

Study of safety and performance of the developed esophageal variceal band ligation

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ABSTRACT

Background: Esophageal variceal bleeding is a major complication causing mortality in cirrhotic patients. In Thailand, limited access to banding ligator equipment due to high prices compared to government healthcare reimbursement rates exists. This study aims to develop efficient, accessible equipment for distribution within the country while reporting on its safety and efficacy.

Methods: We developed a locally manufactured esophageal varices band ligator and conducted a multicenter study across three provincial hospitals. We enrolled cirrhotic patients undergoing EGD for esophageal varices bleeding or surveillance, requiring endoscopic esophageal banding ligation to evaluate the equipment's safety and efficacy. The primary outcome was the technical success rate of immediate endoscopic esophageal banding ligation, defined as successful hemostasis after banding ligation. The secondary outcome was the clinical success rate of hemostasis at 72 hours post-endoscopic banding ligation.

Results: Sixteen cirrhotic patients were enrolled, with 81.3% were male and a mean age of 54.3±9.0 years. Most patients (93.8%) underwent elective endoscopy for esophageal varices surveillance. The number of bandings performed ranged from 1 to 4. The technical

success rate was 100%, with all patients (16/16) achieving immediate hemostasis without complications, totaling 41 bandings. Additionally, the clinical success rate at 72 hours post-endoscopic banding ligation was also 100%, with no occurrences of recurrent bleeding observed.

Conclusion: Our study demonstrates the safety and efficacy of the locally manufactured esophageal banding ligator developed by our research team, with a remarkable success rate of 100% in achieving immediate hemostasis and preventing recurrent bleeding post-treatment. Further studies involving larger-scale trials to validate its safety profile and efficacy, leading to widespread adoption in various provinces nationwide, are warranted.

INTRODUCTION

Cirrhosis significantly contributes to morbidity and mortality among individuals with chronic liver disease worldwide. In 2019, it was related to 2.4% of global fatalities (1). The leading cause of death in these patients is liver-related complications, with esophageal variceal bleeding being a major concern resulting from portal hypertension in decompensated cirrhosis (2). The standard and effective treatment for esophageal variceal bleeding is esophagogastroduodenoscopy (EGD) with esophageal variceal ligation (EVL). This procedure effectively treats bleeding and prevents further episodes.

Currently, the mortality rate from variceal bleeding has significantly decreased, with rates ranging from 6-12% in cases where patients receive timely and effective treatment (3). However, according to report data from Thailand, the mortality rate from variceal bleeding within the country is as high as 19% (4), significantly higher than in other countries such as the United States. This discrepancy partly reflects challenges in accessing effective treatment.

In Thailand, there are significant limitations to the use of banding ligation equipment, primarily due to the high price compared to the government's healthcare reimbursement rates. This situation results in many individuals in the population being unable to access treatment. Additionally, there are two limitations related to the equipment itself. First, the one-way clutch mechanism, designed to prevent improper rotation, imposes considerable friction on the inner surface during operation, leading to inconsistent prevention of reverse rotation. Second, the small metal components within the clutch are susceptible to corrosion, making them fragile and potentially hindering users from adjusting the tension of the cord as desired.

Therefore, the study aims to develop an effective and affordable esophageal banding ligation equipment for distribution within the country, with the goal of performing as well as or better than existing market options. Clinical safety and efficacy testing results are reported to study its clinical efficacy, generate confidence and acceptance, and ensure product quality through real-world clinical usage evaluations. This initiative aims to reduce medical costs for both hospitals and patients by providing commercially viable treatment options at government reimbursement rates, ultimately improving patient access to treatment.

MATERIALS AND METHODS

Study design and participants

The study is a collaboration between the Faculty of Medicine and the Faculty of Engineering at Chulalongkorn University, Thailand, and Popolo Co., Ltd., in conjunction with medical professionals from various regions in the country, is conducting research and development on a locally manufactured esophageal varices band ligator (**Figure 1**).

Furthermore, Popolo Co., Ltd. is actively advocating for medical industry standards in the country under the supervision of the Medical Device Control Division of the Food and Drug Administration. By aligning with ASEAN Common Submission Dossier Template (CSDT) standards, the company is preparing to register medical devices at the regional level.

The study was conducted at multicenter across three provincial hospitals, including Queen Savang Vadhana Memorial Hospital in Chonburi province, King Mongkut Memorial Hospital in Phetchaburi province, and Surin Hospital in Surin province. We enrolled cirrhotic patients aged 18 years and above who were hospitalized due to upper gastrointestinal bleeding from esophageal varices, as well as patients who visited outpatient clinics meeting the criteria for esophagogastroduodenoscopy (EGD) for esophageal varices surveillance. Endoscopic esophageal banding ligation was performed for therapeutic hemostasis in patients with bleeding and for prophylaxis in patients undergoing surveillance. Endoscopists who perform procedures on patients are experienced gastroenterologists with over 5 years of experience in performing EGD and esophageal banding ligations. The selection of patients requiring esophageal ligation depends on the endoscopist's decision. Baseline patient characteristics, underlying chronic liver diseases, and laboratory profiles were collected on the same date.

All information was collected from electronic medical records. All participants signed informed consent forms before participating in the research study. The study protocol was approved by the Institutional Review Board of the Faculty of Medicine, Chulalongkorn University (IRB No.775/65), and was conducted in accordance with the Helsinki Declaration of 1983.



Figure 1. The esophageal banding ligations developed by the research team

Outcomes

The primary outcome was the technical success rate of immediate endoscopic esophageal banding ligation, defined as successful hemostasis after banding ligation. The secondary outcome was the clinical success rate of hemostasis at 72 hours after endoscopic banding ligation. A flow diagram of patient enrollment and outcomes was shown in **Figure 2**.

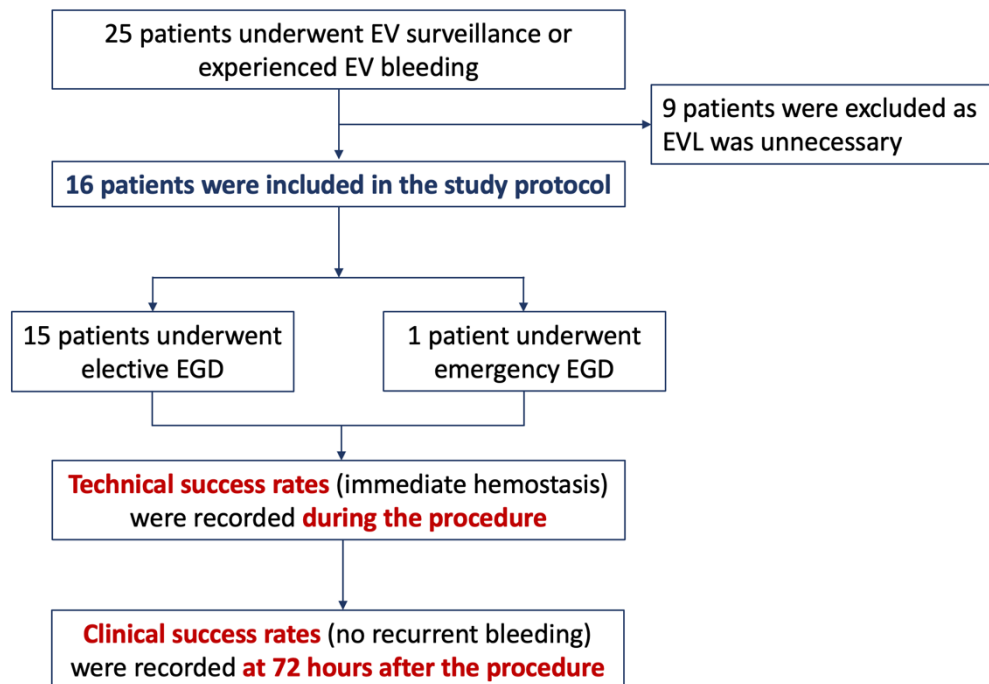


Figure 2. Flow diagram of patient enrollment

Statistical analysis

This study is an experimental biomedical research in the form of a clinical medical device trial. It is designed as a pilot study to determine the sample size, with 12 participants representing the sample group of patients with esophageal variceal bleeding in cirrhosis, without other significant comorbidities, according to the theory of sample size determination for experimental devices [Julious, 2005 #5].

RESULTS

Baseline patient characteristics

We enrolled 16 cirrhotic patients who met the criteria and underwent endoscopy with esophageal variceal ligations. Among them, 13 (81.3%) were male with a mean age of 54.3 ± 9.0 years. Alcoholic cirrhosis was the most common etiology, present in 9 (56.3%) patients, followed by HBV, HCV, and NASH in 2 (12.5%) patients each, and cryptogenic cirrhosis in 1 (6.2%) patient. Most patients (93.8%) underwent elective endoscopy for esophageal varices surveillance. The number of bandings performed ranged from 1 to 4 (Table).

Outcomes

For the primary outcome, which was the technical success rate, all patients (16/16) achieved immediate hemostasis without complications, totaling 41 bandings. Additionally, the clinical success rate at 72 hours post-endoscopic banding ligation was also 100%, with no occurrences of recurrent bleeding observed.

Table. Baseline characteristics of cirrhotic patients undergoing endoscopy with esophageal variceal ligations (n=16).

No	Site	Age	Sex	Cirrhosis etiologies	Endoscopic type	Number of banding	Technical success (immediate)	Clinical success (72 hours)
1	1	55	M	HBV	Elective	4	Yes	Yes
2	1	54	M	Alcohol	Elective	3	Yes	Yes
3	1	64	F	Alcohol	Elective	4	Yes	Yes
4	1	65	M	HBV	Elective	2	Yes	Yes
5	1	61	M	Alcohol	Emergency	2	Yes	Yes
6	2	43	M	Alcohol	Elective	3	Yes	Yes
7	2	49	M	Alcohol	Elective	2	Yes	Yes
8	2	43	M	Alcohol	Elective	2	Yes	Yes
9	2	58	F	Alcohol	Elective	3	Yes	Yes
10	2	44	M	Cryptogenic	Elective	3	Yes	Yes
11	2	73	M	Alcohol	Elective	2	Yes	Yes
12	3	62	M	NASH	Elective	3	Yes	Yes
13	3	43	M	Alcohol	Elective	2	Yes	Yes
14	3	57	F	NASH	Elective	3	Yes	Yes
15	3	53	M	HCV	Elective	2	Yes	Yes
16	3	45	M	HCV	Elective	1	Yes	Yes

DISCUSSION

We conducted a pilot study to assess the safety and performance of a locally manufactured esophageal varices band ligator. This study focused on evaluating the technical success rate, which indicates successful hemostasis during banding ligation procedures, reflecting the efficacy of the equipment. Additionally, we examined the clinical success rates of esophageal variceal ligations, defined as successful hemostasis or no recurrent bleeding within 72 hours post-endoscopic banding ligations, representing both the efficacy and safety of the equipment. The study yielded promising results, with both technical and clinical success rates reaching an impressive 100% among all 16 patients and 41 banding ligations. These findings suggest that our equipment offers a high level of efficacy and reliability in achieving immediate hemostasis during procedures and preventing recurrent bleeding post-treatment.

Furthermore, reports from endoscopists performing EGD and esophageal banding ligations indicated a high level of satisfaction and no operational issues. Therefore, the study concludes that the new esophageal banding ligator developed by our research team can be used efficiently and safely. Subsequent studies will focus on assessing market pricing and access to the equipment in Thailand under the national health insurance scheme, potentially replacing imported devices with high prices from abroad. Additionally, further studies will involve larger-scale trials to validate its safety profile and efficacy, leading to widespread adoption in various provinces nationwide.

CONCLUSION

Our study demonstrates the safety and efficacy of the locally manufactured esophageal banding ligator developed by our research team, with a remarkable success rate of 100% in achieving immediate hemostasis and preventing recurrent bleeding post-treatment. Further studies involving larger-scale trials to validate its safety profile and efficacy, leading to widespread adoption in various provinces nationwide, are needed.

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