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Endoscopic Scleroligation is a Superior New Technique for Preventing Recurrence of Esophageal Varices

Takashi Tajiri, Masahiko Onda, Hiroshi Yoshida, Yasuhiro Mamada, Nobuhiko Taniai,
Matsuomi Umehara, Masahito Toba and Kiyohiko Yamashita

First Department of Surgery, Nippon Medical School

Abstract

This study compared a new method, endoscopic scleroligation, intravariceal injection sclerotherapy followed by ligation plus extravariceal injection sclerotherapy, with ligation plus extravariceal injection sclerotherapy. Fifty-nine patients with cirrhosis and esophageal varices were treated by endoscopic scleroligation (ESL group, n=28) or ligation plus extravariceal injection sclerotherapy (EVL+extraEIS group, n=31). The demographics and clinical characteristics of the two treatment groups were similar, as was the rate of complete eradication with initial treatment. However, the 1- and 3-year cumulative recurrence rates in the ESL group (3.8% and 22.4%) were very significantly lower than those in the EVL+extraEIS group (48.3% and 81.0%) ($p<0.0001$). The overall survival rates in the two groups were similar. In conclusion, endoscopic scleroligation is superior to ligation plus extravariceal injection sclerotherapy in preventing variceal recurrence. The efficacy of intravariceal injection sclerotherapy before ligation is believed to arise from the eradication of feeder vessels.

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Key words: esophageal varices, endoscopic ligation, endoscopic sclerotherapy, combination therapy

Introduction

Endoscopic injection sclerotherapy (EIS) is an established treatment for esophageal varices. Endoscopic variceal ligation (EVL) has been used increasingly because of its safety and simplicity and because no sclerosant is used. EIS can be accomplished by either intravariceal injection sclerotherapy (intraEIS) or extravariceal injection sclerotherapy (extraEIS). IntraEIS obliterates interconnecting perforating veins and the veins feeding esophageal varices. ExtraEIS and EVL achieve local eradication,

but do not disrupt interconnecting perforating and feeder vessels¹. Combination therapy incorporating EVL and EIS has been compared with EVL alone²⁻⁴. The technique in these trials involved ligation first, followed by intraEIS^{2,3} or extraEIS⁴. Beginning in November 1994, we developed a new technique for combining EVL and EIS called endoscopic scleroligation (ESL)⁵, in which intraEIS is performed before ligation.

This study compared intraEIS followed by EVL plus extraEIS (ESL) with EVL plus extraEIS (EVL+extraEIS) as therapy for esophageal varices with respect to efficacy, complications, recurrence of esophageal varices, and survival, retrospectively.

Correspondence to Takashi Tajiri, MD, First Department of Surgery, Nippon Medical School, 1-1-5 Sendagi, Bunkyo-ku, Tokyo 113-8603, Japan
E-mail: tajirit@nms.ac.jp
Journal Website (<http://www.nms.ac.jp/jnms/>)

Patients and Methods

Patients

The subjects were patients with cirrhosis and esophageal varices admitted between January 1995 and December 1998. Liver cirrhosis was diagnosed based on liver biopsy or suggested based on radiologic findings and clinical presentation. Patients with a history of endoscopic or surgical treatment of esophageal varices were excluded.

Classification

All patients underwent endoscopic examination using the Japan Society for Portal Hypertension and Esophago-gastric Varices Grading System⁶.

The criteria included color (white [Cw] or blue [Cb]), form (small and straight [F 1], nodular [F 2], or large or coiled [F 3]), presence of the red color sign ([RC]), and location (superior [Ls], medial [Lm], or inferior [Li]).

Methods

Endoscopic treatment sessions were carried out at weekly intervals whenever possible by three expert endoscopists using a television endoscopy system with computer stored endoscopic images. The following portion of the procedure was the same in both groups. Following premedication with an intramuscular injection of scopolamine butylbromide (20 mg) and intravenous injection of atropine sulfate (0.25 mg), pentazocine (15 mg), hydroxyzine (25 mg), and diazepam (5 mg), a one-channel endoscope was introduced. A flexible endoscopic sheath (Sumitomo Bakelite, Tokyo, Japan) was positioned to permit reinsertion of the endoscope and to prevent aspiration.

ESL group

The endoscope was removed and attached to a pneumo-activate EVL device (Sumitomo Bakelite) and an adoral balloon. The endoscope was reinserted and, after inflating the balloon, a 22 gauge needle was inserted into the target varix 2 to 3 cm proximal to the gastroesophageal junction. Sclerosant,

5% ethanolamine oleate with iopamidol (5% EOI), was infused into the varix and flow was monitored by x-ray fluoroscopy to confirm filling of the feeder vessel or the pericardiac venous plexus⁷. Suction was maintained at the puncture point while the needle was in the varix. As the varix was pulled into the ligator cap, the needle was also pulled, and EVL was accomplished by injection of air into the tube^{5,8}. The same procedure was repeated for other variceal columns in the lower esophagus. No additional injections were performed, and the intensive ligation method, which consists of ligating as many varices as possible, was used^{9,10}. In the second and subsequent treatment sessions, extraEIS was performed using 1% polidocanol¹¹.

EVL + extraEIS group

The endoscope was removed and attached to a pneumo-activate EVL device (Sumitomo Bakelite). The endoscope was reinserted, and varices were ligated using the intensive ligation method. In the second and subsequent treatment sessions, extraEIS was performed using the same method as ESL with 1% polidocanol as the sclerosant.

The end point of primary treatment was the failure to detect any residual varices between the ulcers created by EIS or EVL during the first hospitalization.

Follow-up

Endoscopic evaluation was performed 3 months after primary treatment. Variceal eradication was assessed based on the consensus of at least four expert endoscopists using a television endoscopy system with computer stored endoscopic images. The presence of F1 varices, or the RC sign was taken as evidence of incomplete eradication. Follow-up endoscopy was performed at 3- to 6-month intervals. Variceal bleeding, F 2 or F 3 varices, the RC sign, or intramucosal venous dilatation was taken as evidence of recurrence. Recurrent varices were treated by extraEIS with 1% polidocanol. Patients who refused additional therapy or did not keep appointments for a period of 6 months were counted as follow-up losses.

Statistical analysis

The cumulative bleeding rates were calculated using the Kaplan-Meier method. Differences in bleeding rates were analyzed using the log-rank test. The Mann-Whitney U test or chi-square test were used to compare the patients in the ESL and EVL + extraEIS groups. A p value < .05 was considered statistically significant.

Results

The ESL and EVL + extraEIS groups consisted of 28 and 31 patients, respectively (**Table 1**). The two groups were comparable with regard to sex, age, Pugh's modification of Child's grading system (Child-Pugh grade), etiology of cirrhosis, timing of treatment, initial endoscopic findings, and mean length of follow-up. No patient was lost in follow-up in either group.

There were no treatment failures or deaths during the period of hospitalization (**Table 2**). The two groups were similar in terms of the number of treatment sessions, number of O-rings placed, and total volume of sclerosant injected. No bleeding from treatment-induced esophageal ulcers occurred during hospitalization, and no serious treatment-related complications requiring active treatment or prolonged hospitalization occurred in either group.

Eradication was incomplete 3 months after primary treatment in 2 patients (7.1%) in the ESL group and 2 patients (6.5%) in the EVL + extraEIS group. All 4 patients had F 1 RC (+) varices, and extraEIS was carried out as an additional treatment.

The mean length of follow-up after primary treatment of patients with complete eradication was 32.0 ± 17.0 months in the ESL group (n=26) and 32.5 ± 18.1 months in the EVL + extraEIS group (n=29). According to Kaplan-Meier analysis, the 1- and 3-year cumulative recurrence rates were 3.8% and 22.4% in the ESL group and 48.3% and 81.0% in the EVL + extraEIS group. The overall rate of variceal recurrence was significantly lower in the ESL group than in the EVL + extraEIS group (p<0.0001) (**Fig. 1**).

Esophageal varices recurred in 5 patients in the ESL group. Endoscopic examination at the time of recurrence revealed F 1 RC (+) varices and intramucosal venous dilatation in the lower esophagus in the 4 patients who did not suffer variceal bleeding, and extraEIS was administered as additional treatment. One patient had acute esophageal bleeding after drinking a massive amount of alcohol, and F 1 RC (-) varices without intramucosal venous dilatation in the lower esophagus was observed endoscopically. EVL was performed to stop the bleeding, and extraEIS was administered as additional treatment.

Table 1 Demographics and Clinical Characteristics of Patients Undergoing Endoscopic Treatment of Esophageal Varices

	ESL	EVL + extraEIS	p value
No. of patients	28	31	
Gender (Female/Male)	9/19	12/19	NS
Age (yrs) *	61.9 ± 8.3	60.8 ± 10.4	NS
Child-Pugh (A/B/C)	4/19/5	6/17/8	NS
Etiology of cirrhosis			
Viral hepatitis/ alcoholism	21/7	25/6	NS
Timing of treatment			
Prophylactic/ Elective	17/11	19/12	NS
Endoscopic findings			
Form (2/3)	21/7	23/8	NS
Color (white/blue)	21/7	21/10	NS
Red color sign (+ /2 + /3 +)	16/9/3	15/10/6	NS
Follow-up (months) *	32.5 ± 16.6	32.2 ± 17.5	NS

* mean \pm SD ESL, endoscopic scleroligation; EVL, endoscopic variceal ligation; extraEIS, extravariceal injection sclerotherapy

Table 2 Outcome of Variceal Eradication by Endoscopic Therapy

	ESL	EVL + extraEIS	p value
No. of patients	28	31	
No. of treatment sessions	3.3 ± 0.7	3.1 ± 1.0	NS
No. of O-rings	14.6 ± 5.5	13.0 ± 4.3	NS
Total volume of sclerosant (ml)	18.4 ± 4.8	17.7 ± 9.1	NS
Volume of 5% EOI (ml)	6.4 ± 1.6	—	
Volume of 1% polidocanol (ml)	11.9 ± 4.9	17.7 ± 9.1	< .02
Eradication *			
Complete/Incomplete	26/2	29/2	NS
Complications			
Retrosternal pain	8 (28.6%)	8 (25.8%)	NS
pyrexia (> 38°C)	6 (21.4%)	5 (16.1%)	

Data are expressed as mean ± SD * Evaluated endoscopically 3 months after primary treatment

ESL, endoscopic scleroligation; EVL, endoscopic variceal ligation; extraEIS, extravariceal injection sclerotherapy; EOI, ethanolamine oleate with iopamidol

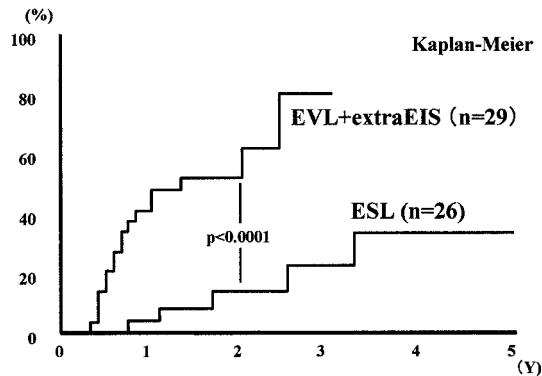


Fig. 1 Cumulative recurrence rate after complete eradication of esophageal varices
ESL, endoscopic scleroligation; EVL, endoscopic variceal ligation; extraEIS, extravariceal injection sclerotherapy.

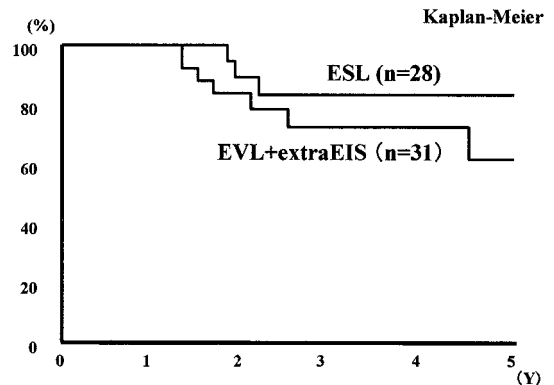


Fig. 2 Cumulative survival rate after primary treatment
ESL, endoscopic scleroligation; EVL, endoscopic variceal ligation; extraEIS, extravariceal injection sclerotherapy.

Esophageal varices recurred in 17 patients in the EVL + extraEIS group. Endoscopic examination at the time of recurrence revealed F 1 RC (+) varices in 12 patients, F 1 RC (2+) varices in 3 patients, including the one who bled, and F 2 RC (2+) varices in 2 patients. Intramucosal venous dilatation in the lower esophagus was observed in all patients. Additional treatment by EVL followed by extraEIS was performed in 11 of these patients, and extraEIS was performed in 6 patients.

Based on Kaplan-Meier analysis, the 1- and 3-year cumulative survival rates were 100% and 83.9%, respectively, in the ESL group and 100% and 73.1%,

respectively, in the EVL + extraEIS group (Fig. 2). The difference in the overall survival rate between the two groups was not significant. No deaths related to upper gastrointestinal hemorrhage occurred in either group. Three patients in the ESL group and 7 patients in the EVL + extraEIS group died of liver failure during follow-up.

Discussion

A number of investigators have examined the efficacy of combination therapy using EVL and EIS for the treatment of esophageal varices²⁻⁴. Saeed et al.²

and Laine et al.³ compared a single treatment session using a combination of EVL and low-volume EIS with EVL alone and concluded that EVL alone is superior to combination therapy. Their EVL was performed first followed by intraEIS immediately proximal to the ligature. The limitation of this method is that only half the feeding vessels are treated because the sclerosant is injected into varix proximal to the ligature, so the distal vessels are not sclerosed.

EVL followed by EIS is intrinsically different from EIS followed by EVL, and furthermore, combination therapy using intraEIS and EVL is different from extraEIS and EVL. EVL and extraEIS both eradicate varices locally without any effect on interconnecting perforating or feeding vessels¹. In contrast, because intraEIS is performed prior to ligation in ESL, all interconnecting perforating veins and feeder vessels are obliterated. Takase et al.⁷ concluded that the obliteration of feeder vessels is essential for the prevention of recurrence. The present study supports that conclusion in that the incidence of variceal recurrence in patients treated by ESL is lower than in patients treated by EVL + extraEIS, even though both methods were equally effective initially in completely eradicating esophageal varices.

The incidences of treatment-related complications associated with ESL and EVL + extraEIS were similar, as were the survival rates. However, despite the lack of difference in survival, a high recurrence rate diminishes the quality of life. This fact alone is sufficient to recommend ESL as endoscopic treatment for esophageal varices.

In conclusion, ESL is equal to EVL + extraEIS in eradicating esophageal varices, and is associated with a lower recurrence rate. Obliteration of feeder vessels by intraEIS prior to EVL is thought to be responsible for ESL's ability to prevent variceal recurrence.

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