Chapter 30
Endoscopic Treatment of Esophageal Varices: Combination of Endoscopic Variceal Ligation and Endoscopic Injection Sclerotherapy

Manabu Yamamoto and Hiroaki Suzuki

Abstract Endoscopic variceal ligation (EVL) was developed by Stiegmann et al. and has been performed using a device that allows aspiration and ligation of varices using rubber bands (O-rings). The advantage of this mechanical therapy rests on elimination of the need for injection of the sclerosant or tissue glues and, hence, obviation of many complications known to be associated with injection therapies. EVL was introduced to Japan by the authors in 1989, and thereafter, it became the first-line procedure especially for acute variceal bleeding.

On the other hand, in our initial experience of EVL in 1989, 20 out of 23 patients with esophageal varices showed an eradication effect as high as 86.9%; however, complete eradication (F_0) could only be observed in five patients (21.7%). To obtain better results, we then performed additional endoscopic injection sclerotherapy (EIS) using 1% polidocanol, which resulted in a 100% eradication effect with 43.5% complete eradication.

We perform EVL/EIS combined therapy for the prevention of variceal bleeding, and for acute bleeding cases, we have found EVL to be superior to other hemostatic options.

In this chapter, we introduce the historic aspect of EVL as well as our technical improvements including the development of an original device.

Keywords EVL · EIS · Polidocanol · Esophageal varices · Endoscopic treatment

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K. Obara (ed.), *Clinical Investigation of Portal Hypertension*,
https://doi.org/10.1007/978-981-10-7425-7_30

30.1 Introduction

Endoscopic variceal ligation (EVL) was developed by Stiegmann et al. [1] and has been performed using a device that allows aspiration and ligation of varices using rubber bands (O-rings). The advantage of this mechanical therapy rests on elimination of the need for injection of the sclerosant or tissue glues and, hence, obviation of many complications known to be associated with injection therapies. EVL was introduced to Japan by the authors in 1989 [2] and 150 patients with esophageal varices and 20 with gastric varices had been treated by March 1995 [3].

30.2 Results of the Previous Studies

In our initial experience of EVL in 1989, 20 out of 23 patients with esophageal varices showed an eradication effect as high as 86.9%. However, our endpoint of the therapy, complete eradication (F_0) [4], could only be observed in five patients (21.7%). To obtain better results, we then performed additional endoscopic injection sclerotherapy (EIS) using 1% polidocanol, and a 100% eradication effect (become F1 or F0 after the therapy) with 43.5% complete eradication was achieved [5]. The average volume of injected 1% polidocanol was 15 mL, which was less than a quarter of the dose used for patients who were treated by EIS alone. For three patients with active bleeding during this period, quick and secure hemostasis was achieved after a single ligation onto the bleeding point. There were no complications related to EVL alone or EVL with EIS.

30.3 Procedure of EVL/EIS Combined Therapy

30.3.1 Technique

Our first-line procedure for the treatment of esophageal varices is called EVL/EIS combined therapy where EVL is performed with ELS using 1% polidocanol in the same series of treatments. However, EVL without EIS [6–8] is still performed for patients with severe complications such as hepatic failure, renal failure, and disseminated intravascular coagulation (DIC).

EVL/EIS combined therapy is performed in a manner similar to conventional EIS in a sedated patient. An overtube that allows repeated endoscope insertion and withdrawal is attached to the endoscope before the survey endoscopic examination. After the survey examination of the upper gastrointestinal tract, the overtube is gently inserted, followed by withdrawal of the endoscope. The EVL device is then mounted and the loaded endoscope is reinserted through the overtube.

In patients bleeding from esophageal varices, a careful endoscopic examination is performed to find the bleeding point. If the bleeding point is found, direct ligation

(Fig. 30.1) onto the bleeding varix will be attempted [9]. In most of the cases, a single ligation is required to obtain complete hemostasis, but additional multiple ligations are recommended to supplement its efficacy. If the bleeding point cannot be found, EVL is started from slightly cephalad to the esophagogastric junction, and all varices are ligated with the spiral ligation method (Fig. 30.2) until the variceal blood flow has decreased and complete hemostasis can be obtained [10]. Additional EVL and/or EIS should be performed within a week after the initial treatment, and it should be repeated until complete eradication is achieved. For elective and

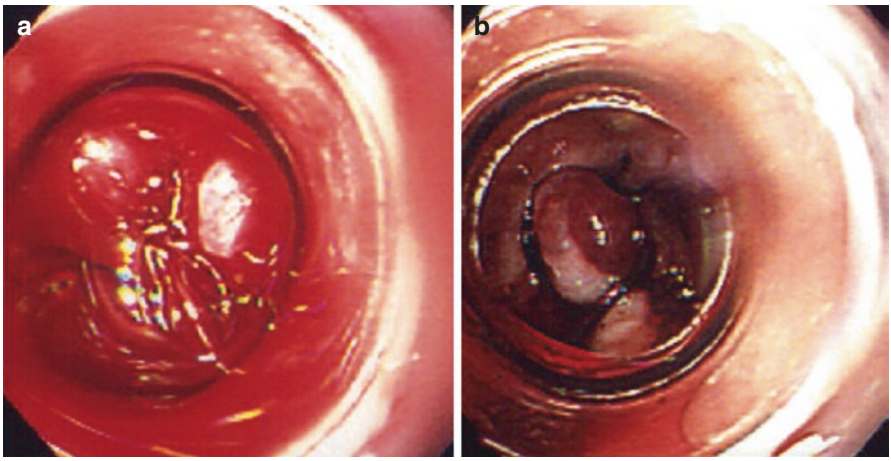

Fig. 30.1 If the bleeding point is found, place the device loaded endoscope directly onto the bleeding point and endoscopic ligation is performed. (**a**) Spurting bleeding was found through the EVL device. (**b**) Bleeding point was ligated and the complete hemostasis was obtained immediately

Fig. 30.2 If the bleeding point cannot be found, endoscopic ligation is started from slightly cephalad to the EG junction, and all varices are ligated with the spiral ligation method until the hemostatic effect is obtained

prophylactic patients, spiral ligations are performed initially. This method was developed to prevent unexpected esophageal strictures caused by healing of post-EVL ulcers [11]. In general, 2–3 individual ligations are attempted for each variceal channel up to a total of 8–12 ligations. A second session is held in a week after the initial treatment, and if there are varices larger than F_2, EVL is performed again. Such additional ligations should not be attempted near the post-EVL ulcer to prevent the severe bleeding by the ulcer tear. In our experience, additional ligation should be performed at least half an inch away from the post-EVL ulcer for the best prevention of bleeding. If the varices are smaller than F_1 or there is not enough space to add the safety ligation, EIS using 1% polidocanol is then performed. This is mainly attempted paravariceally on the distal esophagus to create the whole round ulcerations and reepithelialization of the esophageal wall. EIS is repeated every week until the complete eradication is achieved.

30.3.2 Outcomes of the Treatment

Overall outcome for 150 patients treated by EVL/EIS therapy showed 96% eradication which was as high as the eradication rate from our EIS trial (92%) [3]. From the viewpoint of the variceal form, 66 patients had F_3, 79 had F_2, and 5 had F_1 varices before the treatment. After a series of EVL/EIS therapy sessions, these statistics were improved to 6 patients with F_2, 67 with F_1, and 77 with F_0 (Fig. 30.3).

The details of the EVL/EIS therapy are as follows. EVL was performed for 180 sessions with an average of 1.2 sessions for each patient and 1530 ligations were attempted with 10.2 ligations per patient. Additional EIS was performed in a total of 285 sessions and the average number of sessions was 1.9 per patient. Altogether, 3800 mL of 1% polidocanol was injected and 25.3 mL was the average dose for each EVL/EIS session. This means the volume of injected sclerosant was decreased by a quarter from that used in EIS alone, and an average of 2.8 sessions were required to obtain the eradicating effect compared with 3.2 sessions for EIS alone. For the 17 patients who had active bleeding at the time of initial treatment, 10 direct ligations and 7 spiral ligations were performed, and 100% hemostasis was achieved [3].

There were five complications that required endoscopic treatment: two esophageal strictures (1.3%) and three post-therapeutic bleeding (2.0%). Strictures were

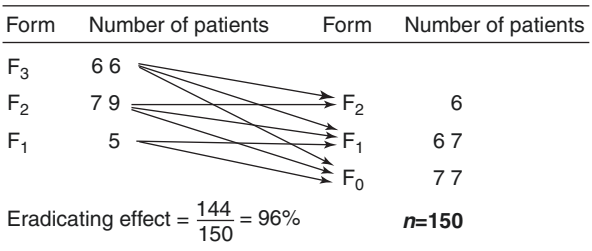

Fig. 30.3 Eradicating effect of EVL/EIS combined therapy ($n = 150$)

successfully treated by single or multiple endoscopic dilations and the bleeding was controlled by additional EIS. There were no deaths related to EVL/EIS therapy.

Recurrence of the varices was noted in 25 out of 41 patients (61%) who were followed up for more than 3 years. For such patients, additional endoscopic therapies were carried out mostly on an outpatient basis when recurrence was found. One or two sessions of low-volume EIS were required to obtain satisfactory results without any complications.

30.3.3 Improvement of the Device

EVL is very effective and easy to perform. However, we thought that the original device needed minor modifications to maximize the effectiveness of the therapy. Our problems with for the conventional device were as follows:

1. Visual field of the device attached to the endoscope is too narrow to observe the target varices and surroundings carefully.
2. Suction and/or irrigation to maintain a clear view during the treatment is limited since a trip wire occupies the endoscopic working channel.
3. The O-ring is not always released when ligation is performed in a retroflexed fashion.

To solve these problems, we first made a transparent EVL device with the cooperation of the original device manufacturer. This modification was fairly effective and the visual field of the endoscope became 70% more than the gray-colored device [12]. Then we also developed a new "pneumatic EVL device" to solve the other problems [13]. The pneumatic EVL device consists of a clear two-layer cylinder (an inner cylinder which the O-ring is stretched over and a sliding cylinder), air tube, and O-ring plate (Fig. 30.4). This device pushes the O-ring off with the sliding cylinder, which is activated by air injection, while the conventional device pulls a trip wire to move an inner cylinder toward the endoscope to release the O-ring. To load the device, the cylinder is first secured to the distal end of an endoscope followed by air tube taped over the endoscope. This allows us to keep the endoscopic working channel clear with suction and irrigation or to insert an injector needle for simultaneous EIS. By this mechanism, the O-ring can always be released even if the endoscope is fully retroflexed. Moreover, the O-ring plate eliminates complicated cylinder changing work and helps to prevent the transmission of blood-borne diseases to medical personnel. The O-ring plate has eight rubber bands and there is a preloading hole in the center of the plate to load and reload the O-rings smoothly. Prior to each O-ring loading, the device should be inserted to the preloading hole to push the sliding cylinder back to the working position. Then move the device onto the O-ring cylinder and push down vertically to complete the loading. From a questionnaire that we issued, it appeared that medical personnel appreciated this improvement very much more than we thought.

Insertion of an endoscopic overtube at the outset of the procedure facilitates withdrawal and reinsertion of the endoscope for multiple ligations and prevents unexpected aspiration of blood to the respiratory organs. However, complications related to the overtube insertion such as esophageal injury or perforations are reported [13]. To perform EVL more safely, we also developed the flexible overtube (Fig. 30.5) which is made of thinner silicon than the original one and reinforced by spiral wire like the esophageal prosthesis. The tip of a flexible tube is cut obliquely to prevent esophageal injury, and at the proximal end, anti-deflate film is placed to maintain a better visual field during the EVL. Unfortunately, the pneumatic EVL

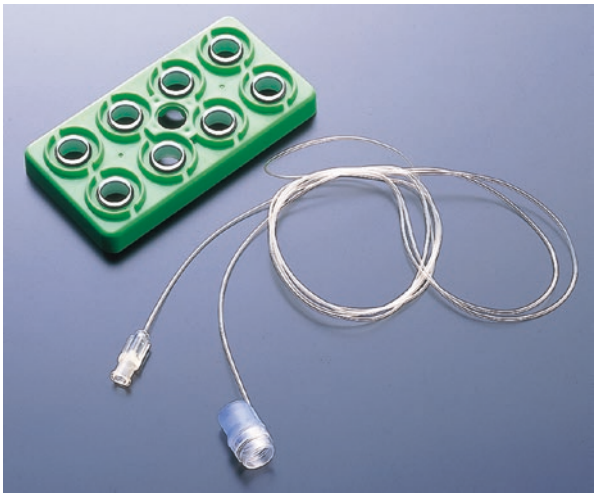

Fig. 30.4 The pneumatic EVL device consists of a friction fit clear cylinder, air tube, and syringe connector. The O-ring plate is equipped with eight rubber bands and a preloading hole in the center of the plate

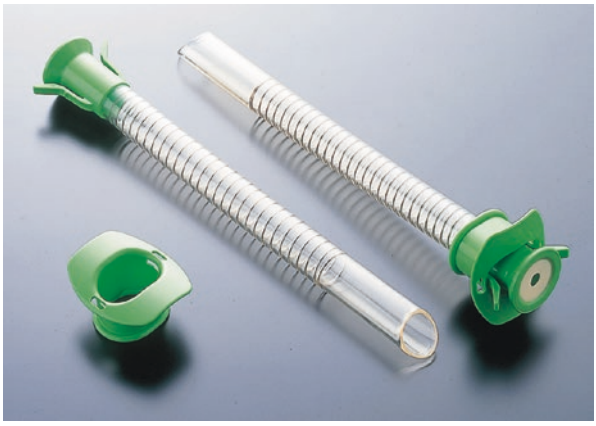

Fig. 30.5 The flexible overtube consists of a detachable mouthpiece and an overtube. The tip of the tube is obliquely cut and the soft silicon tube is reinforced by a spiral coil. Anti-deflate film is placed at the proximal end of the tube

device and the flexible overtube are currently available only in Japan due to patent issues, but we expect similar modifications will be made in each country to perform safer and easier EVL for patients suffering from variceal bleeding.

30.4 Discussion

The effects of EVL were examined experimentally using Jensen's portal hypertensive canine model by Stiegmann et al. [1]. Three to seven days following ligation of varices, slough of variceal tissue and shallow ulcerations were observed at all treatment sites. From 14 to 21 days after the treatment, there were minimal residual varices and no evidence of full-thickness esophageal injury. Sites where previously shallow ulcers had appeared were healed, and microscopic findings showed the full-thickness replacement of vascular structures in the submucosa with maturing scar tissue. An intense inflammatory response was present and reepithelialization of treated sites had occurred by the 21st day. The authors thought that the shallow ulcers produced at each ligated site resulted in little risk of bleeding and probably represented evidence of an effective treatment. Our follow-up animal study also paralleled to the results from their report [14].

Goff et al. [15] compared the patients who underwent EVL with those who underwent EIS and with untreated controls. They all had esophageal varices. Patients treated with EIS had a greater incidence of stricture formation, but esophageal manometric studies did not show persistent long-term differences among those three groups.

EVL was examined in both uncontrolled and prospective randomized studies and compared with EIS [3, 16–20]. Goff et al. [18] studied 146 consecutive nonselected patients with variceal hemorrhage who were treated by EVL for control of acute hemorrhage and were then serially treated to achieve variceal eradication. Control of active variceal hemorrhage was accomplished in 94% of 33 patients who were actively bleeding at the time of index endoscopy. Variceal obliteration was achieved in 79% of the 125 patients who remained in the trial for more than 30 days with a mean of 5.5 endoscopic treatment sessions. Recurrent hemorrhage occurred in 44% and the overall survival rate in 146 patients who entered the study was 73% at a mean follow-up of 15 months. A total of four treatment-related non-bleeding complications were observed. Data from prospective randomized trials [19, 20] support the contention that EVL is at least as effective as EIS for prevention of recurrent hemorrhage and resulted in comparable survival while inflicting a minimum risk of non-bleeding complications.

Reveille et al. [21] combined EVL with low-volume EIS and reported that combination therapy may theoretically result in more rapid variceal obliteration because of the additive effects of mechanical stasis by EVL and intimal damage by EIS. Their experience consisted of 46 patients and eradication was accomplished in 76% of

patients with a mean of 3.1 treatment sessions. The rebleeding rate was 30% with one death resulting from hemorrhage. Overall survival at 6 months was 85%. These data support the contention that the more rapid eradication may be possible with combined EVL/EIS. They concluded that further confirmation of these data is needed before solid conclusions can be drawn, and we confirmed in our uncontrolled trial that the combination therapy is superior to EVL alone [3].

30.5 Conclusion

Endoscopic treatment for esophageal varices is already an accomplished procedure, but we should be trying to improve the technique and/or develop a new procedure to obtain better results. We consider that the most important issue for the management of esophageal varices is having as many therapeutic options as we can and selecting the best therapy for each patient.

References

1. Stiegmann GV, Sun JH, Hammond WS. Results of experimental endoscopic esophageal varix ligation. Ann Surg. 1988;54:105.
2. Yamamoto M, Suzuki H, Aoki T, et al. Endoscopic variceal ligation (in Japanese). Endosc Dig. 1990;2:269.
3. Yamamoto M, Suzuki H. Efficacy of endoscopic variceal ligation for esophageal varices (in Japanese). Surgery. 1995;57:657.
4. The Japan Society for Portal Hypertension. The general rules for study of portal hypertension (in Japanese). 3rd ed. Tokyo: Kanehara & Co., Ltd.; 2013.
5. Ohnishi T, Yamamoto M, Aoki T, et al. Combination of endoscopic variceal legation and endoscopic sclerotherapy with 1% polidocanol: effect on esophageal varices (in Japanese). Prog Dig Endosc. 1991;39:157.
6. Stiegmann GV, Yamamoto M, Goff JS, Reveille RM. Technique and current results of endoscopic of variceal ligation. Prog Dig Endosc. 1991;39:11.
7. Stiegmann GV, Yamamoto M. Approaches to the endoscopic treatment of esophageal varices. World J Surg. 1992;16:1034.
8. Yamamoto M, Stiegmann GV. Current status of band ligation for esophageal varices. Probl Gen Surg. 1992;9:477.
9. Stiegmann GV, Yamamoto M. Endoscopic techniques for the management of active variceal bleeding. Gastrointest Endosc Clin N Am. 1992;2:59.
10. Yamamoto M, Suzuki H. Technique and current results of endoscopic variceal ligation (in Japanese). Rinsho Geka. 1994;49:411.
11. Yamamoto M. Endoscopic variceal ligation. Phys J. 1992;1:66.
12. Yamamoto M, Suzuki H. A technical commentary: endoscopic variceal ligation (in Japanese). Clin Gastroenterol. 1995;10:161.
13. Yamamoto M, Suzuki H. Endoscopic variceal ligation: is the procedure really safe, easy and effective (in Japanese). Endosc Dig. 1995;7:19.
14. Yamamoto M, Suzuki H. Endoscopic injection sclerotherapy for esophageal varices (in Japanese). Tokyo: Endoscopic Variceal Ligation; 1992. p. 201–8.

15. Goff JS, Reveille RM, Stiegmann GV. Endoscopic sclerotherapy versus endoscopic variceal ligation: esophageal symptoms, complications and motility. Am J Gastroenterol. 1988;83:1240.
16. Hall RJ, Lilly JR, Stiegmann GV. Endoscopic esophageal varix ligation: technique and preliminary results in children. J Pediatr Surg. 1988;23:1222.
17. Saeed Z, Michaletz P, Winchester C, et al. Endoscopic variceal ligation in patients who have failed sclerotherapy. Gastrointest Endosc. 1990;36:572–4.
18. Goff JS, Reveille RM, Sun JH, Stiegmann GV. Three years experience with endoscopic variceal ligation (EVL) for treatment of bleeding varices. Endoscopy. 1992;24:401.
19. Stiegmann GV, Goff JS, Michaletz-Onody PA, et al. Endoscopic sclerotherapy as compared with endoscopic ligation for bleeding esophageal varices. N Engl J Med. 1992;326:1527.
20. El-Newihi H, Migicovsky B, Laine L. A prospective randomized comparison of sclerotherapy and ligation for the treatment of bleeding esophageal varices (abstract). Gastroenterology. 1991;100:A59.
21. Reveille RM, Goff JS, Stiegmann GV, Stauffer JT. Combination endoscopic variceal ligation (EVL) and low volume sclerotherapy (ES) for bleeding esophageal varices: a faster route to variceal eradication (abstract). Gastrointest Endosc. 1991;37:243.