

Endoscopic Variceal Ligation Compared with Sclerotherapy for Treatment of Bleeding Esophageal Varices in Decompensated Cirrhosis- A Single Center Experience

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Abstract

Objectives: Acute variceal bleeding is a catastrophic complication of liver cirrhosis. We aim to compare the efficacy of endoscopic variceal band ligation (EVL) and endoscopic injection sclerotherapy (EIS), the two most commonly used procedures used for therapy of variceal hemorrhage.

Materials and Methods: We conducted a retrospective analysis from hospital records in 111 patients in EVL arm and 103 patients in EIS arm. Primary endpoints of the study were incidence of rebleeding and death. Secondary endpoints were adverse effects of EVL and EIS, variceal eradication and variceal recurrence after eradication.

Results: The initial hemostat rate was similar in both groups (EVL, 94.6%; EIS, 96.1%). However, the EVL group required fewer mean sessions to eradicate varices (4.4 ± 1.6 vs. 5.8 ± 2.1), fewer blood transfusions, lower rates of rebleeding (14.4% vs. 26.2%), lower mortality (7.2% vs. 13.6%) and higher variceal eradication after 12 months follow-up (86% vs. 73%) compared to the EIS group.

Conclusion: EVL scored over EIS in terms of efficacy, complications, and mortality. The probability of patients remaining bleed-free was higher ($p < 0.01$) in the EVL group than the EIS group. Hence, EVL is a safer and more effective option than EIS for initial and long-term control of bleeding.

Keywords: Cirrhosis; Endoscopic Variceal Ligation; Endoscopic Sclerotherapy; Variceal Bleed

Abbreviations

EVL: Endoscopic Variceal Band Ligation; EIS: Endoscopic Sclerotherapy; UGIB: Upper Gastrointestinal Bleeding; HVPG: Hepatic Venous Pressure Gradient; EV: Esophageal Varices; TIPS: Transjugular Intrahepatic Portosystemic Shunt; ESL: Endoscopic Scleroligation

Introduction

Liver cirrhosis is a chronic, progressive, and irreversible disease resulting in portal hypertension, defined as hepatic sinusoidal pressure ≥ 6 mm Hg. One of the major complications of portal hypertension is formation of varices at the gastroesophageal junction. These varices are a major cause of upper gastrointestinal bleeding (UGIB) and represent the second most common cause of death in cirrhosis [1]. An elevated hepatic venous pressure gradient (HVPG) has the strongest correlation with rebleeding risk and mortality, with variceal bleeding occurring at HVPG > 12 mmHg [2,3]. With recent advances in technology allowing for more precise care, the mortality rate has come down. Chalasani, *et al.* reported six-week mortality to be 17.5% in a cohort of 231 patients [4]. Rebleeding in non-treated patients occurs in 47 - 84% cases with a corresponding 20 - 70% mortality rate [5].

There are several therapeutic options to control acute variceal bleeding, each with its own benefits and shortcomings. Upper gastrointestinal endoscopy is the diagnostic procedure of choice and can be combined with sclerotherapy or band ligation for the treatment of EVs. Other therapies include vasoactive drugs (vasopressin, octreotide), tamponade and transjugular intrahepatic portosystemic shunt (TIPS).

The mechanisms by which EVL and EIS achieve variceal sclerosis diverge in several ways. The effect induced by EVL is localized to the submucosa, whereas the chemical effect of EIS is deeper, reaching the perforating veins and paraesophageal collaterals. In EVL, application of bands lead to mechanical strangulation of varices causing tissue necrosis, fibrosis and hence obliteration, while the intravariceal EIS obliterates both interconnecting perforating veins and feeding veins of EVs. The efficacy of EIS has been estimated at up to 95% for treatment of active bleed but has also been associated with a higher risk of complications. By eliminating the sclerosing agent, EVL carries a lower rate of complication.

However, there's significant cost difference between EVL and EIS which becomes a major consideration during treatment especially in resource constrained regions.

Aim of the Study

The current retrospective study aims to compare the efficacy of these two commonly used approaches.

Materials and Methods

Patients

We conducted a retrospective cohort study in adult cirrhotic patients presenting with UGIB who underwent endoscopy within 24 hours of presentation. Patients referred to our center after EIS or EVL treatment were also included in the study. We excluded patients presenting with non-variceal bleed, taking vasoactive drugs, and who did not achieve hemostasis after initial EVL/EIS or underwent surgical treatment for portal hypertension. Informed consent was taken from all participants in the study. Patients received EVL or EIS as per the discretion of the endoscopist. Data records from 273 patients strictly within the inclusion criteria were included as part of the study. After UGIE, ten patients with non-variceal bleeding, three patients with surgical treatment and forty six patients (20 after EVL; 26 after EIS) whose active bleeding did not stop after index treatment were excluded. Thus, 214 patients available for evaluation, 111 in the EVL arm and 103 in EIS arm, were analysed as per intention-to-treat analysis.

Endpoints

Primary endpoints of the study were rebleeding and death. Secondary endpoints were adverse effects of EVL and EIS, variceal eradication and variceal recurrence after eradication with EVL or EIS.

Statistical analysis

All data was expressed as mean ± standard deviation. Significance of data was established using the Chi-square test or the Student t test. In all tests, p-value was established as 0.05.

Results and Discussion

Out of 273 patients, 214 patients were included in final analysis with 111 in the EVL arm and 103 in EIS arm. The patient characteristics of the two groups are compared in table 1.

Patient characteristics	Group 1: EVL (n = 111)	Group 2: EIS (n = 103)
Age (years)	43.7 ± 14.3	40.9 ± 13.9
Gender (M:F)	76:35 (68.5%:31.5%)	78:25 (75.7%: 24.3%)
Previous treatment EVL	8 (7.2%)	11 (10.7%)
EIS	2 (1.8%)	5 (4.8%)
Hepatitis C infection	21 (18.9%)	17 (16.5%)
Hepatitis B infection	28 (25.2%)	19 (18.4%)
Alcohol consumption	62 (55.8%)	67 (65%)

Table 1: Comparison of patient characteristics between endoscopic variceal ligation (EVL) and endoscopic injection sclerotherapy (EIS) groups.

Index endoscopy, which was done as emergency procedure, served as both a diagnostic tool and a therapeutic modality. The comparative data of endoscopic findings of the two groups has been shown in table 2. After index endoscopy, patients were treated endoscopically with either of the two procedures. Initial hemostat rate was defined as no evidence of bleeding for 72 hours post-endoscopic treatment and was similar in both groups viz 94.6% in EVL group and 96.1% in EIS group. The requirement of blood transfusions was also higher in the EIS group as compared to EVL during the course of treatment and follow-up (2.1 ± 1.3, 1.4 ± 1.1, p < 0.05).

	Group 1 (EVL) n = 111	Group 2 (EIS) n = 103
Grading of esophageal varices		
Grade 2	4	39
Columns 1/2/3	0/4/0	4/24/11
Grade 3	91	50
Columns 1/2/3	11/28/52	4/20/26
Grade 4	16	14
Columns 1/2/3	0/3/13	0/4/10
Evidence of gastropathy	25 (22.5%)	7 (6.8%)
Gastric varices (GVs)	17 (15.3%)	8 (7.7%)
Gastric mucosal abnormalities	1 (0.9%)	2 (1.9%)
Duodenal bulb deformity	0 (0.0%)	1 (0.97%)

Table 2: Comparison of findings of index endoscopy between endoscopic variceal ligation (EVL) and endoscopic injection sclerotherapy (EIS) groups.

Patients were scheduled for follow-up endoscopy and repeat procedure as needed every 3 weeks. Mean follow-up period for EVL group was 4.8 ± 2.1 weeks as compared to 7.2 ± 2.4 weeks in EIS group.

In the EVL group, variceal eradication was achieved in 96/111 patients (86.5%), while treatment failed in 7/111 (6.3%) patients and 8/111 patients (7.2%) died during the course of treatment. On the other hand, in the EIS group, eradication was achieved in 76/103 patients (73.8%), while treatment failed in 13/103 (12.6%) patients and another 14/103 (13.6%) died during the course of the study. The mean number of sessions required to eradicate varices was less in the EVL group as compared to the EIS group (4.4 ± 1.6 vs. 5.8 ± 2.1). In general, 1.4 ± 0.5 more sessions were necessary in the EIS group compared with the EVL group ($p < 0.05$). The overall success rate of EVL to eradicate varices was significantly higher than the EIS group ($p < 0.05$). In the EVL group, 96 patients that achieved eradication were followed up to verify recurrence. Variceal recurrence occurred in 21/96 (21.9%), 17 of which were subjected to EVL again and rest 4 underwent EIS, all according to patient characteristics and consent. In the EIS group, 18/76 (23.7%) showed recurrence, and were treated again with EIS in 10 and EVL in 8 patients. There was not any significant difference in recurrence rate between patients in the EVL and EIS arm. Whether or not a patient experienced rebleeding was considered an important indicator of the procedures' efficacy. The rate of rebleeding was significantly higher among patients treated with EIS (26.2%) than those who underwent EVL (14.4%) ($p < 0.05$). The main source of rebleeding was recognized as esophageal varices (EVs) in both the groups (81.5% in EIS and 81.2% in EVL group). Other sources of rebleeding including GVs, treatment-induced ulcers and portal gastropathy, were limited in both groups. Major and minor complications were also significantly higher in patients treated with EIS as charted in table 3.

	EVL (Group 1) n = 111	EIS (Group 2) n = 103
Rebleeding during treatment or follow up	16 (14.4%)	27 (26.2%)
Esophageal varices (EVs)	13	22
Gastric varices (GVs)	2	3
Treatment induced ulcer	0	1
Portal gastropathy	1	1
Major complications		
Large ulcer	2 (1.8%)	4 (3.9%)
Stricture	0 (0.0%)	1 (0.97%)
Esophageal erosions	1 (0.9%)	0 (0.0%)
Congestive gastropathy	1 (0.9%)	1 (0.97%)
Minor complications		
Retrosternal discomfort	3 (2.7%)	4 (3.9%)
Transient fever	1 (0.9%)	3 (2.9%)
Dysphagia/Odynophagia	3 (2.7%)	5 (4.8%)
Disappearance of GVs after EVs treatment	12/17 (70.6%)	6/8 (75%)

Table 3: Comparison of complications between endoscopic variceal ligation (EVL) and endoscopic injection sclerotherapy (EIS) groups.

Endoscopic variceal band ligation (EVL) was first described by Stiegmann, *et al.* in 1986 and is now considered the gold standard intervention for EV [6]. It is highly effective in achieving immediate hemostasis and decreases subsequent rebleeding [7]. Endoscopic injection sclerotherapy (EIS) is a procedure which predates EVL but has slowly fallen out of favor. However, it still remains a widely used technique in resource constrained regions due to its simplicity, cost-effectiveness and efficiency. Apart from endoscopic therapies, there have been a number of surgical procedures developed to manage EVs, including shunting and non-shunting procedures. A variety of newer techniques

have also been developed in recent years, some of them following alternate regimens of EVL and EIS, and some using combinations of endoscopic treatment and interventional radiology. These methods, though not very widely studied, have been shown to reduce long-term rates of rebleeding and retreatment in patients with EV. Another technique called endoscopic scleroligation (ESL) has been introduced, a method in which intravariceal EIS is performed before ligation. New modalities such as this one has exacerbated the existing controversy surrounding the choice of therapy for bleeding varices. We conducted this retrospective study with the goal of comparing endoscopic variceal ligation and sclerotherapy for management of acute variceal bleeding. We followed patients to study the success of endoscopic treatments and monitor for possible complications. Similar to prior studies, the initial hemostat rate was not significantly different between the EVL (94%) and EIS (96%) groups, indicating the significant immediate benefit from both the procedures [7,8]. Eradication, which was defined as disappearance of varices or decrease to grade 1 when bands could no longer be applied, was achieved with serial endoscopic treatment sessions and avoidance of alcohol during the treatment period. The mean number of sessions required to eradicate varices was significantly lower with EVL than EIS, which is consistent with the earlier reports [8,9].

Our EIS group showed significantly higher rebleeding during one-year follow-up when compared with the EVL group, thus contradicting a few reports of higher recurrence after EVL [10]. Also, our analysis revealed that most rebleeding was caused by recurrence of EVs, and less often by other sources like GVs, treatment-induced ulcers and portal gastropathy. The sharp difference in rebleeding rate in favor of EVL is mainly due to the smaller sessions required for treatment, which reduces the vulnerable phase of endoscopic treatments [11]. Our study demonstrated trend towards higher incidences of rebleeding and both major and minor complications after EIS as compared to EVL as demonstrated in table 3. This is in accordance with previous study by Ali, *et al.* which demonstrated significantly higher incidence of fever after EIS as compared to EST. Also, they found trend towards higher incidence of retrosternal pain, nausea and vomiting in the EIS group [9].

Sclerotherapy has been associated with a variety of significant local and systemic complications, in particular esophageal ulceration and stricture formation [12,13]. The number of patients who developed esophageal stricture (n = 1) and large ulcers (n = 4) in our EIS group is lower than reported in other studies [14]. This relatively low incidence of stricture may be due to the fixed small volume of sclerosant used at each session, postponing of sessions when ulcers were encountered, and routine use of pantoprazole after each procedure. In EVL group, on the other hand, there were only 2 cases of large ulcers and no stricture formation. There were no major complications in either arm, or no significant difference was observed between the two groups with respect to minor complications.

A review of the literature showed a higher incidence of death associated with EIS than with EVL [10,12,14]. In the present study, mortality was also significantly higher in the EIS group than in the EVL group. Of note, the actual cause of death varied between groups. Most of the mortality in the EIS cohort was attributable to rebleeding and its associated complications (82%, n = 14), while in the EVL cohort, progressive liver failure (62%, n = 5) was the leading cause of death, followed distantly by rebleeding (37%, n = 3). This finding is in perfect accordance with an earlier report by Stiegmann, *et al* [15]. Major complications like large ulcers and strictures in the EIS group had no direct influence on mortality.

There's considerable cost difference between EVL and EIS which may influence availability of the procedures in certain constrained regions. The cost of a ligation device with six elastic bands was estimated to be around \$400.00 which was significantly higher to a sclerosis needle and substance. The average cost of EVL and EIS per session is estimated to be around \$120 and \$65 respectively in northern India.

Conclusion

Our results support the previous randomized controlled trials that compared ligation and sclerotherapy in the management of acute variceal bleeding in adults. Although both techniques were equally effective for the initial arrest of active variceal bleeding, EVL demonstrated significant advantages over EIS in terms of efficacy and safety. However, given cost difference and resource availability, sclerother-

apy could be considered as a possible alternative treatment for variceal upper gastrointestinal bleeding in resource constrained regions with limited financial and technical abilities.

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