Clinical characteristics and efficacy of endoscopic treatment of gastrointestinal ectopic varices: A single-center study

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INTRODUCTION

Ectopic varices (EcVs) are a heterogeneous group of venous shunts located anywhere within the mesenteric vascular bed, with the exception of the gastroesophageal region, which is considered separate. In general, EcVs include duodenal varices (DVs), ileal varices, jejunal varices, small bowel varices (SBVs), colonic varices (CVs), rectal varices (RVs), biliary varices, peritoneal varices, and anastomotic varices (SVs), among others.

Abstract

Background: Ectopic varices (EcVs) may cause massive bleeding, which can be difficult to control, with a high rate of mortality. The purpose of this study was to analyze the clinical characteristics of EcVs and the efficacy of endoscopic treatment.

Methods: From January 2008 to July 2017, the clinical data of 150 patients with EcVs in our center were retrospectively collected and analyzed.

Results: One hundred and fifty patients with EcVs (male 74.7%), with a mean age of: 54.1 ± 14.6 years were included. The prevalence of EcVs was 0.92% in gastrointestinal varices. Cirrhosis was the most common cause of EcVs (67.0%). The rates of bleeding were 57.14%, 4.34%, 30.0%, 33.3%, and 100% in the duodenal varices rectal varices, colonic varices, anastomotic varices, and small bowel varices, respectively. An age under 55 years, varices in the duodenum, and erythema were considered risk factors for EcV bleeding. Endoscopic treatments were performed in 15 patients with EcV bleeding. The follow-up period of the patients who underwent endoscopic treatment ranged from 0.5 to 24 months. The overall rate of treatment success was 73.33% for endoscopic treatment of EcV bleeding. The overall rates of rebleeding and mortality during 2 years were as high as 53.3% and 26.7%, respectively.

Conclusion: Age, erythema, and the location of EcVs are considered risk factors for EcV bleeding, and the rate of bleeding is higher in patients with duodenal varices than in those with other EcVs. Endoscopic treatment is safe, effective, and feasible for controlling EcV bleeding.

Keywords: Clinical characteristics, ectopic varices, endoscopic treatment

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EcV bleeding is responsible for 1%-5% of all variceal bleeding.[3-4]

Few studies have focused on EcVs. The prevalence of EcVs varies substantially because of different locations and inspection methods. In a large population-based study, Al-Mofarreh et al.[5] reported that DVs had a prevalence of 0.2% under gastroscopy. In patients with portal hypertension (PH), the prevalence was 0.4% under gastroscopy.[6] In patients with intrahepatic portal hypertension (IPH) who underwent angiography, the prevalence was as high as 40%. The prevalence of RVs in patients with cirrhosis was 28%-56%, and the prevalence of RVs in patients with extrahepatic portal occlusion was 63%-94%.[7-8]

EcVs can cause massive bleeding, and the diagnosis and bleeding control are difficult. The risk of bleeding from EcVs was reported to be four times that of esophageal varices (EVs).[10] Although many treatment strategies and techniques have been utilized to manage EcV bleeding, the rates of mortality and rebleeding of EcVs are as high as 40% and 60%, respectively.[10-15] The best treatment modalities for EcV bleeding have not yet been established. Endoscopic treatment is currently the most common therapeutic modality for EcV bleeding and is less invasive and technically difficult than surgery and radiological interventions such as the transjugular intrahepatic portal systemic shunt (TIPS) procedure, balloon-occluded retrograde transvenous obliteration (BRTO), and double balloon-occluded embolotherapy (DBOE), although its efficacy and safety are still unknown. The purpose of this study was to further analyze the clinical characteristics of EcVs and the efficacy of endoscopic treatments for EcV bleeding.

METHODS

Patients

All patients who were endoscopically diagnosed with EcVs between January 2008 and July 2017 in our digestive endoscopy center, were included for retrospective analysis. Patients with varices only in the esophagus and stomach, such as solitary EVs, isolated gastric varices (IGVs), and gastroesophageal varices (GOVs), were excluded.

The types of gastric varices (GVs) were classified into GOV1, GOV2, IGV1, and IGV2 according to Sarin’s criteria[16]: GOV1, varices continuous with EVs and extending along the lesser curvature of the stomach below the gastroesophageal junction; GOV2, varices continuous with EVs and extending along the greater curvature toward the fundus; IGV1, varices located in the fundus without associations with EVs; and IGV2, varices located anywhere in the stomach except for the fundus.

Data collection

All patient data with regard to demographic characteristics (age and sex), endoscopic findings (variceal diameter, erythema, the site of bleeding lesions, etc.) were collected. In addition, the etiology of underlying EcVs, complications or adverse events, laboratory results, Child-Pugh classification, and model for end-stage liver disease (MELD) scores were collected during hospitalization. An acute bleeding episode was defined as 120 h.[17] Follow-up data from patients who underwent endoscopic treatment were collected for 2 years or until or death, TIPS treatment or liver transplantation after enrollment.

Outcomes and definitions

The primary outcomes included treatment success, rebleeding, and mortality. The secondary outcomes were immediate hemostasis, initial hemostasis, and adverse events. Immediate hemostasis was defined as the cessation of bleeding within 5 min after endoscopic intervention.[18]

Initial hemostasis was defined as the cessation of bleeding at the time of therapeutic endoscopy, followed by stable vital signs, no drop in hemoglobin (Hb), and no rebleeding within 24 h.[17,19]

Treatment success was defined as no death or need to change therapy, which was defined by the occurrence of one of the following (based on the Baveno criteria[17]) within 120 h of treatment: (a) fresh hematemesis or nasogastric aspiration of at least 100 mL of fresh blood at least 2 h after therapeutic endoscopy, (b) the development of hypovolemic shock, or (c) a 3-g decrease in Hb (a 9% drop in hematocrit) within any 24-h period if no transfusion was administered.

Rebleeding was defined as clinically significant rebleeding manifested as hematemesis or melena after 120 h resulting in any of the following: (a) hospital admission, (b) blood transfusion, (c) a 3-g decrease in Hb, or (d) death within 6 weeks.[17] Adverse events included all conditions possibly related to the endoscopic procedure. Complications included conditions caused by EcV bleeding or underlying EcVs rather than endoscopic procedure-induce conditions. High-risk varices were defined as medium-to-large varices or small EVs with red signs.[17,20]

Endoscopic treatment

Endoscopic treatment was performed using an Olympus GIF-Q260J video endoscope (Olympus Optical
Corporation, Tokyo, Japan) for EcVs. Endoscopic band ligation (EBL) was performed in patients with EcV bleeding, which was carried out with multiband devices (Wilson-Cook Medical, Winston-Salem, NC, USA). An intravariceal or a paravariceal injection of 10–30 mL of lauromacrogol per session (Tianyu Pharmaceutical, Zhejiang, China) was administered through a 23 G injection needle (Boston Scientific Interject-M00518301; Boston Scientific, USA). Each injection contained different volumes (1.0–4.0 mL) as needed, and each EcV was injected with no more than 8 mL of lauromacrogol. An intravariceal injection of N-butyl-cyanoacrylate (Beijing Compont Medical Devices Co. Ltd, Beijing, China) was administered to target the EcVs after flushing the needle with isotonic sodium chloride. Each injection contained different volumes (0.5–2.0 mL) as needed and an equal volume of lipiodol or 20% glucose. To decrease the risk of a variceal tear, the tip of the needle was withdrawn before the glue had set, and a catheter was held in place for 3–4 s to prevent leakage of the tissue adhesive. The sandwich technique was used. Cyanoacrylate was injected into EcVs with lauromacrogol or normal saline before and after tissue adhesive injection. All treatments were carried out by experienced endoscopists.

Statistical analysis
Statistical analyses were performed using SPSS software, version 23.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables are expressed as mean ± standard deviation (mean ± SD) and were analyzed by Student’s t-test. Qualitative data were evaluated using χ² or Fisher’s exact tests. Univariate analysis for predictors of EcV bleeding was performed by logistic regression analysis, and all variables with P values less than 0.05 were further analyzed using the forward Wald method in a multivariate analysis. The cumulative survival and rebleeding rates were determined by the Kaplan-Meier method, and differences between two groups were evaluated by the log-rank test. All tests were two-tailed, and P values less than 0.05 were considered statistically significant.

RESULTS
Clinical and endoscopic characteristics of the study patients
Between January 2008 and July 2017, 623,628 sessions of endoscopic diagnosis and treatments (including gastroscopy, colonoscopy, enteroscopy, duodenoscopy, and capsule endoscopy) were performed in our endoscopy center. A total of 16,271 patients were diagnosed with varices in the gastrointestinal (GI) tract, 150 patients of whom [88 (58.7%) inpatients; 62 (41.3%) outpatients] were diagnosed with EcVs and were included in this study. The flow chart for inclusion and exclusion is shown in Figure 1. Among 150 patients with EcVs, 22 patients were endoscopically diagnosed with GI bleeding from EcVs instead of EVs and GVs. Of these, 22 patients with EcV bleeding, 15 (10 with DVs, 4 with RVs, and 1 with SVs) underwent endoscopic treatment at the start of this study, and the other 7 (7/22) patients only received medical therapy, including blood volume resuscitation, octreotide or terlipressin, and antibiotic prophylaxis. The demographic and clinical characteristics of the patients with EcVs are summarized in Table 1. The mean age was 54.10 ± 14.60 years, and 112 (74.7%) were males. Cirrhosis [59, (67.0%)] was the most common cause of EcVs in hospitalized patients, followed by noncirrhosis in 29 (33.0%) patients. The causes of cirrhosis and noncirrhosis are presented in Table 2. The most common cause of cirrhosis was chronic hepatitis B, which was found in 34 (38.6%) patients, followed by alcoholic liver disease in 9 (10.2%) patients. The cause of EcVs in outpatients was unknown because of lack of complete medical records. The mean MELD score of the 59 patients with cirrhosis...
was 9.58 ± 4.43, and Child-Pugh grades A, B, and C were assigned to 24 (40.7%), 26 (44.1%), and 9 (10.2%) patients, respectively.

One hundred and fifty patients diagnosed with EcVs underwent a total of 186 sessions of endoscopic treatment, and the endoscopic findings are presented in Table 3. The overall endoscopy detection rate of EcVs was 2.98/10,000 (186/623,628). The prevalence of EcVs was 0.92% (150/162,71) in GI varices. The constituent ratios of EcVs were 14.0%, 76.6%, 6.7%, 2.0%, and 0.6% in DVs, RVs, CVs, SVs, and SBVs, respectively. The mean diameter of EcVs was 0.60 ± 0.44 cm. Of the 21 patients with DVs, varices in the descending portion of the duodenum was found in 14 (66.7%) followed by the bulb portion of the duodenum in six patients (28.5%) and others in one (4.8%) patient. The bleeding rates of DVs, RVs, CVs, SVs, and SBVs were 57.1% (12/21), 4.34% (5/115), 30.0% (3/10), 33.3% (1/3), and 100% (1/1), respectively. The proportion of DVs was significantly higher in patients with GI bleeding than in those without bleeding (12 patients, 54.6% vs. 9 patients, 7.0%; \(P < 0.001\)). Among 150 patients with EcVs, 54 (36.0%) patients had other varices (EVs or GV), while 12 (54.6%) of 22 patients with EcV bleeding had EVs or GV, 6 (6/12) of whom had a history of EV bleeding and received endoscopic treatment for secondary prophylaxis, and the remaining 6 (6/12) patients who had high-risk EVs or GV underwent endoscopic treatments for primary prophylaxis at the time of initial diagnosis.

Factors associated with EcV bleeding
Twenty-two patients experienced bleeding from EcVs. We performed logistic regression analysis to identify risk factors for EcV bleeding. On univariate analysis, age under 55 years, cirrhosis, varices in the duodenum, erythema, and variceal diameter (>0.75 cm) were found to be risk factors for EcV bleeding [Table 4]. Subsequently, on multivariate analysis, and age under 55 years, varices in the duodenum, and erythema were confirmed to significantly increase the odds of EcV bleeding [Figure 2].

Endoscopic treatments for EcV bleeding
Nine patients underwent EBL for EcV bleeding, and six received other endoscopic modalities. Endoscopic injection therapy (EIT) included endoscopic sclerosis injection, cyanoacrylate injection, and a combination of cyanoacrylate with sclerotherapy injection in this study. The clinical outcomes of endoscopic treatments for EcV bleeding are summarized in Table 5. The overall rates of immediate hemostasis, initial hemostasis, and treatment success were 100% (15/15), 86.7% (13/15), and 73.3% (11/15), respectively. Four (26.7%) patients experienced failed bleeding control and presented the hematemesis, melena or hematochezia within 120 h after endoscopic treatments. Of these four patients, one patient underwent EBL again, and

Table 1: Demographic and clinical characteristics of 150 patients with EcV

| Characteristics                        | Number of patients [n (%)] |
|----------------------------------------|---------------------------|
| Male                                   | 112 (74.7)                |
| Age (mean±SD) (years)                  | 54.10±14.60               |
| Inpatients/Outpatients                 | 88 (58.7)/62 (41.3)       |
| Cirrhosis                              | 59 (39.3)                 |
| Noncirrhosis                           | 29 (33.0)                 |
| CTP classification                     | A 24 (40.7); B 26 (44.1); C 9 (10.2) |
| Variceal diameter (Mean±SD) (cm)       | 0.60±0.44                  |
| MELD score (Mean±SD) (n=59)            | 9.58±4.43                  |

EcV, ectopic varices; SD, standard deviation; CTP, Child-Turcotte-Pugh score; MELD, model for end-stage liver disease

Table 2: The causes of cirrhosis and noncirrhosis in hospitalized patients

| Causes                               | Number of patients [n (%)] |
|--------------------------------------|---------------------------|
| Total                                | 88 (100)                  |
| Cirrhosis                            | 59 (67.0)                 |
| HBV                                  | 34 (38.6)                 |
| Alcoholic liver disease              | 9 (10.2)                  |
| Schistosomiasis                      | 4 (4.6)                   |
| Alcoholic + HBV                      | 4 (4.6)                   |
| HBV + Schistosomiasis                | 3 (3.4)                   |
| Alcoholic + Schistosomiasis          | 1 (1.1)                   |
| HCV                                  | 1 (1.1)                   |
| PBC                                  | 1 (1.1)                   |
| Idiopathic cirrhosis                 | 2 (2.3)                   |
| Noncirrhosis                         | 29 (33.0)                 |
| Superior mesenteric vein thrombosis  | 3 (3.4)                   |
| Cavernous Transformation of Portal Vein | 1 (1.1)                  |
| Pancreas-related diseases            | 3 (3.4)                   |
| Cryptogenic PH                       | 22 (25.0)                 |

PH, portal hypertension; HBV, hepatitis B virus; HCV, hepatitis C virus; PBC, primary biliary cholangitis

Figure 2: (a) Erythema of varices in the duodenal bulb; (b) Erythema of varices in the duodenal descending portion; (c) Erythema of rectal varices; (d) Erythema of colonic varices
hemostasis was successfully achieved, while another patient received endoscopic sclerotherapy injection (lauromacrogol), and hemostasis was successful. The remaining two patients, who were diagnosed with endoscopy-induced ulcerative bleeding, received medical treatment and successfully stopped bleeding. The rate of initial hemostasis was not significantly different between EBL and EIT [88.9% (8/9) vs. 83.3% (5/6); P > 0.05]. The rate of treatment success was comparable between the two groups [77.8% (7/9) vs. 66.7% (4/6); P > 0.05].

The follow-up period of the patients who underwent endoscopic treatment ranged from 0.5 to 24 months. Eight (53.3%) patients developed rebleeding during the follow-up period. Of these eight patients, one (1/8) patient who experienced three episodes of bleeding received endoscopic sclerotherapy injection (lauromacrogol), and hemostasis was successful; four (4/8) patients underwent endoscopic cyanoacrylate injection, three (3/4) of whom successfully achieved hemostasis, but one (1/4) patient with failed bleeding control underwent the TIPS procedure at 2 weeks after initial endoscopic treatments, and hemostasis was successfully achieved. Massive ulcerative bleeding at the site of a varix where initial endoscopic treatment was performed was observed in one (1/8) patient; although successful hemostasis was achieved by medical therapy, he ultimately died from liver failure 16 months after successful treatment. The remaining two (2/8) patients developed massive bleeding in the 7th and 11th months and eventually died. One patient died from hepatic encephalopathy in the 15th month. The overall mortality rate was 26.7% (4 patients) during the follow-up period. Although the rate of rebleeding was not found to be significantly different between the two groups [44.4% (4/9) vs. 66.7% (4/6); P = 0.617] [Figure 3], patients receiving EBL seemed to have a lower rebleeding rate than those receiving EIT. The mortality rate was comparable between the two groups [22.2% (2/9) vs. 33.3% (2/6); P = 0.706] [Figure 4].

Endoscopy-induced peptic ulcer or ulcerative bleeding was the main adverse event in four (26.7%) patients. Other adverse events, such as embolism, abdominal pain,

Table 3: Endoscopic characteristics of 150 patients with EcV

| Endoscopic characteristics | Number of patients [n (%)] |
|---------------------------|---------------------------|
| **Type of EcV**            |                           |
| DV                        | 21 (14.0)                 |
| RV                        | 115 (76.7)                |
| CV                        | 10 (6.7)                  |
| SV                        | 3 (2.0)                   |
| SBV                       | 1 (0.6)                   |
| **Diameter of varices (mean±SD) (cm)** | 0.60±0.44 |
| Erythema                  | 17 (11.3)                 |
| Erosion                   | 3 (2.0)                   |
| **Locations of DV (n=21)** |                           |
| Duodenal bulb             | 6 (28.5)                  |
| Duodenal descending part  | 14 (66.7)                 |
| Other                     | 1 (4.8)                   |
| **EcV coexisting with EVs or GVVs** | 54 (36.0) |
| **EcV bleeding**          | 22 (14.7)                 |
| **Endoscopic treatment**  | 15 (10.0)                 |

EcVs, ectopic varices; DVs, duodenal varices; RVs, rectal varices; CVs, colonic varices; SVs, anastomotic varices; EcVs, esophageal varices; SBVs, small bowel varices; EVs, gastric varices; SD, standard deviation

Table 4: Logistic regression analysis for risk of EcV bleeding

| Variable                              | Univariate OR 95%CI P | Multivariate OR 95%CI P |
|---------------------------------------|-----------------------|-------------------------|
| Age (>55 vs. ≤55 years)               | 0.178 0.057-0.557 0.003 | 0.159 0.027-0.938 0.042 |
| Sex (male vs. female)                 | 2.384 0.64-8.557 0.183 |                           |
| Etiology (LC vs. non-LC)              | 8.94 1.68-24.9 0.001 |                           |
| Distribution (duodenum vs. non-duodenum) | 15.867 5.396-46.657 0.000 | 8.508 1.884-38.426 0.005 |
| Erythema (absent vs. present)         | 0.034 0.01-0.115 0.000 | 0.028 0.005-0.169 0.001 |
| Coexistence with other varices (absent vs. present) | 0.457 0.183-1.141 0.094 |                           |
| Diameter of EcV (≤0.75 vs. >0.75 cm)  | 0.132 0.050-0.350 0.000 |                           |
| ALB (g/L)                             | 0.933 0.861-1.012 0.094 |                           |
| INR                                   | 2.516 0.211-29.981 0.465 |                           |
| MELD score                            | 1.004 0.877-1.150 0.948 |                           |
| CTP score                             | 0.564 0.121-2.629 0.446 |                           |

OR, odds ratio; CI, Confidence Interval; EcV, ectopic varices; LC, liver cirrhosis; CTP, Child-Turcotte-Pugh score; MELD, model for end-stage liver disease; ALB, albumin; INR, international normalized ratio
performed, and fever, were not observed in any patients who underwent endoscopic treatment, including hepatic encephalopathy was observed in three (20.0%) patients and spontaneous peritonitis in two (13.3%) patients.

**DISCUSSION**

EcVs are portosystemic collaterals located anywhere in the GI tract outside the region of the esophagus and stomach. The prevalence of EcVs is low in patients with PH compared to patients with EVs and GV. The prevalence of EcV bleeding is generally accepted to account for 1%–5% of all variceal bleeding. Previous studies reported that the overall endoscopy detection rate of EcVs was 0.06% in a large population study, and the prevalence rates of DVs were 0.2% and 0.4% in patients who underwent gastroscopy screening and patients with PH who underwent gastroscopy, respectively. The prevalence of RVs ranged from 10%–40% in patients with PH who underwent colonoscopy, and so on. The causes of EcV bleeding included PH (intrahepatic and extrahepatic), surgical procedures involving abdominal organs and vessels, anomalies of venous outflow vessels, abdominal vascular thromboses, rare familial conditions, and so on. DVs and RVs have also been reported to be caused by EBL for EVs/GVs. In this study, we found that cirrhosis was the most common cause of EcVs, which is consistent with other reported cases.

The locations of EcVs varied, which generally included the duodenum, small intestine, colon, rectum, peritoneum, and so on. Norton et al. reviewed 169 patients with EcV bleeding and identified bleeding in the duodenum in 17% of the patients, the rectum in 8% of the patients, the peritoneum in 9% of the patients, the jejunum or ileum in 17% of the patients, and the peristomal area in 26% of the patients. Oey et al. reported that 23% of patients had bleeding in the duodenum, while 17% of patients had bleeding in the rectum. Our study found that the prevalence of RVs was higher than that of DVs, which is consistent with a Japanese study. However, many previous studies have reported that the prevalence of DVs was higher than that of RVs. The reason for this may be participant difference in the studies. All patients with and without bleeding from EcVs were included in Watanabe’s study by Watanabe et al. and our study, while only patients with EcV bleeding were included in the study of Norton et al.

Many studies have shown a significant discrepancy between Eastern and Western countries in respect of location of DVs. In the United States and Europe, the bulb part of the duodenum was the most common site of DVs, followed by the descending part. However, in Asian countries, such as Japan and China, the descending part was the main location of DVs, followed by the duodenal bulb. In the present study, the duodenal bulb part was the most frequent location of DVs followed by the duodenal descending part. This discrepancy may be due to the different ethnicities of patients with DVs and the experience of endoscopists.

**Table 5: The clinical outcomes of endoscopic treatment for EcV bleeding**

| Results                          | Number of patients [n (%)] |
|---------------------------------|---------------------------|
| Total                           | 15                        |
| Immediate hemostasis            | 15 (100)                  |
| Initial hemostasis              | 13 (86.7)                 |
| Treatment success               | 11 (73.3)                 |
| Rebleeding                      |                           |
| Day 5 to 6 weeks                | 4 (26.7)                  |
| 7 weeks to 6 months             | 2 (13.3)                  |
| 7 months to 1 year              | 2 (13.3)                  |
| Mortality                       | 4 (26.7)                  |
| <1 year                         | 2 (13.3)                  |
| 1 year to 2 years               | 2 (13.3)                  |
| Complications                   |                           |
| Hepatic encephalopathy          | 3 (20.0)                  |
| Spontaneous peritonitis         | 2 (13.3)                  |
| Adverse events                  | 4 (26.7)                  |

EcV, ectopic varices

Bleeding from RVs rarely occurs, with a frequency from 0.6% to 3.6%, and DV bleeding accounted...
for 1%–3% of all varices and was often a serious, life-threatening condition.\[15,49\] In this study, we found that the rate of bleeding was higher in patients with DVs than in patients with other EcVs. Upper GI bleeding from DVs is often neglected and misdiagnosed. Therefore, we recommend that when endoscopists encounter acute obscure gastrointestinal bleeding in patients with PH, the descending part of the duodenum and then the distal portion should be observed.

Currently, the treatment of bleeding EcVs is still challenging. Although various treatment modalities, including medication, endoscopic treatments, TIPS treatment, BRTO, and surgical treatment, have been used to control bleeding EcVs, the optimal treatment has not yet been established. Currently, endoscopic treatment is one of the most common modalities for the management of EcV bleeding. Most guidelines and consensuses have recommended endoscopic treatments as the first-line therapy to control bleeding of EVs or GVVs.\[41-43\] However, the efficacy and safety of endoscopic treatment for acute EcV bleeding must be further elucidated. In this study, the overall rates of immediate hemostasis and initial hemostasis were 100% and 86.7%, respectively, which are comparable to those in previous studies reporting rates of hemostasis of 80%–100%,\[13,29,44,45\] suggesting that endoscopic therapy is effective for controlling bleeding. Previous studies have found that the rebleeding rate was 16%–60% after endoscopic treatment for EcV bleeding,\[44-47\] while the overall rebleeding rate was 53.3% in our study.

The all-cause mortality rate after endoscopic treatment for EcV bleeding was reported to be 25.0%–60.0% within 1 year and reached 80% within 2 years,\[13,30,44-47\] which is higher than our findings. However, the mortality rate related to bleeding was 10%–20% within 1 year,\[13,46,47\] which is comparable to our study (13.3%). The high mortality rate of EcVs may be due to different endoscopic therapeutic modalities, the types of EcVs, and the severity of liver function in our study. We previously performed a systematic review of all published evidence to evaluate the effectiveness and safety of endoscopic treatments for DV bleeding and found that the rates of rebleeding and mortality following endoscopic treatment for DV bleeding were 8.9% and 13.9%, respectively.\[48\] This discrepancy may be associated with the variable definition of “rebleeding” in the published literature and a publication bias in this systematic review. Overall, endoscopic treatment is an effective option for controlling EcV bleeding, but the long-term efficacy may be poor.

Endoscopic therapies include mechanical therapies (band ligation) and injection therapies (EIS and ETA). However, few studies have compared the efficacy of different endoscopic therapies for EcV bleeding. A retrospective study reported by Sato et al.\[45\] compared the efficacy of EBL and EIS in the treatment of RVs. This study showed that all patients were successfully treated, and the recurrence rate of RVs was comparable between the two groups (55.6% vs. 33.3%, P > 0.05), while the rebleeding rate was significantly higher in the EBL group than in the EIS group (44.4% vs. 0%, P < 0.05), suggesting that EIS was superior to EBL in the treatment of RVs. In the present study, the rates of hemostasis, rebleeding, mortality, and adverse events were not significantly different between the EBL group and the EIT group, showing that both endoscopic techniques were comparable with regard to efficacy and safety for the treatment of EcV bleeding. However, the aforementioned a systematic review showed that endoscopic tissue adhesive injection may be preferable in the management of DV bleeding.\[48\] Given the small number of patients in our study, prospective controlled studies with large sample sizes are required to compare the efficacy and safety of different endoscopic treatments for EcV bleeding.

The present strategy for EcV bleeding in our institution is presented in Figure 5. Considering that bleeding from EcVs is substantial and fatal, an easy, quick, safe, and effective therapeutic method should be recommended. Compared with interventional radiology and surgical procedures, endoscopic techniques are easier, less invasive, and less expensive.\[47,49\] Therefore, endoscopic treatment was selected as a preferred option to control bleeding in the initial therapy for EcV bleeding in our institution. Published studies have reported that interventional radiology has been increasingly used for EcV bleeding, and that good clinical outcomes have been achieved.\[10,32,33,50\] A systematic review presented by Copelan et al.\[46\] reviewed 32 patients who underwent angiographic occlusion for DV bleeding (including 21 patients treated with BRTO for DV bleeding) and showed that 87.5% of the patients were successfully treated. Only 2 (6.25%) patients developed rebleeding from DVs, and 2 (6.25%) patients died from bleeding and acute renal failure. AEs (sepsis and duodenal ulcers) occurred in only 2 patients. When hemodynamic stability is achieved, interventional radiological procedures should be attempted to prevent rebleeding from EcVs. If bleeding fails to be controlled with endoscopic treatment, interventional radiology should be initiated. Studies have shown that surgical methods had high rates of rebleeding and mortality of up to 57% and 80%, respectively.\[14,53\] Nevertheless, if endoscopic techniques and interventional radiologic procedures fail to control bleeding or are not feasible, surgical procedures should be considered in patients with Child-Pugh class A or noncirrhotic EHPVO.\[52\]
Our study sufficiently summarized the clinical and endoscopic characteristics of patients with EcVs, identified risk factors for EcV bleeding, and assessed the safety and efficacy of endoscopic treatments for EcVs bleeding. However, several deficiencies exist in this study. First, this is a retrospective study, and only one-tenth of the patients underwent endoscopic treatment. Second, the data was incomplete for outpatients.

**CONCLUSION**

EcVs represent a rare condition with a low frequency of bleeding. Age, erythema, and the locations of EcVs are considered risk factors of EcV bleeding, while the rate of bleeding is higher in patients with DVs than in patients with other EcVs. Endoscopic treatment is safe, effective, and feasible and may be selected as the first-line therapeutic method for controlling EcV bleeding. When bleeding fails to be controlled, interventional radiology may be considered for second-line therapy. However, these conclusions must be further confirmed through large-scale, multicenter randomized controlled trials.

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**Conflicts of interest**

There are no conflicts of interest.

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