Endoscopic Sclerotherapy and Band Ligation in Secondary Prophylaxis of Esophageal Variceal Treatment

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ABSTRACT

Background: *Variceal bleeding is the most severe outcome of portal hypertension. Endoscopic sclerotherapy and band ligation are endoscopic treatment modalities for both active variceal bleeding and secondary prophylaxis. Endoscopic sclerotherapy has been carried out in Sardjito hospital since 1998, while band ligation has only been carried out since 2007 year. The aim of this study was to evaluate the long-term result of endoscopic sclerotherapy and endoscopic band ligation in secondary prophylaxis of esophageal variceal eradication.*

Method: *This is not a prospective study and is not randomized. The results of patients who underwent endoscopic sclerotherapy and endoscopic band ligation from July 2003 to June 2009 were compared. Patients were evaluated for re-bleeding and recurrence rates.*

Results: *Two hundred and seventy seven patients underwent endoscopic sclerotherapy and endoscopic band ligation during the period. One hundred and nine patients with varices eradication data; 49 patients who underwent sclerotherapy and 60 patients who underwent band ligation were followed for 1-119 (15.54 ± 20.70) months. The numbers of sessions for eradication were 4.33 ± 1.16 and 2.23 ± 0.59 for endoscopic sclerotherapy and endoscopic band ligation respectively ($p < 0.001$). Re-bleeding and recurrence rates were 38.64% and 84.21% for endoscopic sclerotherapy, and 25.93% and 70% for endoscopic band ligation ($p > 0.05$).*

Conclusion: *Endoscopic band ligation is more effective than sclerotherapy in the eradication of esophageal varices.*

Keywords: *esophageal varices, sclerotherapy, band ligation, secondary prophylaxis*

INTRODUCTION

Esophageal varices occurs in 50-60% of patients with liver cirrhosis.[1] Variceal bleeding is the most serious complication of portal hypertension, and occurs in one third of patients with esophageal varices.[2] In 60-90% of cases, the source of bleeding in patients with cirrhosis is esophageal varices.[1] Esophageal varices bleeding is associated with mortality. The mortality rate of variceal bleeding is approximately 20-30% and can reach 50% in some case series.[1,3]

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The treatment of patients with esophageal varices is intended to eradicate the varices or reduce the portal pressure. This can be achieved by pharmacology, endoscopy, surgery, or radiology.[4] Prevention of esophageal varices bleeding can be achieved before the first bleeding (primary prophylaxis) and after bleeding occurs (secondary prophylaxis) to prevent re-bleeding.[5,6,7] Re-bleeding of varices is very common. Patients who did not receive therapy after the first bleeding episode have a 60% risk of re-bleeding.[1] Several studies have shown that the re-bleeding rate was decreased by 40% and overall survival rate was increased by 20% with beta-blocker. However, this therapy sometimes raises several issues such as non-responder and contraindications for its usage.[8]

Sardjito hospital has been providing endoscopic sclerotherapy procedure since 1998, and ligation procedure since 2007. Endoscopic sclerotherapy and

band ligation is almost entirely done as secondary prophylaxis to esophageal varices. In this study, the patients who had undergone endoscopic sclerotherapy and/or endoscopic band ligation to be evaluated by comparing the results of sclerotherapy to ligation in eradication, re-bleeding rates, and recurrence of esophageal varices.

METHOD

In this study, during the period of July 2003-June 2009 there were 277 patients who had undergone endoscopic sclerotherapy and/or endoscopic band ligation at the Sardjito hospital. Varices eradication program in this study was executed as secondary prophylaxis. Therapy in the era of sclerotherapy was performed every 1-2 weeks until varices eradication was achieved, followed by repeated endoscopy every 1-3 months or if re-bleeding occurs. In the era of ligation, the therapy was conducted every 2-4 weeks until varices eradication was accomplished, followed by repeated endoscopy every 1-3 months or if re-bleeding occurs. All patients receive oral propranolol or isosorbid mononitrate as a combination of endoscopic therapy.

Endoscopic sclerotherapy and ligation are performed with hyosin bromide premedication unless contraindicated, in outpatients and inpatients. Endoscopic tools used were the Olympus® endoscopes in the era of sclerotherapy and Fujinon® EG-270 N5 and EG-250 WR5 in the era of ligation. Sclerotherapy was carried out paravariceal starting from superior of 2 cm distal esophagus using 1% polidokanol (Aethoxysclerol®) with 23 gauge sclerotherapy needle Olympus® NM-3K(E), whereas ligation was performed on the same position using a multiple band ligator set.

The size of the varix was assessed with grade 1 to 3 according to the classification of Japanese Study Society for Portal Hypertension. Grade 1 varix was defined as varices that collapsed with air inflation, grade 2 did not collapse with inflation and did not close the lumen, whereas grade 3 was large varix which closed the lumen.[1] A varix was considered eradicated if it vanished (optimal sclerosis) or reached grade 1. Recurrence of new varix that require therapy after eradication was called a recurrence, and bleeding after the first therapy was referred to as re-bleeding.

Statistical analysis in this study used SPSS 13.0. To assess the mean differences, independent sample t-test was used for data with normal distribution and the Mann Whitney U for data with abnormal distribution. Chi-square test was used to assess differences in categorical variables. Results with $p < 0.05$ are considered statistically significant.

RESULTS

This study is not a prospective study and was not randomized. Patients were divided into two groups of ligation therapy or sclerotherapy due to the differences in the era of availability of facilities. There were secondary data of 277 patients who had undergone endoscopic sclerotherapy and/or ligation. The number of patients who underwent sclerotherapy were 109 (39.35%) patients, ligation were 147 (53.07%) patients, and both therapy were 21 (7.58%) patients. Patients with varices eradication data were 109, aged between 15-80 (56.3 ± 12.6) years old, and consist of 86 (78.90%) male and 23 (21.10%) female. The etiologies of portal hypertension were cirrhosis of the liver in 106 (97.25%) patients, hepatocellular carcinoma in 2 (1.83%) patients and pancreatic cancer in 1 (0.92%) patient. A total of 49 patients underwent sclerotherapy, while 60 patients underwent ligation, with data that could be followed for 1-119 (15.54 ± 20.70) months. The number of therapy sessions needed to achieve eradication of varices was significantly less in the ligation group compared to the sclerotherapy group, which was 2.23 ± 0.59 times vs. 4.33 ± 1.16 times, with $p < 0.001$.

Table 1. Characteristics of patient with eradication

Variable	n (%)
Sex	
Male	86 (78.9)
Female	23 (21.1%)
Etiology	
Portal hypertension	106 (97.25)
Carcinoma	2 (1.83)
Pancreatic cancer	1 (0.92)
Procedure	
Sclerotherapy	49 (44.95)
Ligation	60 (55.05)

Table 2. Eradication, re-bleeding, and recurrence of esophageal varices with endoscopic therapeutic modalities

	Sclerotherapy	Band ligation	p
Eradication			
Session (times)	4.33 ± 1.16	2.23 ± 0.59	
Period (month)	2.63 ± 2.63	1.71 ± 1.50	< 0.001
Re-bleeding (%)	38.64	25.93	0.27
Recurrence (%)	84.21	70.00	0.21

The rate of re-bleeding in endoscopic ligation (25.93%) was lower compared to endoscopic sclerotherapy (38.64%) but statistically was not significantly different with $p > 0.05$. The number of therapy sessions before re-bleeding was 1 time in 9 patients, 2 times in 6 patients, 3 times in 5 patients, > 3 times in 5 patients who underwent sclerotherapy,

whereas in patients who underwent ligation was 1 time in 5 patients and 2 times in 1 patient. Patients with minimum 3 months follow-up data since stated varices eradicated were assessed for recurrence. There were 76 patients with relevant data. The period of time for recurrence are listed in table 2. The recurrence rate was also lower in the ligation group (70%) compared to sclerotherapy group (84.21%) but these differences did not reach statistical significance $p > 0.05$.

Table 3. The time period of recurrence by endoscopic therapeutic modalities

	Period (months)			
	1- < 3	3 - < 6	6 - < 12	≥ 12
Sclerotherapy	3.23 %	32.26 %	19.35 %	45.16 %
Band ligation	15.38 %	15.38 %	38.46 %	30.77 %

DISCUSSION

Endoscopic sclerotherapy and ligation are the modalities of endoscopic therapy for active variceal bleeding as well as for secondary prophylaxis.[1] Sclerotherapy is done by injecting sclerosant into the varix to cause thrombosis or by injecting it close to the varix to induce submucosal fibrosis.[2] Endoscopic band ligation was developed based on hemorhoid ligation technique using rubber band to ligate the basal of the varix.[2,9,10] Esophageal mucosa and submucosa in the variceal column are snared, causing strangulation, peeling, and even fibrosis, and produce variceal obliteration.[4,9,10] Both of these treatment modalities have advantages and disadvantages of its own. Sclerotherapy can cause some significant complications such as deep esophageal ulcers, bleeding of the ulcers, esophageal stricture, pleural effusion, and mediastinitis.[1,10,11] Complications of ligation tend to be lower.[11] A meta-analysis confirms the benefits of endoscopic ligation compared to sclerotherapy regarding re-bleeding, local complications, time to variceal obliteration, and short term recurrence.[2,3,8]

Endoscopic variceal ligation was developed in an attempt to discover an effective way to deal with esophageal varices by endoscopy with fewer complications than sclerotherapy.[9,12] As with sclerotherapy, endoscopic ligation of varices require multiple sessions/times to eradicate the varices. Ligation is usually repeated 7-10 days after the initial session.[12] In this study, ligation was repeated 2-4 weeks after the initial session. Some advantages of ligation compared to sclerotherapy may be related to the faster achievement of variceal obliteration. Studies conducted by Shafgat et al, Laine et al and Stiegmann et al showed that the mean times to obliteration with ligation were 2 sessions, 4.1 sessions and 4 sessions respectively, while with sclerotherapy the obliteration time were 5 sessions, 6.2 sessions and 5 sessions respectively. In this study, similar results were obtained. Obliteration with ligation requires fewer sessions i.e. 2.2 sessions whereas with sclerotherapy 4.3 sessions.[12,13,14] Meanwhile studyes conducted by Kuran et al, Zargar et al, Sharin et al contradicts the results of this study.[1,15,16]

Generally re-bleeding occurs in the time interval between initial endoscopic therapeutic sessions and the time of obliteration. Most studies show that rebleeding occurrence after initial therapy, followed by repeated therapy with the aim of varices eradication tend to be fewer by ligation than by sclerotherapy (27% vs. 45% cumulative re-bleeding rate in eight randomized trial).[17] Similar results were shown in this study (26 % vs. 39%), although these figures do not differ significantly in statistics ($p = 0.27$). A number of other studies agree with this, with different percentages and significance.[1,12-16]

There are fewer study that state the recurrence rate of esophageal varices after eradication by sclerotherapy compared to ligation. Recurrence rate reported in various literature and studyes differ from one another. The differences of recurrence rate of esophageal varices after eradication by sclerotherapy and by ligation are generally not statistically significant.

A number of studies compare the mortality in patients treated with ligation or sclerotherapy. A meta-analysis that included those five trials showed that mortality after ligation was lower than after sclerotherapy (24 vs. 31%).[9] The possible reason for the improvement of survival rate after ligation compared to sclerotherapy may be the lower rate of complications associated with ligation.[17] In this study, we were not able to analyze the survival rate due to lack of data.

According to the guidelines, the current choice for secondary prophylaxis is beta blocker, band ligation, or both for patients who previously did not receive any primary prophylaxis.[5,6,7] Band ligation should be added in patients receiving beta blocker for primary prophylaxis and experiencing bleeding.[5] Sclerotherapy is performed if ligation is not possible. Sclerotherapy may be needed to complete the eradication of small or recurrent varices.[3] Previous randomized trials reports have shown that band ligation produced fewer re-bleeding, mortality, and local complications than sclerotherapy. Endoscopic band ligation is also apparently the most appropriate endoscopic modalities according to our study. Re-bleeding and recurrence rate may be similar between sclerotherapy and ligation, but ligation eradicates varices faster with less number of sessions required than sclerotherapy.

CONCLUSION

Endoscopic band ligation is more effective than endoscopic sclerotherapy in eradicating esophageal varices.

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