Investigation Report On Endoscopic Management of Esophagogastric Variceal Bleeding By Chinese Endoscopists

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Abstract

Background: To explore potential differences in the endoscopic management of esophagogastric variceal bleeding (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 varix (EGV) classification, emergency treatment, and primary and secondary prevention 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 ($P > 0.05$). The majority of endoscopists (95.29%) offered EGV screening for patients with liver cirrhosis. LDRf classification was selected by 82.35% of endoscopists. Endoscopy + medication was preferred (42.35%) for primary prevention of moderate-to-severe EGVs. There was no statistical difference in emergency intervention time for active EGVB ($P > 0.05$). The first choice of emergency treatment for EGVB was combination treatment (40%). Tissue adhesive embolization was selected for gastric variceal bleeding by 74.12% of endoscopists; TIPS/PTVE were selected as remedial measures by 48.23%–52.94% of endoscopists. In addition, 67.06% of endoscopists selected 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 prevention. The choice of laboratory indicators did not differ with length of experience ($P > 0.05$).

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

Background

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 the initial bleeding episode may exceed 50% [1]. Patients who experience a first hemorrhage without treatment have an up to 60% risk of rebleeding. Recently, with advances in diagnosis and treatment, the mortality rate of EGVB has decreased significantly [1, 2] to approximately 12–22% [3–5]. Therefore, disease screening, prevention, and treatment options for patients with cirrhosis and portal hypertension complicated with EGVs have a great impact on survival and prognosis. However, there are no unified guidelines nor a consensus on the diagnosis and treatment of EGVB.

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 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 lay a theoretical foundation for the formulation of clinical guidelines for the diagnosis and treatment of EGVB.

Methods

Subjects

Endoscopists from 85 hospitals in 62 cities from 26 provinces were contacted. 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 People's Liberation Army General Hospital and the Fifth Medical Center of the People's Liberation Army General Hospital approved the study.

Survey

Gastroenterologists/endoscopists who performed endoscopic treatment for EGVB were contacted via email. The questionnaire items involved the academic experience of each participant; the screening and classification of EGVBs by doctors with different lengths of experience; and the primary prevention, emergency treatment, and secondary prevention of EGVB of varying degrees of severity. The questionnaire also included a limited number of high-quality endoscopic images. All the questions were listed step by step on the questionnaire.

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 progressive problems (primary and recurrent bleeding). For each question, only the option that was most commonly selected by the subjects was analyzed.

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 (ANOVA) was used to compare treatment options and the basis of their selection. If ANOVA indicated a significant difference, the Bonferroni multiple comparison test was performed to check for significant pairwise differences. The *t*-test was used to compare differences between two groups. The mean values and standard deviations of important parameters were determined. Median values were provided for each variable. All analyses were performed using SPSS v22, and $P < 0.05$ was considered to indicate statistically significant differences.

Results

The questionnaires of 85 endoscopists from 85 hospitals were divided into 3 groups according to their length of experience: 5–10 years, 16 endoscopists; 11–20 years, 22 endoscopists; and 21 years or more, 47 endoscopists. 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 prevention, emergency treatment, secondary prevention, and remedial measures for different situations.

The most common responses for each of the 16 questions are listed below (Table 1).

Table 1
Most common responses to questions in the questionnaire for EGV management

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 years	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 GVVs were treated simultaneously	57.65%
Primary prevention of gastric varices	Endoscopic therapy	42.35%
Timing of intervention after hematemesis	12–24 h	30.59%
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 week	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; GV, gastric varix; EVL, endoscopic variceal ligation; HI, histoacryl injection; TIPS, transjugular intrahepatic portosystemic shunt; PTVE, percutaneous transhepatic variceal embolization		

(1) To the question “whether to start routine screening for EGV after diagnosis of cirrhosis,” most endoscopists (95.29%) answered “yes.”

(2) For patients with compensated liver cirrhosis and no EGVs, more than half of the endoscopists choose a screening interval of once every 2 years.

- (3) For the classification of EGVs, 82.35% of endoscopists chose the location, diameter, and risk of bleeding (LDRf) classification.
- (4) For medium-to-large EVs without bleeding (Fig. 1), endoscopic therapy with medication was most commonly selected as the primary prevention measure, while endoscopic combination therapy was selected as the most satisfactory treatment option.
- (5) For patients with medium-to-large esophageal varicose veins with gastric varicose veins without bleeding, 57.65% of endoscopists chose simultaneous treatment of esophageal varices and gastric varices (GVs) as a primary preventive measure.
- (6) Most endoscopists chose endoscopic treatment for bulging GV without bleeding.
- (7) For patients with cirrhosis and hematemesis, the most commonly selected endoscopic intervention time was 12–24 h.
- (8) For bleeding esophageal varices (Fig. 2), ligation and multiple treatments were selected as the main measures, and 52.94% of endoscopists chose transjugular intrahepatic portosystemic shunt (TIPS) or percutaneous transhepatic variceal embolization (PTVE) as the next step when endoscopic treatment was unsatisfactory.
- (9) For esophageal varices with blood clot or thrombus (recent bleeding focus), 81.81% of endoscopists placed the first ligation trap on the anal side of the blood clot if ligation was used for treatment.
- (10) For the treatment of GV vein rupture and hemorrhage, the proportion of endoscopists who chose tissue adhesive embolization was 74.12% and 91.76%, respectively, and most endoscopists chose TIPS/PTVE as a remedial measure.
- (11) For patients with acute upper gastrointestinal bleeding (Figs. 3–5), 67.06% of endoscopists recommended secondary prevention within 1 week after the intervention to stop bleeding, and most endoscopists chose the combination of medication and endoscopy for secondary prevention.
- (12) For isolated GV veins and ectopic varicose veins, tissue adhesive embolization was the preferred option for more than half of the endoscopists.
- (13) Among the treatment options for primary and secondary prevention of varicose veins, endoscopy combined with medication therapy was most commonly selected by endoscopists, and there was no statistical difference in the choice of treatment among the 3 groups (Fig. 6).
- (14) A comparison of endoscopic treatment options for different bleeding sites showed no significant difference in the choice of treatment for ruptured EGVs among the 3 groups (Table 2).

Table 2

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

Endoscopic treatment option	5–10 years of experience (n = 16 endoscopists)	11–20 years of experience (n = 22 endoscopists)	≥ 21 years of experience (n = 47 endoscopists)	P value
Treatment option for esophageal variceal rupture and bleeding (Fig. 2): Combination of treatment regimens	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. 3): 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. 4): 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. 5): HI	56.25%	59.09%	55.32%	> 0.08
TIPS, transjugular intrahepatic portosystemic shunt; PTVE, percutaneous transhepatic variceal embolization; HI, histoacryl injection				

(15) There was no significant difference in the selection of laboratory indicators between the groups with 5–10 years (n = 16) and 11–20 years (n = 22) of experience; most endoscopists with 21 years or more of experience did not have personalized requirements for laboratory indicators (Fig. 7).

(16) The treatment options selected by the endoscopists were mainly based on the guidelines in the literature and the doctors' experience, and there was no statistical difference among the 3 groups (Fig. 8).

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. Our questionnaire received a high response rate, which shows that the questions posed in the questionnaire received much attention. It is expected that the answers to these questionnaires will be of reference to readers, endoscopists, and researchers worldwide.

It is generally believed that the clinical practice of endoscopists may be influenced by many factors, such as personal experience, previous training, operational skills, guidelines, and academic publications. Through a comprehensive comparative analysis of 85 questionnaires (Table 1), we found that the responses to the questionnaire items did not significantly differ among endoscopists with different lengths of experience. 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. The guidelines suggest that patients with compensated cirrhosis without varicose veins should undergo gastroscopy every 2 years; those with mild varicose veins should undergo gastroscopy every year, and those with decompensated cirrhosis should undergo gastroscopy every 0.5–1 year [6]. For patients with compensated liver disease without EGVB, 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 5–10 years, 11–20 years, and ≥ 21 years groups, respectively). The risk of EGVB in cirrhosis is estimated to be 5–15% per year [7]. Endoscopic screening of EGVs is essential in patients with cirrhosis complicated with venules or varicose veins, and the time interval of screening should be shortened. Therefore, the Expert Consensus on Diagnosis and Treatment of EGVB in Cirrhotic Portal Hypertension, Chinese Medical Association (2019) [8] recommended that patients with compensated cirrhosis without varicose veins be reexamined using endoscopy every 2–3 years; patients with compensated cirrhosis and mild varicose veins be reexamined using endoscopy every 1–2 years; and patients with liver hardness < 20 kPa and platelet count $> 150 \times 10^9/L$ be allowed to opt out of endoscopic screening.

In terms of the diagnosis and treatment criteria for EGVs, 82.35% of endoscopists chose the LDRf classification, which is in line with the eligibility of Chinese patients. The LDRf classification criteria [9] not only provide a basis for the diagnosis and prognosis of EGVs but also provide normative guidance for the selection of treatment timing and methods. According to statistics [10], the incidence rate of both the formation and aggravation of EGVs is approximately 7% per year. The incidence of hemorrhage from the first rupture of esophageal and gastric varices within 1 year is approximately 12%. The incidence of re-rupture bleeding is approximately 60%. The mortality rate within 6 weeks of esophageal and gastric variceal hemorrhage is 15–20% [10]. Therefore, the screening, prevention, and treatment of EGVs are particularly important for patients with cirrhosis and portal hypertension, and endoscopic therapy and the combination of endoscopic and drug therapy remain the preferred choices over drug therapy alone (Fig. 6).

The purpose of primary prevention is to prevent the formation and progression of varicose veins in order to prevent moderate-to-severe varicose vein rupture and bleeding, and the occurrence of complications as well as to improve the survival rate. A prospective study [6] found that the incidence of bleeding during 1, 3, and 5 years of follow-up was 16%, 36%, and 44%, respectively. The same study reported that the annual bleeding rate for patients with Child-Pugh class A cirrhosis with small varicose veins and no red rash was 4%, while the rate for patients with Child-Pugh class C cirrhosis with large varicose veins and a red rash was 65%. Because GV bleeding is more serious and has a higher mortality rate than esophageal variceal

bleeding, it is necessary to identify high-risk GV patients in time and intervene early to prevent large-diameter GV bleeding. Early intervention and bleeding prevention can improve not only the quality of life of these patients but also the survival rate of patients with cirrhosis. The guidelines recommend primary prevention for patients with moderate-to-severe varicose veins and high bleeding risk, and recommend the use of non-selective β -blockers or endoscopic variceal ligation (EVL) to prevent the first episode of bleeding from varicose veins [6]. Portal shunt surgery, portal evascularization surgery, and TIPS cannot fundamentally change the hemodynamic status of portal hypertension, and are not recommended as measures to prevent the first episode of bleeding [6, 11]. Gastroendoscopy can identify the site of bleeding under direct vision and can simultaneously be used for hemostasis treatment, which has made it the preferred diagnostic/treatment method for EGVB [6]. However, the timing of endoscopic diagnosis and treatment remains controversial [12, 13]. Endoscopic treatment for active bleeding at different sites achieved a high degree of uniformity among the different groups in our study, with consistent rates of 78.72–95.74% (Table 2). The first choice of emergency treatment for acute esophageal variceal bleeding was a combination of various methods (40%). GVs occur in approximately 50% of patients with liver cirrhosis, and is closely related to the severity of liver disease. The incidence of isolated GVs is 33.0–72.4%, and the incidence of bleeding within 2 years is approximately 25% [6]. Because the gastric fundus veins are abundant and superficial, they are prone to varicosity. The venous blood flow at this site is abundant and fast. Once ruptured, fatal massive hemorrhage can occur. For the treatment of GV bleeding, 74.12% of endoscopists chose tissue adhesive embolization, because tissue adhesive has the characteristics of coagulation, rapid hemostasis, and definite effect; TIPS/PTVE was chosen by 48.23–60% of the endoscopists for patients with failed endoscopic treatment of EGVB.

The purpose of secondary prevention is to prevent rebleeding in patients who have already had a bleeding episode, and thereby reduce the rebleeding and mortality rates. In terms of the timing of secondary prevention and treatment of varicose veins, 67.06% of endoscopists chose endoscopic intervention within 1 week after hemostasis. Secondary prevention measures include drug therapy, endoscopic therapy, surgical treatment, and interventional therapy. EVL, endoscopic variceal sclerotherapy, and tissue adhesive embolization are the main measures used for secondary prevention. When choosing one of these treatment methods, endoscopists should take into account the location, diameter, and risk factors for varicose veins [8]. Most authors believe that combination therapy is better than monotherapy [8, 14]. In terms of treatment options, endoscopic therapy and endoscopic-drug combination therapy were selected by 44.71% and 49.41% of endoscopists, respectively. In terms of the selection of laboratory indexes for secondary prevention, those 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. 7).

After the failure of emergency treatment or endoscopic treatment for primary and secondary prevention, TIPS was the preferred choice of treatment for most endoscopists. According to the guidelines in the literature [15, 16], TIPS was given priority after the failure of endoscopic and drug treatment for patients with Child-Pugh class A or B disease, and surgical shunts were considered when there was no sufficient treatment preparation for TIPS or when TIPS was contraindicated. Ectopic varices are varices outside the

esophagus and stomach in patients with portal hypertension [17]. Although rare, ectopic variceal bleeding accounts for 2–5% of variceal bleeding related to portal hypertension, and its mortality rate can be as high as 40% [18]. The pathological characteristics of ectopic varicose veins 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. Finally, 70.59% of the respondents offered endoscopic treatment for more than 50 cases of EGVs per, 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. 8). 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.

Conclusions

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.

Abbreviations

EGVs, esophagogastric varices;

EGVB, esophagogastric variceal bleeding;

TIPS, transjugular intrahepatic portosystemic shunt;

PTVE, percutaneous transhepatic vein embolization;

LDRf classification, location, diameter, and risk of bleeding classification

Declarations

Ethics approval and consent to participate: This study was approved by the ethics committee of the People's Liberation Army General Hospital and the Fifth Medical Center of the People's Liberation Army General Hospital. All procedures performed in the study involving human participants were in accordance

with the ethical standards of the 1964 Declaration of Helsinki and its later amendments. Written informed consent was obtained from all the patients or their immediate family.

Consent for publication: Not applicable.

Availability of data and materials: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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Authors' contributions: WHZ designed, collected the questionnaires and was a major contributor in writing the manuscript. YLW analysed the data and was a contributor in writing the manuscript. JDC and YDL were contributors in distributing and collecting the questionnaires. EQLH designed, distributed and analysed the questionnaires. All authors read and approved the final manuscript.

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Figures

Figure 1

Medium-to-large esophageal and gastric varices without bleeding

Figure 2

Esophageal varices with bleeding

Figure 3

Varicose cardia veins with bleeding

Figure 4

Rupture and bleeding of gastric fundus varices

Figure 5

Ectopic varicose veins (duodenal varicose veins)

Figure 6

Proportion of treatment options selected by endoscopists for the primary and secondary prevention of varicose veins

Figure 7

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

Figure 8

Basis of treatment selection by endoscopists