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Endoscopic treatment for gastroesophageal varices in patients with cirrhosis: a survey comparing between developed and developing countries



Wenhui Zhang^{1,2†}, Ning Kang^{3†}, Yanling Wang^{2†}, Fulong Zhang⁴, Jianbo Xue¹ and Enqiang Linghu^{5*}

Abstract

Background In this survey, we compared endoscopists' approach to treatment of gastroesophageal varices (GOV) in patients with cirrhosis between developed and developing countries. The objective of this study was to undertake a comparative analysis of the approaches employed by endoscopists in developed and developing countries with regard to the treatment of GOV in patients with cirrhosis.

Methods Between Jan 2019 to Aug 2019, we administered a questionnaire-based online survey internationally via e-mail. A total of 148 endoscopists from five countries were invited to participate in the survey, and 93 responses were received (response rate: 62.8%). The questionnaire covered several aspects: characteristics of the respondents, primary prophylactics, endoscopic therapy, and secondary prophylactics for acute variceal bleeding (AVB). The answers were compared between developed and developing countries using the chi-square test. For all tests, a *P* value of < 0.05 was considered significant.

Results There was a significant difference between developed and developing countries in practice settings (P=0.001), the years of independent gastroenterology or endoscopic practice (P=0.036), treating non-hemorrhagic large gastric varices with medicine (P=0.019), and selection of preferred initial endoscopic therapy for active gastric fundic variceal bleeding (P=0.015). Notably, developed and developing countries did not significantly differ in terms of treatment of non-hemorrhagic esophageal varices (P=0.076), initial endoscopic therapy for active gastric cardia variceal bleeding (P=0.272), timing of secondary prophylaxis (P=0.104), timing of endoscopy (P=0.073), measures for secondary prophylaxis (P=0.166), and basis for the selection of management preferences (P=0.278).

Conclusion There were some differences in the practice of endoscopists for GOV in patients with cirrhosis between developing and developed countries. We speculate that these differences may affect the costs, management of primary bleeding, and chances of rebleeding in GOV. Furthermore, the equipment and technical conditions

[†]Wenhui Zhang, Ning Kang, Yanling Wang these authors contributed equally to this work.

*Correspondence: Enqiang Linghu linghuenqiang30120@126.com

Full list of author information is available at the end of the article



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of different hospitals may also significantly influence the endoscopist's choice of treatment modality. We hope that future studies will place greater emphasis on this aspect as continuing education of and providing updated equipment to endoscopists are of paramount importance.

Keywords Gastroesophageal varices, Variceal bleeding, Survey, Portal hypertension, Therapeutic endoscopy, Transjugular intrahepatic portosystemic shunt, Primary prophylaxis, Secondary prophylaxis, Band ligation, Tissue adhesive injection

Background

The rupture of gastroesophageal varices (GOV) is a serious complication in patients with cirrhosis [1, 2]. Despite the recent advancements in treatment, acute variceal bleeding (AVB) is associated with a concerningly high mortality rate of $\sim 20\%$ at 6 weeks [2, 3]. The prevalence of gastroesophageal varices (GOV) in patients with portal hypertension is 17-25%, whereas esophageal varices (EV) are found in up to 85% of these patients. Although EV are more prevalent and frequently present with bleeding, bleeding from gastroesophageal varices (GOV) tends to be more severe, with a 3-year incidence rate of 16–45% and a higher mortality rate [4-6]. The available evidence suggests that gastroesophageal varices type 2 (GOV2) and isolated gastric varices type 1 (IGV1) located on the proximal side of the greater curvature of the cardia present with an elevated risk of rebleeding and mortality and high likelihood of endoscopic treatment failure. Therefore, it is important to manage GOV with the risk of bleeding, including primary prevention for bleeding, treatment for AVB, and secondary prevention for rebleeding.

For patients with AVB, combined treatment with vasoactive drugs, prophylactic antibiotics, and endoscopic techniques is the recommended standard of care. However, many promising new modalities have emerged, such as the combination of coil and glue injection for management of gastric varices and hemostatic powder application [2, 7]. However, the practice of treating GOV is still faced with numerous challenges: (1) The efficacy of endoscopic treatment in AVB is not clear within 24 h of the treatment. (2) There are no guidelines on primary prevention of gastric varices [6, 8]. (3) It is important to know what measures have been taken by the endoscopist, and any regional differences in the practice currently remain unknown.

Currently, there are discrepancies in medical conditions and professional development across different regions. Furthermore, there is a dearth of research examining the current status of GOV treatment. Therefore, we initiated this study to understand the current status of fundal varicose vein treatment in developed and developing countries, identify current problems and directions for improvement, and provide data and useful references for the development of fundal varicose vein treatment in the future.

Methods

Subjects

We included three developed countries (the United States, Poland, and Greece) and two developing countries (Egypt and Brazil). We invited 148 endoscopists from the above countries to participate in an e-mail-based survey and received 93 answered questionnaires, indicating a response rate of 62.8%. To ensure that participants had adequate practical knowledge and skills relevant to the study, all invited endoscopists were required to have at least 5 years of clinical experience in endoscopic practice. The ethics committee of the Fifth Medical Center of Chinese People's Liberation Army General Hospital approved the study.

Inclusion criteria

(1) All of the information sought on the characteristics was obtained in the responses. (2) All questions of the questionnaire had been answered by the interviewee. (3) Except for the last question in the questionnaire, a single answer was provided for all other questions.

Evaluation of gastroesophageal varices

Mild: Gastroesophageal varices are straight or tortuous, without the red sign. **Medium**: (1) Gastroesophageal varices are straight or tortuous, with the red sign. (2) Gastroesophageal varices are serpentine or bulging, without the red sign. **Large**: (1) Gastroesophageal are serpentine or bulging, with the red sign. (2) Gastroesophageal varices are beaded or nodular [9].

Questionnaire

The items included in this questionnaire were determined by consultation and discussion with members of the collaborative group, comprising gastroenterologists, hepatologists, and endoscopists. The questionnaire (supplementary file) was divided into five parts as described below, with all parts except for *the last one* presented as single-choice questions.

The first part queried the following characteristics of the respondent, all questions are single choices: (1) Country of practice, (2) Participant's name, (3) Participant's e-mail address, (4) Years of independent gastroenterology /endoscopic experience, (5) practice settings, and (6) How many patients with gastric varices does the participant's institution treat in a year. The second part of the questionnaire queried about the primary prophylactic given for the bleeding of GOV as follows: (1) In a patient with non-bleeding medium or large esophageal varices, how do you prevent bleeding? (2) In patients with non-bleeding large gastric varices, what do you do?

The third part queried the participants about the timing of the preferred endoscopic treatment for the bleeding of GOV as follows: (1) When do you perform endoscopy in a hemodynamically stable patient with fresh blood hematemesis and cirrhosis? (2) What is your preferred initial endoscopic therapy for active gastric cardia variceal bleeding? (3) What is your preferred initial endoscopic therapy for gastric fundic variceal bleeding?

The fourth part queried about secondary prophylactic measures for the bleeding of GOV in cirrhosis as follows: (1) When do you start measures to prevent rebleeding and secondary prophylaxis after acute (esophageal or gastric) variceal bleeding in patients with cirrhosis? (2) What is your preferred secondary prophylactic measure?

The fifth part queried the participants about their preferred endoscopic treatment: What is the basis for the selection of the above management preferences?

Data processing

We converted the continuous variables in the questionnaire to the categorical variables as follows:

- 1. Years of independent gastroenterological/endoscopic practice: 5–10 years, 10–20 years, and > 20 years.
- 2. How many patients with gastric varices are treated at your institution in a year: 0–5 cases, 5–20 cases, 20–50 cases, and > 50 cases.
- When do you perform endoscopy in a hemodynamically stable patient with fresh blood hematemesis and cirrhosis: <2 h, 2–6 h, 6–12 h, 12–24 h, and >24 h after admission.
- 4. When do you start secondary prophylaxis after acute (esophageal or gastric) variceal bleeding in patients with cirrhosis: <1 week, 1–4 weeks, 1–6 months, >6 months.

Table 1	Years of independent gastroenterological/endoscopic
practice	

Location	Years of independent	N (%)	X ² P
	practice		value
Developed country	5–10	12 (21.1%)	0.036*
	10-20	24 (42.1%)	
	>20	21 (36.8%)	
Developing country	5–10	16 (44.4%)	
	10-20	8 (22.2%)	
	>20	12 (33.3%)	

* Developed country (the United States, Poland, and Greece); developing country (Egypt and Brazil); * P < 0.05, ** P < 0.01

Statistical analysis

All analyses were performed with SPSS 23.0 software. The counts (N) and the percentages (%) are provided for all categorical variables. The following parameters were compared between the two groups using the chi-square test: years of independent gastroenterological/endoscopic practice, practice settings, the number of gastric varices treated at the endoscopist's institution in a year, for non-hemorrhagic medium-to-large esophageal varices, the number of non-hemorrhagic large gastric varices treated with medicine, timing of endoscopy for patients with bleeding, the preferred initial endoscopic therapy for active gastric cardia variceal bleeding, the preferred endoscopic treatment of gastric fundic variceal bleeding, the timing of secondary prevention for bleeding, primary measures taken for secondary prevention, and the basis for the selection of management preference.

For non-normally-distributed continuous variables, the Mann–Whitney U test was performed to compare the developed and developing countries. Multiple response analysis was used to analyze descriptive statistics for multiple choice questions, and percentage of cases was provided for each variable. For all tests, a P value of < 0.05 was considered significant.

Results

Respondent characteristics

A total of 93 questionnaire responses were included in the study (Table 1), and their geographical distribution was as follows: 57 from developed countries (Greece, n=43; the United States, n=9; and Poland, n=5) and 36 from developing countries (Brazil, n = 21 and Egypt, n = 15). Among all respondents, the majority of endoscopists worked in academic hospitals (73.7%) in developed countries and in hybrid hospitals (61.1%) in developing countries. The practice settings for endoscopists significantly differed between developed and developing countries (χ^2 = 38.809, *P* = 0.001). Most endoscopists had been practicing for more than 20 years in both regions (developed 36.8%, developing 33.3%); however, the years of independent gastroenterological or endoscopic practice significantly differed between developed and developing countries (χ^2 = 6.622, *P* = 0.036). Endoscopists in developing countries managed more gastric varices at their institutions; 14 endoscopists (38.9%) from developing countries reported treating more than 50 cases of gastric varices each year, whereas only 2 endoscopists (3.5%)from developed countries reported treating more than 50 cases of gastric varices each year, suggesting that the number of gastric varices annually treated by endoscopists significantly differed between developed and developing countries (χ^2 = 19.750, *P* < 0.001). The majority of respondents in developed countries are employed in academic hospitals. Furthermore, endoscopists in developed

Table 2 Selection of primary preventive measures for gastroesophageal variceal hemorrhage

Treatment of	Treatment	Developed country	Developing country N (%)	χ²	
		N (%)		Р	
				value	
Non-bleeding medium-to-large esophageal varices	Endoscopic therapy	8 (14.0%)	11 (30.6%)	0.076	
	Oral beta blocker therapy	29 (50.9%)	11 (30.6%)		
	Both endoscopic intervention and drug therapy	20 (35.1%)	14 (38.9%)		
Non-bleeding large gastric varices	Prophylactic endotherapy	8 (14.0%)	13 (36.1%)	0.019*	
	Follow up	8 (14.0%)	7 (19.4%)		
	Medical treatment	41 (71.9%)	16 (44.4%)		

* P < 0.05, ** P < 0.01

Table 3 Timing of endoscopy for a hemodynamically stable paties	nt with fresh blood hematemesis
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Treatment of	Timing	Developed country	Developing country	χ ²
		N (%)	N (%)	P value
Hemodynamically stable patient with fresh blood hematemesis and hepatic cirrhosis	<2 h	15 (26.3%)	7 (19.4%)	0.073
	2–6 h	21 (36.8%)	6 (16.7%)	
	6–12 h	16 (28.1%)	18 (50.0%)	
	12–24h	5 (8.8%)	5 (13.9%)	
	>24 h	0 (0.0%)	0 (0.0%)	

* Timing is the amount of time a patient is admitted to the hospital for endoscopy

countries have better access to new guidelines and treatment modalities than endoscopists in developing countries. This may have an impact on regional differences in treatment choice. In addition, a greater proportion of endoscopists in developing countries treat more than 50 patients per year. Therefore, it is reasonable to assume that the disease burden of GOV is higher in developing countries.

Primary prevention for the bleeding of GOV in cirrhosis

Among treatment options for non-bleeding mediumto-large esophageal varices, most endoscopists in developed countries chose oral beta-blocker therapy (50.9%), whereas most endoscopists in developing countries chose both endoscopic intervention and drug therapy (38.9%). The choice of treatment for non-hemorrhagic mediumto-large esophageal varices did not significantly differ between developed and developing countries (χ^2 = 5.153, *P* = 0.076).

For treating gastric varices, in developed countries, most endoscopists chose medicine to manage non-hemorrhagic large gastric varices (71.9%), and relatively fewer endoscopists chose prophylactic endoscopic treatment (14.0%) or follow-up (14.0%). Conversely, in developing countries, nearly half of endoscopists chose prophylactic endoscopic treatment (36.1%) or follow-up (19.4%). These findings suggest that compared with developing countries, in developed countries, endoscopists were significantly more likely to use medicine to manage non-hemorrhagic large gastric varices ($\chi^2 = 7.882$, P = 0.019; Table 2).

Timing of endoscopy and preferred endoscopic treatment measures for the bleeding of GOV

For patients who were hemodynamically stable and had fresh blood hematemesis from GOV, most endoscopists in developed countries chose endoscopic examination within 12 h of admission [2–6 h (36.8%), 6–12 h (28.1%), < 2 h (26.3%)]. Even in developing countries, endoscopists chose to perform endoscopy within 12 h of admission; however, a relatively higher proportion of endoscopists chose endoscopy within 6–12 h of admission (50.0%). The timing of endoscopy for patients with bleeding did not significantly differ between developed and developing countries (χ 2 = 6.974, *P* = 0.073; Table 3).

For patients with active gastric cardia variceal bleeding, most endoscopists in developed countries chose endoscopic band ligation (35.1%) and tissue adhesive injection (29.8%) as the preferred initial endoscopic therapy, whereas most endoscopists in developing countries chose tissue adhesive injection as the preferred initial endoscopic treatment (47.2%) to manage the gastric cardia varices. Moreover, compared with endoscopists in developed countries, a greater proportion of endoscopists in developing countries chose sclerotherapy as the preferred initial endoscopic therapy (8.8% vs. 11.1%). The selection of the preferred initial endoscopic therapy for active gastric cardia variceal bleeding did not significantly differ between developed and developing countries (χ^2 =3.901, *P*=0.272).

For patients with active gastric fundic variceal bleeding, the initial endoscopic therapy preferred by the majority of endoscopists was tissue adhesive injection in both

value

Treatment of	Preferred treatment	Developed country	Developing country	X ²	
		N (%)	N (%)	P valu	
Active gastric cardia variceal bleeding	Endoscopic band ligation	20 (35.1%)	10 (27.8%)	0.272	
	Sclerotherapy	5 (8.8%)	4 (11.1%)		
	Tissue adhesive injection	17 (29.8%)	17 (47.2%)		
	Combination of above	15 (26.3%)	5 (13.9%)		
Gastric fundic variceal bleeding	Endoscopic band ligation	2 (3.5%)	0 (0.0%)	0.015*	
	Sclerotherapy	8 (14.0%)	0 (0.0%)		
	Tissue adhesive injection	38 (66.7%)	34 (94.4%)		
	Combination of above	9 (15 8%)	2 (5.6%)		

 Table 4
 Preferred initial endoscopic therapy for gastric variceal bleeding

* P<0.05, ** P<0.01

 Table 5
 Secondary prophylaxis after acute variceal bleeding

Treatment of	Timing/Treatment	Developed country	Developing country	X ²
		N (%)	N (%)	P value
Time to take secondary preventive measures	<1 week	30 (52.6%)	12 (33.3%)	0.104
	1 week to 1 month	27 (47.4%)	23 (63.9%)	
	1–6 months	0 (0.0%)	1 (2.8%)	
	>6 months	0 (0.0%)	0 (0.0%)	
Gastric fundic variceal bleeding	Medication	4 (6.8%)	1 (2.8%)	0.166
	Endoscopic therapy	4 (6.8%)	7 (19.4%)	
	Interventional therapy (TIPS, PTVE, etc.)	2 (3.4%)	0 (0.0%)	
	Medication and endoscopic therapy	49 (83.1%)	28 (77.8%)	

* Medication is oral beta blocker therapy

developed (66.7%) and developing (94.4%) countries. The preferred endoscopic treatment of gastric fundic variceal bleeding differed between endoscopists from developed and developing countries ($\chi^2 = 10.469$, P = 0.015; Table 4).

Secondary prophylaxis after the rebleeding of GOV

The secondary prophylaxis time for cirrhosis after acute (esophageal or gastric) variceal bleeding was within 1 week (52.6%) or 1-4 weeks (47.4%) in developed countries and 1-4 weeks (63.9%) in developing countries. The timing of secondary prophylaxis did not significantly differ between endoscopists in developed and developing countries ($\chi^2 = 4.523$, P = 0.104).

Most endoscopists chose medication and endoscopic therapy as the preferred secondary prophylactic measures in both developed (83.1%) and developing countries (77.8%). The measures for secondary prophylaxis did not significantly differ between endoscopists in developed and developing countries ($\chi^2 = 5.0749$, P = 0.166; Table 5).

Basis for the selection of the above management preference

When they were asked about the factors influencing the selection of the above management measures, endoscopists in both developed and developing countries acknowledged the following as influencing factors: personal preference and experience, published medical evidence or literature, and national or local society guidelines. However, the influence of published medical evidence was more on endoscopists in developing countries than on those in developed countries. There was no significant difference in factors affecting endoscopists in developing and developed countries (P = 0.278; Table 6).

For primary prevention strategies for non-bleeding large gastric varices, there are more physicians in developed countries who prefer pharmacological treatment and have better adherence to guidelines.

Discussion

Our findings validated that endoscopists in developed and developing countries have differences in their practices to manage GOV in patients with cirrhosis. Researches have shown that compared with no intervention, which typically presents with high risk of esophageal varices in individuals with cirrhosis and no previous history of bleeding, the use of beta-blockers, endoscopic ligation, or ligation combined with beta-blockers can reduce the mortality. However, the effect of the intervention on esophageal varices remains uncertain [10].

Our survey revealed that endoscopists in developing countries used a combination of endoscopy and medicine to prevent bleeding from medium or large non-hemorrhagic esophageal varices, whereas they prescribed oral β -blockers as the primary prophylaxis for the bleeding of esophageal varices.

Factor under consideration	Developed country	Developing country	Mann- Whiteov II tost
	N (%)	N (%)	P value
Your personal preference and experience	27 (47.4%)*	12 (33.3%)*	0.278
Mentor's teachings	7 (12.3%)*	9 (25.0%)*	
Lectures at local or national meetings	5 (8.8%)*	4 (11.1%)*	
National or local society guidelines	18 (31.6%)*	9 (25.0%)*	
Published medical evidence or literature	20 (35.1%)*	18 (50.0%)*	

Table 6 The basis for the selection of the above management preferences

*Case percentage of multiple response analysis

Notably, gastric varices are rarer than the esophageal varices, and their bleeding is more severe than that of esophageal varices [11]. To our knowledge, there is no guideline to recommend any prevention measures for gastric varices [6, 12]. In our survey, among the various measures for the primary prevention for non-hemorrhagic large gastric varices, most endoscopists in developed countries administered drug therapy, whereas some physicians in developing countries chose drug therapy, and some chose follow-up or endoscopic therapy. More high-quality clinical studies are needed to confirm the efficacy of primary prevention measures for gastric varices bleeding.

Some guidelines recommend that endoscopy should be performed within 12 h of hemodynamic resuscitation in patients with suspected AVB, and conversely, if the patient's vital signs are unstable, the patient should undergo endoscopic treatment safely as soon as possible. However, the recommendation level for undergoing endoscopic treatment for AVB is not high [7]. Other studies have shown that performing endoscopy within 6 h of gastroenterology consultation for acute upper gastrointestinal bleeding was not associated with a lower incidence of mortality or rebleeding than performing it within 24 h [8, 12]. Our survey found that most endoscopists in developed countries performed endoscopy within 2-6 h of admission, whereas most endoscopists in developing countries performed endoscopy within 6–12 h of admission. More research evidence is needed on the timing and preferred measures of endoscopy to reduce mortality and rebleeding in patients with AVB.

Guidelines have recommended tissue adhesives for the treatment of gastric varices [6]. Many studies have provided strong evidence in favor of the efficacy and global recognition of cyanoacrylate injection for bleeding of gastric varices [2, 13-15]. However, our investigation found that some endoscopists in developed countries still chose endoscopic band ligation as the preferred treatment, whereas some endoscopists in developing countries still chose sclerotherapy as the preferred treatment. This may have an impact on the rate of re-bleeding in GOV; however, further research is needed in this regard. These differences in the choice of treatment may be

attributable to disparities in medical resources and technological capabilities among different hospitals, as well as varying levels of awareness of the guidelines among endoscopists. In most developed countries, endoscopists take secondary preventive measures within 1 week of AVB in patients with cirrhosis. Conversely, in developing countries, endoscopists usually proceed with secondary prevention between 1 week and 2 months since AVB. Endoscopic ligation reportedly has fewer adverse events than sclerotherapy, and using a transjugular intrahepatic portosystemic shunt may lead to fewer instances of rebleeding than endoscopic ligation [4, 16]. Endoscopy in combination with drug therapy is the first-line therapy to prevent rebleeding after AVB [7, 17, 18]. Most interviewees regarded drug or endoscopic therapy as the preferred secondary preventive measure, which was consistent with guideline recommendations [7].

Our survey was aimed at exploring the differences between developed and developing countries in terms of their practices for GOV in cirrhosis, which we believe have not been explored before. To our knowledge, this study is the first step in investigating the best approach of primary or secondary prophylaxis for the bleeding of GOV in cirrhosis patients with different geographical, economic, and cultural backgrounds. Despite the existence of endoscopic therapy for several decades, our study identified that further improvements are needed in both the understanding of the indications for this therapy and the technical proficiency required in its clinical practice. It is our contention that the most pressing issue currently is the need to enhance the proficiency of endoscopists and to further improve the medical equipment related to endoscopic therapy, particularly in developing countries. In addition, the findings of the present study showed that while most physicians in developing countries (94.4%) selected tissue adhesive injection as the primary prevention strategy for fundal varices, endoscopists in developed countries made more varied choices. We believe that this difference may be attributed to economic factors and medical resources. This study had several limitations. (1) The research questionnaire was distributed via email and did not encompass a sufficiently large number of countries and subjects, which may have resulted in

nonrepresentative data. (2) Given that the capabilities of each center in terms of treatment options vary, some hospitals did not have access to cyanoacrylate or transjugular intrahepatic portosystemic shunt/balloon-occluded retrograde transvenous obliteration therapy, and the endoscopist's choice of treatment may also be significantly influenced by these technical factors. Taken together, it is not possible to exclude the possible influence of differences in healthcare resources on the results of the study. (3) Individual patient data were not collected in this study, and thus, it was not possible to count the proportion of patients who received different treatment modalities or to evaluate the impact of treatment measures on patient prognosis. (4) Unfortunately, due to the lack of information about the management policies of governments in different regions, we are unable to understand the regional variability in government management and how this informs global health strategies. (5) The selection of countries to participate in the study was not done in a way that would avoid bias resulting from geographical concentration or imbalance of medical resources. Overall, endoscopists in developing and developed countries were found to have different practice patterns. We speculate that these different practice patterns may affect the costs, management of primary bleeding, and chances of rebleeding in GOV. Conversely, continuing education is important for all endoscopists, which can decrease the differences in terms of the preference for endoscopic treatment, which typically result from the differences in training, local practice patterns, and specific equipment in developed and developing countries. However, more clinical research is needed to better explore these differences in the future. We believe that this information will be useful to your readers, endoscopy educators, and researchers around the world.

Conclusions

There is a paucity of consensus among endoscopists in both developing and developed countries regarding the preferred initial endoscopic therapy for non-bleeding medium-to-large esophageal varices, active gastric cardia variceal bleeding, and gastric fundic variceal bleeding in patients with cirrhosis. Similarly, there is considerable variation in the time of secondary prophylaxis after acute (esophageal or gastric) variceal bleeding in patients with hepatic cirrhosis. The findings of this study indicate that the medical burden and prognosis of patients with cirrhotic gastroesophageal varices vary between developing and developed countries. Further high-quality clinical research is required to identify more appropriate treatments for gastroesophageal varices in patients with cirrhosis. In addition, it is of paramount importance to provide continuing education and training for endoscopists.

Abbreviations

- GOV Gastroesophageal varices
- AVB Acute variceal bleeding
- TIPS Transjugular intrahepatic portosystemic shunt

Supplementary Information

The online version contains supplementary material available at https://doi.or g/10.1186/s12876-025-03758-6.

Supplementary Material 1

Acknowledgements

None.

Author contributions

WZ: Project administration; Writing - review & editingNK: Data curation; Formal analysis; Writing - original draftYW: Data curationFZ: InvestigationJX: MethodologyELH: Conceptualization; ValidationAll authors read and approved the final manuscript.

Funding None

None.

Data availability

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

Declarations

Ethics approval and consent to participate

The ethics committee of the Fifth Medical Center of Chinese People's Liberation Army General Hospital approved the study. The need for written informed consent was waived by the Fifth Medical Center of Chinese People's Liberation Army General Hospital ethics committee due to no personal patient information is involved. This study was conducted following the principles of the 1975 Declaration of Helsinki.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

¹Department of Gastroenterology, Beijing Daxing District People's Hospital, 26 Huangcun West Road, Daxing district, Beijing 102699, China ²Endoscopy Center, The Fifth Medical Center of Chinese PLA General Hospital, 100 Xisihuan middle road, Fengtai district, Beijing 100039, China ³Institute of Portal Hypertension, The First Hospital of Lanzhou University, 1 Donggangxi road, Chengguan district, Lanzhou 730099, Gansu, China ⁴Department of Gastroenterology, Hangzhou Xixi Hospital, Hangzhou 310023, China

⁵Department of Gastroenterology, The First Medical Center of Chinese PLA General Hospital, 28 Fuxing road, Haidian district, Beijing 100853, China

Received: 4 July 2024 / Accepted: 4 March 2025 Published online: 15 March 2025

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