

Frequency of Re-bleeding after Esophageal Variceal Banding in Cirrhotic patients at 3 weeks

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ABSTRACT

Background: Acute esophageal variceal bleeding is a deadly complication in cirrhotic patients. Without proper treatment recurrent bleeding occurs in 30–40% within next 2–3 days, and upto 60% within 1 week.

Aim: To determine frequency of re-bleeding after esophageal variceal banding in cirrhotic patients during 3 weeks.

Study design: Descriptive study

Place and duration: Department of Medicine, Lahore General Hospital, Lahore. Six months from 03-03-2015 to 02-09-2015.

Methods: Total 220 patients with active variceal bleeding were included in this study. On identification of bandable varices, endoscopic bands were applied. Patients were followed for 3 weeks for history of hematemesis or melena or fall in hemoglobin of 2grams or more and endoscopy performed and endoscopic findings noted.

Results: Out of 220 patients, 115(52.3%) were males and 105(47.7%) were females, patients ranged between 20-70 years of age with mean age of 54.86±9.83 years.

According to Child-Pugh Classification 23 patients (10.5%) were Child A, 64 patients (29%) were Child B and 133 patients (60.5%) belonged to Child Class C. Red wale markings were observed in 132 patients (60%). Evidence of re-bleed observed in 14 patients (6.4%). Amongst these 14 patients 13(92.8%) had more than 2 columns of varices and belonged to child class C, all 14(100%) had red wale marks

Conclusion: Endoscopic variceal Band Ligation is an effective modality for control of esophageal variceal bleeding. Re-bleeding after variceal banding was 6.4%. Major factors contributing to re-bleeding were number of columns of varices, presence of red signs and severity of cirrhosis.

Keywords: Cirrhosis of liver, Esophageal variceal banding, Re-bleeding

INTRODUCTION

Cirrhosis is a major cause of mortality and morbidity throughout the world¹. It is also a common cause of mortality amongst Pakistani population and a leading cause of admission in our hospitals, making it a major health burden². Cirrhosis is by far the most common cause of portal hypertension which is the main cause of esophageal varices. Approximately 59% percent of patients with cirrhosis develop esophageal varices, and one-third of these patients experience esophageal variceal bleeding (EVB) with a risk of mortality of 17–42% per bleeding episode³.

Recurrent bleeding is common without prophylactic treatment⁴, the risk varies between 8-35% within 2 years of follow up⁵. In another series, the risk of recurrent bleeding was as high as 60%⁶ with a mortality rate of 33%⁷. In a local study re-bleeding was seen in 33(19.1%) of the 173 patients analyzed after variceal band ligation⁸. Prevention of

re-bleeding is therefore a major goal in patients in whom the initial bleeding episode has been successfully controlled⁹.

Acute variceal bleeding is managed with endoscopic therapy⁹ and endoscopic variceal band ligation is now treatment of choice. Endoscopic band ligation controls bleeding by causing thrombosis and scarring of the vessel [6]. Band ligation has also been used successfully for the treatment of re-bleeding. Various studies have attempted at identifying the risk factors of re-bleeding. In one series, major risk factors identified for re-bleeding were volume of ascites, number of bands applied, severity of varices and prolonged PT¹⁰.

Variceal re-bleed is associated with high mortality rate and limited work has been done to identify the incidence and frequency of early re-bleeding after band ligation and the risk factors associated with rebleeding in our population. The rationale of this study is to evaluate the frequency and risk factors of re-bleeding after band ligation

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of esophageal varices to see effectiveness of therapy in our population.

The objective of the study was to determine the frequency of re-bleeding after variceal banding of bleeding esophageal varices in cirrhotic patients within 3 weeks.

OPERATIONAL DEFINITION

Variceal bleeding: Presence of hematemesis /melena or blood in NG tube in last 24 hours and endoscopy shows esophageal varices.

Re-Bleeding: Re-Bleeding is defined as new hematemesis or melena within 3 weeks of banding and/or fall in hemoglobin of 2gms or more of pre-discharge level within 3 weeks post banding.

Red wale marking: Red wale marks are longitudinal dilated venules appearing like red streaks on the surface of the varix

Cirrhosis: Defined by clinical and laboratory indicators of liver dysfunction calculated by Child Pugh Classification along with coarse echotexture of liver on ultrasonography diagnosed at least 6 months ago.

MATERIALS AND METHODS

This descriptive study was conducted in the Gastroenterology Division, Medical Unit-I, Lahore General Hospital, Lahore. Study was carried out over a period of six months from 03-03-2015 to 02-09-2015. With confidence level of 95% and 5% margin of error population size for this study is 220 patients with an expected percentage of re-bleeding in 17% of cases after variceal banding.

Sampling technique was non probability consecutive sampling

Inclusion Criteria

1. Both males and females between Age 18 to 70 years.
2. Patients having cirrhosis (due to any etiology) for at least 6 months presenting with variceal bleed as per operational definition.
3. Patient with bandable varices on endoscopy.

Exclusion Criteria

1. Upper GI bleeding due any other cause apart from portal hypertension eg. Peptic ulcer bleed assessed by endoscopy.
2. History of treatment for variceal bleeding in past.
3. Patients with history of non-cirrhotic portal hypertension.
4. Patients with portal vein thrombosis
5. Patients taking NSAIDs and antiplatelets drugs.
6. Patients with history of Transjugular intrahepatic portosystemic shunts or surgical decompression for portal hypertension.

Data collection procedure: Approval for this research proposal was sought from Hospital Ethical Committee. All patients presenting to Emergency and Endoscopy Services of Lahore General Hospital meeting the above mentioned inclusion and exclusion criteria were offered to be enrolled in this study. Informed written consent was taken from all participating patients. All data was collected on preformed proforma including age, gender, etiology and class of cirrhosis. Upper gastrointestinal endoscopy was performed using high definition Fujinon Endoscope 9.2mm (Fujifilm Holdings Corporation, USA) by single endoscopist who has 2 years experience of band ligation and endoscopic findings were noted.

On identification of bandable varices, endoscopic bands were applied using Saeed 6 shooter Endoscopic Band Ligator (Cook Inc, Bloomington, Indiana, USA). Post banding patients were followed for any history of an episode of hematemesis or melena and endoscopy performed immediately. Fall in hemoglobin level of 2gms or more of pre-discharge at 3 weeks was also considered a sign of re-bleeding.

Data analysis: Collected data was entered into SPSS version 12 and analyzed. The quantitative variables like age was presented as mean and standard deviation. The qualitative variables like gender and frequency of re-bleeding was presented as frequency and percentages. Data was stratified for severity of cirrhosis according to Child's Pugh classification, number of varices, age of different patient groups, presence or absence of red signs to deal with effect modifiers. Post stratification Chi Square was applied. P value ≥ 0.05 was significant.

RESULTS

A total 220 patients were included during 6 months period, patients ranged between 20-70 years of age with mean age of 54.86 ± 9.83 years. Out of 220 patients, 115 (52.3%) were males while remaining 105 patients (47.7%) were females.

According to Child-Pugh Classification, 23 patients (10.5%) belonged to Child Class A, 64 patients (29.0%) had Child B and 133 patients (60.5%) belonged to Child C Cirrhosis.

Out of 220 patients, 95 patients (43.2%) had 1-2 columns of varices and 125 patients (56.8%) had 3-4 columns.

Duration of cirrhosis was 1-10 years in 209 patients (95.0%) and 11-20 years in 11 patients (5.0%). Mean duration of cirrhosis was 5.09 ± 2.78 years

Red wale markings were observed in 132 patients (60%) while 88 patients (40%) had no such markings. Evidence of re-bleeding was observed in 14 patients (6.4%)

Stratification for age, child class, presence of red wale marking and number of columns of varices with regard to evidence of re-bleed carried out and presented in tables 1 to 4. Regarding gender 7 out of 14 (50%) patients were males and rest of the 7(50%) were females.

Table1: Stratification for age with regard to evidence of re-bleed

| Age (Year) | Evidence of re-bleed | | Total |
|------------|----------------------|--------|-------|
| | Present | Absent | |
| 20-50 | 3 | 55 | 58 |
| 51-60 | 5 | 92 | 97 |
| 61-70 | 6 | 59 | 65 |
| Total | 14 | 206 | 220 |

Chi Square=.273 P value=0.529

Table2: Stratification for Child-Pugh classification with regard to evidence of re-bleed

| Child pugh classification | Evidence of re-bleed | | Total |
|---------------------------|----------------------|--------|-------|
| | Present | Absent | |
| A | 0 | 23 | 23 |
| B | 1 | 63 | 64 |
| C | 13 | 120 | 133 |
| Total | 14 | 206 | 220 |

Chi Square=6.636 P value=0.036

Table3: Stratification for presence of Red wale marking with regard to evidence of re-bleed

| Size of varices | Evidence of re-bleed | | Total |
|---------------------|----------------------|--------|-------|
| | Present | Absent | |
| No red wale marking | 0 | 88 | 88 |
| Red wale marking | 14 | 118 | 132 |
| Total | 14 | 206 | 220 |

Chi Square=9.968 P value=0.002

Table4: Stratification for number of columns of varices with regard to evidence of re-bleed

| No. of variceal columns | Evidence of re-bleed | | Total |
|-------------------------|----------------------|--------|-------|
| | Present | Absent | |
| 1-2 | 1 | 94 | 95 |
| 3-4 | 13 | 112 | 125 |
| Total | 14 | 206 | 220 |

Chi Square=7.915 P value=0.005

DISCUSSION

Formation of Esophageal varices is the most common complication of liver cirrhosis and portal hypertension. The reported prevalence of esophageal varices in cirrhotic patients fluctuates within a wide range and is around 60% (ranging from 24 to 80%)¹¹. Variceal bleeding occurs in 30% of patients with

cirrhosis and portal hypertension¹² and each episode has a mortality risk between 30% and 70%¹³. Esophageal and gastric variceal bleeding is a major source of morbidity and mortality in patients with portal hypertension from various causes, including end-stage liver disease and cirrhosis. Nearly 90% of patients with cirrhosis develop esophageal varices sometime in their lifetime, of which 30% bleed^{12,15}. Once varices have developed, they increase in size and eventually cause variceal bleeding. The study by the North Italian Endoscopy Club identified the variceal size, the degree of liver failure assessed by the Child-Pugh classification and endoscopic "red signs" as the major independent risk factors of the first variceal bleeding episode¹². The rate of variceal size enlargement from small to large is also not well defined, with reported prevalence ranging between 8 and 31% per year¹⁴.

Endoscopic band ligation is now established as standard therapy for the management of bleeding esophageal varices. Esophageal variceal band ligation has significantly reduced the frequency of variceal bleeding, mortality and complications and has replaced endoscopic injection sclerotherapy as the first line therapy in oesophageal variceal bleeding^{16,17}.

However this treatment has a high recurrence rate, also needs advanced technique and incurs high cost^{18,19}. The utility of band ligation in gastric varices is limited. Endoscopic variceal band ligation is mostly performed in the in-patient setting and is effective in primary and secondary prophylaxis of bleeding oesophageal varices in patients with cirrhosis¹⁶.

In our study, risk of re-bleeding following successful control of the initial bleeding episode with band ligation, was observed in 14(6.4%) patients which is quite low in frequency as compared to study done by Abbasi A et al i.e., 19.1%⁸ and the difference in frequency is because of the fact that they included every patient with indication for band ligation but in our study we excluded the patients with previous band ligation, portal vein thrombosis and non cirrhotic portal hypertension, in another study done by Harewood GC²⁰ rebleeding was reported to be 9.3% which is similar to results of our study. In present study, re-bleeding after esophageal variceal banding in cirrhotic patients was 6.4%. Our results are consistent with a study from Turkey reported re-bleeding rate 6.1%²¹. Another study carried out in Germany reported 3.9% bleeding rate²². While a local study documented 3.2% bleeding rate after variceal band ligation²³. These results are close to our study.

Other studies found rates of re-bleeding ranged between 10% and 50%^{24,25,26}. A relatively wide variation in rates of recurrent bleeding may be due, at least in part, to technical differences among studies,

such as variations in the interval between sessions or in the number of bands placed during each session²⁷. Whether these or other technical differences can affect the outcome has not been adequately investigated. Other possible confounding factors, such as the time since the initial bleeding episode, alcohol use or non-use, and the treatment used to stop the bleeding, may also affect the results of treatment. Among different trials, there may be differences in the characteristics of the population treated, such as the cause or the severity of portal hypertension, or in the definition of end points such as recurrent bleeding²⁸.

In our study the major factors contributing to re-bleeding were the number of columns of varices, presence of red wale marks and severity of cirrhosis. All 14 patients that had evidence of re-bleeding had red wale marks at the initial endoscopy which is consistent with data from international study by Merli M et al²⁹. 13 out of 14 (92.8%) patients had more than 2 variceal columns. In 125 patients had more than 2 columns and 13 (10.4%) out of these patients had rebleeding, while 95 patients had less than 2 columns on initial endoscopy and only 1 (1%) out of these patients had evidence of re-bleeding.

13 out of 14 (92.8%) patients belonged to Child Class C while only one (7.1%) patient belonged to Child B. None of the patients had Child A cirrhosis. In total 133, 64 and 33 patients belonged to child C, B and A respectively, and 13 (9.77%), 1 (1.5%) and none had re-bleeding, showing that risk of rebleeding is significantly greater in patients with severe liver disease which is consistent with study done by D'Amico G³⁰.

Age was another factor that was studied in relation to frequency to re-bleeding. 6 (42.8%) patients were between 61-70 years of age, 6 (35.7%) patients were between 51- 60 years and only 3 (21%) patients were younger than 50 years however this result was not statistically significant. Frequency of re-bleeding was similar in both male and female patients. Age factor has not been studied as risk factor for rebleeding in international studies.

Limitations of the study were a short follow up interval. Patients were not followed up till the eradication of varices. Other confounding factors like use of alcohol were not considered. Use of medications, other than NSAIDs and antiplatelet drug, was not considered. Endoscopic variceal Band ligation is an operator dependent procedure, and banding in our study was not done by a single operator which can also influence the results.

CONCLUSION

Endoscopic variceal Band Ligation is an effective modality of treatment for control of esophageal variceal bleeding. The major factors contributing to re-bleeding were the number of columns of varices, presence of red wale marks and severity of cirrhosis. Increasing age was another factor that increased the risk of re-bleeding.

Disclosure: None

Conflict of Interest: None

REFERENCES

1. Starr SP, Raines D. Cirrhosis: Diagnosis, Management and Prevention. *Am Fam Physician* 2011;84:1353-9.
2. Almani SA, Memon AS, Memon AI, Shah MI, Rahpoto MQ, Solangi R. Cirrhosis of liver: Etiological factors, complications and prognosis. *LUHMS* 2008; 61-66.
3. Blei AT. Portal hypertension and its complications. *Curr Opin Gastroenterol.* 2007;23:275-82.
4. Augustin S, González A, Genescà J. Acute esophageal variceal bleeding: Current strategies and new perspectives. *World J Hepatol* 2010; 2:261-74.
5. De Franchis R. Endoscopy critics vs endoscopy enthusiasts for primary prophylaxis of variceal bleeding. *Hepatology* 2006;43:24-6.
6. Biecker E. Portal hypertension and gastrointestinal bleeding: Diagnosis, prevention and management. *World J Gastroenterol* 2013;19:5035-50.
7. Bari K, Garcia-Tsao G. Treatment of portal hypertension. *World J Gastroenterol* 2012;18: 1166-75.
8. Abbasi. A, Bhutto. AR, Bhatti KI, Mahmood K, Lal Keshav Outcome of band ligation in oesophageal varices: *J Pak Med Assoc* 2013;63:983-7.
9. Kchaou AO, Kharrat J, Mir K, Houda B, Abdelli N, Ajmi S et al. Variceal Band Ligation in the Prevention of Variceal Bleeding: A Multicenteric Trial, *Saudi J Gastroenterol* 2011;17:105-9.
10. Xu L, Ji F, Xu QW, MQ. Risk factors for predicting early variceal rebleeding after endoscopic variceal ligation. *World J Gastroenterol* 2011;28:17:3347-52.
11. Pascal JP, Cales P, Desmorat H. Natural history of esophageal varices. In: Bosch J, Rodes J, editors. Recent advances in the pathophysiology and treatment of portal hypertension. *Serono Symposia Review No. 22; Rome, Italy; 1989. p. 127-42.*
12. North Italian Endoscopic Club for the study and treatment of Esophageal Varices. Prediction of the first variceal hemorrhage in patients with cirrhosis of the liver and large esophageal varices. *N Engl J Med* 1988;319:983-9.
13. Pagliaro L, D'Amico G, Sorensen TIA, 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.

14. Cales P, Desmorat H, Vinel JP, et al. Incidence of large oesophageal varices in patients with cirrhosis: application to prophylaxis of first bleeding. *Gut* 1990;31:1298-302.
15. Grace ND. Diagnosis and treatment of gastrointestinal bleeding secondary to portal hypertension. American College of Gastroenterology Practice Parameters Committee. *Am J Gastroenterol* 1997;92:1081-91.
16. Garcia-Tsao G, Sanyal AJ, Grace ND, Carey W. Prevention and management of gastroesophageal varices and variceal hemorrhage in cirrhosis. *Hepatology* 2007;46:922-38.
17. Santos MM, Tolentino LH, Rodrigues RA, Nakao FS, Rohr MR, de Paulo GA, et al. Endoscopic treatment of oesophageal varices in advanced liver disease patients. *European J Gastroenterol Hepatol* 2011;23:60-5.
18. Karsan HA, Morton SC, Shekelle PG, Spiegel BM, Suttrop MJ, Edelstein MA, et al. Combination endoscopic band ligation and sclerotherapy compared with endoscopic band ligation alone for the secondary prophylaxis of esophageal variceal hemorrhage: a meta-analysis. *Dig Dis Sci* 2005; 50:399-406.
19. Ding SH, Liu J, Wang JP. Efficacy of α -adrenergic blocker plus 5-isosorbide mononitrate and endoscopic band ligation for prophylaxis of esophageal variceal rebleeding: A meta-analysis. *World J Gastroenterol* 2009;15:2151-5.
20. Harewood GC. Factors predicting success of endoscopic variceal ligation for secondary of esophageal variceal bleeding. *J Gastroenterol Hepatol* 2006 Jan 21 237-41
21. Kuran S, Oguz D, Parlak E, Asil M, Cicek B. Secondary prophylaxis of esophageal variceal treatment: Endoscopic sclerotherapy, band ligation and combined therapy - long-term results. *Turkish J Gastroenterol* 2006;17:103-9.
22. Petrasch F, Grothaus J, Mossner J, Schiefke I, Hoffmeister A. Differences in bleeding behavior after endoscopic band ligation: a retrospective analysis. *BMC Gastroenterology* 2010;10:5.
23. Hameed K, Saeed A, Khan Y, Khan IM, Javed M. Endoscopic band ligation: an ideal procedure to manage bleeding oesophageal varices. *Ann Pak Inst Med Sci* 2007; 3:234-7.
24. Garcia-Pagan JC, De Gottardi A, Bosch J. Review article: the modern management of portal hypertension--primary and secondary prophylaxis of variceal bleeding in cirrhotic patients. *Aliment Pharmacol Ther* 2008;28:178-86.
25. Silvanou S, Potenza I, Debernardi Venon W. Endoscopic variceal ligation for prophylaxis of esophageal variceal bleeding: Technical aspects and outcome. *Dig Liv Dis* 2009;41S:167-9.
26. Chandrasekhara V, Yepuri J, Sreenarasimhaiah J. Clinical predictors for recurrence of esophageal varices after obliteration by Endoscopic Band ligation. *Gastrointest Endosc* 2007;65:148-150.
27. Nguyen KC, Nguyen TH. Efficacy of endoscopic multi-site band ligation in eradicating esophageal varices. *Gastrointest Endosc* 2009;69:222.
28. Spaander MC, Darwish Murad S, van Buuren HR, Hansen BE, Kuipers EJ, Janssen HL. Endoscopic treatment of esophagogastric variceal bleeding in patients with noncirrhotic extrahepatic portal vein thrombosis: A long-term follow-up study. *Gastrointest Endosc* 2008;67:821-7.
29. Merli M, Nicolini G, Angeloni S, et al. Incidence and natural history of small esophageal varices in cirrhotic patients. *J Hepatol* 2003; 38:266.
30. D'Amico G1, De Franchis R; Cooperative Study Group. Upper digestive bleeding in cirrhosis. Post-therapeutic outcome and prognostic indicators. *Hepatology*. 2003 Sep;38(3):599-612.