Splenectomy with endoscopic variceal ligation is superior to splenectomy with pericardial devascularization in treatment of portal hypertension

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AIM: To investigate the therapeutic efficacy and complications of splenectomy with endoscopic variceal ligation (EVL) and splenectomy with pericardial devascularization (i.e. Hassab’s operation) in patients with portal hypertension.

METHODS: A total of 103 patients with liver cirrhosis and portal hypertension were randomly selected to receive either splenectomy with EVL (n = 53, group A) or Hassab’s operation (n = 50, group B).

RESULTS: The portal blood flow volume, the presence of portal vein thrombosis, gastric emptying time, free portal venous pressure (FPP) before and after the operation were determined. Patients were followed up for up to 64 mo with an average of 45 mo, and the Dagradi classification of variceal veins and the grading of portal hypertension gastropathy (PHG) were evaluated. It was found that all esophageal varices were occluded or decreased to grade II or less in both groups. There was little difference in the recurrence rate of esophageal varices (11.9% vs 13.2%) and the re-bleeding rate (7.1% vs 5.3%) between groups A and B.

CONCLUSION: The results suggest that splenectomy with EVL achieves similar therapeutic efficacy to that of Hassab’s operation in terms of the recurrence rate of esophageal varices and the re-bleeding rate, but the former results in fewer and milder complications.

Key words: Portal hypertension; Splenectomy; Endoscopic varices ligation; Hassab’s operation

INTRODUCTION

Recurrent bleeding occurs in over 70% of portal hypertension patients with a variceal bleeding history[1]. It is a general consensus that all patients with a variceal bleeding history should accept further treatment to prevent re-bleeding. Surgical operations still play a role in this process[2,3]. Since hepatitis-induced cirrhosis is the main cause of portal hypertension in China, which is associated with increased hepatocellular damage and worsened liver function, splenectomy with pericardial devascularization (i.e. Hassab’s operation) has been widely used because of its minor influence on liver function[3,4]. However, this operation has its limitations, including a high incidence of portal vein thrombosis, serious gastric mucosa damage and gastric emptying delay after operation[5-8]. The benefits of endoscopic management in preventing re-bleeding have been explicitly illustrated in a series of well designed randomized controlled trials[9,10]. Sclerotherapy significantly decreases the recurrence of bleeding and mortality, but it is associated with serious complications, the most common of which are esophageal strictures and bleeding from treatment-induced ulcers[3,4]. More recently, endoscopic variceal ligation (EVL) has been proven as an endoscopic therapy at least as effective as sclerotherapy, but with fewer complications. Meta-analyses have revealed that variceal ligation can more significantly reduce re-bleeding than sclerotherapy (POR = 0.53, 95% CI: 0.42 to 0.67), without significant heterogeneity amongst trials[12,13]. However, EVL still results in the re-bleeding rate as high as 30%, and does not help to relieve...
portal hypertension and hypersplenism\[14\].

Theoretically, combining splenectomy with EVL should relieve not only portal hypertension but also hypersplenism, and thus prevent the bleeding of esophageal varices\[13\]. Meanwhile, avoiding the procedure of devascularization may overcome its associated limitations as mentioned above. In this study, we compared the therapeutic efficacy of splenectomy combined with EVL with that of Hassab's operation and their respective complications in patients with portal hypertension.

**MATERIALS AND METHODS**

**Patients**
From January 1999 to June 2002, 103 consecutive patients (61 males and 42 females) with portal hypertension caused by hepatitis-induced cirrhosis were admitted to the Third Affiliated Hospital of Sun Yat-Sen University Hospital. All these patients were recruited in this prospective study.

The inclusion criteria included clinically diagnosed portal hypertension caused by hepatitis-induced cirrhosis in patients with endoscopically confirmed esophageal varices and a history of upper gastrointestinal hemorrhage, and functional hepatic reserve of grade A or B according to the Pugh-modified Child's scales.

The exclusion criteria included portal hypertension caused by reasons other than hepatitis-induced cirrhosis in patients with functional hepatic reserve of grade C by the Child-Pugh classification, peptic ulcer or other gastrointestinal complications, severe diseases in major organs other than in liver and/or age over 70 years.

The recruited patients were randomly assigned to group A or B with the use of opaque, sealed envelopes that contained a treatment assignment derived from computer-generated random numbers. Randomization was stratified according to the severity of liver failure (assessed by the Child-Pugh classification system). All the patients were cared for at the Department of General Surgery, Third Affiliated Hospital of Sun Yat-Sen University, Guangzhou, China. A written informed consent was obtained from all the patients, and the trial was approved by the Ethics Committee of Sun Yat-Sen University.

The study protocol is shown in Figure 1.

**Pre-operative endoscopic examination**
All the patients received a pre-operative endoscopic examination. The esophageal varix was evaluated by Dagradi classification\[16,17\], while the portal hypertensive gastropathy (PHG) was graded as mild, moderate or severe as previously described\[8,9\].

**Gastric emptying assessment**
Gastric emptying was assessed with a standardized scintigraphy method\[24,25\]. In brief, a test meal was prepared by mixing sixty grams of fat-parched flour (16 g protein, 3.24 g fat and 80 g carbohydrate, 924.7 KJ per 100 g) with hot water containing 37-74 mBq of 99mTc-DTPA to form a portion of semi-solid general meal. Each patient consumed a portion of the test meal within 5 min at a sitting position. Time to half-emptying of gastric contents, lag-phase calculation and residual gastric contents at 60, 120 and 240 min were calculated by a GENESYS SPECT system (ADAC, Laboratories, Milpitas, CA, USA).

**Splenectomy combined with endoscopic varices ligation**
Patients assigned to group A (n = 53) initially underwent routine splenectomy, and EVL was performed right after the splenectomy. After local application of lidocaine, an endoscope (GIF 240 or 260, Olympus Optical, Tokyo) was introduced, and ligation was carried out 6-12 times by placing a single rubber band (Bard Interventional Products, Tewksbury, Mass USA) over a varix each time. The ligation was repeated every 2 wk till the varices completely disappeared under the endoscope.

**Hassab's operation**
Patients assigned to group B (n = 50) underwent Hassab's operation as previously described in detail by Yang and Qiu\[3\]. In brief, extended left subcostal incision or L incision of the left upper abdomen was used for extreme splenomegaly. After routine splenectomy, the gastric branch and 5-8 small branches of the gastric coronary veins were disconnected. The esophageal branch was disconnected and suture-ligated. The gastric posterior vein was ligated by suturing, and then the left subphrenic vein was ligated as well\[21\]. In addition, the arteries accompanied by the veins including the left gastric artery, left gastroepiploic artery, gastric posterior artery and left subphrenic artery, were disconnected.

**Determination of portal vein hemodynamics**
Free portal venous pressure (FPP) was measured before and after splenectomy (after the first EVL in group A) by inserting the measuring tube in the main portal vein through the right gastroepiploic vein during the operation, as described previously\[22\].

**Color Doppler ultrasound**
Color Doppler ultrasound detection was performed 2 wk before and 3 wk after the operation by a color Doppler ultrasound system (Biosound AU 4, Esaote, Italy). For each measurement, at least 3 reproducible patterns were created to calculate the mean maximum portal blood velocity (Vmean) to ensure the measurement accuracy. Mean portal blood velocity (Vmean) was calculated (cm/s) by the equation “Vmean = 0.57 × Vmax” as described by Moriyasu et al\[23\]. The cross-sectional area (cm²) was also recorded at the site of the main portal vein where the portal blood velocity was measured. Portal blood flow volume (PBF) was obtained (mL/min) by the equation “PBF = Area × Vmean × 60”.

**Follow-up of patients**
All patients were followed up by endoscopy at wk 2, 4 and 12 after operation, and every 12 wk thereafter (Figure 1). Gastrointestinal symptoms such as refractory hiccup, bilious vomiting, hematemesis and dark stools were recorded. The Dagradi classification and PHG grading were evaluated at the follow-up endoscopy as described above.
Statistical analysis
Values were expressed as mean ± SD. Mean differences between the two groups were calculated by unpaired *t* test. Mann-Whitney test was used for the analysis of ranked data. The comparison of categorical data was performed by the χ² test. *P* < 0.05 (2-tailed test) was considered statistically significant.

RESULTS

Efficacy on esophageal varices
A total of 154 EVLs were performed in group A, with a mean of 3.2 (2-5) EVL sessions per patient. All esophageal varices were occluded or decreased from grade III to grade II (Dagrade classification) in both groups.

A total of 80 patients were followed up for 24.5-64 mo with an average of 45 mo. Eleven patients in group A and 12 patients in group B were not followed up due to death or other reasons (3 died of liver cancer, 5 died of hepatic failure, 15 lost contact). The recurrence rate of esophageal varices was 11.9% (5/42) in group A and 13.2% (5/38) in group B, while the re-bleeding rate was 7.1% (3/42) in group A and 5.3% (2/38) in group B (*P* > 0.05).

Complications
No patients in both groups died of operation-related complications. The common complications included infection, worsened liver function (i.e. increasing jaundice), refractory ascites and pleural effusion. The incidence of complications in group B was higher than that in group A (60% vs 32.1%, *P* < 0.01). Mild pharyngodynia and/or retrosternal pain were found in most patients in group A, but they were relieved 3-5 d later without medical treatment. Esophageal ulcer-induced re-bleeding was found in 2 patients at 2 wk after the operation, but the bleeding was stopped by repeated EVL and medical treatment. Incomplete portal vein thrombosis was found in 7 patients (13%) in group A as detected by color Doppler ultrasound, and disappeared after anticoagulation treatment. In group B, 14 patients (28%) suffered from portal vein thrombosis (*P* < 0.01, compared with group A), while one patient presented with widespread thrombi in the main portal vein and the portal vein branch, and died of sponge-like lesions in the portal vein and liver function failure 6 mo after the operation, despite thrombolysis treatment. Significant differences were found in the incidence of refractory hiccup, bilious vomiting and the degree of gastric motility between the two groups (*P* < 0.05) (Table 1).

Endoscopic follow-up of PHG
The PHG grading increased significantly after the operation in patients of group B, but not in patients of group A (Table 2). The percentage of patients with severe PHG after the operation was 20.8% in group A and 52.0% in group B (*P* < 0.05) (Table 2). Three patients in group B suffered from hematemesys, which was evidenced by dark stools and/or a positive fecal occult blood test more than

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**Table 1** Incidence of complications after operation

| Complications               | Group A (n = 53) | Group B (n = 50) | Value |
|-----------------------------|------------------|------------------|-------|
|                            | n    | %    | n    | %    | χ²  | *P*  |
| Total cases with complications | 17   | 32.1 | 30   | 60   | 4.85 | 0.01 |
| Refractory ascites          | 3    | 5.7  | 9    | 18   | 4.65 | 0.03 |
| Pleural effusion            | 5    | 9.4  | 16   | 32   | 5.63 | 0.02 |
| Esophageal ulcer            | 2    | 3.8  | 0    | 0    | 6.56 | 0.03 |
| Portal vein thrombosis      | 5    | 9.4  | 11   | 22   | 3.25 | 0.03 |
| Refractory hiccup           | 2    | 3.8  | 15   | 30   | 5.46 | 0.02 |
| Bilious vomiting            | 3    | 5.7  | 16   | 32   | 3.65 | 0.01 |

Figure 1 The study protocol and the number of patients studied.
1 wk, and further confirmed as PHG-related hemorrhage by endoscopic examination.

**Alteration of gastric empty time**

No significant difference was found in gastric emptying time between the two groups at each time point before and after the operation. Moreover, the gastric emptying time did not change after the operation in both groups (Table 3).

**Alterations of portal vein pressure and hemodynamic variables**

In both groups after the operation, the directions of the portal venous flow were maintained towards the liver, but the FPP, V_max and the blood flow were decreased significantly compared with those before the operation ($P < 0.05$). However, there was no significant difference in the changes of these variables between the two groups ($P > 0.05$) (Table 4).

### DISCUSSION

Portosystemic shunt and Hassab's operation are commonly used in the treatment of portal hypertension. Although both operations are effective in control of bleeding, portosystemic shunt has increasingly been replaced by devascularization in recent years in China because of its technical difficulty and poor long-term outcome. A prospective study of 435 cases showed that the 5- and 10-year survival rates of patients after devascularization are 94.1% and 70.0%, respectively, while the recurrent bleeding rate is 6.2% and 13.3%, respectively. The same study also showed that the bleeding control rate of emergency operation is 96.9%, and the overall operative mortality rate is only 4.5%. However, the portal blood flow may decrease to some extent and re-bleeding is likely to occur because of the portal hyperdynamic state, and gastric congestion may exacerbate portal hypertensive gastropathy.

With the introduction of multishot band devices which allow the placement of 5-10 bands at a time, EVL has become a more effective method with fewer side effects compared with previous operations. After several repeated sessions at 2 wk intervals, obliteration of varices can be achieved in about 90% of patients. However, since portal hypertension and hypersplenism cannot be eliminated by EVL, resulting in the recurrence of varices after EVL, 20%-75% of patients require repeated EVL sessions. As the hyperkinetic circulatory state of the splenic vein is a potential factor for the development of bleeding in esophageal varices, we believe that splenectomy in combination with EVL may eliminate not only hypersplenism but also the hyperkinetic circulatory state of the portal vein system, which may prevent the recurrence of esophageal varices after EVL.

In the present study, splenectomy in combination with EVL showed a similar efficacy to Hassab's operation in the treatment of esophageal varices and in the prevention of re-bleeding. However, the former demonstrated several advantages over the latter, including a lower incidence of overall and individual complications such as refractory ascites, pleural effusion, esophageal ulcer, portal vein thrombosis, refractory hiccup and bilious vomiting and lower percentage of patients with severe PHG.

EVL may cause fibrosis in the mucous layer where the esophageal varices are located, but has no effect on the formation of collateral circulation in the muscular layer. Moreover, EVL may not injure the collaterals of the portal vein near the esophagus, thus decreasing the portal vein pressure by keeping the natural portal azygous shunt. In addition, EVL is a safe operation with few mild complications that can be tolerated by patients even with poor liver functions, thus allowing the extension of the indications for such a surgical intervention.

Thrombosis in the portal vein is a major complication of...
devascularization, which may be caused by the decreased blood flow in the portal vein system, porto-azygos disconnection, damage to the endangium and increased platelets after splenectomy. Acute thrombosis in the portal vein may lead to intestinal infarction, which is characterized by abdominal pain, hematochezia and diffuse peritonitis\(^5\). In our study, portal vein thrombosis was present in 28% (14/50) of patients receiving Hassab’s operation and 13% (7/53) of patients receiving splenectomy in combination with EVL, indicating that the latter can offer a significant benefit for patients with portal vein thrombosis.

In addition to portal vein thrombosis, vagal nerve injury is another commonly reported complication of devascularization\(^6\), which may greatly increase the incidence of gastric emptying delay and bilious vomiting by decreasing the gastric motivation. It is presumably a major cause for PHG. However, this kind of injury is likely to be related to the operational skills. Theoretically, devascularization may accompany a higher incidence of gastric emptying delay. However, no difference was found in the gastric emptying time between the two groups in the present study, suggesting that this phenomenon cannot be ascribed to any influence of EVL on gastric emptying.

Based on the observations of the present study, splenectomy in combination with EVL is as effective as Hassab’s operation in preventing the recurrence of esophageal varices and the re-bleeding rate, but has a lower incidence of PHG than Hassab’s operation. However, repeated EVL sessions (an average of 3.2 times) are necessary to maintain the occlusion of varices, which requires long-term follow-up and thus increasing the cost of therapy.

In conclusion, splenectomy in combination with EVL achieves a similar therapeutic efficacy to Hassab’s operation in terms of the recurrence rate of esophageal varices and the re-bleeding rate, but the former results in fewer and milder complications.

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