Therapeutic effects of endoscopic variceal ligation combined with partial splenic embolization for portal hypertension

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Methods: From May 1999 to May 2002, 41 cases with cirrhosis and portal hypertension underwent EVL-PSE. Hemodynamics of the main portal vein (MPV), the left gastric vein (LGV) and azygos vein, including maximum velocity, flow rate and vein diameter, were assessed by Doppler ultrasonography.

Results: One case died from pulmonary artery embolism. One case complicated with splenic abscess was successfully managed by laparotomy. The esophageal varices and hypersplenism were well controlled after EVL-PSE in other patients. After EVL-PSE, the flow rate and velocity of MPV was significantly reduced (P<0.05), as well as the flow rate of the LGV and azygos vein. During the follow-up, no recurrent bleeding was found.

Conclusion: Being more convenient and less invasive, EVL-PSE is hopeful to be a proper intervention strategy for portal hypertensive patients with impaired hepatic function or those intolerant to shunting or devascularization surgery.

INTRODUCTION
Recently, various non-surgical and less invasive treatments for liver cirrhosis and portal hypertension have been developed and accepted world-wide. However, these more up-to-date methods have their drawbacks, respectively. We introduced a new strategy combining endoscopic variceal ligation with partial splenic embolization (EVL-PSE) and examined its therapeutic features. The present study was thus designed to determine, in a controlled and prospective manner, whether this intervention would decrease the risk of variceal bleeding and improve the hypersplenism in cirrhotic patients effectively. In the meantime, we investigated the portal hemodynamic changes before and 1 week after EVL-PSE by Color Doppler Flow Imaging (CDFI).
Scanning was performed with patients in a supine position and the portal vein and left gastric vein were visualized via a transabdominal way while imaging of the azygos vein was through suprasternal fossa. The blood flow velocity was calculated from Doppler spectral traces of 4-6 s with 1 to 10 mm sampling volume adjusted according to the respiration and the mean values were calculated as the mean blood flow velocity. To avoid equipment and operator variability, all examinations were performed using the same equipment by the same ultrasonogist.

Statistical analysis
Analyses were performed by using SPSS10.0 statistical packages. The results are presented as mean±SD and were considered to be significant if P<0.05. The data analyses before and 1 week after EVL-PSE of portal hypertensive patients were made using the paired t-test. Analysis of variance was used to verify differences between groups.

RESULTS
Efficacy of EVL-PSE on varices occlusion and bleeding control
EVL-PSE was performed successfully in all 41 cases. A total of 128 EVLs were done, with a mean of 3.1 (2-5) EVLs per patient. All esophageal varices were occluded. Nine cases with active variceal bleeding underwent successful emergent EVL. One patient suffered a recurrent bleeding 11 d after the initial intervention and received a repeated EVL with perfect result. No recurrent bleeding was observed in the other 40 cases during hospitalization, and no case presented with another hemorrhagic event during 2-24 mo follow-up (mean 9.9 mo).

Changes of laboratory parameters after EVL-PSE
The effect on blood routine examination is shown in Table 2, where a significant increment was observed both for leukocytes and thrombocytes 1 and 2 weeks after EVL-PSE. The changes of hemoglobin contents throughout the operation was of nostastistical significance.

| Table 2 Changes of laboratory parameters after EVL-PSE |
|-----------------------------------------------|
| Hemoglobin (g/ L) | WBC (x10^9/ L) | Platelet (x10^9/ L) |
|-----------------|----------------|--------------------|
| Before EVL-PSE  | 104±14         | 2.9±0.6            | 55±11             |
| 1 wk after EVL-PSE | 117±12   | 7.4±1.5            | 102±18            |
| 2 wk after EVL-PSE | 119±16   | 6.1±1.2            | 120±24            |

**P<0.05 vs before EVL-PSE.**

Gross and pathologic changes of spleens
Forty cases showed significantly smaller spleens after PSE, and the shrinkage degree correlated well with the infarcted area. One patient underwent splenectomy 2 wk after PSE. Grossly the spleen presented with grey regions of segmental infarction, and microscopic examination suggested degeneration and necrosis of the splenic parenchyma with proliferation of surrounding fibrous tissue.

Adverse effects and complications
The majority of patients had EVL-related mild angina and/or retrosternal pain, which usually palliated spontaneously 3-5 d later without any special management. Forty cases had different degrees of fever and pain in left upper quadrant. The fever was usually around 38 °C and lasted 3-7 d with an exception of 28 d. One patient had splenic abscess and recovered after operation. Another case died 2 d after PSE due to pulmonary arterial embolism.

Color doppler ultrasound changes
Comparisons of Doppler parameters before EVL-PSE between the cirrhotic patients and controls are listed in Table 3. Significant differences were found in blood flow, blood flow rate and diameters of the main portal vein (MPV), left gastric vein (LGV) and azygos vein between the two groups. Table 4 presents the effects of EVL-PSE on the collateral branches of main portal vein and azygos vein. The diameters of MPV before and after the operation showed no difference, while the blood flow and blood flow rate decreased significantly, as well as the blood flow-rates of LGV and azygos vein.

DISCUSSION
What is the therapeutic strategy for portal hypertension? As medical doctors, we have been working on it assiduously. Poor hepatic function and impaired tolerance to the operation make it very important and of great clinical significance to explore an optimal strategy both effectively and the least invasively for portal hypertensive patients.

EVL is the widely accepted treatment for the bleeding of esophageal varices because of its definite efficacy, more convenience and safety and minor invasiveness. it, however, had a much longer course of treatment and the rate of recurrent hemorrhagic events in the short term was as high as 15-36%, especially before the varices were completely occluded[8-10]. EVL alone had no effect on hypersplenism, either. PSE is a new interventional radiological method for the treatment of hypersplenism secondary to portal hypertension. Generally,
30-40% of splenic infarction by PSE could improve hypersplenism, and 50-60% would affect favourably the portal pressure[7]. We discovered that the hypertrophic spleen would shrink more or less when the infarcted area reached 30-60%, with a significant increase of white blood cells and platelets in the peripheral blood (P<0.05), which suggested that PSE could improve the hypersplenism effectively. Former study demonstrated similar results. The content of hemoglobin changed little during PSE, because it was correlated much closely with the patients’ bleeding history and the amount of transfusion.

The current study revealed no changes of the diameters (P>0.05) of MPV as well as its significantly lower blood flow velocity and decreased blood flow rate after EVL-PSE. Traditional opinions held that portal blood flow after splenectomy or devascularization procedures would not decrease even would increase, while more up-to-date discoveries researched that portal blood flow decreased as a result of devascularization, similar to that of decompressive shunts surgery[10-12]. We found the similar results to a further degree, that is, the diameter of MPV after PSE showed no difference, the portal blood flow decreased significantly, however. Some held the opinion that the increased blood flow in portal hypertension come mainly from the splenic vein. PSE decreased the reflux of splenic vein, therefore, the blood flow of MPV decreased as well as its pressure. EVL-PSE decreased the blood flow and pressure of MPV equivalent to the conjoint effects of splenectomy and devascularization. The hemodynamic changes of MPV may be not quite the same because of individual difference, from which some scholars concluded that interventional therapy should be based on the patients’ hemodynamic conditions individually. We found in the portal hypertension group enlarged LGVs and hepatofugal blood flow in the pre-operation examination, which both indicated the patency of the esophagocardiac collateral circulation. LGV dilated and its blood flow decreased after EVL-PSE, which probably were results of the increased blood flow of the mucosa in the fundus and gastric body after repeated ligation. The gastric mucosa might be damaged more severely as a consequence. We should go further to identify its long-term effects. The diameter and blood flow velocity were strikingly higher in portal hypertension patients than controls before EVL-PSE (P<0.01). Some studies reported the same conclusions. They considered that measurement of the azygos blood flow was of importance for the patients’ treatment and prognosis[13]. Main branches of the portosystemic collateral circulation being cut-off, the diameter and blood flow-rate of azygos vein decreased significantly after EVL-PSE (P<0.01). However, they were still higher than that of the controls, indicating that other shunts for the superior vena cava, such as the periesophageal veins and abdominal wall veins accounted for the flow of azygos vein to a great extent.

Except for an ectopic embolism resulting from inappropriate operation, the main complications in our study were PSE-related pain in left upper quadrant and mild to moderate fever, which could be relieved by a small dose of NSAID such as mezolin, etc. satisfactorily. Spleen abscesses was diagnosed 2 wk after EVL-PSE in one case, and the patient whose spleen parenchyma was infarcted very much (about 70%) was recovered and discharged after splenectomy. Infarcted area more than 60% would induce more complications. Strengthened antibiotic use together with intestinal preparation and especially, perfect operation were the key points for a favorable result with less complications.

The esophageal varices were completely obliterated by EVL-PSE in 40 patients, with an average of 3.1 EVLs per patient. No case except one suffered recurrent bleeding during hospitalization and follow-up. In contrast, the obliteration rate of esophageal varices was 80-91% by EVL alone, with an average of 4 EVLs per patient, and with a recurrent bleeding rate as high as 15-17.1%[11]. EVL-PSE was superior to EVL alone. The underlying mechanism might be that PSE could decrease the blood flow of MPV, and the consequent pressure lowering of portal vein made varices less viable to recur. Conclusively, EVL-PSE was effective in the treatment of esophageal variceal hemorrhage and hypersplenism secondary to portal hypertension, and it could also decrease the total EVLs needed to make the varices occluded and the rate of short-term recurrent bleeding. The reduction of blood flow of MPV lowered the risk of recurrent bleeding after EVL. Being very convenient and little invasive, EVL-PSE is probably the first choice of intervention at strategy for portal hypertensive patients with impaired hepatic function or those intolerant to shunting or devascularization surgery.

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