The Risk Factors for Bleeding of Fundal Varices in Patients with Liver Cirrhosis

Eui Ju Park*, Jae Young Jang*, Ji Eun Lee*, Soung Won Jeong*, Sae Hwan Lee*, Sang Gyune Kim*, Sang-Woo Cha*, Young Seok Kim*, Young Deok Cho*, Hong Soo Kim*, Boo Sung Kim*, and Yong Jae Kim†

*Institution for Digestive Research, Digestive Disease Center, Department of Internal Medicine, †Department of Radiology, Soonchunhyang University Hospital, Soonchunhyang University College of Medicine, Seoul, Korea

Background/Aims: The relationship between portal hemodynamics and fundal varices has not been well documented. The purpose of this study was to understand the pathophysiology of fundal varices and to investigate bleeding risk factors related to the presence of spontaneous portosystemic shunts, and to examine the hepatic venous pressure gradient (HVPG) between fundal varices and other varices.

Methods: In total, 85 patients with cirrhosis who underwent HVPG and gastroscopic examination between July 2009 and March 2011 were included in this study. The interrelationship between HVPG and the types of varices or the presence of spontaneous portosystemic shunts was studied. Results: There was no significant difference in the HVPG between fundal varices (n=12) and esophageal varices and gastro-esophageal varices type 1 (GOV1) groups (n=73) (17.1±7.7 mm Hg vs 19.7±5.3 mm Hg). Additionally, there was no significant difference in the HVPG between varices with spontaneous portosystemic shunts (n=28) and varices without these shunts (n=57) (18.3±5.8 mm Hg vs 17.0±8.1 mm Hg). Spontaneous portosystemic shunts increased in fundal varices compared with esophageal varices and GOV1 (8/12 patients [66.7%] vs 20/73 patients [27.4%]; p=0.016). Conclusions: Fundal varices had a high prevalence of spontaneous portosystemic shunts compared with other varices. However, the portal pressure in fundal varices was not different from the pressure in esophageal varices and GOV1. (Gut Liver 2013;7:704-711)

Key Words: Cirrhosis; Hypertension, portal; Hepatic venous pressure gradient; Fundal varices; Portasystemic shunt, surgical

INTRODUCTION

Portal hypertension is defined as a pathological increase of portal pressure gradient resulting in the formation of portal-systemic collaterals that shunt part of the portal blood flow to the systemic circulation bypassing the liver. Clinically significant portal hypertension is diagnosed when clinical manifestations of the disease appear or when portal pressure gradient exceeds the threshold value of 10 mm Hg. Gastric varices (GVs) are found in approximately 22% to 57% of cirrhotic patients with portal hypertension. Although the rates of bleeding in GVs have been reported to be lower than those in esophageal varices (EVs), rupture from GVs, particularly from fundal varices (FVs), tends to be more severe, requiring more transfusions and having a higher mortality rate. Gastroesophageal varices type 2 (GOV2) and isolated GVs are referred to as gastric FVs, together. Gastric FVs are frequently supplied from the short gastric vein, drain blood from the fundus into the splenic vein, in contrast to gastroesophageal varices type 1 (GOV1) which are known to be supplied from the left (coronary) gastric vein. Therefore, the characteristics and clinical outcomes are different between these two. EVs are known to be frequently supplied from the left (coronary) gastric vein. So, EVs and GOV1 have similar hemodynamics. In a study by Sarin et al., the prevalence of large EVs in GOV1 was more commonly associated with large EVs than with GOV2 and the majority of GOV1 disappeared within 6 months after the obliteration of EVs, whereas GOV2 did not. However, few reports exist on hemodynamic features of FVs and risk factors for FVs bleeding in association with the presence of portasystemic shunt.

In this study, we investigated hepatic venous pressure gradient (HVPG) of gastric FVs with the presence of spontaneous...
portosystemic shunts as compared with EVs and GOV1 to clarify the hemodynamics of FVs.

MATERIALS AND METHODS

1. Patients

During the period from July 2009 to March 2011, 85 patients with liver cirrhosis who had EVs or GVs or both were investigated with HVPG measurements at Soonchunhyang University Hospital, Seoul, South Korea. All patients had liver cirrhosis diagnosed on the basis of imaging findings, histologic findings, clinical symptoms, and biochemistry findings. Exclusion criteria included hemodynamic instability, severe comorbidity disease, uncontrolled bleeding tendency, and use of vasoactive drugs in the previous 2 weeks.

After the measurement of HVPG, they were tracked for follow-up observation retrospectively to determine whether they had variceal bleeding based on the history of hematemesis or melena and endoscopic findings. The mean follow-up period was 419 days (range, 36 to 652 days). In acute variceal bleeding, HVPG was evaluated within 2 weeks after the endoscopic treatment. The correlation between the results of HVPG measurements and endoscopically assessed degrees of varices was analyzed. The diagnosis of GVs was confirmed using endoscopy by the agreement of two experienced endoscopists. This study was approved by the local institutional review board and conducted in accordance with the principles set forth in the Declaration of Helsinki. Written informed consent was obtained from all patients.

2. Variceal bleeding

Variceal bleeding was classified as bleeding during follow-up and past variceal bleeding. Variceal bleeding during follow-up was defined as presence of gastrointestinal bleeding signs (e.g., hematemesis, melena, unexplained anemia) and endoscopic findings after HVPG measurement. Past variceal bleeding was defined as history of endoscopic therapeutic procedures within 3 months from HVPG measure time.

3. HVPG measurement

HVPG measurements of patients were performed after overnight fasting using electrocardiogram and vital sign monitoring by an experienced radiologist. Under local anesthesia and under aseptic conditions, the venous introducer was placed in the right jugular vein. HVPG was estimated from the measurements of the wedged hepatic venous pressure (WHVP) and free hepatic venous pressure, respectively. WHVP was measured while occluding the hepatic vein when the tracing was stable. Adequate occlusion of the hepatic vein was checked using an injection of contrast dye that shows typical wedged pattern without the reflux of contrast. These measurements were duplicated before the catheter was withdrawn. The HVPG was measured at least three times to demonstrate the reproducible values. In the cirrhotic liver, the pressure of the static column of blood created by balloon inflation could not be decompressed at the sinusoidal level due to sinusoidal narrowing and disruption of the normal inter sinusoidal architecture by fibrosis and nodule formation. For this reason, WHVP equilibrated with portal pressure.8,9

4. Classification of GVs

We used the classification system proposed originally by Sarin et al.2 GOV are varices that extend from the esophagus into the stomach. GOV were further subclassified as GOV1 (EVs extending down to cardia or lesser curvature) and GOV2 (EVs extending to gastric fundus).3 In order to make hemodynamic and clinical correlations, EVs and GOV1 were classified as group 1 because they have similar hemodynamic, and GOV2 were classified as group 2. The endoscopic findings of GVs or EVs were classified into three types: F1, small or tortuous; F2, medium-sized or beady; and F3, enlarged, nodular or tumor-shaped according to the General Rules for Recording Endoscopic Findings set by the Japanese Research Society for Portal Hypertension and Hashizumeet classification.

5. Portosystemic shunts

A postcontrast computed tomography (CT) was performed to confirm the presence of a portosystemic shunts in all patients. The collaterals that connect gastric veins (short gastric veins, posterior gastric veins, left and right gastric veins) and the left renal vein observed in abdominal CT were defined as gastrorenal shunts. Splenorenal shunts were noted as the connections between the splenic vein and the left renal vein.

6. Statistical analysis

Data was expressed as mean±SD, range, or number (%) as appropriate. When comparing the baseline characteristics of patients in two different groups, chi-square test and Fisher exact test were used for categorical data, and Student t-test and Mann-Whitney U test were used for continuous variables. The result with p<0.05 by 2-tailed test was considered significant. Data analysis was performed using SPSS version 17.0 for Windows (SPSS Inc., Chicago, IL, USA).

RESULTS

1. Baseline characteristics

Patient characteristics are summarized in Table 1. Eighty-five patients (69 men, 16 women; mean age, 55.6 years) with liver cirrhosis were enrolled in this investigation. The majority of patients had alcohol-related (46.1%) or hepatitis B virus-related (38.8%) cirrhosis. Group 1 (EVs and GOV1) consisted of 73 (85.9%) patients and group 2 (GOV2) consisted of 12 (14.1%) patients. Taking β-blocker history was not differentiated between two groups. There were 28 portosystemic shunts of which the
majority were gastrorenal and splenorenal shunts.

2. Interrelationship between HVPG and types of varices and shunt

The mean HVPG of group 1 was 17.1±7.7 mm Hg and that of group 2 was 19.7±5.3 mm Hg (p=0.114) (Fig. 1A). The HVPG of varices with and without portosystemic shunts were 18.3±5.8 and 17.0±8.1 mm Hg, respectively (p=0.195) (Fig. 1B).

Portosystemic shunts were found in 20 patients (27.4%) in group 1 and eight patients (66.7%) in group 2 (p=0.016) (Table 2).

3. Relationship between HVPG and variceal bleeding history, endoscopic finding

The HVPG of varices with and without variceal bleeding history were 18.2±6.9 and 16.6±8.1 mm Hg, respectively (p=0.428). In subgroup analysis with group 1 and group 2, there was no

### Table 1. Baseline Characteristics of the Patients

| Characteristic                  | Group 1 (EVs+GOV1*) | Group 2 (GOV2*) | p-value |
|---------------------------------|---------------------|-----------------|---------|
| Gender, male/female             | 73 (57/16)          | 12 (12/0)       | 0.072   |
| Age, yr                         | 55.2±9.1 (31-71)    | 58.3±10.0 (48-79)| 0.297   |
| Cause                           |                     |                 |         |
| HBV/HCV/Alcohol/Others†         | 29/1/33/10          | 4/0/7/1         | 0.830   |
| Taking β-blocker                | 24 (32.9)           | 5 (41.7)        | 0.552   |
| HVPG                            | 17.1±7.7            | 19.7±5.3        | 0.268   |
| Endoscopic finding              |                     |                 |         |
| Small (F1)/Medium (F2)/Large (F3)| 27/30/16           | 5/4/3           | 0.879   |
| Portosystemic shunt             | 20 (27.4)           | 8 (66.7)        | 0.016*  |
| Child-Pugh score                | 6.8±1.7             | 8.67±2.2        | <0.01*  |
| MELD score                      | 9.75±4.2            | 11.83±4.3       | 0.115   |
| Laboratory findings             |                     |                 |         |
| Hemoglobin, g/dL                | 11.1±10.5           | 10.5±2.0        | 0.351   |
| Platelet, x10^12/μL             | 108.6±53.0          | 135.3±73.8      | 0.132   |
| INR                             | 1.2±0.2             | 1.4±0.4         | 0.005*  |
| Albumin, g/dL                   | 3.2±0.6             | 2.9±0.4         | 0.048*  |
| Bilirubin, mg/dL                | 2.1±2.8             | 3.5±3.9         | 0.127   |
| Creatinine, mg/dL               | 0.8±0.3             | 0.7±0.2         | 0.092   |

Data are presented as number (%), mean±SD (range), or mean±SD.

HBV, hepatitis B virus; HCV, hepatitis C virus; HVPG, hepatic venous pressure gradient; MELD, model for end-stage liver disease; INR, international normalized ratio.

*Gastric varices (GOV1+GOV2)=33 (38.8% of total varices); †Others, cryptogenic (n=9)/autoimmune (n=1)/primary biliary cirrhosis (n=1).

Fig. 1. (A) The hepatic venous pressure gradient (HVPG) was not different between groups 1 and 2. (B) The HVPG of varices was not different between those varices with portosystemic shunts and those varices without shunts.
difference in the HVPG and variceal bleeding history.

The HVPG of varices with large size (F2 and F3) were significantly higher (18.7±7.4 mm Hg vs 15.4±7.2 mm Hg, p=0.049). However, red color sign was not significance.

4. Endoscopic finding between group with variceal bleeding and without

In the variceal bleeding groups, endoscopic findings of F2 and F3 were significantly higher (81.3% vs 50.9%, p=0.006) and red color sign was presented more frequently than the group without variceal bleeding (70.5% vs 42.2%, p=0.045). Endoscopic findings of F2 and F3 (odds ratio, 5.73; confidence interval, 1.602 to 20.484; p=0.007) showed association with variceal bleeding after multiple adjustments. F2/F3 and presence of red color sign were not differentiated between group 1 and group 2 with variceal bleeding, respectively (p=0.06, p=0.637).

5. The comparison of bleeding risk factors between group 1 and group 2 with bleeding

There were 32 cases of variceal bleeding (37.6%) including past bleeding history associated with endoscopic treatment (Tables 3 and 4). There were 26 cases (35.6%) of variceal bleeding in group 1 and six cases (50.0%) in group 2 (p=0.355). During follow-up, six patients (19%) in group 1 and two patients (33.3%) in group 2 had variceal bleeding according to history data and endoscopic findings. HVPG, presence of shunt, taking of β-blocker, Child-Turcotte-Pugh score, model for end-stage liver disease (MELD) score were not differentiated significantly between two bleeding groups. There was no difference in the frequency of bleeding between the group with portosystemic shunt and the group without (p=0.246) (Fig. 2A). In group 2, patients without portosystemic shunt had a significantly higher frequency of bleeding compared to patients with portosystemic shunt (p=0.014) (Fig. 2B).

All the patients without portosystemic shunt in group 2 experienced bleeding from varices at least once. Variceal bleeding in group 2 with more portosystemic shunt number tended to be less frequent than in those without (p=0.065).

6. Correlation between HVPG and hepatic function

The correlation between HVPG and Child-Pugh score and MELD score were examined. There was a positive and significant correlation between HVPG and Child-Pugh score (r=0.438, p=0.000) (Fig. 3A). MELD score also showed a positive and significant correlation with the HVPG (r=0.343, p=0.001) (Fig. 3B).

DISCUSSION

It is generally believed that mean portal pressure in patients with GVs is lower than that in patients with EVs, because spontaneous portosystemic splenorenal or gastrorenal shunts are more common in GVs than in EVs. Contrary to what was traditionally thought, HVPG in gastric FVs was not different from that of EVs in the current study despite high prevalence of spontaneous portosystemic shunts in comparison with EVs. The

Table 2. Summary of Portosystemic Shunts

| Value                        |     |
|-----------------------------|-----|
| Total no. of portosystemic shunt | 28 (32.9) |
| Group 1 (n=73)              | 20 (27.4) |
| Gastrorenal shunt           | 5 (25.0) |
| Splenorenal shunt           | 10 (50.0) |
| Gastrorenal shunt with splenorenal shunt | 0 |
| Others                      | 5 (25.0) |
| Group 2 (n=12)              | 8 (66.7) |
| Gastrorenal shunt           | 4 (50.0) |
| Splenorenal shunt           | 1 (12.5) |
| Gastrorenal shunt with splenorenal shunt | 3 (37.5) |
| Others                      | 0 |
| p=0.016                     |     |

Data are presented as number (%).

Table 3. Summary of Variceal Bleeding

| Value                        |     |
|-----------------------------|-----|
| Total no. of patients with bleeding | 32 (37.6) |
| Group 1                      | 26 (81.2) |
| Past bleeding with endoscopic treatment | 20 (77.0) |
| Bleeding during follow-up    | 4 (15.3) |
| Both past bleeding and bleeding during follow-up | 2 (7.7) |
| Group 2                      | 6 (18.8) |
| Past bleeding with endoscopic treatment | 4 (66.7) |
| Bleeding during follow-up    | 2 (33.3) |
| p=0.355                     |     |

Data are presented as number (%).

Table 4. Summary of Site Variceal Bleeding

| Value                        |     |
|-----------------------------|-----|
| Total no. of patients with bleeding | 32 (37.6) |
| Group 1                      | 26 (81.2) |
| Esophageal varices bleeding  | 24 (92.3) |
| Gastric varices bleeding     | 0 |
| Esophageal and gastric varices bleeding | 2 (7.7) |
| Group 2                      | 6 (18.8) |
| Esophageal varices bleeding  | 2 (33.3) |
| Gastric varices bleeding     | 2 (33.3) |
| Esophageal and gastric varices bleeding | 2 (33.3) |
| p<0.01                      |     |

Data are presented as number (%).
interrelationships between the types and degrees of spontaneous portal systemic shunts and portal vein pressure have not been clarified yet. It is generally believed that spontaneous portal systemic shunting occurs as portal vein pressure increases. Vascular resistance against portal blood flow increases in cirrhosis, inducing the congestion of blood in the splenic and mesenteric veins that lie upstream portal trunk. As blood stagnates in the stagnant route, hepatofugal collateral vessels are created as escape routes that involve veins of the esophagus, stomach, pelvis (hemorrhoids), retroperitoneum, liver, abdominal wall, and other areas. One might expect that as the collateral circulation develops, the portal vein pressure would fall. However, the inconsistent relationship between spontaneous portal systemic shunting and portal vein pressure remains one of the much challenging issues for the understanding of the hemodynamics in portal hypertension. In a study by Ohnishi et al., there was a tendency of progressively high values of portal vein pressure being associated with increasing total collateral circulation up to certain levels. To understand the interrelationship between the increase of portal vein pressure and the type and degree of spontaneous portosystemic shunts, it is necessary to use a large number of patients for the follow-up observations of the development of spontaneous portosystemic shunts in connection with increased portal vein pressure.

Hemodynamic studies have shown that patients with varices always have a considerable increase of portal pressure gradient or its equivalent, the HVPG in cirrhosis. Measurement of the HVPG has been proposed for the following indications: 1) to monitor portal pressure in patients taking drugs; 2) as a prognostic marker; 3) as an end-point in trials using pharmacologic...

Fig. 2. (A) There was no difference in the frequency of bleeding between the group with portosystemic shunts and the group without the shunts. (B) Group 2, without portosystemic shunts, had a significantly higher frequency of bleeding.

Fig. 3. The hepatic venous pressure gradient (HVPG) had significant positive correlation with both (A) the Child-Pugh score and (B) model for end-stage liver disease (MELD) score.
agents for the treatment of portal hypertension; 4) to assess the risk of hepatic resection in cirrhotic patients; and 5) to investigate the cause of portal hypertension.

HVPG was correlated with the liver function and risk of variceal bleeding. The threshold portal pressure gradient or HVPG of about 12 mm Hg is needed for varices to bleed, as was prospectively validated in a placebo-controlled trial of prophylactic propranolol. However, for GV, portal pressure gradient of ≥12 mm Hg is not required for bleeding to occur and a large proportion of bleedings still occur below this threshold, probably related to the high incidence of spontaneous gastrorenal shunts among GV patients. A number of studies have now shown that a significant proportion of GV bleed at portal pressure gradient <12 mm Hg. In our study, HVPG relationship between with and without variceal bleeding groups was not differentiated as similar previous study.

In the study of Villanueva et al., the intervals to HVPG remeasurement for therapeutic response evaluation were 3 months. However, there are currently no clear guidelines that define the optimal time and interval for HVPG measurement. We analyzed by the limitation to past bleeding as within 3 months from HVPG measurement time. We found no significant association of HVPG level with the history of bleeding.

The important predictors of bleeding from GV include the presence of large varices, red color sign, and advanced Child-Pugh stage. In this study, variceal size (F2/F3) and presence of red color sign were higher in variceal bleeding group similar to previous study. However, difference according to GOV type was not revealed. Variceal rupture in gastric FVs with portosystemic shunt had a less frequent than in those without. This means gastric FVs without gastrosystemic shunt or splenorenal shunt could be a risk factor for gastric fundal variceal bleeding. Most FVs are fed by the short or posterior gastric vein and drain to the inferior vena cava through well developed gastrorenal shunt. Patient’s varices without gastrorenal shunt had thinner veins and a lower blood-flow volume than with. However, the hemodynamics was more complicated than that in the without gastrorenal shunt group. The portal hemodynamics of GV without gastrorenal shunt was not well known. Matsumoto et al. showed that it is likely to develop high risk FVs after the occlusion of gastric FVs with gastrorenal shunt. Sakai et al. reported that patients with gastrorenal shunt showed a significantly lower recurrence rate of FVs after sclerotherapy compared with patients without it. And, in previous study, worsening of FVs was reported after balloon occluded retrograde transvenous obliteration (B-RTO) in long-term follow-up. It was suggested that reflux into the left gastric vein of these patients in who blood flow from the gastric wall vessels and the left gastric vein drained into gastrorenal shunt increased after B-RTO. Increased hepatofugal flow in the left gastric vein after B-RTO is also thought to have caused FVs. Surgical distal splenorenal shunt was effective in controlling gastric variceal haemorrhage. This suggests that portosystemic shunt has a role of limiting the increase of portal pressure to a certain level and is the main route for reducing the portal venous pressure.

Although a prospective study involving a large number of patients is needed, it is possible to reduce gastric fundal variceal bleeding by reducing the portal flow to GV through newly made gastroscopic shunt. Under the similar principle, the transjugular intrahepatic portosystemic shunt stent (TIPSS) has been evaluated for its effectiveness in the management of gastric fundal variceal bleeding. TIPSS is clearly very effective in controlling active bleeding and has been considered to be effective as a secondary prophylaxis, but still carries a fairly high rate of hepatic encephalopathy. However, the severity of gastric fundal variceal bleeding and the associated mortality is significantly high. Therefore gastroscopic shunt could be utilized as a new method to prevent gastric fundal variceal bleeding. Gastric fundal variceal bleeding with an increased number of portosystemic shunt tended to be less frequent. This suggests that increased shunting has a support role of limiting the increase of portal pressure to a certain level. However, our study is too small to prove result. More controlled and large scale studies are needed.

This study examined the severity of liver disease, as defined by MELD score or Child-Pugh score, in association with the HVPG. It is well known that patients with advanced cirrhosis have greater magnitudes of portal hypertension and Child’s class is associated with portal venous pressure.

One clear limitation of our study is its retrospective study design. The other limitation is the use of endoscopy to diagnose GV. Standard endoscopy underestimates the true prevalence of pathologically dilated gastric veins in patients with portal hypertension. GV lie in the submucosa, deeper than EVs, and GV may not be clearly distinguishable from gastric rugae. Endoscopic ultrasonography have shown that a significant number of GV were not evident in endoscopy. However, endoscopy still is recommended most frequently as a standard for the diagnosis of GV because it is the best noninvasive tool.

In previous reports, HVPG was significantly lower in patients with GV than those without. In our study, FVs had high prevalence of spontaneous portosystemic shunts compared with EVs and GOV1, but portal pressure in FVs was not different from that of EVs and GOV1. Because our study was designed by similar hemodynamic classification according to major blood supply (EVs/GOV1 vs FVs) and investigated small number of patients, this suggests that makes HVPG results unlike the previous study.

These findings indicate that the development of spontaneous portosystemic shunt may steal a part of portal venous flow and keep the portal venous pressure from increasing beyond a certain level. In this study, all the patients without portosystemic shunt in fundal variceal group experienced bleeding from varices at least once. Since gastric FVs without gastroscopic
shunt had to bleed more frequently than those with it, producing gastroesophageal varices. A prospective, randomized, controlled trial involving a large group of patients.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

REFERENCES

1. Bosch J, Berzigotti A, García-Pagán JC, Abraldes JG. The management of portal hypertension: rational basis, available treatments and future options. J Hepatol 2008;48 Suppl 1:S68–S92.

2. Sarin SK, Lahoti D, Saxena SP, Murthy NS, Makwana UK. Prevalence, classification and natural history of gastric varices: a long-term follow-up study in 568 portal hypertension patients. Hepatology 1992;16:1343–1349.

3. Hosking SW, Johnson AG. Gastric varices: a proposed classification leading to management. Br J Surg 1988;75:195–196.

4. Ryan BM, Stockbrugger RW, Ryan JM. A pathophysiological, gastroenterologic, and radiologic approach to the management of gastric varices. Gastroenterology 2004;126:1175–1189.

5. Al-Osaimi AM, Caldwell SH. Medical and endoscopic management of gastric varices. Semin Intervent Radiol 2011;28:273–282.

6. Watanabe K, Kimura K, Matsutani S, Ohto M, Okuda K. Portal hemodynamics in patients with gastric varices. A study in 230 patients with esophageal and/or gastric varices using portal vein catheterization. Gastroenterology 1988;95:434–440.

7. Arakawa M, Masuzaki T, Okuda K. Pathomorphology of esophageal and gastric varices. Semin Liver Dis 2002;22:73–82.

8. Bosch J, García-Pagán JC, Berzigotti A, Abraldes JG. Measurement of portal pressure and its role in the management of chronic liver disease. Semin Liver Dis 2006;26:348–362.

9. Parikh S. Hepatic venous pressure gradient: worth another look? Dig Dis Sci 2009;54:1178–1183.

10. D’Amico G, Pagliaro L, Bosch J. The treatment of portal hypertension: a meta-analytic review. Hepatology 1995;22:332–354.

11. Tripathi D, Therapondos G, Jackson E, Redhead DN, Hayes PC. The role of the transjugular intrahepatic portosystemic stent shunt (TIPS) in the management of bleeding gastric varices: clinical and haemodynamic correlations. Gut 2002;51:270–274.

12. Chao Y, Lin HC, Lee FY, et al. Hepatic hemodynamic features in patients with esophageal or gastric varices. J Hepatol 1993;19:85–89.

13. Matsumoto A, Hamamoto N, Nomura T, et al. Balloon-occluded retrograde transvenous obliteration of high risk gastric variceal am. J Gastroenterol 1999;94:643–649.

14. Ohsahi K, Nakayama T, Koen H, et al. Interrelationship between type of spontaneous portal systemic shunt and portal vein pressure in patients with liver disease. Am J Gastroenterol 1985;80:561–564.

15. Viallet A, Marleau D, Huet M, et al. Hemodynamic evaluation of patients with intrahepatic portal hypertension. Relationship between bleeding varices and the portohepatic gradient. Gastroenterology 1975;69:1297–1300.

16. Lebrec D, De Fleury P, Rueff B, Nahum H, Benhamou JP. Portal hypertension, size of esophageal varices, and risk of gastrointestinal bleeding in alcoholic cirrhosis. Gastroenterology 1980;79:1139–1144.

17. García-Tsao G, Groszmann RJ, Fisher RL, Conn HO, Atterbury CE, Glickman M. Portal pressure, presence of gastroesophageal varices and variceal bleeding. Hepatology 1985;5:419–424.

18. Groszmann RJ, Bosch J, Grace ND, et al. Hemodynamic events in a prospective randomized trial of propranolol versus placebo in the prevention of a first variceal hemorrhage. Gastroenterology 1990;99:1401–1407.

19. Conn HO, Grace ND, Bosch J, et al. Propranolol in the prevention of the first hemorrhage from esophagogastric varices: a multicenter, randomized clinical trial. The Boston–New Haven–Barcelona Portal Hypertension Study Group. Hepatology 1991;13:902–912.

20. Villanueva C, Balanzó J, Novella MT, et al. Nadolol plus isosorbide mononitrate compared with sclerotherapy for the prevention of variceal rebleeding. N Engl J Med 1996;334:1624–1629.

21. Kim T, Shijo H, Kokawa H, et al. Risk factors for hemorrhage from gastric fundal varices. Hepatology 1997;25:307–312.

22. Kameda N, Higuchi K, Shiba M, et al. Management of gastric fundal varices without gastro-renal shunt in 15 patients. World J Gastroenterol 2008;14:448–453.

23. Sakai T, Iwao T, Oho K, Toyonaga A, Tanikawa K. Influence of extravariceal collateral channel pattern on recurrence of esophageal varices after sclerotherapy. J Gastroenterol 1997;32:715–719.

24. Katoh K, Sone M, Hirose A, Inoue Y, Fujino Y, Onodera M, Balloon-occluded retrograde transvenous obliteration for gastric varices: the relationship between the clinical outcome and gastrorenal shunt occlusion. BMC Med Imaging 2010;10:2.

25. Thomas PG, D’Cruz AJ. Distal splenorenal shunting for bleeding gastric varices. Br J Surg 1994;81:241–244.

26. Rees CJ, Nylander DL, Thompson NP, Rose JD, Record CO, Hudson M. Do gastric and esophageal varices bleed at different portal pressures and is TIPS an effective treatment? Liver 2000;20:253–256.

27. Irani S, Kowdle K, Kozaek R. Gastric varices: an updated review of management. J Clin Gastroenterol 2011;45:133–148.

28. Braillon A, Cales P, Valla D, Gaudy D, Geoffroy P, Lebrec D. Influence of the degree of liver failure on systemic and splanchic haemodynamics and on response to propranolol in patients with cirrhosis. Gut 1986;27:1204–1209.

29. Wang YW, Huo TI, Yang YY, et al. Correlation and comparison of the model for end-stage liver disease, portal pressure, and serum sodium for outcome prediction in patients with liver cirrhosis. J Clin Gastroenterol 2007;41:706–712.
30. Ripoll C, Groszmann R, García-Tsao G, et al. Hepatic venous pressure gradient predicts clinical decompensation in patients with compensated cirrhosis. Gastroenterology 2007;133:481-488.

31. Lo GH, Lai KH, Cheng JS, Huang RL, Wang SJ, Chiang HT. Prevalence of paraesophageal varices and gastric varices in patients achieving variceal obliteration by banding ligation and by injection sclerotherapy. Gastrointest Endosc 1999;49(4 Pt 1):428-436.

32. Thabut D, Moreau R, Lebrec D. Screening for esophageal varices: endoscopy, other tools, or endoscopy and other tools? Hepatology 2008;47:1434-1436.

33. Kim MY, Baik SK, Suk KT, et al. Measurement of hepatic venous pressure gradient in liver cirrhosis: relationship with the status of cirrhosis, varices, and ascites in Korea. Korean J Hepatol 2008;14:150-158.