

Investigation report on endoscopic management of esophagogastric variceal bleeding by Chinese endoscopists

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Abstract

Background: Esophagogastric variceal bleeding (EGVB) is a potentially life-threatening complication of portal hypertension. Endoscopic treatment combined with pharmacotherapy remains the mainstay in the management of acute variceal bleeding.

Aim: This article intends to highlight the potential differences in the endoscopic management of EGVB in China.

Methods: A cross-sectional descriptive study was conducted. Endoscopists from 85 hospitals in 62 cities from 26 provinces were contacted by email. The items in questionnaire involved academic experience, screening, esophagogastric varices (EGV) classification, emergency treatment, and primary and secondary prophylaxis of EGVB by endoscopists with different lengths of experience.

Results: A total of 85 questionnaires were collected. There was no statistical difference in the selection of items (P < .05 indicated statistical significance). The majority of endoscopists (95.29%) offered EGV screening for patients with liver cirrhosis. The location, diameter, and risk factor classification was selected by 82.35% of endoscopists. Endoscopy + medication was preferred (42.35%) for the primary prophylaxis of moderate-to-severe EGVs. There was no statistical difference in emergency intervention time for active EGVB (P > .05). The response "patients receive emergency endoscopic intervention within 12 hours" was selected by 61.2% of the endoscopists. The preferred emergency treatment for EGVB was combination treatment (40%). Tissue adhesive embolization was selected for the treatment of gastric variceal bleeding by 74.12% of endoscopists; transjugular intrahepatic portosystemic stent shunt/percutaneous transhepatic variceal embolization were selected as remedial measures by 48.23% to 52.94% of endoscopists. In addition, 67.06% of endoscopists elected to perform secondary prophylaxis and treatment within 1 week after hemostasis. Endoscopy and endoscopy + medication were selected by 44.71% and 49.41% of endoscopists, respectively, for secondary prophylaxis. The choice of laboratory indicators did not differ with length of experience.

Conclusions: There was no statistical difference in the endoscopic management of EGVB among Chinese endoscopists. The selection of diagnosis/treatment schemes was mainly based on guidelines and physician experience.

Abbreviations: EIS = endoscopic injection sclerotherapy, EGVB = esophagogastric variceal bleeding, EGVs = esophagogastric varices, EVL = endoscopic variceal ligation.

Keywords: endoscopy, esophagogastric variceal bleeding, liver cirrhosis, primary prophylaxis, questionnaire, secondary prophylaxis.

1. Introduction

Esophagogastric variceal bleeding (EGVB) is a common complication of liver cirrhosis and the main cause of death in patients with liver cirrhosis. Approximately 30% of patients with cirrhosis and portal hypertension develop bleeding from ruptured esophagogastric varices (EGVs), and the mortality rate of patients with the initial bleeding episode may exceed 50%.^[1] The risk of rebleeding is up to 60% for patients who experience a first hemorrhage without treatment. Recently, with advances in diagnosis and treatment of EGVB, the mortality rate has decreased significantly^[1,2] to approximately 12% to 22%.^[3-5] Therefore, screening, prevention, and treatment options for patients with cirrhosis and portal hypertension complicated with EGVs will greatly impact the survival and prognosis.

The present study hypothesized that the choice of endoscopic therapy for EGVB would be influenced by many factors, such as physician experience, training received, and published guidelines. Thus, differences in the clinical practices of endoscopists

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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may lead to different options being offered for the diagnosis and treatment of EGVB, which in turn would lead to different final therapeutic outcomes. Therefore, we conducted a nationwide online survey to explore the potential differences in the endoscopic diagnosis and treatment of EGVB in China, including differences in the screening, classification, grading, and treatment options offered by Chinese endoscopists. The results of this survey are expected to inform stakeholders involved in updating existing guidelines.

2. Methods

2.1. Subjects

This study was conducted from October 2018 to June 2019. Endoscopists from 85 hospitals in 62 cities from 26 provinces were contacted. The inclusion criteria were as follows: endoscopists from member institutions of the Esophageal and Gastric Varices Group of the Chinese Medical Association, and endoscopists from local tertiary care hospitals, which represented the quality of local medical care. Subjects with incomplete or unanswered responses to the questionnaire were excluded. The survey involved the diagnosis and treatment habits and methods of endoscopists in the east, west, south, north, and central regions of China. The ethics committee of the Fifth Medical Center of the People's Liberation Army General Hospital approved the study.

2.2. Survey

Gastroenterologists/endoscopists who performed endoscopic treatment for EGVB were emailed a 2-part questionnaire; the first part focused on the general information of the participants, and the second part included 16 questions about EGVs, which were further divided into 4 parts: diagnosis and classification, primary prophylaxis, emergency treatment, and secondary prophylaxis. The questionnaire items involved the academic experience of each participant; the screening and classification of EGVs; and the primary prophylaxis, emergency treatment, and secondary prophylaxis of EGVB. The questionnaire also included a limited number of high-quality endoscopic images. All the questions were listed step by step on the questionnaire.

2.3. Data processing

Each question included multiple options related to clinical guidelines and practices. All the questions in the questionnaire were designed in a step-by-step form, and were both related to and compared with each other. Each condition was associated with disease progression (primary and recurrent bleeding). For each question, only the option that was most commonly selected by the subjects was analyzed.

2.4. Statistical analysis

All categorical variables were presented as counts (N) and percentages (%). The chi-square test was used to compare classification variables between endoscopists with different lengths of experience. Analysis of variance was used to compare treatment options and the basis of their selection. If analysis of variance indicated a significant difference, the Bonferroni multiple comparison test was performed for post hoc pairwise differences. The *t* test was used to compare differences between 2 groups. The mean values and standard deviations of important parameters were presented. Median values were provided for each variable. All data analyses were performed using SPSS *v*22 software (Chicago, USA), and *P* < .05 was considered as statistically significant differences.

3. Results

All 85 questionnaires were collected. The questionnaires of the 85 endoscopists, each of whom held a title of attending physician or above, from 85 hospitals were divided into 3 groups according to the duration of endoscopic experience. The choice of treatment regimen and professional evaluation of the diagnoses and treatments proposed by endoscopists with different lengths of experience were compared and analyzed. Each questionnaire consisted of 16 questions that covered EGV screening, primary prophylaxis, emergency treatment, secondary prophylaxis, and remedial measures for different situations.

The responses to each of the 16 questions are presented in Tables 1 and 2, and Figs. 1–9. Among the 16 questions, the following questions elicited responses with a relatively high consistency (over 80%): whether patients with cirrhosis are routinely screened (Yes, 95.29%), diagnostic criteria

Table 1

Most common res	ponses to questions	in the questionnaire f	or EGV management.
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Question	Most common response	Rate	
Whether patients with cirrhosis are routinely screened	Yes	95.29%	
Screening frequency for patients with compensated cirrhosis without varicose veins	2 yrs	54.12%	
Diagnostic criteria for varicose veins	LDRf classification	82.35%	
Treatment of choice for primary prevention of moderate-to-severe varicose veins	Endoscopy + drugs	42.35%	
Endoscopic therapy of choice for primary prevention	EVL/EIS/HI combined therapy	49.41%	
Primary prevention approach	EVs and GVs were treated simultaneously	57.65%	
Primary prevention of gastric varices	Endoscopic therapy	42.35%	
Timing of intervention after hematemesis	<6 h	34.12%	
Treatment of esophageal variceal hemorrhage	Ligation or combination therapy	40.00%	
Remedial measures for treatment failure	TIPS/PTVE	52.94%	
Treatment of cardiac varicose vein rupture and hemorrhage	HI	74.12%	
Remedial treatment for treatment failure	TIPS/PTVE	48.23%	
Treatment of gastric variceal hemorrhage	HI	91.76%	
Remedial measures for treatment failure	TIPS/PTVE	60.00%	
Timing of intervention for secondary prevention	Within 1 wk	67.06%	
Preferred treatment for secondary prevention	Drug + endoscopy	49.41%	
Treatment of choice for isolated gastric varices	HI	52.94%	
Preferred treatment for duodenal varicose veins	HI	54.12%	

EGVs = esophagogastric varices, EV = esophageal varix, EVL = endoscopic variceal ligation, GV = gastric varix, HI = histoacryl injection, LDRf = location, diameter, and risk factor, PTVE = percutaneous transhepatic variceal embolization, TIPS = transjugular intrahepatic portosystemic shunt.

Table 2

Comparison of most commonly selected endoscopic treatment options for different bleeding sites.

Endoscopic treatment option	5 to 10 years of experience (n = 16 endoscopists)	11 to 20 years of experience (n = 22 endoscopists)	≥21 years of experience (n = 47 endoscopists)	<i>P</i> value
Treatment option for esophageal variceal rupture and bleeding (Fig. 3): Combination of treatment regimens (ligation + other en- doscopic treatment)	37.50%	40.90%	40.40%	>0.05
Preferred option after failure of the above treatment: TIPS/ PTVE	68.75%	59.09%	51.06%	>0.05
Treatment for rupture and hemorrhage of cardiac varicose vein (Fig. 4): HI	75.00%	77.27%	80.85%	>0.05
Preferred option after failure of the above treatment: TIPS/ PTVE	50%	68.18%	51.06%	>0.05
Treatment for rupture and bleeding of gastric fundus varices (Fig. 5): HI	87.50%	95.45%	95.74%	>0.06
Preferred option after failure of the above treatment: TIPS/ PTVE	68.75%	86.36%	61.70%	>0.07
Treatment option for ectopic variceal rupture and bleeding (Fig. 6): HI	56.25%	59.09%	55.32%	>0.08

HI = histoacryl injection, PTVE = percutaneous transhepatic variceal embolization,

TIPS = transjugular intrahepatic portosystemic shunt.

for varices (location, diameter, and risk factor (LDRf) classification, 82.35%), and treatment of gastric varices hemorrhage (histoacryl injection, 91.76%). Questions that elicited responses with a relatively low consistency (≤40%) were timing of intervention after hematemesis (<6 hours, 34.12%) and treatment of esophageal variceal hemorrhage (ligation or combination therapy, 40.00%). The consistency of the responses to the remaining 9 questions ranged from 42.35% to 74.12%. No significant difference was detected in the responses to each item in the between-group analyses. In particular, for the item "duration of endoscopic intervention for acute bleeding," which was the question with the lowest response consistency, 29, 23, 28, and 5 subjects selected < 6 hours, 6 to 12 hours, 12 to 24 hours, and > 24 hours, respectively. A total of 94.1% of the respondents chose to complete emergency endoscopy within 24 hours in the above setting.

4. Discussion

To explore differences in the clinical practice of endoscopic treatment of EGVB, we obtained satisfactory responses from Chinese endoscopic physicians with different academic backgrounds, practice conditions, and clinical experience. It is expected that the answers to these questionnaires will be of reference to readers, endoscopists, and researchers worldwide.



Figure 1. Medium-to-large esophageal and gastric varices without bleeding.



Figure 2. Time-step number of patients receiving emergency endoscopic intervention.



Figure 3. Esophageal varices with bleeding.

We believe that the clinical practice of endoscopists may be influenced by many factors, such as personal experience, previous training, operational skills, guidelines,^[6] and academic



Figure 4. Cardiac varices with bleeding.



Figure 5. Rupture and bleeding of gastric fundus varices.

publications. Through a comprehensive comparative analysis of 85 questionnaires (Table 2), we found that the responses to the questionnaire items did not significantly differ among endoscopists with different lengths of experience. This finding indicates that like more experienced clinicians, even doctors with relatively little experience can obtain good uniformity in the diagnosis and treatment of EGVs after undergoing good medical education and short-term clinical practice. China has a vast territory, and the economic development of different regions is uneven; thus, there are certain differences in the quality of medical care available. The Esophageal and Gastric Varices Group of the Society of Digestive Endoscopy of the Chinese Medical Association has been working hard to carry out continuing medical education programs in various forms, including online and offline academic activities, training, and case sharing. The present study showed that "medical homogeneity" may have been achieved among endoscopists with different lengths of experience through these efforts.

Our research showed that the majority (95.29%) of endoscopists agreed with the statement that patients with cirrhosis should receive endoscopic screening for EGVs, which is consistent with the recommendations of consensus guidelines.^[7] In consideration of the risk of EGVB, the Expert Consensus



Figure 6. Ectopic varices (duodenal varices).

on the Diagnosis and Treatment of EGVB in Cirrhotic Portal Hypertension, Chinese Medical Association (2019) recommended that patients with compensated cirrhosis without varices be reexamined using endoscopy every 2 to 3 years.^[8,9] For these patients, most participants in the 3 groups tended to recommend a screening interval of 2 years (38.25%, 53.19%, and 68.18% of endoscopists in the 5 to 10 years, 11 to 20 years, and ≥ 21 years groups, respectively). With increasing experience, a higher proportion of endoscopists tended to shorten the interval between reexaminations. The reason for this may be that with increasing experience, more cases of EGVB are encountered, and endoscopists may be more determined to detect the occurrence of varices as early as possible to reduce the risk of bleeding through patient education and corresponding treatment.

For terms of the diagnosis and treatment criteria for EGVB, 82.35% of endoscopists chose the LDRf classification, which is in line with the eligibility of Chinese patients. The LDRf classification criteria^[10] not only provide a basis for the diagnosis and prognosis prediction of EGVs but also provide normative guidance for the selection of treatment timing and methods. The letter "L" stands for location; the letter "D" stands for diameter; the "Rf" stands for risk factor, and is divided into scores 0, 1, and 2. Compared with previous classification methods, the LDRf classification is simple and more meaningful for guiding clinical decision-making. Since the release of the LDRf classification, it has gradually been accepted by Chinese gastroenterologists/endoscopists, and has also been written into China's guidelines for the diagnosis and treatment of EGVs.^[9,11] China is a country with a large number of patients with liver diseases, including about 7 million patients with liver cirrhosis. Digestive endoscopists have done extensive work on the diagnosis and treatment of esophageal varices, but few high-quality studies are available in this field. Because the LDRf classification is easy to use, covers the entire digestive tract, can guide treatment, and is widely used in China, we hope that our findings will aid research design and data-summation efforts.

The screening, prevention, and treatment of EGVs are particularly important for patients with cirrhosis and portal hypertension because of the morbidity and mortality of EGVB.^[12] This study found that for medium-to-large EGVs, endoscopic therapy and the combination of endoscopic + drug therapy remains preferred choices over drug therapy alone for both primary and secondary prophylaxis (Fig. 7). The Baveno VII version



Figure 7. Proportion of treatment options selected by endoscopists for the primary and secondary prophylaxis of varices.

recommended combination therapy for secondary prophylaxis. For primary prophylaxis, endoscopy can be used if nonselective beta blockers cannot be tolerated.

The 2008 Chinese Consensus on the Prevention and Treatment of Esophageal and Gastric Variceal Hemorrhage in Cirrhotic Portal Hypertension recommended that emergency endoscopic therapy should be administered within 48 hours. The 2015 revision did not recommend a specific timing for endoscopic therapy, but suggested that the timing and method of endoscopic therapy should be determined according to the experience of the physician and the medical/technical conditions in the hospital. It was found in this study that 61.2% of patients could receive emergency endoscopic examination/treatment within 12 hours as recommended by Baveno VI, and 34.1% of them received urgent endoscopy within 6 hours. Those who received intervention after 12 hours were further divided into 2 categories: 32.9% within 12 to 24 hours and 5.9% after 24 hours (Fig. 2). The possible causes were inferred as Chinese vast territory and unbalanced distribution of medical resources. For many hospitals, it is difficult to carry out emergency endoscopy at night/weekend; hence, most doctors choose to carry out emergency endoscopy intervention within 12 to 24 hours (32.9%). In the future, it is in urgent need to accelerate the process of medical homogenization in China, and more doctors should be trained to perform endoscopic treatment for acute EGV rupture and hemorrhage in accordance with the latest international guidelines.

As the preferred diagnostic/treatment method for EGVB, gastroendoscopy can identify the site of bleeding under direct vision and can simultaneously be used for hemostasis treatment.^[7] Endoscopic treatment for active bleeding at different sites achieved a high degree of uniformity among the different groups in our study (Table 2). The first choice of emergency treatment for acute esophageal variceal bleeding was a combination of various methods (40%). Treatment strategies included endoscopic injection sclerotherapy (EIS), esophageal varix ligation (EVL), and tissue adhesive embolization. These choices differ from the recommendations in the UK guidelines, which only recommend EVL for the emergency endoscopic treatment of acute esophageal variceal bleeding.^[13] A recent study indicates that EIS and EVL are both efficient emergency endoscopic treatment strategies for acute esophageal variceal bleeding, and EIS should not be dismissed as an economical and effective emergency endoscopic treatment strategy for acute esophageal variceal bleeding.^[14] In addition, the guidelines in Japan, another Asian country, recommend both EVL and EIS for the treatment of esophageal varices.^[15] The above findings suggest that there exists a certain gap between the East and the West in the understanding and application scope of sclerotherapy.

Because the gastric fundus varices are abundant and superficial, they are prone to varicosity. The venous blood flow at this



Figure 8. Requirements of laboratory indexes for EGVs among endoscopists with different lengths of experience (years). ALB = albumin, INR = international normalized ratio, N = neutrophil count, PLT = platelets.

site is abundant and fast. Once ruptured, fatal massive hemorrhage can occur. For the treatment of gastric varix bleeding, 74.12% of endoscopists chose tissue adhesive embolization, because tissue adhesive has the characteristics of coagulation, rapid hemostasis, and definite effect; transjugular intrahepatic portosystemic stent shunt/percutaneous transhepatic variceal embolization was chosen by 69.4% of the endoscopists for patients with failed endoscopic treatment of EGVB. The LDRf classification not only records the location and diameter of varices but also has significance for guiding treatment. We found good consistency in the endoscopists' choice of classification system for the treatment of variceal bleeding in different parts of the country, indicating that the LDRf classification is widely used in China. Standardization of treatment can benefit more patients and prevent doctors from providing treatment plans based on personal experience, which may result in poor treatment outcomes. It should be noted that the treatment of EGVs involves multidisciplinary participation. After the failure of endoscopic hemostasis, most endoscopists choose to cooperate with interventional radiologists.

In terms of the timing of secondary prophylaxis and treatment of varices, 67.06% of endoscopists chose endoscopic intervention within 1 week after hemostasis. Secondary prophylaxis measures included drug therapy, endoscopic therapy, surgical treatment, and interventional therapy. EVL, endoscopic variceal sclerotherapy, and tissue adhesive embolization were the main measures used for secondary prophylaxis. Most endoscopists believed that combination therapy was better than monotherapy.^[9,16] In terms of treatment options, endoscopic therapy and endoscopic + drug combination therapy were selected by 44.71% and 49.41% of endoscopists, respectively. Liver cirrhosis should not be regarded as a single end-stage disease, but as a group of systemic diseases that can be staged according to significant clinical symptoms. It can lead to leukopenia, thrombocytopenia, decreased albumin, and reduced coagulation factor synthesis, which may increase the risk of infections and intraoperative bleeding as well as delayed wound repair. There is no relevant research on the impact of these factors on endoscopic treatment. In terms of the selection of laboratory indexes for secondary prophylaxis, endoscopists with more than 20 years of experience did not have clear requirements for laboratory indexes, while those with less than 20 years of experience had certain requirements for these indexes and strove to be safe and effective (Fig. 8). The reason may be that younger doctors are more cautious with higher requirements for various indicators, and they expect to achieve higher surgical safety.

Ectopic varices are varices outside the esophagus and stomach in patients with portal hypertension.^[17] Although rare, ectopic variceal bleeding accounts for 2% to 5% of variceal



bleeding related to portal hypertension, and its mortality rate can be as high as 40%.^[18] The pathological characteristics of ectopic varices (for example, duodenal varices) are thinner venous walls and larger diameter, which can cause greater wall tension and lead to a high bleeding rate.^[19] In our study, 54.12% endoscopists chose tissue adhesive embolization for the treatment of ectopic variceal bleeding, after considering its pathological characteristics. Finally, 70.59% of the respondents offered endoscopic treatment for more than 50 cases of EGVs per year, which reflects the wide application of the treatment methods and the consistency of treatment schemes. The choice of treatment-related indicators did differ among the study groups, but the differences were not statistically significant. The selection of treatment options was mainly based on the guidelines in the literature and personal experience (Fig. 9). In other words, Chinese endoscopists may gradually accumulate personal experience based on the guidelines in the literature, which are themselves based on evidence-based medicine.

To our knowledge, this is the only study that focuses on the clinical practice patterns in the endoscopic management of EGVB. In conclusion, Chinese endoscopists mainly choose the appropriate treatment for patients based on evidence-based medicine such as consensus guidelines, which has no relationship with the length of experience. Moreover, endoscopists achieved high consistency in disease screening, treatment options, and corresponding treatment principles. There was no significant difference in the practice modes of endoscopic treatment of EGVB among endoscopists in different hospitals in China. The treatment scheme was mainly selected according to the guidelines in the literature and personal experience, which had a certain impact on the treatment scheme.

4.1. Limitation

The 85 hospitals covered are all public hospitals, and no private, academic, or hybrid hospitals were included, which may have caused a selection bias. Moreover, all 85 endoscopists were from hospitals that were members of the Chinese Esophageal and Gastric Varices Group, which means that they had abundant experience in this field. If the scope of the survey were to be widened to include private hospitals and academic hospitals, the survey results might be a little different.

4.2. Strengths

About 84% of Chinese patients choose public hospitals for treatment (2020 statistics), so this study basically represents the choice of mainstream doctors. The investigated hospitals cover the east, west, north, south, and central parts of China, thereby avoiding the impact of regional differences. The endoscopists who participated in the questionnaire survey were distributed across different age groups, and are thus representative of all endoscopists in China.

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Author contributions

Zhang WH designed, collected the questionnaires and was a major contributor in writing the manuscript. Wang YL analyzed the data and was a contributor in writing the manuscript. Chu JD and Liu YD were contributors in distributing and collecting the questionnaires. LingHu EQ designed, distributed and analyzed the questionnaires. All authors read and approved the final manuscript.

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