Endoscopic variceal ligation as primary prophylaxis for oesophageal variceal bleeding at a Malaysian tertiary hospital

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ABSTRACT

Objective: Approximately one-third of patients with esophageal varices will develop bleeding which is a major cause of morbidity and mortality in patients with liver cirrhosis. Currently, the two most widely used modalities to prevent variceal bleeding are pharmacologic and oendoscopic variceal band ligation (EVL). However, EVL has been associated with significant complications. Hence we aim to evaluate and to identify the epidemiology, demography, and complications of EVL at our local Malaysian tertiary hospital.

Method: This is a retrospective study of all the patients that had undergone endoscopic variceal surveillance at the Gastroenterology endoscopy unit, Serdang Hospital from 1st January 2015 to 31st March 2017. Patients' demography, aetiologies of liver cirrhosis, platelet level and international normalised ratio (INR) prior banding procedure, and the post EVL complications were recorded and further analysed with SPSS version 16.

Results: In this study, 105 patients were screened for varices. Fifty-five of them had undergone EVL, with a quarter of the patients requiring repeated ligation. There was a male preponderance with 76.4%. 56.4% of patients were in age from 40-59 years. The majority of our patients were of the Malay ethnicity. The major aetiology for liver cirrhosis in our patients was viral hepatitis with Hepatitis C (31.0%), and Hepatitis B (20.0%). Most of our patients had platelet count >50,000 and INR <1.5 prior to EVL. There was no major complication in all of our subjects.

Conclusion: EVL is relatively safe and feasible treatment for prevention of oesophageal variceal bleeds with a low complication rate.

KEY WORDS:
Endoscopic variceal ligation (EVL), Esophageal variceal bleeding, cirrhosis

INTRODUCTION

Liver cirrhosis leads to progressive complication of portal hypertension. The pathophysiology of portal hypertension involved vascular resistance due to the architectural distortion of the liver from fibrosis and intrahepatic vasoconstriction due to the reduction of endogenous nitric oxide production. Subsequently, this results to in the formation of portosystemic collaterals which can be divided into esophagogastric varices and ectopic varices, which occur elsewhere in the gastrointestinal tract.[1] Approximately 50% patients with liver cirrhosis have gastroesophageal varices and one-third of them will develop variceal haemorrhage.[2,3]

The yearly rate of oesophageal variceal bleeding is 5-15% with the highest risk in patients with large varices, presence of red wale marks, and patients with decompensated cirrhosis.[4] Variceal haemorrhage is associated with up to 30% mortality[2,5] and as high as 70% risk of recurrent haemorrhage within one year of the bleeding episode.6 Hence primary prophylaxis aims to prevent variceal haemorrhage in patients with oesophageal varices with no previous history of variceal bleeding.

Generally, there are two modality of primary prophylaxis for oesophageal varices bleeding which are medically with NSBB and endoscopically by performing EVL. Medical therapy with NSBB is recommended in patients with small oesophageal varices that have not bled. A meta-analysis of six trials of up to the year 2004 have reported 42.7% adverse events in EVL group which includes the most common complication of ligation-induced ulcers, dysphagia and chest pain. This means nearly one in two patients who have undergone EVL developed some minor complications. Severe complication occurred in 3.7% of patients who have undergone EVL which included ligation-induced oesophageal ulcer bleeds in eight patients with two fatal outcomes and overtube-induced oesophageal perforation in one patient.[7]

As for patients with medium/ large varices either NSBB or EVL are recommended, and the decision should depend on the patient's characteristics and preferences, local resources, and expertise.[3] EVL is achieved by suction and ligating the varix in a banding device attached to the tip of the endoscope, which is quite similar to the technique applied for ligation of internal haemorrhoids. Nowadays, multiband ligators are often used. Two meta-analyses of trial comparing EVL and NSBB in this group of patients have showed that EVL is associated with a small but significant reduction of risk of variceal bleeding (4% vs 13%) but also shown no benefit with regards to mortality.[7,8]

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Table I: Frequency of EVL performed as primary prophylaxis for esophageal variceal bleeding in patient

Frequency of EVL, n	Number of patients, n (%)
1	41 (74.5%)
2	9 (16.4%)
3	4 (7.3%)
4	1 (1.8%)

Table III: The patients' platelet counts and INR prior to EVL

Laboratory investigations	Frequency, n (%)
Platelet count	
>50,000	65 (97.0%)
<50,000	2 (3.0%)
no FBC	8
INR	
<1.5	50 (78.1%)
1.5-2	11 (17.2%)
>2	3 (4.7%)
no INR	11

Table II: Characteristics of the patients whom have undergone EVL as primary prophylaxis for esophageal variceal bleeding

Variable	Frequency, n (%)
Gender	
Male	42 (76.4%)
Female	13 (23.6%)
Ethnicity	
Malay	28 (51.0%)
Chinese	14 (25.4%)
Indian	10 (18.2%)
Others	3 (5.4%)
Age group	
20-39	11 (20.0%)
40-59	31 (56.4%)
>60	13 (23.6%)
Etiology of cirrhosis	
NASH	2 (3.6%)
Hepatitis B	11 (20.0%)
Hepatitis C	17 (31.0%)
Crytogenic	13 (23.6%)
Alcoholic	9 (16.4%)
Hep B&C	2 (3.6%)
Others	1 (1.8%)

There was no previous published study on EVL as primary prophylaxis for oesophageal variceal bleeding in Malaysia. Hence, this study was carried out to evaluate and to identify the epidemiology, demography and complications of EVL specifically focusing on the safety aspect of EVL at our local Malaysian tertiary hospital.

MATERIALS AND METHODS

This was a retrospective study of all patients who had done oesophago-gastro-duodenoscopy (OGDS) for variceal screening at the Gastroenterology endoscopy unit, Serdang Hospital from 1st January 2015 to 31st March 2017. These patients encompassed those with underlying liver cirrhosis and follow up at the Hepatology Clinic, Serdang Hospital, and newly diagnosed cases of liver cirrhosis that were internally referred from other departments such as general medical department, general surgical department, as well as referrals from local district hospitals. A total of 105 patients were screened during this period. Only 55 patients who had undergone EVL were included. Individual who had EVL as treatment for bleeding oesophageal varices were excluded from our study. All the EVL procedures were performed by our three qualified gastroenterologists, with sedation of midazolam and fentanyl.

The patient's records were traced from the Hospital Information System (EHIS). Specific data such as patient ethnicity, gender, age, aetiology of liver cirrhosis, platelet count and INR prior EVL and complication of EVL were extracted and further analysed. The complications of EVL which we looked for were the severe adverse events such as ligation-induced ulcers bleed, post EVL stricture, severe chest pain, oesophageal perforation and death.

The analysis was done using EXCEL and SPSS for Windows version 16.0.

This research was registered in accordance with the National Medical Research Register Malaysia.

RESULTS

From 1st January 2015 to 31st March 2017, 105 patients with liver cirrhosis had undergone OGDS for variceal surveillance. EVL was performed in 55 of them. EVL was performed once in 74.5% of the patients, while fourteen patients (25.5%) required repeated EVL during the time frame of the study which sums up to a total of 75 procedures. Table I shows the frequency of EVL performed as primary prophylaxis in our patients.

The characteristic of the patients in our study issummarised in Table II.

There was a male preponderance with 76.4%.

In terms of age, more than half of the patients (56.4%) were in for 40-59 years, while a quarter of patients were more than 65 years old.

The majority of our patients were of Malay ethnicity (51.0%), followed by Chinese (25.4%), Indian (18.2%) and others (5.4%).

The aetiologies for liver cirrhosis in our patients were mainly viral hepatitis (54.6%) predominantly Hepatitis C, cryptogenic (23.6%), alcoholic (16.4%), and NASH (3.6%).

The patients' platelet counts and INR prior to the EVL procedure were traced, and they are summarized in Table III. Eight of the EVL procedures' platelet count were not documented. Among the 67 procedures which had platelet count prior, 65 (97.0%) of them had platelet count more than 50,000/mcL, and only two (3.0%) patients had platelet count less than 50,000/mcL.

INR was not documented for 11 of the EVL procedures. Among the 64 procedures which had INR prior, 50 (78.1%) had INR below1.5.

No major adverse events were documented in all the patients whom EVL were performed as primary prophylaxis at our Gastroenterology Endoscopy unit. No mortality was reported during EVL procedures as well.

DISCUSSION

76.4% of our patients who have undergone EVL were male. This corresponded to a study which was performed in New Delhi, India comparing EVL and propanolol as primary prevention whereby 73% of subjects who have undergone EVL were male.[9] On a separate case control study in France studying the predictive factors of bleeding related to post-banding ulcer following EVL in cirrhotic patients, we have noted that the demographic of their subjects in term of gender were similar to ours.[10] We attribute this to the higher prevalence of liver cirrhosis in male as compared to female, which was also supported by a retrospective local study on the epidemiology of liver cirrhosis in Malaysia showing that 68.9% of patient with liver cirrhosis were male.[11] Moreover, more males are known to be exposed to high risk behaviors behaviours such as intravenous illicit drug abuse and sexual promiscuity which were the risks factors to viral hepatitis, and alcohol drinking.

In our study majority of patients were from 40-59 years old. This corresponded to the mean age of patients with liver cirrhosis in Malaysia which is 58.8 years old.[11]

The major cause of liver cirrhosis in our subjects undergoing EVL was chronic hepatitis C infection (31.0%), followed by cryptogenic (23.6%), chronic hepatitis B (20.0%), alcoholic (16.4%) and NASH (3.6%). Over the years, there is a wave of change in the aetiology of liver cirrhosis in Malaysia. A six-year study (1982-1988) in the National University of Malaysia had shown that the commonest aetiology of chronic liver disease was alcohol-associated (36.0%), followed by idiopathic (34.0%), chronic hepatitis B (33.0%).[12] A similar study performed in the University Malaya Medical Centre from 2006-2009, has recorded chronic hepatitis B as the main cause of liver cirrhosis (46.1%), followed by chronic hepatitis C (18.5%), cryptogenic (15.4%) and alcoholic (12.6%).[11] Our study had shown the similar causes of liver cirrhosis as the University Malaya Medical Centre where at the viral hepatitis was the major aetiology of the liver cirrhosis. This may represent a gradual increase in cases of viral hepatitis associated liver cirrhosis, and a reduction of alcohol associated liver cirrhosis in Malaysian population. As the aetiology of liver cirrhosis in each ethnicity was further studied, we found that the most common cause of liver cirrhosis in Malays was chronic hepatitis C (39%), followed by chronic hepatitis B (32%); forty-three percent of the Chinese patients had cryptogenic liver cirrhosis; and alcoholic liver cirrhosis remained the commonest cause in Indians (70%). This result was consistent with one of our local study, in which the aetiology of liver cirrhosis had a peculiar pattern based on ethnicity differences in alcohol intake and in the prevalence of viral hepatitis.[11]

Preliminary studies suggest that viral eradication by using antiviral therapy with nucleoside analogues in the treatment of chronic hepatitis B,[13] and peginterferon plus ribavirin or lately direct-acting antiviral (DAA) in the treatment of Hepatitis C[14] may arrests fibrosis progression and delay progression of varices, and to further decrease the risk of bleeding in patients. However, viral hepatitis especially chronic hepatitis C remains the major aetiology of liver cirrhosis among our patients undergoing EVL. This could be explained by the underutilization of antiviral therapy in our clinical practice due to limited medical budget.

A meta-analysis of sixteen randomised trials in patients with medium to high risk varices have shown that three endoscopic sessions are required to eradicate a varices, and at least thirty-three endoscopic procedures are required to prevent one bleeding episode.[15] 25.5% of our subjects required repeated EVL with the highest number of EVL performed was four times in one of the subjects.

EVL procedure is associated with complications. However, the complication most frequently reported was minor, such as dysphagia, and post ligation retrosternal non-cardiac chest pain.[16] Major adverse events such as life threatening bleeding from banding induced ulcers, oesophageal perforation, and oesophageal stricture formation were rare.[15,17-19]. Following EVL, a local ulcer was usually found due to a sequence of pathological changes. EVL induced variceal thrombosis with varying degrees of ischemic necrosis leading to detachment of the rubber band.[1,20] Subsequently, a shallow ulcer would occur and healed within 2-3 weeks allowing the development of fibrosis in sub mucosa. Complication of EVL usually occurred in case of premature detachment of rubber band before variceal thrombosis which may explain bleeding episodes from esophageal ulcers following EVL.[2] No major complication was reported among the patients performed EVL as primary prophylaxis in our study. No guideline regarding the safe level of patient's platelet count and INR prior EVL as primary prophylaxis. Even though 3.0% of subjects have platelet count below 50,000/mcL, and 21.9% have INR above1.5, there was no major complication of EVL especially bleeding, documented in our study. The complication rate in our hospital was lesser compared to the average of 3.7% from a meta-analysis of six trials.[7] Hence, prophylactic EVL was considered efficient and safe in preventing oesophageal variceal bleeding.

The main limitation of this study was that the data were collected retrospectively, thus making this study liable to missing and inaccurate data. There was no follow up on some patients and hence we were unable to comment on long term morbidity or mortality post EVL. Incomplete documentation of blood tests prior the procedure, e.g. platelet count and INR was our limitation as well. Moreover, we had poor documentation of minor adverse event in most of our patients. The sample size of our study was small and hence may not be a representative of the intended population.

CONCLUSION

In conclusion, EVL is very safe and feasible treatment for prevention of oesophageal variceal bleeds in patients

with medium/large size varices. EVL could be safely performed if patients' platelet counts more than 50,000/mcL and INR below1.5. All the patients with liver cirrhosis should be offered endoscopy variceal surveillance, and EVL should be performed if indicated.

Our hospital is a government funded tertiary hospital, aiming to provide cost efficient, universal and comprehensive services to the public. However, as most patients required repeated OGDS with EVL to eradicate the varices, this method may not be cost efficient especially when there is no difference in term of mortality rate if compared with using NSBB. Hence, larger sample sized, prospective study should be conducted to investigate the cost effectiveness of EVL compared to NSBB. Further refining of clinical and endoscopic scoring systems is warranted to stratify the cirrhotic patients into high- and low- risk groups for variceal haemorrhage. By practising the scoring system in triaging individuals for endoscopy variceal surveillance can substantially reduce the demand for endoscopy.

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CONFLICT OF INTEREST

All the authors have declared no competing conflict of interest.

FINANCIAL DISCLOSURE

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