Digestive Diseases and Sciences, Vol. 51, No. 2 (February 2006), pp. 352–358 (© 2006)
DOI: 10.1007/s10620-006-3137-8

Improved Prognosis of Cirrhosis Patients with Esophageal Varices and Thrombocytopenia Treated by Endoscopic Variceal Ligation Plus Partial Splenic Embolization

KENJI OHMOTO, MD, NAOKO YOSHIOKA, MD, YASUYUKI TOMIYAMA, MD, NORIKUNI SHIBATA, MD, MICHIHIKO TAKESUE, MD, KOJI YOSHIDA, MD, MAKOTO KUBOKI, MD, and SHINICHIRO YAMAMOTO, MD

The aim of this study was to assess the efficacy of the combination of endoscopic variceal ligation (EVL) and partial splenic embolization (PSE) compared with EVL alone in cirrhosis patients with thrombocytopenia. In a prospective study, 84 cirrhosis patients with esophageal varices and thrombocytopenia (platelet count $<50{,}000/mm^3$) underwent EVL plus PSE ($N = 42$) or EVL alone ($N = 42$). Primary end points assessed during the follow-up period included the recurrence of varices, progression to variceal bleeding, and death. Comparison between combined treatment and variceal ligation alone by multivariate analysis showed a hazard ratio of 0.44 for the recurrence of varices ($P = 0.02$), 0.19 for progression to variceal bleeding ($P = 0.01$), and 0.31 for death ($P = 0.04$). These results suggest that the combination of EVL plus PSE can prevent the recurrence of varices, progression to variceal bleeding, and death in cirrhosis patients with esophageal varices and thrombocytopenia.

KEY WORDS: liver cirrhosis; portal hypertension; esophageal varices; thrombocytopenia; endoscopic variceal ligation; partial splenic embolization.

Esophageal varices are a common complication of liver cirrhosis. Bleeding from varices often occurs in the first year after their diagnosis (1, 2) and the mortality rate due to the first hemorrhage is about 30% to 50% (3–5). The 1-year risk of rebleeding after an index variceal bleed is 70%, and the mortality rate is 50% for each subsequent episode (6). However, bleeding or rebleeding can be prevented in many patients either by medical treatment with a nonselective ß-blocker or by endoscopic variceal ligation (EVL). Nonselective ß-blocker therapy is the most widely studied form of prophylaxis and has been shown to reduce the risk of bleeding but not the mortality rate. EVL is more effective than propranolol for the primary prevention of variceal bleeding (7, 8). However, varices often recur quite rapidly after treatment by EVL (9, 10), so various combination therapies, such as EVL plus pharmacologic treatment (11), EVL plus sclerotherapy (12, 13), and EVL plus radiologic intervention (14, 15), have been tried to improve the outcome. With regard to the risk factors for variceal bleeding, large esophageal varices have a significantly higher risk of bleeding than small varices (16–20), while thrombocytopenia and splenomegaly are independent predictors of bleeding from large varices (21–26). Unfortunately, the best method for management of esophageal varices in patients with hypersplenism,

Manuscript received December 7, 2004; accepted June 2, 2005.
From Division of Hepatology, Department of Medicine, Kawasaki Medical School, Okayama, Japan.
Address for reprint requests: Kenji Ohmoto, MD, Division of Hepatology, Department of Medicine, Kawasaki Medical School, 577 Matsushima, Kurashiki, Okayama 701-0192, Japan; ohmotok@med.kawasaki-m.ac.jp.

TABLE 1. CLINICAL CHARACTERISTICS OF THE PATIENTS

	EVL + PSE group (n = *42*)	*EVL group* (n = *42*)	P *value*
Age (years) (mean ± SD)	60.2 ± 10.4	62.3 ± 9.6	0.25
Gender (male/female)	30/12	28/14	0.64
Etiology of cirrhosis			0.16
Hepatiti B virus	9	4	
Hepatiti C virus	25	33	
Alcoholic liver damage	8	5	
Child-Pugh score			0.38
Class A	12	11	
Class B	21	19	
Class C	9	12	
Presence of HCC	16 (38%)	12 (29%)	0.35
Variceal size (Fl/F2/F3)	0/30/12	0/22/20	0.20
Variceal bleeding on admission	14 (33%)	17 (40%)	0.50
EVL sessions (mean ± SD)	2.7 ± 1.5	3.1 ± 1.9	0.21
Bands consumed (mean ± SD)	15.8 ± 5.3	18.2 ± 7.1	0.11
Platelet count ($\times 10^3/mm^3$) (mean ± SD)	41 ± 7	43 ± 5	0.43
Follow-up period (years) (mean ± SD)	4.8 ± 2.2	4.2 ± 2.1	0.26

Note. EVL, endoscopic variceallligation: PSE, partial splenic embolizition: HCC hepatocellular carcinoma.

especially those with thrombocytopenia, is still unclear (27). In patients with hypersplenism, partial splenic embolization (PSE) was introduced by Spigos *et al.* (28) for the treatment of leukopenia and thrombocytopenia. We have also found that cirrhosis patients with hypersplenism and thrombocytopenia showed long-term improvement of their hematological profile and liver function and promoted long-term survival after PSE (29). Therefore, prevention and treatment of ruptured esophageal varices is expected to improve the prognosis of liver cirrhosis patients who have esophageal varices associated with splenomegaly and thrombocytopenia and cannot be treated by liver transplantation.

In the present study, we prospectively evaluated the usefulness of EVL combined with PSE versus EVL alone for the treatment of cirrhosis patients with esophageal varices and severe thrombocytopenia.

PATIENTS AND METHODS

Patients. From July 1995 to April 2004, 84 cirrhosis patients who were not potential candidates for orthotopic liver transplantation and had large untreated varices (F2/F3: 52/32 patients), hypersplenism, and thrombocytopenia (platelet count $<50{,}000/mm^3$) were admitted to our hospital. Among them, 42 patients underwent EVL plus PSE and complete endoscopic eradication of their varices was achieved (EVL+PSE group). The other 42 patients were treated with EVL alone (EVL group). Patients qualifying for this prospective study were randomly assigned to receive either EVL plus PSE or EVL alone according to a computer-generated randomization sequence. The two groups were well matched with respect to clinical characteristics such as the mean age, gender, etiology (including hepatitis B virus, hepatitis C virus, and alcoholism), Child-Pugh class, presence of hepatocellular carcinoma (HCC), variceal size, performance of emergency EVL for variceal bleeding on admission, number of EVL sessions, number of bands used for eradication of varices, mean platelet count, and follow-up period (Table 1). This study was approved by the ethics committee for clinical investigations of our medical school and conformed to the Helsinki Declaration. Each patient was informed of the aims of the study and the nature of the protocol and gave written consent to participation.

Endoscopic Variceal Ligation and Partial Splenic Embolization. EVL was performed using a standard endoscope (XQ-200; Olympus Optical Co., Ltd., Tokyo) with a pneumoactived single ligator (Sumitomo Bakelite Co., Ltd., Tokyo) and an overtube. Varices were sequentially ligated, starting from the most distal lesion in the esophagus, and EVL was repeated at weekly intervals until complete eradication of varices was achieved.

PSE was performed using the Seldinger method and small amounts of embolic material were injected until there was a 60% to 80% reduction in splenic blood flow. We evaluated the hemodynamics of the left gastric vein based on the results of splenic arteriography performed before and after PSE. The arteriograms were reviewed independently by two investigators.

In patients with large varices, prophylactic EVL was performed even if the varices were not bleeding. PSE was done 1 week before EVL and vasoactive drugs or nonselective ß-blockers such as propranolol were not given. In patients with active variceal bleeding, emergency EVL was performed first to achieve hemostasis, and PSE was done 1 week later.

Follow-up. After treatment, follow-up endoscopy was performed twice at 3-month intervals and then was done every 6 months if there was no recurrence. If bleeding recurred, emergency endoscopy was performed to identify the source. If esophageal varices were determined to be responsible, EVL was performed to arrest the bleeding. The maximum, minimum, and mean follow-up period was 8.3, 0.5, and 4.8 years, respectively, in the EVL plus PSE group, versus 7.5, 0.3, and 4.2 years in the EVL group. The end points of the study were recurrence of

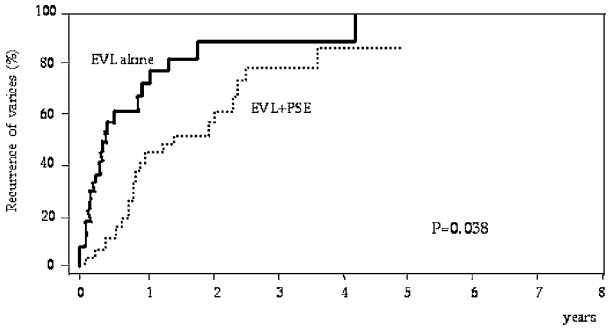

Fig 1. The cumulative recurrence rate of varices was significantly lower in the EVL + PSE group than in the EVL group.

esophageal varices, bleeding from the varices, death, and loss to follow-up.

Definitions. Eradication of varices was defined as nonvisualization of any varices or the presence of only fibrosed varices resistant to ligation. Recurrence of varices was defined as the detection of new varices after eradication had previously been achieved. Variceal bleeding was defined on the basis of the follows findings: (1) active variceal bleeding, (2) clot overlying a varix that resists removal by washing, (3) a white plug overlying a varix, or (4) esophageal varices and fresh blood in the stomach without any other potential sources of bleeding. The final decisions regarding eradication, recurrence, and bleeding were made on the basis of agreement between two experienced endoscopists.

Statistical Analysis. Statistical analysis was carried out using the SPSS software package (SPSS, Inc., Chicago, IL). The chi-square test was employed to assess the homogeneity of groups. Cumulative incidences were plotted by the Kaplan-Meier method, and the significance of differences was examined by the log-rank test. Identification of factors that were predictive of the recurrence of varices, bleeding from varices, and mortality was performed with a Cox proportional hazards model. Univariate analysis was performed first and then multivariate analysis was done using the significant factors identified by the univariate analysis. A P value of <0.05 was considered to indicate statistical significance.

RESULTS

Recurrence of Varices. During follow-up, 28 patients (67%) from the EVL + PSE group and 37 patients (88%) from the EVL group developed new varices that required prophylactic retreatment. The EVL + PSE group showed a significantly lower incidence of new varices ($P = 0.038$) (Figure 1). The results of the univariate and multivariate analyses are reported in Table 2. Multivariate analysis identified only one independent factor that influenced the recurrence of varices, which was treatment with EVL plus PSE ($P = 0.02$; hazard ratio = 0.44; 95% CI, 0.22–0.89).

Variceal Bleeding. Variceal bleeding occurred in 7 patients (17%) from the EVL + PSE group and 14 patients (34%) from the EVL group, and it was significantly less common in the former group ($P = 0.024$) (Figure 2). Comparison of EVL + PSE with EVL alone by multivariate analysis showed that the hazard ratio for variceal bleeding was 0.19 (95% CI, 0.05–0.69; $P = 0.01$) (Table 3).

Survival. Twenty-one patients (50%) from the EVL + PSE group and 29 patients (69%) from the EVL group died during the observation period. The survival rate was significantly higher after EVL + PSE for patients in any Child's class ($P = 0.042$) (Figure 3). Only 2 of 21 patients (10%) from the EVL + PSE group died of variceal bleeding, versus 10 of 29 patients (34%) from the EVL group. Therefore, the incidence of death related to variceal bleeding was significantly lower after EVL + PSE than

TABLE 2. FACTORS PREDICTING VARICEAL RECURRENCE

Variable	*Univariate analysis (*P *value)*	*Multivariate analysis (*P *value)*	*Hazard ratio (95% CI)*
Age	0.71	—	—
Gender	0.76	—	—
Etiology of cirrhosis	0.77	—	—
Presence of HCC	0.88	—	—
Child-Pugh score	0.04	0.24	—
Laboratory data			
White blood count	0.34	—	—
Red blood count	0.003	0.13	—
Total bilirubin	0.01	0.14	—
ALT	0.26	—	—
Albumin	0.16	—	—
Prothrombin time	0.62	—	—
Ammonia	0.11	—	—
Treatment			
Prophylactic EVL	0.0003	0.08	—
Emergency EVL	0.0009	0.73	—
EVL+PSE	0.003	0.02	0.44 (0.22–0.89)

Note. CI, confidence interval; HCC, hepatocellular carcinoma; ALT, alanine aminotransferase; EVL, endoscopic varicealligation; PSE, partial splenic embolization.

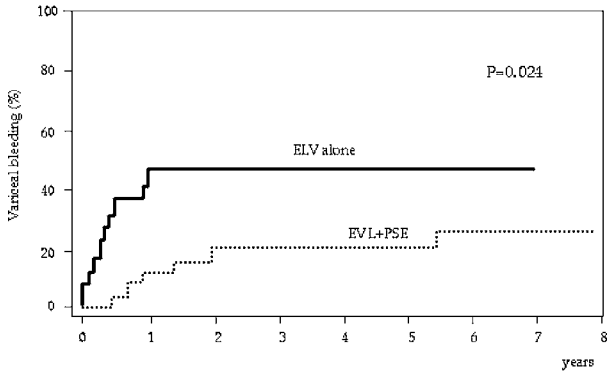

Fig 2. The cumulative variceal bleeding rate was significantly lower in the EVL + PSE group than in the EVL group.

after EVL alone ($P = 0.041$). By multivariate analysis, only the presence of HCC at diagnosis and treatment by EVL + PSE were independent predictors of mortality, with the hazard ratios being 6.03 (95%CI, 1.88–19.33; $P = 0.004$) and 0.31 (95%CI, 0.12–0.79; $P = 0.04$), respectively (Table 4).

Effect of Partial Splenic Embolization. The mean ± SD splenic embolization rate was 68% ± 12%, which was assessed after 1–2 weeks on the basis of enhanced CT findings. In the patients undergoing PSE, the platelet count, serum albumin level, and prothrombin activity all showed a significant increase after treatment and remained significantly elevated for the next 5 years. In addition, the Child-Pugh score showed significant improvement at 1, 2, and 5 years after PSE (Table 5).

During angiography at the time of PSE, the left gastric vein was visualized distal to the liver in 31 patients (74%). In all of these patients, the left gastric vein was opacified more slowly after PSE and its diameter was smaller than before the procedure.

Adverse Effects. EVL caused a few complications, such as deep ulcers and stricture of the esophagus. Regarding the adverse effects of PSE, transient fever, left-sided chest pain, and anorexia were observed in all of the patients, but there were no serious complications.

DISCUSSION

Endoscopic procedures such as EVL and sclerotherapy have been widely used to control acute variceal bleeding and to prevent further bleeding episodes. Recent studies and a meta-analysis have shown that EVL is superior to sclerotherapy in terms of bleeding, survival, and stricture formation, as well as the number of treatment sessions required to achieve the obliteration of varices (30, 31). EVL is also more effective than propranolol for the primary prevention of variceal bleeding (7, 8). However, esophageal varices often recur soon after the performance of EVL (9, 10), so the use of this method in isolation seems to have limitations.

In patients with large esophageal varices, the platelet count is one of the important predictors of variceal bleeding (21–26), but the optimum management of varices in patients with thrombocytopenia is still not well understood (27). Since the report by Spigos *et al.* (28), PSE has been used to treat cirrhosis patients with hypersplenism and EVL has been combined with PSE to prolong the duration of variceal eradication (14, 15). We prospectively evaluated the impact of treatment with EVL plus PSE on the

TABLE 3. FACTORS PREDICTING VARICEAL BLEEDING

Variable	*Univariate analysis (*P *value)*	*Multivariate analysis (*P *value)*	*Hazard ratio (95% CI)*
Age	0.81	—	—
Gender	0.46	—	—
Etiology	0.52	—	—
Presence of HCC	0.90	—	—
Child-Pugh score	0.05	0.29	—
Laboratory data			
White blood count	0.22	—	—
Red blood count	0.0002	0.09	—
Total bilirubin	0.009	0.26	—
ALT	0.47	—	—
Albumin	0.39	—	—
Prothrombin time	0.09	—	—
Ammonia	0.44	—	—
Treatment			
Prophylactic EVL	0.004	0.21	—
Emergency EVL	0.03	0.68	—
EVL+PSE	0.003	0.01	0.19 (0.05–0.69)

Note. CI, confidence interval; HCC, hepatocellular carcinoma; ALT, alanine aminotransferase; EVL, endoscopic variceal ligation; PSE, partial splenic embolization.

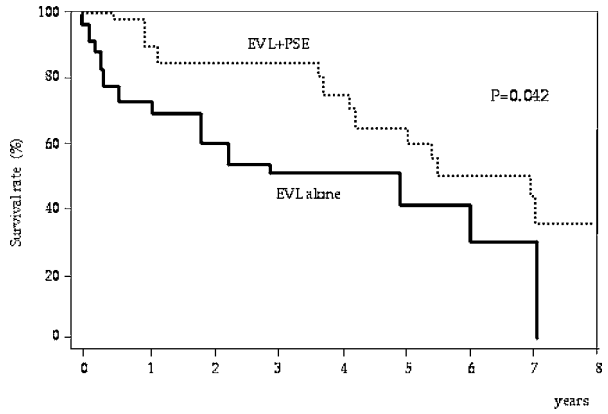

Fig 3. The cumulative survival rate was significantly higher in the EVL + PSE group than in the EVL group.

long-term prognosis of cirrhosis patients with esophageal varices and severe thrombocytopenia. We found that multivariate analysis demonstrated the usefulness of EVL plus PSE for reducing the recurrence of esophageal varices and variceal bleeding in patients with cirrhosis, hypersplenism, and thrombocytopenia. Moreover, this combined therapy significantly decreased the risk of death from variceal bleeding.

It has been reported that cirrhosis patients treated with PSE show long-term improvement of their hematological abnormalities and also of their hepatic functional reserve after PSE (29). Although the mechanism by which PSE improves liver function is still unclear, it has been suggested that immunological factors and hemodynamic changes are involved (32–35). Regarding the former mechanism, an experimental study has shown that the spleen suppresses liver regeneration following partial hepatectomy, suggesting the production of suppressive factors by the spleen (36). In addition, a clinical study has suggested that the spleen regulates inflammation and fibrosis in the liver (33). Thus, PSE may decrease the levels of splenic inhibitory factors such as cytokines, which have an adverse influence on hepatic regeneration. Regarding hemodynamic changes after PSE, Hirai *et al.* (37) suggested that a decrease in portal blood flow and a relative increase in mesenteric blood flow may decrease liver congestion after PSE, and may also increase the supply of nutrients and cytokines derived from the alimentary tract. In our previous study, mesenteric hepatopetal blood flow showed a relative increase following PSE and the liver volume was increased at 2 years after PSE, so hepatic regeneration is probably involved in the improvement of liver function (29).

In the present study, the left gastric vein was visualized in 31 of 42 patients when angiography was performed at the time of PSE. After PSE, blood flow through the left gastric vein (which is distal to the liver) decreased in these patients, suggesting a reduction in the blood supply to the esophageal varices. Accordingly, PSE seems to be a useful adjunctive therapy for esophageal varices, and the above-mentioned effects may have made an important contribution to decreasing variceal recurrence or bleeding and increasing survival among our patients receiving combined therapy.

We found that the combination of EVL plus PSE did not cause any serious complications, and its relative safety emphasizes the usefulness of this method for treating patients with esophageal varices and thrombocytopenia.

TABLE 4. FACTORS PREDICTING DEATH

Variable	*Univariate analysis (*P *value)*	*Multivariate analysis (*P *value)*	*Hazard ratio (95% CI)*
Age	0.97	—	—
Gender	0.96	—	—
Etiology	0.42	—	—
Presence of HCC	0.001	0.004	6.03 (1.88–19.33)
Child-Pugh score	0.02	0.56	—
Laboratory data			
White blood count	0.99	—	—
Red blood count	0.02	0.33	—
Total bilirubin	0.69	—	—
ALT	0.58	—	—
Albumin	0.02	0.65	—
Prothromibin time	0.28	—	—
Ammonia	0.17	—	—
Treatment			
Prophylactic EVL	0.24	—	—
Emergency EVL	0.83	—	—
EVL+PSE	0.03	0.04	0.31 (0.12–0.79)

Note. CI, confidence interval; HCC, hepatocellular carcinoma; ALT, alanine aminotransferase; EVL, endoscopic variceal ligation; PSE, partial splenic embolization.

TABLE 5. CHANGES IN THE PLATELET COUNT AND LIVER FUNCTION PARAMETERS AFTER PARTIAL SPLENIC EMBOLIZATION

	Before	*1 year*	*3 years*	*5 years after PSE*
Platelet count ($\times 10^3$/mm^3)	41 ± 7	110 ± 43‡	108 ± 53‡	98 ± 45‡
Albumin (g/dL)	3.1 ± 0.4	3.4 ± 0.5†	3.4 ± 0.6†	3.5 ± 0.5†
Prothrombin activity				
(%)	52 ± 12	68 ± 16‡	73 ± 13‡	67 ± 13‡
(INR)	1.6 ± 0.4	1.3 ± 0.3‡	1.2 ± 0.2‡	1.3 ± 0.2‡
Child-Pugh score	7.8 ± 1.8	7.1 ± 18†	6.7 ± 1.7†	6.9 ± 1.3†

Nate. PSE, partial splenic embolization; INR, international normalized ratio.
†$P < 0.01$ vs. before. ‡$P < 0.001$ vs.before.

In conclusion, EVL plus PSE may prevent the development of new varices, progression of variceal bleeding, and death of cirrhosis patients with esophageal varices and thrombocytopenia who cannot undergo liver transplantation. However, further studies are required to develop more useful therapies because the mortality rate of such patients remains high.

REFERENCES

1. The Northern Italian Endoscopic Club for the Study and Treatment of Esophageal Varices: Prediction of the first variceal hemorrhage in patients with cirrhosis of the liver and esophageal varices. N Engl J Med 319:983–989, 1988
2. Burroughs AK, Mezzanotte G, Phillips A, McCormick PA, McIntyre N: Cirrhotics with variceal hemorrhage: the importance of the time interval between admission and the start of analysis for survival and rebleeding rates. Hepatology 9:801–807, 1989
3. Novis BH, Duys P, Barbezat GO, Clain J, Bank S, Terblanche J: Fibreoptic endoscopy and the use of the Sengstaken tube in acute gastrointestinal haemorrhage in patients with portal hypertension and varices. Gut 17:258–263, 1976
4. Graham D, Smith JL: The course of patients after variceal hemorrhage. Gastroenterology 80:800–809, 1981
5. Silverstein FE, Gilbert DA, Tedesco FJ, Buenger NK, Persing H: The national ASGE surveys on upper gastrointestinal bleeding. áU. Clinical prognostic factors. Gastrointest Endosc 27:80–93, 1981
6. D'Amico G, Pagliaro L Bosch J: Pharmacological treatment of portal hypertension: an evidence-based approach. Semin Liver Dis 19:475–505, 1999
7. Sarin SK, Lamba GS, Kumar M, Misra A, Murthy NS: Comparison of endoscopic ligation and propranolol for the primary prevention of variceal bleeding. N Engl J Med 340:988–993, 1999
8. Aoki N, Kajiyama T, Beck R, Cone RW, Soma K, Fukui T: Decision analysis of prophylactic treatment for patient with high-risk esophageal varices. Gastrointest Endosc 52:707–714, 2000
9. Baroncini D, Milandri GL, Borione D, Piemontese A, Cennamo V, Billi P, Dal Monte PP, D'Imperio N: A prospective randomized trial of sclerotherapy versus ligation in the treatment of bleeding esophageal varices. Endoscopy 29:235–240, 1997
10. Hou MC, Lin HC, Lee FY, Chang FY, Lee SD: Recurrence of esophageal varices following endoscopic treatment and its impact on rebleeding: comparison of sclerotherapy and ligation. J Hepatol 32:202–208, 2000
11. Banares R, Albillos A, Rincon D, Alonso S, Gonzalez M, Ritz-del-Arbol L, Salcedo M, Molinero LM: Endoscopic treatment versus endoscopic plus pharmacologic treatment for acute variceal bleeding: a meta-analysis. Hepatology 35:609–615, 2002
12. Hou MC, Chen WC, Lin HC, Lee FY, Chang FY, Lee SD: A new "sandwich" method of combined endoscopic variceal ligation and sclerotherapy versus ligation alone in the treatment of esophageal variceal bleeding: a randomized trial. Gastrointest Endosc 53:572–578, 2001
13. Singh P, Pooran N, Indaram A, Bank S: Combined ligation and sclerotherapy versus ligation alone for secondary prophylaxis of esophageal variceal bleeding: a meta- analysis. Am J Gastroenterol 97:623–629, 2002
14. Taniai N, Onda M, Tajiri T, Toba M, Yoshida H: Endoscopic variceal ligation (EVL) combined with partial splenic embolization (PSE). Hepatogastroenterology 46:2849–2853, 1999
15. Taniai N, Onda M, Tajiri T, Yoshida H, Mamada Y: Combined endoscopic and radiologic intervention to treat esophageal varices. Hepatogastroenterology 49:984–988, 2002
16. Beppu K, Inokuchi K, Koyanagi N, Nakayama S, Sakata H, Kitano S, Kobayashi M: Prediction of variceal hemorrhage by esophageal endoscopy. Gastrointest Endosc 27:213–218, 1981
17. Zoli M, Merkel C, Magalotti D, Marchesini G, Gatta A, Pisi E: Evaluation of a new endoscopic index to predict first bleeding from the upper gastrointestinal tract in patients with cirrhosis. Hepatology 24:1047–1052, 1996
18. Lay CS, Tsai YT, Teg CY, Shyu WS, Guo WS, Wu KL, Lo KJ: Endoscopic variceal ligation in prophylaxis of first variceal bleeding in cirrhotic patients with high-risk esophageal v arices. Hepatology 25:1346–1350, 1997
19. Merkel C, Zoli M, Siringo S, van Buuren H, Magalotti D, Angeli P, Sacerdoti D, Bolondi L, Gatta A: Prognostic indicators of risk for first variceal bleeding in cirrhosis: a multicenter study in 711 patients to validate and improve the North Italian Endoscopic Club (NIEC) index. Am J Gastroenterol 95:2915–2920, 2000
20. Jensen DM: Endoscopic screening for varices in cirrhosis: findings, implications, and outcomes. Gastroenterology 122:1620–1630, 2002
21. Chalasani N, Imperiale TF, Ismail A, Sood G, Carey M, Wilcox CM, Madichetty H, Kwo PY, Boyer TD: Predictors of large esophageal varices in patients with cirrhosis. Am J Gastroenterol 94:3285–3291, 1999
22. Zaman A, Hapke R, Flora K, Rosen HR, Benner K: Factors predicting the presence of esophageal or gastric varices in patients with advanced liver disease. Am J Gastroenterol 94:3292–3296, 1999

23. Rajvanshi PR, Kowdley KV: Prediction of varices in patients with cirrhosis. A high-stakes numbers game? J Clin Gastroenterol 34:4–5, 2002
24. Madhotra R, Mulcahy HE, Willner I, ReubenA: Prediction of esophageal varices in patients with cirrhosis. J Clin Gastroenterol 34:81–85, 2002
25. Thomopoulos KC, Labropoulou-Karatza C, Mimidis KP, Katsakoulis EC, Iconomou G, Nikolopoulou VN: Non-invasive predictors of the presence of large oesophageal varices in patients with cirrhosis. Dig Liver Dis 35:473–478, 2003
26. Giannini E, Botta F, Borro P, Risso D, Romagnoli P, Fasoli A, Mele MR, Testa E, Mansi C, Savarino V, Testa R: Platelet count/spleen diameter ratio: proposal and validation of a non-invasive parameter to predict the presence of oesophageal varices in patients with liver cirrhosis. Gut 52:1200–1205, 2003
27. Van Os EC, Kamath PS, Gostout CJ, Heit JA: Gastroenterological procedures among patients with disorders of hemostasis: evaluation and management recommendations. Gastrointest Endosc 50:536–543, 1999
28. Spigos DG, Jonasson O, Mozes M, Capek V: Partial splenic embolization in the treatment of hypersplenism. Am J Roentgenol 132:777–782, 1979
29. Ohmoto K, Iguchi Y, Miyake I, Ohno S, Yamamoto S: Long-term evaluation of partial splenic embolization for liver cirrhosis and hepatocellular carcinoma accompanied by hypersplenism. Hepatol Res 11:73–83, 1998
30. Laine L, Cook D: Endoscopic ligation compared with sclerotherapy for treatment of esophageal variceal bleeding. A meta-analysis. Ann Intern Med 123:280–287, 1995
31. De la Peña J, Rivero M, Sanchez E, Fábrega E, Crespo J, Pons-Romero F: Variceal ligation compared with endoscopic sclerotherapy for variceal hemorrhage: prospective randomized trial. Gastrointerst Endosc 49:417–423, 1999
32. Porter BA, Frey CF, Link DP, Lantz BM, Pimstone NR: Splenic embolization monitored by the video dilution technique. Am J Roentgenol 141:1063–1065, 1983
33. Sato K, Tanaka M, Tanikawa K: The effect of spleen volume on liver regeneration after hepatectomy. A clinical study of liver and spleen volumes by computed tomography. Hepatogastroenterology 42:961–965, 1995
34. Hidaka H, Kokubu S, Saigenji K, Isobe Y, Maeda T: Restoration of thrombopoietin production after partial splenic embolization leads to resolution of thrombocytopenia in liver cirrhosis. Hepatol Res 23:265–273, 2002
35. Tajiri T, Onda M, Yoshida H, Mamada Y, Taniai N, Kumazaki T: Long-term hematological and biochemical effects of partial splenic embolization in hepatic cirrhosis. Hepatogastroenterology 49:1445–1448, 2002
36. Ohira M, Umeyama K, Taniura M, Yamashita T, Morisawa S: An experimental study of a splenic inhibitory factor influencing hepatic regeneration. Surg Gynecol Obstet 164:438–444, 1987
37. Hirai K, Kawazoe Y, Yamashita K, Kumagai M, Tanaka M, Sakai T, Inoue R, Eguchi S, Majima Y, Abe M, Toyonaga A, Tanikawa K: Transcatheter partial splenic arterial embolization in patients with hypersplenism: a clinical evaluation as supporting therapy for hepatocellular carcinoma and liver cirrhosis. Hepatogastroenterology 33:105–108, 1986