

## Original Article

# Endoscopic variceal ligation with multi-band technique for treating upper gastrointestinal hemorrhage

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Received May 18, 2016; Accepted May 24, 2016; Epub June 15, 2016; Published June 30, 2016

**Abstract:** Objective: Esophageal varices (EV) and gastric varices (GV) rupture hemorrhage in advanced cirrhotic patients is a serious medical condition and requires immediate treatment. This clinical study aims to find out a more efficient way of using endoscopic variceal ligation (EVL) in treating variceal bleeding and hypotension caused by upper gastrointestinal hemorrhage, and to compare the long-term therapeutic effect of single-band and multi-band ligation techniques. Methods: Sixty-seven patients with clinical diagnosed cirrhosis and massive hematemesis were admitted to hospital through emergency room visits. The blood pressure (Bp) of these patients was between 60-82/30-55 mmHg, and their hemoglobin (Hb) levels were in the range of 50-87 g/L. All patients were given fluid resuscitation and somatostatin or terlipressin to reduce portal vein pressure. Patients with Hb level lower than 60 g/L were also given blood transfusion. When patients' Bp stabilized at 78-86/50-55 mmHg and Hb reached 55-60 g/L, endoscopic variceal ligation techniques were immediately applied to stop bleeding. Patients were randomly divided into single-band and multi-band ring ligation groups, while some patients accompanying with GV was treated by injecting in the bleeding gastric varices with sequential sclerosing agent, tissue adhesive and sclerosing agent (named as "sandwich" injection therapy). In the multi-bands treatment group, two to four bands were applied on the varices. The number of bands used for varices were dependent on the severity of EV. In another group of patients (single-band group), only one band was used on varices. Results: All sixty-seven patients were found to have EV by gastroscopic examination, and fifty-three of them had accompanying GV. Sixty-six of these sixty-seven cases were rescued successfully by using immediate endoscopic variceal ligation treatment within 24 hours after bleeding. One exception is a patient who still had bleeding even after EVL and sclerotherapy because he had been treated with Sengstaken-Blakemore tube for three days and that might cause erosion and ulcers in his esophagus. Among the thirty-five multi-band ligation treated patients, eight patients' EV were completely eradicated, and twenty-one patients' EV were mostly eradicated. Varicose veins disappeared in 82.8% of the multi-band treated patients. In single-band ligation treated group which comprises of thirty two patients, EV were completely eradicated in five patients and EV were mostly eradicated in fourteen patients. Varicose veins disappeared in 59.4% of these single-band treated patients. One-year follow-up results showed that the EV recurrence rate in the multi-bands ligation group was 5.7%, which was significantly lower than the rate of 18.7% in the single-band ligation group. No esophageal stenosis was observed in either groups. Conclusion: Patients with EV and/or GV rupture hemorrhage can be rescued successfully by endoscopic variceal ligation therapy. The long-term efficacy of the multi-band ligation technique is superior to single-band ligation.

**keywords:** Endoscopic variceal ligation, multi-band technique, upper gastrointestinal hemorrhage

## Introduction

Esophageal varices (EV) and/or gastric varices (GV) bleeding is a common complication in patients with advanced liver cirrhosis and por-

tal hypertension [1]. EV and/or GV rupture hemorrhage can lead to hemorrhagic shock, and the consequence is usually fatal unless the bleeding is quickly stopped [2, 3]. The effective method to control and reduce the EV and (or)

GV rupture hemorrhage is fading or eradicating EV and GV [3]. Endoscopic treatment of EV and GV and the subsequent bleeding is commonly used and effective, especially for patients with upper gastrointestinal hemorrhage caused by EV rupture. The current endoscopic treatment techniques on EV and GV includes ligation, sclerotherapy, tissue adhesive injection and combinations of these methods [4]. For variceal ligation method, many physicians use a single-band ring ligation technique. This method usually needs to be used more than once in order to fade the EV, and it can rarely eradicate varicose veins completely. Therefore, we tried to improve it by using a multi-band ligation technique. We compared the results between the group of using multi-band ligation and another group of using single-band ligation to treat massive hemorrhage in upper gastrointestinal tract.

### Materials and methods

#### *Patients*

Sixty-seven patients with advanced liver cirrhosis were enrolled in this study from March 2013 to September 2015. Fifty are male patients and seventeen are female patients. Their ages range from 25 to 82 years old ( $52.37 \pm 11.62$ ). They were all admitted through emergency visits with massive hematemesis as the main complaint. Among these patients, the etiological factors of advanced liver cirrhosis include chronic hepatitis B virus (CHB) (57 cases), chronic hepatitis C virus (CHC) (3 cases), schistosomiasis (9 cases, of which 4 cases with CHB) and chronic alcoholic liver disease (3 cases, of which 1 cases with CHB).

#### *Treatments*

Patients were all conscious at the time when they were admitted to hospital, but their limbs were cool and wet. Their blood pressure (Bp) was in the range of 60-82/30-55 mmHg (1 mmHg=0.133 kPa), and the hemoglobin (Hb) was in the range of 50-87 g/L. All patients were checked for CBC, liver function, coagulation function immediately. While receiving supportive fluid resuscitation, these patients were also given pantoprazole, etamsylate, aminomethyl benzoic acid, vitamin K, somatostatin or terlipressin to stop bleeding and reduce portal vein pressure. Patients with Hb lower than 60 g/L were given blood transfusion to raise the Bp to

the 78-86/50-55 mmHg range and the Hb to the 55-60 g/L range. Immediate endoscopy examination and treatment were performed without narcosis. Patients and their family were informed of the necessity of using these procedures and the possible risks, and consent forms were signed. During the endoscopy examination (Olympus GIF-H260, Japan), we carefully looked for bleeding spots, and gave saline flushing if bleeding sites could not be seen clearly. Patients were randomly assigned into the single-band and the multi-band ligation groups.

According to the Chinese national standards of endoscopic diagnosis and treatment of digestive tract varices and bleeding, all these sixty seven patients belong to severe grade EV [4]. The EV patients accompanied with GV were also treated with the following procedures. First, 3-5 mL sclerosing agent lauromacrogol (10 mL /pack, Shangxi Tianyu Pharmaceutical Company), plus 1-2 mL Glubran tissue adhesive (1 mL/pack, GEM, Italy) and 3-5 mL sclerosing agent lauromacrogol were injected in the varices rapidly [5]. Then the injection needle (1835 type, Boston, American) was taken back into the injection catheter. Injection sites were pressed for 3-5 minutes until there was no active bleeding. Then the gastroscope could be taken out. Next, a seven-band ring ligator (Boston Scientific Corporation, Natick, MA, USA) was attached to the shaft of the endoscope, and then re-intubated into the esophagus again. Obvious EV that laid on the lower esophagus but above the dentate line was chosen to use EVL. After advancing the endoscope toward the varix that needs to be banded, suction force is applied to the varix until "red out" effect occurs and then the band is fired. Patients in the multi-band ligation group were given two rings per unit. The second ligation was applied next to the first site, with 1.5 times of the lens barrel apart horizontally. Moving upwards spirally, three bands or four bands are applied to sites with apparent varices. The gastroscope was taken out again, then a seven-band ring ligator was installed, and the endoscope was inserted into the esophageal once again. All obvious varicose veins were ligated with two-band, three-band or four-band rings. In the single-band ring group, patients were treated according to the conventional EVL technique, i.e., single band was used per unit, spirally and ascendingly.

**Table 1.** Comparison of therapeutic effect between single-band and multi-band ligation

Groups	EV completely disappeared	EV dissipated mostly	Rehaemorrhagia	EV obviously visible but no bleeding
Single-band ligation	5 (15.6%)	14 (43.8%)	6 (18.7%)	7 (21.9%)
Multi-band ligation	8 <sup>1</sup> (22.9%)	21 <sup>1</sup> (60%)	2 <sup>1</sup> (5.7%)	4 <sup>1</sup> (11.4%)
Total	13	35	8	11

Note: All the patients were examined by endoscopy again one or two months after the operations. Completely disappearance: there is no EV but with visible scars; Dissipated mostly: EV seems to be straight or slightly tortuous while it was beaded with the red sign before treatment; Hemorrhage: patients have melena or hematemesis again after therapy. Multi-band ligation group compared with single-band ligation group ( $P<0.05$ ).

All patients were in abrosia for 24 h after the endoscopic therapy, and were given terlipresin injections for 3 days. Patients who had EV only were treated with pantoprazole intravenously for 3-7 days, while the patients who had both EV and GV and operated with the “sandwich” method needed to take esomeprazole orally for 3 months continuously. For patients who were treated with single-band ligation but bled again, they would be treated with multi-band ligation technique.

#### Criteria of EV treatment results

Criteria of EV treatment results were defined as [6]: 1) completely disappearance: there is no EV but with visible scars after ligation; 2) dissipated mostly: EV seems to be straight or slightly tortuous while it was beaded with the red sign before treatment; 3) hemorrhage: after therapy, patients have melena or hematemesis again. All the patients were examined by endoscopy again one or two months after the operations and were followed-up for at least one year. Recurrent bleeding was treated immediately if it occurred.

#### Statistical analysis

All data are presented as mean  $\pm$  standard error of the mean (SEM). Statistical analysis was carried out by SPSS 17.0. T-test and Chi-squared test were performed.  $P$  values of  $<0.05$  (two-tailed) was considered statistically significant, while  $P<0.01$  (two-tailed) was considered obviously significant.

#### Results

Sixty-six patients were rescued successfully by emergency endoscopic treatment within 24 h after bleeding occurred. Unfortunately, there

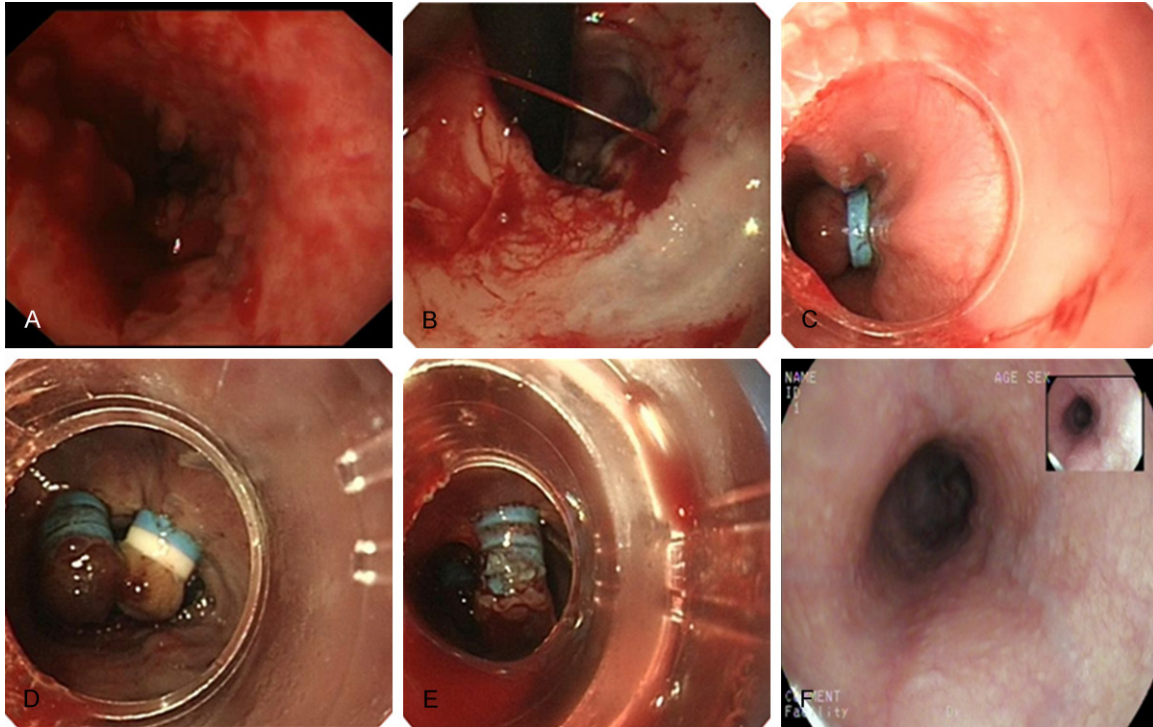
was one patient whose bleeding could not be stopped even with EVL and sclerotherapy both applied. This is probably because the bleeding had been lasting for more than 24 hours, and this patient had been treated with Sengtak-en-Blakemore tube for three days, which could cause the erosion and ulcers in his esophagus.

Two days after endoscopic therapy, this patient died of massive hemorrhage. There were 32 cases in single-band ligation group, including 24 males and 8 females, whose ages were  $52.25\pm 8.72$  years old. In the multi-bands ligation group, there were 35 cases, including 26 males and 9 females, with the ages of  $52.11\pm 8.72$  years old. There was no statistic significant in sex and age between the two groups ( $P>0.05$ ). After the endoscopic therapy operation, their hemorrhage was stopped and their Bp was returned to a normal range. Patients were given liquid diet for two days after the operation, and were discharged from hospital after 3-8 days. In the group of multi-band ligation, eight patients had completely eradicated EV, and twenty-one had mostly eradicated EV. The rate of disappearance of varicose vein was 82.9% in this group. In the single-band ligation group, five patients had completely eradicated EV and fourteen patients had mostly eradicated EV. The rate of disappearance of the varices was 59.4% (Table 1,  $P<0.05$ ). Some treated patients in the single-band group bled again and they were treated with multi-band ligation technique for the second time (Figure 1). During the follow-up with an average time of one year ( $12.16\pm 1.75$  months), six patients in the single-band ligation group suffered from variceal re-bleeding, among those one patient died. Two patients suffered re-bleeding in the multi-band ligation group, and nobody died. The re-bleeding rate of the multi-bands ligation group was significantly lower than that of the single-band ligation group ( $P<0.05$ ). No esophageal stenosis was observed in either group.

#### Discussion

Hemorrhage in digestive tract happens very often in liver cirrhosis patients accompanied

## EVL with multi-band ligation technique



**Figure 1.** Comparison of the single-band and the multi-band ligation technique on varices. A: EV bleeding; B: GV bleeding, and the blood ejected looks like a filament. C: Single-band ligation. Intumescent EV can also be seen upper the ligation ring. D, E: EVL with two, three, or four bands. F: EV shows as a thin wire after multi-band EVL.

with EV and (or) GV. It is one of the most serious complications of esophageal varices due to portal hypertension [7]. Risk factors for variceal bleeding are the big diameter of the varix, presence of red wale signs and an impaired liver function [8-12]. The rehaemorrhagia incidence is 60%~70% within six months after the initial hemorrhage, and the fatality rate is as high as 30%~60% [13-15]. Effective treatment of bleeding and prevention of further hemorrhage are important in reducing mortality and improving the prognosis. EVL is developed from the hemorrhoids ligation technology in the 1950s. In recent years, endoscopic treatment methods were developed rapidly, and the ligation operation were not only used in treating acute EV bleeding (EVB), but also for preventing EVB.

The basic principle of EVL is the same as using elastic rubber ring ligation on hemorrhoids. The ligation device is installed in front of the endoscope, through which the ligation arrives at lower esophagus, and the bleeding varices and conspicuous varicose veins can be ligated [16]. When the blood flow of the ligated varicose vein is blocked, it can cause local inflammation

response and thrombosis of endometrium epithelial of varicose vein, which lead to vascular occlusion. Then the tissue becomes ischemia necrosis and mucous membrane falls off gradually [17, 18]. Partial superficial ulcer will form, and it will be gradually replaced by fibrous scar tissue, and eventually varicose vein is eradicated.

Varicose veins will fade when the mucus member undergoes inflammation, ulcer, fibrosis and scar formation. Sclerotherapy technique is based on this mechanism and is through intravascular injection of hardeners. Its effect can last a long time. However, frequent injection in the same and nearby places can easily cause ulcers, which could be prolonged unhealed. It could also result in difficulty in swallow and induction of esophageal structure. Because EV patients will most likely need to receive the above treatment repeatedly, we choose to inject in different places, reduce the doses of hardeners and increase the time interval of treatments.

Upper gastrointestinal bleeding is often caused by esophageal or gastric varices rupture in cir-



rhosis patients. As a medical emergency, it is usually ferocious, and can become fatal unless being controlled quickly [2]. Therefore, management of those patients has to be rapid and efficient to lower morbidity and mortality [19]. Therefore, catching the treatment opportunity and choosing an appropriate treatment method are critical for saving the patients' lives [2]. In this study, except the one patient died of continuous bleeding, the rescue rate of the 67 patients was as high as 98.5% with emergency gastroscopic treatment when their Bp and Hb were in the range of 70~80/40~50 mmHg and 60 g/L, respectively. It is important that the patients should be treated with this procedure within 24 hours after bleeding.

Endoscopy examination should be undertaken immediately after resuscitation in unstable patients and endoscopic EVL should be used within 24 hours in bleeding patients [2]. The examination provides direct visualization of varicose veins and is very important to confirm the presence of variceal hemorrhage. Endoscopic treatment (e.g., EVL) should be performed at once if there is variceal bleeding [20]. The following are signs of using EVL: active bleeding from a varix; presence of a 'white nipple' fibrin clot overlying a varix; a clot on a varix; the presence of varices without other potential source of bleeding; and fresh blood in the stomach [21]. The most frequent complications of EVL are superficial ulcerations, oesophageal strictures, and delayed bleeding after falling of the rubber rings [25]. Sclerotherapy can be used when band ligation is technically difficult (for example, when there is poor visibility due to too much blood at the bleeding sites) [20-22]. Sclerotherapy is considered less expensive than band ligation.

Emergency endoscopic treatment is the cornerstone for the management of acute variceal bleeding and it is a preferred way to control bleeding [2, 4, 23, 24]. In the 1990s, professor Yun-lin Wu brought the band ring ligation technology into China. However, we found that the long-term efficacy of the traditional single-band ring ligation per unit EVL technique in stopping EV was low. In our practice, EV would always reoccur after the single band ligation, as well as the bleeding. Dr. Wu's group reported using double-band ligation to treat a patient suffering EVB, and in this patient the EV disappeared

and there was no re-bleeding for one and a half years [25]. For our group, we "accidentally" started using the "multi-band" EVL technique. In that accident, the band rings were incarcerated. Eventually all seven rings were set in the same site [26]. The thick EV ligated with seven-band rings, as well as the nearby EVs disappeared after treatment. There was a scar on the ligation place and the EV fading away completely when the patient took another endoscopy examination 7 months after the procedure.

Among the sixty-seven cirrhosis patients with upper gastrointestinal bleeding and hypotension, sixty-six patients' bleeding was stopped successfully through anti-shock treatment and emergency endoscopic treatment at the same time. The detailed procedure of our emergency endoscopy treatment procedure is as the following: First, we choose two apparent EVs above the dentate line, and give two-band ligation separately. Then raise up the scope spirally, and place the two, three, or four-band ring ligation. Compared with traditional mono-band ligation treatment, this method can improve the EV disappearance rate and decrease the re-bleeding rate [25, 26]. Our study proves that EVL with multi-band per point is more effective than the single-band ring ligation.

As stated above, hemostasis patients due to varices have a risk of rehaemorrhagia of about 60% within 1-2 years if left untreated, with a mortality of 33% [14, 27]. Therefore, the second step of a successful treatment of variceal haemorrhagia is the prevention of recurrence, which should be started prior to discharge from hospital. The consensus is to treat these patients with a combination of pharmacological and endoscopic therapy [20, 28]. The effect of this combined therapy has been demonstrated in two randomized studies [29, 30]. For EV, a second therapeutic endoscopy is indicated if the patient is stable [20]. Ligation sessions are performed at 7~14-day intervals until variceal obliteration. Once eradicated, patients should be examined by upper gastrointestinal endoscopy every 3~6 months to evaluate whether there is variceal recurrence and the need to receive more treatment [19]. Vasoactive medication should be given at maximum doses. If endoscopic therapy and vasoactive drugs fail, other measures must be adopted, such as transjugular intrahepatic portosystemic shunt (TIPS), balloon tamponade, or surgery (shunt).

It is also important for each patient to have regular follow-up examinations, including the endoscopic follow-up reviews to check whether the varices relapse. It is also important for patients to take abdomen ultrasound inspection, especially on liver, for every six months, and have liver function test and AFP test every three months. CT inspection is required when there are abnormal findings.

Multi-band ligation for treating EV is relatively a new procedure in China. Further study is needed to determine the most suitable ligation ring number on each bleeding site and how to choose the ligation points. The goal is to eliminate varicose veins more completely, and keep the therapeutic effect longer.

## Acknowledgements

The study was supported by the action plan for scientific and technological innovation from Shanghai Science and Technology Commission (15411950500).

## Disclosure of conflict of interest

None.

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