

Outcome of band ligation in oesophageal varices

Amanullah Abbasi,¹ Abdul Rabb Bhutto,² Khalid Iqbal Bhatti,³ Khalid Mahmood,⁴ Keshav Lal⁵

Abstract

Objective: To find out the outcome of band ligation of oesophageal varices in decompensated chronic liver disease patients.

Methods: The quasi experimental study was conducted at the Jinnah Postgraduate Medical Centre, Karachi, and Civil Hospital, Karachi, unit from September 2007 to August 2011. Subjects were eligible if they had a diagnosis of cirrhosis based on history, physical examination, biochemical parameters and liver biopsy in some cases. Patients with advanced cirrhosis (Child-Pugh class C), antibodies against human immunodeficiency virus, hepatocellular carcinoma, portal vein thrombosis evident on ultrasonography, parenteral drug addiction, current alcohol abuse, previous or current treatment with β -blockers were excluded from the study. All patients were asked about alcohol intake and tested to determine the cause of liver cirrhosis. Tests for other causes of cirrhosis were carried out only if there was a suggestive clue. All patients under-went upper gastrointestinal endoscopy after consent. SPSS 15 was used for statistical analysis.

Results: The age of the 173 patients who met the inclusion criteria ranged from 15 to 85 years, with a mean of 48.39 ± 13.38 years. There were 112 (64.7%) males. High-grade varices were seen in 130 (75.1%) patients, while low-grade varices were observed in 43 (24.9%) on first endoscopy. At initial endoscopy, 111 (64.2%) patients had portal hypertensive gastropathy. The patients were followed up for a mean period of 5.20 ± 2.67 months. Variceal obliteration was achieved in 138 (79.8%), while 33 (19.1%) cases developed re-bleeding. Mean number of endoscopy sessions for these patients were 2.28 ± 0.918 with a maximum of 4.

Conclusion: Band ligation eradicated oesophageal varices with less complications and a lower re-bleeding rate, but at the same time eradication was associated with more frequent development of portal hypertensive gastropathy.

Keywords: Oesophageal varices, Endoscopic band ligation, Portal hypertensive gastropathy. (JPMA 63: 983; 2013)

Introduction

Complications of portal hypertension rank among the top leading causes of death worldwide.¹ Bleeding from oesophagogastric varices in cirrhosis is an emergent condition with high mortality.²⁻⁴ The prevalence of oesophageal varices in patients with cirrhosis has been reported to be around 80%-90%^{5,6} and they develop into variceal haemorrhage at a rate of 10%-30% per year.⁷ Despite substantial improvements in the early diagnosis and treatment of variceal haemorrhage, the mortality from variceal haemorrhage remains high (20%-35%).⁸⁻¹⁰ The 6-week mortality with each episode of variceal haemorrhage is approximately 15% to 20%, ranging from 0% among patients with Child class A disease to approximately 30% among patients with Child class C disease.¹¹⁻¹⁴ In recent years, application of Endoscopic haemostasis has reduced the mortality rate from variceal haemorrhage.¹⁵ For pure oesophageal varices,

endoscopic variceal ligation (EVL) has achieved a good therapeutic effect.¹⁶

Endoscopic therapeutic interventions like sclerotherapy and band ligation have changed the outlook for patients with upper gastrointestinal (GI) bleeding. Sclerotherapy was the initial available modality that led to marked reduction in immediate mortality of cirrhosis due to upper GI bleeding. It is now gradually being replaced by oesophageal varices band ligation which has shown better results in terms of variceal obliteration as well as having fewer side effects like ulceration, perforation and stricture formation than sclerotherapy.¹⁷ However, with increasing use of EVL and sclerotherapy for oesophageal varices, the incidence of fundal varices has increased. In addition, studies have shown that the degree of portal hypertensive gastropathy (PHG) has also shown a worsening trend after the introduction of therapeutic endoscopic interventions for oesophageal varices.¹⁸

In view of excellent results of band ligation as far as obliteration of oesophageal varices is concerned, its effect on development of fundal varices and PHG has raised concern among endoscopists. The aim of the current study was to assess the over-all outcome of band ligation in

.....
^{1,4}Medical Unit-III, ³Department of Cardiology, Civil Hospital Karachi,
²Postgraduate Ward-7, Jinnah Postgraduate Medical Centre, Karachi, ⁵ALYA
 Hospital, Abu Dhabi, UAE.

Correspondence: Amanullah Abbasi. Email: draman_ullah2000@yahoo.com

oesophageal varices in terms of their eradication, recurrence and re-bleeding in addition to its effect on PHG.

Patients and Methods

The quasi-experimental study was conducted at the medical Unit-III of Jinnah Postgraduate Medical Centre (JPMC), Karachi, and the Gastro and Hepatology unit of Civil Hospital Karachi, from September 2007 to August 2011. Subjects were eligible if they had a diagnosis of cirrhosis based on history, clinical examination, and biochemical parameters and, in selected cases, liver biopsy with oesophageal varices presented either due to acute upper GI bleeding or for follow-up. Non-purposive convenient sampling technique was used to enrol the patients. Following detailed history and physical examination, patient's previous medical record was reviewed for aetiology of cirrhosis finding in the first endoscopy, if any, then number of endoscopies till date, and the number of band ligation sessions required for the complete disappearance/eradication of varices. All these patients underwent upper GI endoscopy after informed consent to look for the presence and degree of oesophageal varices and PHG. All endoscopies were performed in a single endoscopy unit, using an Olympus video endoscope GIF 180. The oesophageal varices size was graded as low-grade and high grade using Baveno III. For identification of PHG, Baveno III consensus statement was used.¹⁹

Variceal ligations were performed at 3-week intervals until eradication. Successful variceal eradication was defined as the absence of ligable oesophageal varices. During each session, up to 4 bands were placed beginning in the distal oesophagus using a multiband ligation device (six shooter; Wilson-Cook Inc., Winston-Salem, NC or Speedband; Boston Scientific, Inc., Natick, MA). Minor adverse events included GI discomfort (retrosternal pain or dysphagia). Severe adverse events included bleeding and death.

The primary outcome was variceal obliteration which was defined as the complete disappearance of oesophageal varices or when the sizes of oesophageal varices were too small to be ligated.²⁰ Secondary outcomes like re-bleeding, recurrence of oesophageal varices and minor or major adverse events of EVL procedure were assessed along with its effects on PHG. Recurrence of oesophageal varices was defined as re-appearance of oesophageal varices or enlargement of previous small-size varices that became accessible by EVL.²⁰ Rebleeding from oesophageal varices was defined as the presence of haematemesis and/or malena and the bleeding site was identified to be from oesophageal varices by emergency

endoscopy.²¹ Only those who had a drop in haemoglobin and needed a blood transfusion of 2 or more units were considered to be re-bleeding. When recurrent oesophageal varices or re-bleeding from oesophageal varices were encountered, repeated sessions of EVL were performed until the varices were obliterated once again. After treatment, response rate to treatment, re-bleeding rates, recurrences, effects on PHG and adverse events were evaluated and recorded on a predesigned proforma. Patients who developed re-bleeding were admitted in Intensive care unit and evaluated with diagnostic and/or therapeutic endoscopy. Adjuvant vasoactive treatment and/or blood transfusion were offered whenever needed. Patients who had not responded to EVL were managed through one of the other available treatment modalities (Endoscopic sclerotherapy, balloon tamponade or transjugular intrahepatic portosystemic shunt).

The ethical committee of the institution approved the study protocol.

Statistical analysis was performed using Statistical 15.0 Descriptive analysis was performed for demographic, clinical and radiographic features, and results were presented as mean \pm standard deviation for quantitative variables and frequencies (percentages) for qualitative variables.

Results

Initially, 192 patients who met the inclusion criteria were

Table-1: Baseline characteristics.

Variable	value
Age (years)	48.39 \pm 13.387
Sex, n (%)	
Male	112 (64.7)
Female	61 (35.3)
Aetiology, n (%)	
Hepatitis C	116 (67.1)
Hepatitis B	26 (15.0)
Hepatitis B+C	11 (6.4)
Cryptogenic	20 (11.6)
Child-Pugh Class, n (%)	
A	84 (48.6)
B	79 (45.7)
C	10 (5.8%)
Bilirubin (mg/dl)	1.457 \pm 0.741
Albumin (g/L)	3.178 \pm 0.592
Oesophageal varices	
Low grade	43 (24.9)
High grade	130 (75.1)
Portal Hypertensive Gastropathy, n (%)	111 (64.2)
Mild	88 (50.9)
Severe	23 (13.3)

Table-2: Results.

Outcomes	value
Obliteration, n (%)	138 (79.8)
Recurrence, n (%)	34/138 (24.6)
Re-bleeding, n (%)	33 (19.07)
Portal Hypertensive Gastropathy, n (%)	135/173 (78.03)
Variceal obliteration group	103/138 (74.64)
Re-bleeding group	31/33 (93.94)
Adverse events, n (%)	
Mild events	19 (10.98)
Severe events	3 (1.73)

enrolled, but 19(9.89%) were lost for various reasons (Figure). The final sample size, as such, was 173. The cumulative mean age was 48.39±13.38 years (range: 15-85), with gender-based mean age of 47.43±13.954 years for males and 50.15±12.191 years for female (Table-1).

Patients were followed up for mean period of 5.20±2.67 months. Variceal obliteration was achieved in 138(79.8%) patients, 2 (1.15%) patients had not achieved variceal eradication, rather deteriorated, and were hence, offered combination therapy, while 33 (19.1%) cases developed re-bleeding during the study period and both these type of patients were managed by other modalities or

combination therapies. The bleeding events occurred either from ligation ulcers in 12 (36.36%) patients or from recurrent varices in 21 (63.63%). Mean number of endoscopy sessions for these patients were 2.28±.918 with a maximum of 4. Mean duration since first endoscopy was 5.185 months with a maximum of 18 months. Frequency of PHG was increased from 111 (64.2%) found at initial endoscopy to 135 (78.03%) observed at the final endoscopy. Among them, 90 (66.66%) showed mild PHG whereas severe PHG was noticed in 45 (33.33%) patients.

Nineteen (10.98%) patients experienced minor adverse events like GI discomfort (retrosternal pain or dysphagia), while severe adverse events were noticed in 3 (1.73%) patients.

Discussion

Management of variceal bleeding comprises pharmacologic, endoscopic treatment or combination of the two. Endoscopic sclerotherapy and endoscopic variceal ligation (EVL) are currently practised endoscopic modalities for the treatment as well as prophylaxis of variceal bleeding.

EVL is the gold standard for the treatment of acute bleeding of oesophageal varices. Furthermore, it is also effective in secondary prophylaxis and in primary prophylaxis for patients' who are not suitable candidates for beta blocking agents.

The current study prospectively assessed the overall outcome of EVL in the eradication of oesophageal varices secondary to liver cirrhosis. During the study, 138 (78.8%) subjects achieved eradication/obliteration of varices. A study¹⁷ compared sclerotherapy and band ligation and reached the conclusion that: (i) Endoscopic sclerotherapy and EVL were equally effective in controlling acute bleed; (ii) endoscopic ligation achieved variceal obliteration faster and in fewer treatment sessions; (iii) endoscopic variceal ligation had a significantly lower rate of development of portal gastropathy and re-bleeding, (iv) while both techniques influenced gastric varices equally, there was significantly higher oesophageal variceal recurrence after EVL than sclerotherapy. Meta-analyses of 15 studies that compared EVL against sclerotherapy in the prevention of variceal rebleeding showed that EVL was associated with a lower re-bleeding rate and less frequent and severe complications than sclerotherapy²² Furthermore, the two largest and best designed randomised control trials had to be prematurely terminated because of an increased mortality in the sclerotherapy group.²² It suggested that, variceal eradication is achieved with a lower number of endoscopic sessions with EVL than with

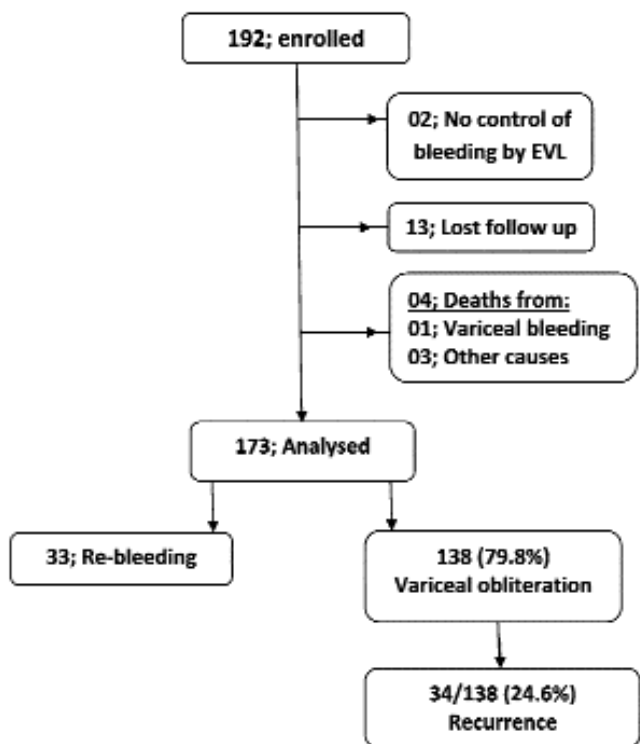


Figure: Patients included in the data analysis. From the 192 patients who enrolled during the observation period, 173 could be analysed in the study.

sclerotherapy, although variceal recurrence is more frequent.²² These suggestions emphasise the fact that there is no role for sclerotherapy as the first-line therapy in the current era.

We observed an overall re-bleeding rate after EVL of 19.07%. This magnitude of re-bleeding is consistent with those reported in studies by other researchers (9% to 19%),^{5,9,23-27} But the main difference among those studies is the indication of EVL; as those studies were performed for primary prophylaxes,^{5,9,23,25,27} secondary prophylaxes²⁴ and control of acute variceal bleeding²⁶ where-as we included subjects who presented with either acute variceal bleeding or for secondary prophylaxis.

Beside the beneficial effect in obliteration of varices by EVL, it has shown disappointing results on PHG. In our study, the frequency of PHG went up (78.03 vs. 64.2%) in subjects who achieved variceal obliteration and these results are in agreement with other researchers.^{28,29} It may be due to the altered haemodynamic following band ligation.³⁰ Many studies found that EVL makes the gastric mucosa more congestive soon after the procedure.^{31,32} This finding was also supported by a study which reported that portal pressure gradient is increased after the obliteration of varices.³³ Further-more, this raised pressure resulted in worsening of PHG and the development of fundal varices, although there are reports that despite the worsening of PHG and the development of fundal varices, there is no change in portal pressure with either sclerotherapy or EVL.³⁴

Variceal obliteration in cirrhotic patients varies with certain factors. Patients surviving a first episode of variceal bleeding have over a 60% risk of recurrence. Because of this, all patients surviving a variceal bleeding should receive active treatments for the prevention of re-bleeding.³⁵ EVL has significantly reduced the frequency of variceal re-bleeding, mortality and complications, and has replaced endoscopic injection sclerotherapy as the first-line therapy in the prevention of oesophageal variceal re-bleeding.¹¹

There were mainly two limitations of our study; first, it was a single-centre study with a limited sample size and follow-up (around four years). Data needs further evaluation on a larger scale and over a longer follow-up duration; second, it was a single-arm study (only the outcome of band ligation) and so not comparable to other available options for oesophageal varices like oral drugs, endoscopic sclerotherapy or their combination.

Conclusion

Band ligation eradicates oesophageal varices with less

complications and a lower re-bleeding rate, but at the same time eradication is associated with more frequent development of PHG.

References

1. Sorbi D, Gostout CJ, Peura D, Johnson D, Lanza F, Foutch PG, et al. An assessment of the management of acute bleeding varices: a multicenter prospective member-based study. *Am J Gastroenterol* 2003; 98: 2424-34.
2. Lay CS, Tsai YT, Lee FY, Lai YL, Yu CJ, Chen CB, et al. Endoscopic variceal ligation versus propranolol in prophylaxis of first variceal bleeding in patients with cirrhosis. *J Gastroenterol Hepatol* 2006; 21: 413-9.
3. Wright AS, Rikkers LF. Current management of portal hypertension. *J Gastrointest Surg* 2005; 9: 992-1005.
4. Stiegmann GV. Endoscopic approaches to upper gastrointestinal bleeding. *Am Surg* 2006; 72: 111-5.
5. Lay CS, Tsai YT, Teg CY, Shyu WS, Guo WS, Wu KL, et al. Endoscopic variceal ligation in prophylaxis of first variceal bleeding in cirrhotic patients with high-risk esophageal varices. *Hepatology* 1997; 25: 1346-50.
6. D'Amico G, Pagliaro L, Bosch J. Pharmacological treatment of portal hypertension: an evidence-based approach. *Semin Liver Dis* 1999; 19: 475-505.
7. Garcia-Tsao G. Current management of the complications of cirrhosis and portal hypertension: variceal hemorrhage, ascites, and spontaneous bacterial peritonitis. *Gastroenterology* 2001; 120: 726-48.
8. Pagliaro L, D'Amico G, Sørensen TI, Lebrec D, Burroughs AK, Morabito A, et al. Prevention of first bleeding in cirrhosis: a meta-analysis of randomized trials of nonsurgical treatment. *Ann Intern Med* 1992; 117: 59-70.
9. Sarin SK, Lamba GS, Kumar M, Misra A, Murthy NS. Comparison of endoscopic ligation and propranolol for the primary prevention of variceal bleeding. *N Engl J Med* 1999; 340: 988-93.
10. D'Amico G, Pagliaro L, Bosch J. The treatment of portal hypertension: a meta-analytic review. *Hepatology* 1995; 22: 332-54.
11. Garcia-Tsao G, Sanyal AJ, Grace ND, Carey W, Practice Guidelines Committee of the American Association for the Study of Liver Diseases; Practice Parameters Committee of the American College of Gastroenterology. Prevention and management of gastroesophageal varices and variceal hemorrhage in cirrhosis. *Hepatology* 2007; 46: 922-38.
12. Villanueva C, Piqueras M, Aracil C, Gómez C, López-Balaguer JM, Gonzalez B, et al. A randomized controlled trial comparing ligation and sclerotherapy as emergency endoscopic treatment added to somatostatin in acute variceal bleeding. *J Hepatol* 2006; 45: 560-7.
13. Abalades JG, Villanueva C, Bañares R, Aracil C, Catalina MV, Garcí A-Pagán JC, et al. Hepatic venous pressure gradient and prognosis in patients with acute variceal bleeding treated with pharmacologic and endoscopic therapy. *J Hepatol* 2008; 48: 229-36.
14. Bosch J, Thabut D, Albillos A, Carbonell N, Spicak J, Massard J, et al. Recombinant factor VIIa for variceal bleeding in patients with advanced cirrhosis: a randomized, controlled trial. *Hepatology* 2008; 47: 1604-14.
15. Carbonell N, Pauwels A, Serfaty L, Fourdan O, Lévy VG, Poupon R. Improved survival after variceal bleeding in patients with cirrhosis over the past two decades. *Hepatology* 2004; 40: 652-9.
16. Sarin SK, Wadhawan M, Agarwal SR, Tyagi P, Sharma BC. Endoscopic variceal ligation plus propranolol versus endoscopic variceal ligation alone in primary prophylaxis of variceal bleeding. *Am J Gastroenterol* 2005; 100: 797-804.
17. Sarin SK, Govil A, Jain AK, Guptan RC, Issar SK, Jain M, et al. Prospective randomized trial of endoscopic sclerotherapy versus

- variceal band ligation for esophageal varices: influence on gastropathy, gastric varices and variceal recurrence. *J Hepatol* 1997; 26: 826-32.
18. de la Pena J, Rivero M, Sanchez E, Fábrega E, Crespo J, Pons-Romero F. Variceal ligation compared with endoscopic sclerotherapy for variceal hemorrhage: prospective randomized trial. *Gastrointest Endosc* 1999; 49: 417-23.
 19. Primignani M, Sarin SK, Battaglia G, D'Amico G, Kamath PS, Lin HC, et al. Baveno III consensus statements: portal hypertensive gastropathy, gastric varices. In: de Franchis R, (ed.). *Portal Hypertension III: Proceedings of the Third Baveno International Consensus Workshop on Definitions, Methodology, and Therapeutic Strategies*. Oxford; Malden, MA: Blackwell Science; 2001; pp 95-6.
 20. Lo GH, Lai KH, Cheng JS, Lin CK, Huang JS, Hsu PI, et al. The additive effect of sclerotherapy to patients receiving repeated endoscopic variceal ligation: a prospective, randomized trial. *Hepatology* 1998; 28: 391-5.
 21. Lo GH, Lai KH, Cheng JS, Hwu JH, Chang CF, Chen SM, et al. A prospective, randomized trial of sclerotherapy versus ligation in the management of bleeding esophageal varices. *Hepatology* 1995; 22: 466-71.
 22. Garcia-Pagan JC, Bosch J. Endoscopic band ligation in the treatment of portal hypertension. *Nat Clin Pract Gastroenterol Hepatol* 2005; 2: 526-35.
 23. Lo GH, Chen WC, Chen MH, Lin CP, Lo CC, Hsu PI, et al. Endoscopic ligation vs. nadolol in the prevention of first variceal bleeding in patients with cirrhosis. *Gastrointest Endosc* 2004; 59: 333-8.
 24. Harewood GC, Baron TH, Song LM. Factors predicting success of endoscopic variceal ligation for secondary prophylaxis of esophageal variceal bleeding. *J Gastroenterol Hepatol* 2006; 21: 237-41.
 25. Lo GH, Lai KH, Cheng JS, Lin CK, Hsu PI, Chiang HT. Prophylactic banding ligation of high-risk esophageal varices in patients with cirrhosis: a prospective, randomized trial. *J Hepatol* 1999; 31: 451-6.
 26. Lo GH, Lai KH, Cheng JS, Lin CK, Huang JS, Hsu PI, et al. Emergency banding ligation versus sclerotherapy for the control of active bleeding from esophageal varices. *Hepatology* 1997; 25: 1101-4.
 27. De BK, Ghoshal UC, Das T, Santra A, Biswas PK. Endoscopic variceal ligation for primary prophylaxis of oesophageal variceal bleed: preliminary report of a randomized controlled trial. *J Gastroenterol Hepatol* 1999; 14: 220-4.
 28. Misra SP, Misra V, Dwivedi M. Effect of esophageal variceal band ligation on hemorrhoids, anorectal varices, and portal hypertensive colopathy. *Endoscopy* 2002; 34: 195-8.
 29. Lo GH, Lai KH, Cheng JS, Hsu PI, Chen TA, Wang EM, et al. The effects of endoscopic variceal ligation and propranolol on portal hypertensive gastropathy: a prospective, controlled trial. *Gastrointest Endosc* 2001; 53: 579-84.
 30. Sato M. Effects of endoscopic variceal ligation on systemic and splanchnic hemodynamics in patients with cirrhosis. *Kurume Med J* 1997; 44: 191-9.
 31. Kanke K, Ishida M, Yajima N, Saito M, Suzuki Y, Masuyama H, et al. Gastric mucosal congestion following endoscopic variceal ligation - analysis using reflectance spectrophotometry. *Nihon Shokakibyō Gakkai Zasshi* 1996; 93: 701-6.
 32. Tayama C, Iwao T, Oho K, Toyonaga A, Tanikawa K. Effect of large fundal varices on changes in gastric mucosal hemodynamics after endoscopic variceal ligation. *Endoscopy* 1998; 30: 25-31.
 33. Korula J, Ralls P. The effects of chronic endoscopic variceal sclerotherapy on portal pressure in cirrhotics. *Gastroenterology* 1991; 101: 800-5.
 34. Pereira-Lima JC, Zanette M, Lopes CV, de Mattos AA. The influence of endoscopic variceal ligation on the portal pressure gradient in cirrhotics. *Hepatogastroenterology* 2003; 50: 102-6.
 35. de Franchis R. Evolving consensus in portal hypertension. Report of the Baveno IV consensus workshop on methodology of diagnosis and therapy in portal hypertension. *J Hepatol* 2005; 43: 167-76.
-