semin Ultra-
Arda K, Ofelli M, Calikoglu U, Olcer T, Cumhur T. Hepatic vein Doppler waveform changes in early stage (Child-Pugh A) chronic parenchymal liver disease. J Clin Ultrasound 1997; 25: 15-19

Gorka W, al Mulla A, al Sebayel M, Altraif I, Gorka TS. Qualitative hepatic venous Doppler sonography versus portal flowmetry in predicting the severity of esophageal varices in hepatitis C cirrhosis. AJR Am J Roentgenol 1997; 169: 511-515

Nagata N, Miyachi H, Nakano A, Nanri K, Kobayashi H, Matsuzaki S. Sonographic evaluation of the anterior liver surface in chronic liver diseases using a 7.5-MHz annular-array transducer: correlation with laparoscopic and histopathologic findings. J Clin Ultrasound 2003; 31: 393-400

Li XH, Wang L, Fang YW, Lu YK. Color Doppler evaluation for the hemodynamics of portal hypertension in liver cirrhosis. Shijie Huaren Xiaohua Zazhi 1999; 7: 453-454

Ohta M, Hashizume M, Kawanaka H, Akazawa K, Tomikawa M, Higashi H, Kishihara F, Tanoue K, Sugimachi K. Prognostic significance of hepatic vein waveform by Doppler ultrasonography in cirrhotic patients with portal hypertension. Am J Gastroenterol 1995; 90: 1853-1857

Aube C, Oberti F, Korali N, Namour MA, Loisel D, Tanguy JY, Valsesia E, Pilette C, Rousselet MC, Bedossa P, Riffllet H, Maiga MY, Penneau-Fontbonne D, Caron C, Cales P. Ultrasonographic diagnosis of hepatic fibrosis or cirrhosis. J Hepatol 1999; 30: 472-478

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

Mutchnick MG, Lerner E, Conn HO. Effect of portacaval anastomosis on hypersplenism. Dig Dis Sci 1980; 25: 929-938

Liangpunsakul S, Ulmer BJ, Chalasani N. Predictors and implications of severe hypersplenism in patients with cirrhosis. Am J Med Sci 2003; 326: 111-116

Bolognesi M, Merkel C, Sacerdoti D, Nava V, Gatta A. Role of spleen enlargement in cirrhosis with portal hypertension. Dig Liver Dis 2002; 34: 144-150

el-Khishen MA, Henderson JM, Millikan WJ, Kutner MH, Warren WD. Splenectomy is contraindicated for thrombocytopenia secondary to portal hypertension. Surg Gynecol Obstet 1985; 160: 233-238

Luo JC, Hwang SJ, Chang FY, Chu CW, Lai CR, Wang YJ, Lee PC, Tsay SH, Lee SD. Simple blood tests can predict compensated liver cirrhosis in patients with chronic hepatitis C. Hepatogastroenterology 2002; 49: 478-481