

Management of acute esophageal variceal bleeding by endoscopic sclerotherapy in technically difficult endoscopic band ligation cases—A population based cohort study

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ABSTRACT

Endoscopic band ligation is regarded as the main therapeutic option for acute esophageal variceal bleeding, while sclerotherapy may be used in the acute setting if ligation is technically difficult. The incidence of difficult-to-perform band ligation in acute esophageal variceal bleeding, as well as the outcome of patients subjected to injection sclerotherapy as an alternative treatment, has not been clearly investigated. Our aim is to study the outcome of patients subjected to injection sclerotherapy in the acute setting of esophageal variceal bleeding when endoscopic band ligation is technically difficult to perform. We included 151 patients with acute esophageal variceal bleeding originating from medium or large sized varices. All patients were planned for EBL as the 1st treatment option (EBL group 61.6%), meanwhile, EIS using 5% ethanolamine oleate was reserved as the 2nd treatment option when EBL was technically difficult (EIS group 38.4%). The mean time to restore hemodynamic stability was significantly prolonged in the EIS group (11.5 ± 6.5 hrs versus 9.5 ± 5.0 hrs, $p = 0.05$). Initial control of bleeding was significantly higher in the EBL group versus the EIS group (96.7% vs 84.5%, $p = 0.021$). Re-bleeding was more among the EIS group (42.9% vs 24.2%, $p = 0.04$). There were no significant differences as regarding mortality and duration of hospital stay. So, a considerable proportion of cases presenting with acute variceal bleeding will have difficulty in performing EBL. In these patients, sclerotherapy is not a waning procedure with an accepted success rate, without much additional complications and without deranging mortality.

Keywords: Esophageal Varices; Band Ligation; Injection Sclerotherapy

1. INTRODUCTION

The management of acute variceal bleeding remains a clinical challenge. Regarding the best endoscopic therapeutic option, a meta-analysis of 10 randomized controlled trials including 404 patients showed an almost significant benefit of endoscopic band ligation in the initial control of bleeding compared to sclerotherapy [1]. At the same time, Baveno IV and V consensuses had repeatedly confirmed that ligation is the recommended method of endoscopic therapy for acute esophageal variceal bleeding although sclerotherapy may be used in the acute setting if ligation is technically difficult [2,3].

The incidence of difficulty to perform band ligation in acute esophageal variceal bleeding, as well as the outcome of patients subjected to injection sclerotherapy as an alternative treatment, has not been clearly investigated.

2. AIM OF THE WORK

Our aim is to study the outcome of patients subjected to injection sclerotherapy in the setting of acute esophageal variceal bleeding in case of technical difficulty to perform band ligation.

3. PATIENTS AND METHODS

This study was approved by the Hepatogastroenterology Department and the Research Board of Cairo University. It included 151 patients with acute bleeding from esophageal varices originating from medium and large sized varices. They were admitted to Gastroenterology unit of

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Air force Hospital, Cairo; during the period from 15 January 2010 till 15 July same year. Patients with bleeding gastric varices, bleeding small sized oesophageal varices, bleeding portal hypertensive gastropathy, hepatic coma or hepatocellular carcinoma were not included in the study.

Patients were resuscitated after relevant history taking and clinical examination. Stabilization of hemodynamics was firstly performed. Blood transfusion was initiated depending upon the severity of bleeding and hemodynamic status with a transfusion target hematocrit of 24% and/or hemoglobin of 8 g/dl. I.V antibiotics were routinely given. Octreotide was started whenever indicated in a dose of 50 µg IV bolus, followed by continuous infusion 50 µg/hr for 2 - 5 days. Further assessment was done including laboratory investigations and abdominal ultrasonography. The severity of bleeding was considered as: mild when pulse rate <100/min, orthostatic hypotension or cold extremities, moderate when pulse rate 100 - 120 beats/min with restlessness or severe when pulse rate >120 beats/min, systolic blood pressure <60 mmHg, severe pallor or oliguria [4]. Endoscopy session was scheduled once the patient's hemodynamics permitted after an informed and written consent. Emergency endotherapy was performed by a single endoscopist, all patients were planned for endoscopic band ligation (EBL) using the Saeed multi-band ligators manufactured by the Wilson-Cook Medical GI endoscopy company as the 1st treatment option to control the acute bleeding episode (EBL group) (**Figure 1**), meanwhile, endoscopic injection sclerotherapy (EIS) using ethanolamine oleate was reserved as a 2nd treatment option when EBL was technically difficult (only when the view of the bleeding source was obscured) (sclerotherapy group) (**Figure 2**).

Varices were assigned grades according to their shape and size: grade F1, small straight veins; grade F2,

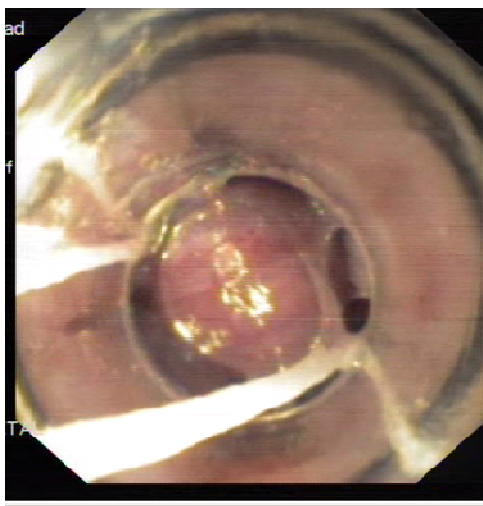


Figure 1. EVL to bleeding varices.

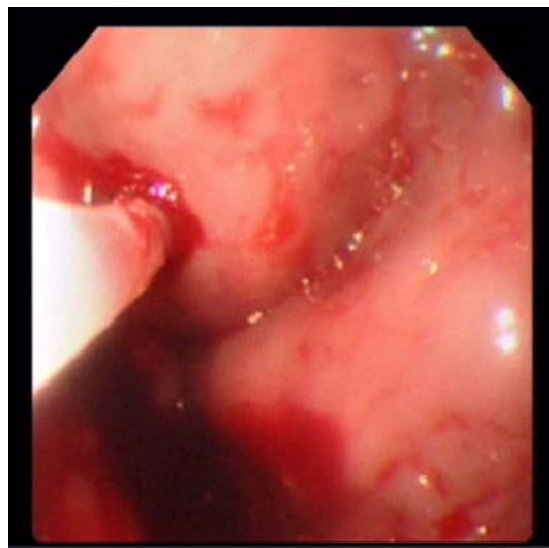


Figure 2. Sclerotherapy for bleeding varices.

slightly enlarged tortuous veins occupying less than one-third of the esophageal lumen; and grade F3, large coil-shaped varices that occupied more than one-third of the esophageal lumen [5].

The assessment for treatment side-effects was performed during hospital stay and included monitoring of symptoms, physical examination and laboratory data. Complications were defined as untoward events related to treatment and require active therapy or prolonged hospitalization. All available patients in both groups were followed up for 42 days for clinical assessment, variceal re-bleeding, and hepatic de-compensation. Failure to control active bleeding was considered according to the UK guidelines [6] as transfusion requirement of 4 units or more and inability to achieve an increase in systolic blood pressure by 20 mm Hg or to 70 mm Hg or more, and/or inability to achieve a pulse rate reduction to less than 100 beat/min or a reduction of 20 beat/min from baseline pulse rate (within the first six hours). Or the occurrence of haematemesis from the six hour point, reduction in blood pressure of more than 20 mm Hg from the six hour point and/or increase in pulse rate of more than 20 beat/min from the six hour point on two consecutive readings an hour apart, transfusion of 2 units of blood or more (over and above the previous transfusions) required to increase the haematocrit to above 27%, or haemoglobin to above 9 g/l. Re-bleeding: was considered as the occurrence of new haematemesis or melena after a period of 24 hours or more of stable vital signs and haematocrit/hemoglobin following an episode of acute bleeding up to 42 days from the acute bleeding episode. Stoppage of bleeding: is considered when there is no haematemesis, stable hemoglobin concentration without blood transfusions, stable hemodynamic conditions at the beginning of the first 24-hour interval from time zero [2].

Patients' data were tabulated and processed using SPSS (10.0) statistical package. Quantitative variables were expressed by means and standard deviation. While qualitative data were expressed by frequency and percent. Qualitative variables were analyzed using Chi-square or Fisher's exact test when appropriate. Quantitative variables were analyzed using student's T-test or Friedman's test when appropriate. In all tests p value was significant when <0.05 .

4. RESULTS

This study included 151 patients with acute esophageal variceal bleeding. They were sub-grouped based on the type of endoscopic intervention into EBL (band ligation) group (93 patients 61.6%) and EIS (sclerotherapy group) (58 patients 38.4%).

The majority of patients in the EBL group had a mild bleeding episode (64.5%) versus none in the sclerotherapy group. While the majority of those in the sclerotherapy group had a moderate bleeding episode (67.2%, p 0.38). Time from admission to patient stabilization was significantly prolonged in the EIS group 11.5 ± 6.5 hrs

versus 9.5 ± 5.0 hrs (p 0.05) (**Table 1**). The post endoscopy outcome is demonstrated in (**Table 2**).

5. DISCUSSION

Bleeding from esophageal varices is a life-threatening complication of portal hypertension which accounts for most of cirrhosis-related mortalities [7,8]. Endoscopic therapy is an integral component of the management of acute variceal bleeding as well as prevention of recurrent bleeding [8,9]. Since it first evolved as a new therapeutic option, EBL has been regarded as a more effective modality than endoscopic injection sclerotherapy in the control of acute hemorrhage with less reported adverse events [10-12]. On the other hand, some studies still advocate the use of sclerotherapy as a better treatment option up to regarding it as the gold-standard treatment [13,14].

Despite the routine standard of care given to patients presenting with hematemesis such as pharmacotherapy and gastric lavage, still up to one third of cases are actively bleeding during endoscopy, and it is this group of patients that poses a challenge to endoscopists and en-

Table 1. Base-line characteristics of EIS and EVL groups.

Parameters	EVL group N: 93 (61.6%)		EIS Group N: 58 (38.4%)		p
	No/%	Mean/SD	No/%	Mean/SD	
Age (years)	52	± 3	53	± 3	0.89
Sex					
Male	52	56%	42	72.5%	0.33
Female	41	44%	16	27.5%	
Previous bleeding attacks	48	51.6%	33	56.9%	0.63
Child Pugh class:					
A	9	9.7%	4	6.9%	0.057
B	37	39.8%	25	43.1%	
C	47	50.5%	29	50%	
Grade of varices					
Grade F2	48	51.6%	28	48.2%	0.85
Grade F3	45	48%	30	51.7%	
Hemodynamic instability	81	87.1%	53	91.4%	0.53
Severity of bleeding					
Mild	60	64.5%	0	0%	<0.01
Moderate	24	25.8%	39	67.2%	
Severe	9	9.7%	19	32.8%	
Time from admission to endoscopy (hrs)	9.5	± 5	11.5	± 6.5	0.05

Table 2. Post-endoscopy outcome in both groups.

Parameters	EVL group N: 93 (61.6%)		EIS Group N: 58 (38.4%)		p
	No/%	Mean/SD	No/%	Mean/SD	
Control of acute bleeding	90	96.7%	49	84.5%	0.021
Re-bleeding	22	24.2%	21	42.9%	0.04
Control of re-bleeding	17/22	77.35	11/19	57.9%	0.23
Incidence of complications among different child-Pugh cases					
Child A	1	1.1%	2	3.4%	
Child B	8	8.6%	14	24.1%	0.079
Child C	6	6.4%	13	22.4%	
Bacterial peritonitis	6	6.4%	11	19%	0.01
Aspiration pneumonia	0	0%	1	1.7%	0.41
Sepsis	1	1.1%	2	3.4%	0.065
Bleeding esophageal ulcer	1	1.1%	2	3.4%	0.065
Chest pain	2	2.2%	5	8.6%	0.01
Fever	1	1.1%	2	3.4%	0.065
Transient arrhythmias	1	1.1%	1	1.7%	0.1
Nausea	1	1.1%	2	3.4%	0.068
Transient dysphagia	2	2.2%	3	5.2%	0.012
Mean hemoglobin (gm/dl)					
Day 1	8.6	±0.34	8.1	±0.36	0.18
Day 5	8.8	±0.34	8.4	±0.31	0.45
Units of packed RBCs	3.1	±1.07	4.1	±1.2	0.01
Hospital stay in days	8.3	±1.9	9.1	±2.6	0.27
Total Mortality	19	20.4%	21	36.2%	0.19

dangers the life of the patient as it has been found to have a negative impact on survival [7,15,16]. In this situation banding may be technically difficult to perform in the presence of continued bleeding, and sclerotherapy may then be necessary [2,3,9,17]. So this means that, whether endoscopists fall for band ligation or sclerotherapy as the preferred treatment, the set up of an emergency endoscopic unit should be equipped with both and the endoscopists should be ready to switch between the 2 modalities.

How frequent is this situation encountered, what is the outcome and what are the sequaele, remained to be investigated. This was the rationale to conduct this study. It was carried in the Air Force hospital on 151 patients with acute variceal bleeding. All included patients had acute esophageal variceal bleeding from medium or large sized varices, while other portal hypertensive bleeding sources

were not included. To ensure homogeneity among these patients, they were all given the same standards of care such as gastric lavage and pharmacotherapy with octerotide and judicious volume expanders. All of them underwent endoscopy whenever they reached hemodynamic stability irrespective of time and all were endoscoped by a single operator. The plan at the time of endoscopy was to perform band ligation as a primary treatment option unless profuse bleeding was encountered to the extent of posing technical difficulty in visualizing and banding the bleeding varix, in the latter condition, switch to sclerotherapy was done.

The studied cases in both groups were comparable in terms of their demographic features. All patients had received pharmacotherapy by octerotide and yet, 38.4% of the studied cases were actively bleeding at endoscopy, profusely enough, to change the decision of treatment

from band ligation to sclerotherapy. Terblanche *et al.* [16], stated that one third of cases are actively bleeding at the time of endoscopy, this finding was made before the advent of octreotide as a recommended treatment. In our study although octreotide was given, still a subset of patients similar to those reported by Terblanche were bleeding profusely at the time of endoscopy (38%). Actually the therapeutic effects of octreotide on the portal and systemic hemodynamics in patients with liver cirrhosis have yielded conflicting results, while some authors showed beneficial effects on the portal hemodynamics, others failed to show any beneficial effects. In an interesting study, Baik *et al.* [18] demonstrated that in patients with acute variceal bleeding, the main effect of octreotide on the HVPG was during the first minute after therapy, whereas thereafter the effect is not sustained and soon the HVPG reverts to base line after 5 mins of therapy. This might explain why patients were still bleeding during endoscopy.

The profuse bleeding at the time of endoscopy (as represented in the sclerotherapy group) was not influenced by the severity of liver disease (as both groups were comparable regarding Child-Pugh class), nor by the grade of varices at the time of endoscopy probably because bleeding might have temporarily reduced variceal size during endoscopy.

All patients underwent endoscopy after attaining hemodynamic stability, and yet the majority of these patients were hemodynamically unstable at the time of presentation (87.1% in the EBL group and 91.4% in the sclerotherapy group), this emphasizes the role of the pre-endoscopic standards of care given to the patients like volume restitution and maintaining the aerobic metabolism by restoring an appropriate delivery of oxygen to the tissues (which depends on oxygen saturation, cardiac output, and hemoglobin concentration) [19]. This also explains why the sclerotherapy group underwent endoscopy after a significantly longer time than the EBL group (9.5 ± 5 hrs in the EBL group versus 11.5 ± 6.5 hrs in the sclerotherapy group) and had a significantly more amount of transfused packed RBCs as compared to the EBL group (4.1 ± 1.2 , versus 3.1 ± 1.07 ; $p 0.01$).

The next point to highlight in this study is the outcome of patients following the emergency endoscopy, it is clear that rapid switching from conventional EBL to sclerotherapy in our patients saved the time that could have been spent over getting a clear view so as to perform EBL, which of course could have endangered the patients' lives. That is why there were no reported differences in the mortalities between the 2 groups nor the duration of hospital stay. However, some of the unfavorable outcomes were significantly reported among the sclerotherapy than the EBL groups. The initial success to control bleeding for both techniques is compatible with

the universally reported figures (around 90%) [20]. However, it was significantly higher in the EBL versus EIS groups (96.7% versus 84.5%; $p 0.02$). Also, bleeding recurrence was significantly less in the EBL versus the EIS groups (24.2% versus 42.9%; $p 0.04$). Lo *et al.* [7], reported 17% rate of re-bleeding with EBL vs. 33% with EIS, Villanueva *et al.* [11], reported 12% incidence rate for re-bleeding for EBL versus 21% for EIS. Krige *et al.* [14], reported that even under optimal conditions, currently available treatment options fail to control initial variceal bleeding or prevent early re-bleeding in up to 20% of patients. The overall analysis of these figures reveals that they match those reported by other authors. However, it is important to emphasize that these studies were randomized and it is supposed that patients with severe bleeding were homogeneously distributed among both the EBL and EIS groups. This was not the case in this study, where the EIS group was a special grouping for those who were actively bleeding and difficult to perform EBL as explained by the significantly higher incidence of moderate and severe bleeding attacks among the EIS group. So the less success rates we encountered in this situation, where the technique might have been deranged due to the severe bleeding, is rather accepted. On the other hand, since the severity of the initial re-bleed has been one of the contributing factors to recurrent bleeding [21], this again explains why the sclerotherapy group had a higher incidence of variceal re-bleeding.

The other reported adverse events like chest pain, dysphagia and bacterial peritonitis were significantly higher in the EIS than the EBL group. These can be attributed mainly to the type of the technique and to a less extent to the severity of bleeding. Randomized trials that compared EBL to sclerotherapy have yielded similar findings, without essentially having difference in the severity of bleeding between both arms. Most of these studies have reported that EBL is generally a safer technique than EIS because it involves a mechanical, less invasive method of variceal obliteration with less systemic and local complications involving the esophageal wall [7,11,22-29]. For example our data of peritonitis were 19% with EIS versus 6.4% with EBL ($p 0.01$). This matches with Laine *et al.* [24], who reported 18% incidence rate of peritonitis in EIS vs. 15.8% in EBL.

6. CONCLUSION

About one third of cases presenting with acute variceal bleeding will have difficult-to-perform EBL due to the severity of active bleeding at the time of endoscopy. In these patients, sclerotherapy is not a waning procedure and is still a technique that can be resorted to with an accepted success rate, without additional complications and without deranging mortality.

7. ACKNOWLEDGEMENTS

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