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Comparison of Outcomes From Sequential Endoscopic Therapy in 60 Patients With Cirrhosis and Esophagogastric Varices Treated at a Provincial and a Tertiary District Hospital

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Data Collection B
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Data Interpretation D
Manuscript Preparation E
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Background: This retrospective study aimed to compare outcomes from sequential endoscopic therapy using a planned, multi-stage eradication approach with combined endoscopic techniques in 60 patients with cirrhosis and esophagogastric varices (EGV) treated at a provincial and a tertiary district hospital.

Material/Methods: Patients receiving secondary prophylaxis of EGV at Pidu District People's Hospital (district tertiary hospital, group A) and Sichuan Provincial People's Hospital (provincial tertiary hospital, group B) between June 1, 2022, and June 30, 2024, were retrospectively included. Group B exhibited more severe baseline disease, including larger portal vein and spleen sizes. Follow-ups at 1, 3, 6, and 12 months assessed clinical symptoms, efficacy, treatment modalities, complications, and compliance.

Results: A total of 60 patients were included, with 30 in group A and 30 in group B. Both groups achieved significant 12-month endoscopic improvements. Severe EGV decreased markedly in group A (73.33% to 6.67%) and group B (83.33% to 20.00%). The red color sign (Rc+) prevalence decreased in group A (96.43% to 11.11%) and group B (93.10% to 34.78%). Group B exhibited reduced mean variceal diameter (1.03 to 0.40 cm) and decreased ascites. Despite differences in specific endoscopic approaches and patient follow-up adherence, the 12-month incidence of major complications was comparable between groups.

Conclusions: Sequential endoscopic therapy demonstrated comparable efficacy and safety in both settings, supporting the safe decentralization of EGV management. However, notable disparities in treatment modality and compliance were observed; thus, future initiatives should prioritize unifying technical training and enhancing patient adherence systems to optimize long-term outcomes.

Keywords: Endoscopy • Esophageal and Gastric Varices • Gastroenterology • Liver Cirrhosis • Retrospective Studies • Tertiary Care Centers

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Introduction

Cirrhosis represents the end-stage of chronic liver disease and can arise from various etiologies. It progresses to decompensated cirrhosis, characterized by portal hypertension, hepatic dysfunction, and severe complications such as esophagogastric varices (EGV), ascites, and hepatic encephalopathy, all of which significantly impair quality of life [1]. Nearly 50% of patients with newly diagnosed cirrhosis present with varices, with an annual incidence of 7% to 8% for new or worsening varices and a 12% yearly risk of first bleeding episode [2]. Esophagogastric variceal bleeding (EGVB) is a life-threatening complication, carrying a 6-week mortality rate of approximately 20% and a rebleeding rate of up to 17% within 6 weeks, despite advances in clinical management [3,4]. Therefore, appropriate treatment of EGVB and prevention of variceal rebleeding are crucial for patients with liver cirrhosis.

Standard care for EGVB includes a combination of vasoactive drugs, prophylactic antibiotics, proton pump inhibitors, endoscopic therapy, and interventional procedures. Among these, endoscopic therapy serves as the first-line strategy for both the primary and secondary prophylaxis of EGVB, and current endoscopic treatments include endoscopic variceal ligation (EVL), endoscopic injection sclerotherapy (EIS), and endoscopic cyanoacrylate injection (ECI) [5]. EVL is effective for esophageal varices, as it mechanically occludes veins but may not address deeper perforating vessels [6]. EIS is useful for gastric varices but carries risks of ulcers, stenosis, or perforation [7]. ECI is the preferred standard for gastric variceal bleeding. It rapidly polymerizes to form a cast, achieving immediate hemostasis [8]. For the endoscopic management of EGV, the currently accepted approach is sequential endoscopic therapy. This strategy is a planned, multi-stage approach utilizing step-by-step endoscopic procedures that combine various techniques—such as EVL, EIS, and ECI—to systematically eradicate esophageal and gastric varices. The primary goals are to reduce the risk of bleeding, promote vascular obliteration, prevent rebleeding, and ultimately decrease patient mortality [9]. To standardize EGV management, major international guidelines, including the Baveno VII consensus, the American Association for the Study of Liver Diseases, and the Asian Pacific Association for the Study of the Liver, strongly recommend EVL as the preferred endoscopic intervention for the secondary prophylaxis of esophageal varices, and ECI as the first-line standard for gastric varices [10-12]. Furthermore, the Asian Pacific Association for the Study of the Liver emphasizes a tailored, sequential approach combining EVL, EIS, and ECI based on specific variceal characteristics to optimize long-term eradication and prevent rebleeding [12].

A critical, yet underexplored, question in real-world practice is whether such complex sequential protocols can be implemented with comparable effectiveness and safety across different healthcare tiers. Provincial tertiary hospitals typically possess advanced resources and expertise. In contrast, district tertiary hospitals are often the first point of contact for a vast patient population, but their capacity to deliver and sustain such intensive management is frequently questioned. Therefore, this retrospective study aimed to compare outcomes from sequential endoscopic therapy in 60 patients with cirrhosis and EGV treated at either a provincial hospital or a tertiary district hospital.

Material and Methods

Patient Selection and Study Design

Patients who underwent sequential endoscopic therapy or secondary prophylaxis of cirrhotic EGV at Pidu District People's Hospital (district tertiary hospital, group A) and Sichuan Provincial People's Hospital (provincial tertiary hospital, group B) between June 1, 2022, and June 30, 2024, were retrospectively included. Hospital admission was driven by natural patient flow (geography, referrals, and disease severity) rather than predefined assignment criteria. All endoscopic examinations and treatments were routinely performed at both institutions. The inclusion criteria were (1) age between 18 and 75 years; (2) decompensated cirrhosis confirmed by ultrasound, computed tomography (CT), or magnetic resonance imaging (MRI) examinations, EGV verified by gastroscopy [13], and a history of related symptoms such as melena or hematemesis; (3) ability to cooperate fully with endoscopic examination, treatment, and follow-up procedures; (4) expected survival time greater than 1 year; and (5) good mental condition and no history of anxiety or depression. The exclusion criteria included (1) gastrointestinal bleeding caused by other etiologies; (2) other severe systemic diseases, such as advanced malignancy, severe coagulopathy, severe hepatic encephalopathy, or refractory massive ascites; (3) unstable vital signs, altered consciousness, or severe cardiac, pulmonary, hepatic, cerebral, or renal failure rendering the patient unsuitable for endoscopic examination or therapy; (4) current pregnancy or breastfeeding; and (5) history of previous surgical or endoscopic treatment for varices. The study protocol was reviewed and approved by the Ethics Committee of Sichuan Provincial People's Hospital. Final approval was obtained from the Ethics Committee of PiDu District People's Hospital (approval No. 2025-52). Written informed consent was obtained from all participants for the treatment and procedures.

Baseline Assessment

All patients underwent comprehensive examinations, including complete blood count, liver and kidney function tests, coagulation profile, ultrasound, tumor marker, and abdominal imaging

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examinations, namely color Doppler ultrasound and multislice computed tomography, alongside other routine clinical indicators. An upper gastrointestinal endoscopy was performed to exclude other concomitant upper gastrointestinal diseases.

Devices and Reagents

Both groups utilized the following: injection needles including the 22 G needle from Micro-Tech (Nanjing) (needle diameter: 22 G, needle length: 4 mm, model: IN02-22423180-J) and the 23 G needle from Boston Scientific (needle diameter: 23 G, needle length: 6 mm, model: M00518301); the 6-shooter multiband ligator from COOK Medical (USA) (model: MBL-6-F); and lauromacrogol injection solution as the sclerosant (Shaanxi Tianyu Pharmaceutical Co, Ltd, National Medical Products Administration, approval No. H20080445).

For endoscopes, group A used the Fujifilm 4450 gastroscope, while group B used either the Olympus CV290 gastroscope or the SonoScape HD-550 gastroscope. For tissue adhesives, group A used Beijing Comate, and group B used Italian GLUBRAN.

Endoscopic Treatment

Both group A and group B adhered to a planned, multi-stage eradication approach using combined endoscopic techniques. This staged approach consisted of the following: (1) initial targeted obliteration during the first endoscopy, prioritizing ECI for gastric varices (when present), and applying either EVL or EIS for esophageal varices (with the specific modality tailored to individual variceal morphology and deep feeders); and (2) scheduled stepwise repeat interventions across follow-ups until complete variceal eradication was achieved. The specific techniques are detailed below

ECI (Gastric Fundus)

Gastric varices located in the gastric fundus were treated first using the "lauromacrogol–tissue adhesive–lauromacrogol" sandwich technique. Under endoscopic retroflexion view in the gastric fundus, the target vein was identified. The needle was advanced, and 2 to 5 mL of lauromacrogol was injected into the target varix. This was immediately followed by rapid injection of 0.5 to 2 mL of cyanoacrylate glue, and then 2 to 5 mL of lauromacrogol (to flush the needle). The needle was then retracted into the sheath, and light pressure was applied to the injection site for 3 seconds before flushing with water and withdrawing the needle. Bleeding from the puncture site was monitored; if present, hemostasis was attempted using needle sheath compression, repeating the sandwich injection if necessary until hemostasis was achieved. Suction was avoided before the glue solidified, to prevent clogging the instrument channel. Finally, the needle sheath was used to probe the treated varix; if soft, additional injection was considered, while a hard texture indicated satisfactory obliteration.

EVL (Esophagus)

After treating gastric varices, the endoscope was withdrawn. The ligation device was attached, and the endoscope was reinserted. Variceal columns starting approximately 1 to 2 cm above the cardia were selected for ligation. Continuous suction was applied until the varix formed a red "red-straw" sign. The ligation ring was then deployed promptly, suction was released, and air was insufflated, resulting in a "purple grape" appearance of the ligated varix. Either a spiral (sequential) or a circumferential (same plane) ligation method was used, based on the variceal pattern, typically placing 4 to 6 bands per session.

EIS (Esophagus)

For esophageal varices, treatment could proceed without scope withdrawal after gastric therapy. The injection needle was inserted into the target varix. Upon confirming blood flashback, a mixture of methylene blue and lauromacrogol (5-10 ml per injection point, total volume not exceeding 40 ml) was injected.

Follow-Up and Sequential Therapy

During scheduled follow-ups at 1, 3, 6, and 12 months, blood tests, abdominal imaging studies, and gastroscopy were performed. In addition to endoscopic treatments, all patients routinely received pharmacological secondary prophylaxis with propranolol throughout the follow-up period, with dosages adjusted according to patient tolerance and target heart rate. Persistent gastric varices underwent repeat ECI. Esophageal varices received supplemental therapy with EVL or EIS based on their recurrent severity.

Assessment Criteria

The clinical and endoscopic outcomes evaluated in this study included variceal eradication efficacy, improvement in severity grading, bleeding risk, and the incidence of complications. These outcomes were objectively evaluated and quantified as follows. Classification of EGV followed the LDRf (Location, Diameter, Risk factor) grading system established by the Chinese Society of Digestive Endoscopy in 2009 [13], as well as the Sarin classification. The severity grading of mild, moderate, and severe presented in our tables for both esophageal and gastric fundal varices was uniformly based on their morphology (form) and size, referencing the guidelines of the Chinese Society of Digestive Endoscopy [14]. Additionally, to align with international size-based criteria, the maximum variceal diameter was quantitatively assessed by visual comparison to endoscopic

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references (a 2.3-mm injection needle sheath for esophageal varices and the 9.0-mm endoscope diameter for gastric varices). The severity of the red color sign (Rc) was graded according to its association with hemorrhage [15]: Rc^+ indicates the presence of red color signs on the variceal surface, suggesting a high risk of impending hemorrhage, whereas Rc^- indicates the absence of red color signs, suggesting a lower immediate risk of bleeding. Upper gastrointestinal bleeding was confirmed by the presence of hematemesis or melena.

Statistical Analysis

Statistical analysis was conducted using R Studio version 4.3.1. Continuous variables are described using medians or means. The *t* test was used to compare the means between the study groups when the data were normally distributed, and the Wilcoxon test was used for variables with a skewed distribution. Categorical variables were expressed as numbers (percentages) and compared using the chi-square test or Fisher exact test. A *P* value <0.05 was considered statistically significant.

Results

Baseline Characteristics

A total of 60 patients were included, with 30 in group A and 30 in group B. The baseline demographic and clinical characteristics are presented in **Table 1**. No significant differences were observed between the 2 groups in terms of sex, age, disease duration, symptoms, disease stage, Child-Pugh classification, portal vein thrombosis rate, and most laboratory blood test indicators.

Group B exhibited a significantly larger main portal vein diameter (1.55±0.30 cm vs 1.33±0.20 cm, *P*=0.001) and spleen size (5.81±0.74 cm vs 5.18±1.07 cm, *P*=0.006) compared with group A. Hematemesis was more frequent in group A (86.67% vs 60.00%, *P*=0.020). Laboratory findings revealed higher aspartate aminotransferase levels (*P*<0.001), higher alkaline phosphatase levels (*P*=0.014), but lower blood urea nitrogen levels (*P*=0.010) in group B.

Initial Treatment Results

At initial presentation, no statistically significant differences were observed in the severity distribution of esophageal varices between group A and group B (*P*=0.794). Severe esophageal varices were prevalent in both groups (73.33% in group A vs 83.33% in group B). Similarly, mean esophageal varix diameter (0.90±0.23 cm vs 1.03±0.43 cm, *P*=0.423) and prevalence of Rc+ (96.43% vs 93.10%, *P*>0.999) were comparable.

For gastric fundal varices, a trend toward higher severity was noted in group B, with 60.00% classified as severe vs 26.67% in group A (*P*=0.051). The mean gastric varix diameter (1.04±1.24 cm vs 0.90±0.56 cm, *P*=0.103) and Rc+ prevalence (62.07% vs 43.33%, *P*=0.150) did not differ significantly.

Table 1. Demographic and baseline characteristics of group A (district tertiary hospital) and group B (provincial tertiary hospital).

Indexes	Group A (n=30)	Group B (n=30)	*P* value
Male, n (%)	19 (63.33)	17 (56.67)	0.598
Age	55.73±12.10	54.77±10.81	0.745
Disease duration, n (%)			0.872
Within 1 month	3 (10.00)	4 (13.33)	
1 month-2 years	9 (30.00)	10 (33.33)	
More than 2 years	18 (60.00)	16 (53.33)	
Alcohol consumption, n (%)	13 (43.33)	6 (20.00)	0.052
Hepatitis, n (%)	16 (53.33)	18 (60.00)	0.602
Autoimmune hepatitis, n (%)	2 (6.67)	5 (16.67)	0.424
Other diseases[1], n (%)	10 (90.9)	4 (100.00)	>0.999
Unknown	19	26	
Antiviral medication, n (%)			0.094
Used	13 (81.25)	18 (100.00)	

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Table 1 continued. Demographic and baseline characteristics of group A (district tertiary hospital) and group B (provincial tertiary hospital).

Indexes	Group A (n=30)	Group B (n=30)	*P* value
Lamivudine	2 (15.38)	0	
Entecavir	11 (84.62)	14 (77.78)	
Tenofovir alafenamide	0	1 (5.56)	
Tenofovir	0	3 (16.67)	
Not used	3 (18.75)	0	
Unknown	14	12	
Child-Pugh classification			0.566
A	16 (53.3)	12 (40.0)	
B	13 (43.3)	16 (53.3)	
C	1 (3.3)	2 (6.7)	
Hematemesis, n (%)	26 (86.67)	18 (60.00)	**0.020**
Melena, n (%)	19 (63.33)	20 (66.67)	>0.999
Ascites, n (%)	3.06±3.54	3.50±3.08	0.224
Liver cancer, n (%)	2 (6.67)	0	0.492
Portal vein thrombosis, n (%)	5 (16.67)	7 (23.33)	0.519
Main portal vein diameter	1.33±0.20	1.55±0.30	**0.001**
Spleen size	5.18±1.07	5.81±0.74	**0.006**
Shunt, n (%)	4 (13.33)	3 (10.00)	>0.999
AST (u/L)	34.20±15.47	53.63±21.05	<0.001
ALB (g/L)	33.46±6.59	34.33±4.30	0.492
ALP (U/L)	102.70±59.69	143.97±78.24	**0.014**
BUN (mmol/L)	7.56±3.68	5.25±2.78	**0.010**
WBC (10^9/L)	6.25±4.62	3.89±2.64	**0.017**
NEU	4.70±4.09	2.42±1.62	**0.012**
LYM	1.08±0.74	0.68±0.35	**0.011**
PT	14.11±2.34	14.11±2.00	0.599
PT-INR	1.23±0.21	1.28±0.19	0.130
APTT	33.11±7.15	27.75±2.69	**<0.001**

Note: "Other diseases" include diabetes mellitus, hypertension, liver cirrhosis, coronary heart disease. AST, aspartate aminotransferase; ALB, serum albumin; ALP, alkaline phosphatase; BUN, blood urea nitrogen; WBC, white blood cell count; NEU, neutrophil count; LYM, lymphocyte count; PT, prothrombin Time; INR, international normalized ratio; APTT, activated partial thromboplastin time.

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Table 2. Initial treatment results of group A (district tertiary hospital) and group B (provincial tertiary hospital).

	Group A (n=30)	Group B (n=30)	*P* value
Esophageal varices			
Severity			0.794
Mild	1 (3.33)	0	
Moderate	5 (16.67)	3 (10.00)	
Severe	22 (73.33)	25 (83.33)	
No	2 (6.67)	2 (6.67)	
Diameter	0.90±0.23	1.03±0.43	0.423
Rc (+)	27 (96.43)	27 (93.10)	>0.999
Gastric fundal varices			
Severity			0.051
Mild	11 (36.67)	4 (13.33)	
Moderate	8 (26.67)	6 (20.00)	
Severe	8 (26.67)	18 (60.00)	
No	3 (10.00)	2 (6.67)	
Classification			0.344
GOV1	19 (70.37)	24 (85.71)	
GOV2	1 (3.70)	0	
IGV1	3 (11.11)	2 (7.14)	
GOV1+GOV2	2 (7.41)	2 (7.14)	
GOV1+IGV1	3 (11.11)	0	
Diameter	1.04±1.24	0.90±0.56	0.103
Rc (+)	18 (62.07)	13 (43.33)	0.150
Rectal varices	0	1 (3.33)	>0.999
Endoscopic treatment			
EVL (rings)	18 (66.67)	10 (33.33)	**0.012**
EIS (injection points)	8 (26.67)	17 (55.17)	**0.026**
Sclerotherapy agent volume	26.63±4.94	24.00±7.11	0.196
ECI (injection points)	26 (86.67)	23 (76.67)	0.506
Tissue adhesive (glue) volume	1.97±1.66	1.87±1.06	0.776
Complications			
Infection	0	0	–
Fever	0	0	–
Liver failure	0	0	–
Pain	9 (30.00)	2 (6.67)	**0.002**
Bleeding	3 (10.00)	2 (6.67)	>0.999

Rc, red color sign; EVL, endoscopic variceal ligation; EIS, endoscopic injection sclerotherapy; ECI, endoscopic cyanoacrylate injection.

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Significant disparities in initial endoscopic management were observed. EVL was performed more frequently in group A (66.67% vs 33.33%, *P*=0.012). EIS was applied more often in group B (55.17% vs 26.67%, *P*=0.026). Volumes of sclerosant (26.63±4.94 mL vs 24.00±7.11 mL, *P*=0.196) and tissue adhesive (1.97±1.66 mL vs 1.87±1.06 mL, *P*=0.776) did not differ significantly. Gastric fundus glue injection was performed at similar rates (86.67% vs 76.67%, *P*=0.506) (**Table 2**).

Follow-Up Results

There was no significant difference in the Child-Pugh classification between the 2 groups at any point during the 1-year follow-up (all *P*>0.05), indicating comparable baseline liver function and similar safety profiles regarding liver function preservation. Throughout the 12-month follow-up, group B consistently demonstrated a significantly larger main portal vein diameter compared with group A at all timepoints (*P*<0.05). Spleen size was significantly larger in group B at the 1-, 3-, and 6-month visits (*P*<0.05), but this difference was no longer statistically significant by 12 months (*P*=0.455). The severity distribution of esophageal varices differed significantly between groups at 1 month (*P*=0.047) and 12 months (*P*<0.001). Group B had a higher proportion of severe cases at 1 month (30.0% vs 8.0%), but this pattern shifted by 12 months.

Group B received significantly more esophageal band ligations at the 1-month (83.33% vs 50.00%, *P*=0.008) and 12-month (56.67% vs 0%, *P*<0.001) timepoints. Conversely, EIS injection points were more frequently applied in group A at the 3-month

Table 3. Postoperative results at 1-, 3-, 6-, and 12-month follow-up for group A (district tertiary hospital) and group B (provincial tertiary hospital).

Indexes	One-month follow-up			Three-month follow-up		
	Group A (n=30)	Group B (n=30)	*P* value	Group A (n=30)	Group B (n=30)	*P* value
Child-Pugh classification			0.588			>0.999
A	14 (53.8)	19 (63.3)		14 (56.0)	16 (53.3)	
B	12 (46.2)	11 (36.7)		10 (40.0)	13 (43.3)	
C	0	0		1 (4.0)	1 (3.3)	
Main portal vein diameter	1.35±0.20	1.58±0.30	**<0.001**	1.37±0.20	1.58±0.30	**<0.001**
Spleen size	5.37±1.18	5.80±0.67	0.050	5.33±1.14	5.76±0.63	**0.029**
AST (u/L)	41.86±32.02	47.70±18.64	**0.039**	44.36±30.87	42.97±21.17	0.833
ALB (g/L)	39.69±8.84	35.37±4.59	**0.021**	38.85±4.67	34.95±6.20	**0.008**
ALP (U/L)	126.86±80.06	139.57±64.35	0.077	144.00±187.33	122.83±59.55	0.669
BUN (mmol/L)	7.27±6.28	9.91±15.59	0.688	34.65±144.36	5.20±2.32	**0.019**
WBC (10^9/L)	4.69±2.92	3.46±1.75	0.067	5.34±2.55	3.42±1.61	**0.004**
NEU	3.32±2.65	2.41±1.50	0.175	4.22±3.25	2.28±1.37	0.002
LYM	0.85±0.41	0.66±0.34	**0.018**	0.87±0.44	0.73±0.31	0.250
PT	14.70±2.17	13.39±1.33	**0.024**	15.08±2.45	13.78±1.71	**0.022**
PT-INR	1.19±0.15	1.22±0.13	0.308	1.16±0.11	1.25±0.16	**0.010**
APTT	35.05±9.85	27.23±2.56	**<0.001**	31.64±4.87	28.38±3.55	**0.002**
Esophageal varices						
Severity			**0.047**			0.531
Mild	10 (40.00)	4 (13.33)		10 (38.46)	14 (46.67)	
Moderate	11 (44.00)	15 (50.00)		8 (30.77)	12 (40.00)	
Moderately severe	0	1 (3.33)		0	0	

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Table 3 continued. Postoperative results at 1-, 3-, 6-, and 12-month follow-up for group A (district tertiary hospital) and group B (provincial tertiary hospital).

Indexes	One-month follow-up			Three-month follow-up		
	Group A (n=30)	Group B (n=30)	*P* value	Group A (n=30)	Group B (n=30)	*P* value
Severe	2 (8.00)	9 (30.00)		6 (23.08)	3 (10.00)	
No	2 (8.00)	1 (3.33)		2 (7.69)	1 (3.33)	
Diameter	0.48±0.13	0.53±0.24	0.756	0.50±0.20	0.40±0.25	**0.026**
Rc (+)	13 (52.00)	12 (46.15)	0.676	13 (59.09)	6 (22.22)	**0.008**
Gastric fundal varices						
Severity			**0.007**			**0.014**
Mild	19 (76.00)	10 (34.48)		1 (3.85)	0	
Moderate	0	3 (10.34)		0	0	
Severe	0	2 (6.90)		12 (46.15)	5 (17.24)	
No	6 (24.00)	14 (48.28)		13 (50.00)	24 (82.76)	
Classification			0.797			0.047
GOV1	14 (46.67)	15 (50.00)		12 (40.00)	4 (13.33)	
GOV2	1 (3.33)	1 (3.33)		0	0	
IGV1	3 (10.00)	1 (3.33)		0	1 (3.33)	
GOV1+GOV2	1 (3.33)	0		1 (3.33)	1 (3.33)	
No	11 (36.67)	13 (43.33)		17 (56.67)	24 (80.00)	
Diameter	0.26±0.08	0.38±0.17	**0.013**	0.35±0.11	0.40±0.30	0.582
Rc (+)	0	1 (3.85)	>0.999	5 (35.71)	0	**0.003**
Rectal varices	0	1 (3.33)	>0.999	0	1 (3.33)	>0.999
Endoscopic treatment						
EVL (rings)	13 (50.00)	25 (83.33)	**0.008**	8 (30.77)	14 (48.28)	0.186
EIS (injection points)	2 (8.33)	4 (13.33)	0.682	9 (34.61)	0	**<0.001**
Sclerotherapy agent volume	25.00±7.07	15.00±6.00	0.219	24.78±0.26	–	–
Gastric fundus						
ECI (injection points)	8 (30.77)	10 (33.33)	0.838	10 (38.46)	4 (13.33)	0.061
Tissue adhesive (glue) volume	0.81±0.26	0.85±0.53	0.731	1.10±0.52	2.25±3.50	0.204
Complications						
Infection	0	0	–	0	0	–
Fever	0	0	–	0	0	–
Liver failure	0	0	–	0	0	–
Pain	0	0	–	2 (7.69)	0	0.211
Bleeding	8 (32.00)	0	**0.001**	9 (34.62)	2 (6.67)	**0.016**

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Table 3 continued. Postoperative results at 1-, 3-, 6-, and 12-month follow-up for group A (district tertiary hospital) and group B (provincial tertiary hospital).

Indexes	Six-month follow-up			Twelve-month follow-up		
	Group A (n=30)	Group B (n=30)	*P* value	Group A (n=30)	Group B (n=30)	*P* value
Child-Pugh classification			0.375			0.475
A	11 (39.3)	17 (56.7)		12 (41.4)	17 (56.7)	
B	16 (57.1)	11 (36.7)		15 (51.7)	11 (36.7)	
C	1 (3.6)	2 (6.7)		2 (6.9)	2 (6.7)	
Main portal vein diameter	1.33±0.20	1.58±0.28	**<0.001**	1.36±0.30	1.63±0.31	**<0.001**
Spleen size	5.33±0.95	5.80±0.65	**0.027**	5.48±0.97	5.75±0.62	0.455
AST (u/L)	35.39±17.60	50.33±36.79	**0.009**	44.27±30.01	49.27±20.95	0.093
ALB (g/L)	38.05±6.88	34.15±5.08	**0.020**	38.32±5.95	35.00±6.07	**0.030**
ALP (U/L)	122.07±94.63	139.73±55.35	**0.036**	121.17±62.32	141.17±67.37	0.222
BUN (mmol/L)	7.07±3.79	6.70±3.75	0.767	8.56±11.49	8.38±14.82	0.147
WBC (10^9/L)	5.16±2.27	3.77±2.48	**0.003**	5.11±2.98	3.67±2.87	**0.002**
NEU	3.59±1.97	2.65±2.10	**0.009**	3.51±2.43	2.63±2.70	**0.008**
LYM	0.98±0.50	0.73±0.42	**0.020**	1.05±0.72	0.65±0.22	**0.035**
PT	19.86±22.87	14.19±1.98	**0.006**	15.96±2.84	14.08±1.95	**0.009**
PT-INR	1.17±0.12	1.29±0.18	**0.011**	1.17±0.25	1.27±0.18	**0.025**
APTT	33.39±6.47	27.65±3.05	**<0.001**	34.32±8.18	28.62±3.56	**0.001**
Esophageal varices						
Severity			0.463			**<0.001**
Mild	19 (67.86)	16 (53.33)		21 (70.00)	13 (43.33)	
Moderate	6 (21.43)	9 (30.00)		0	10 (33.33)	
Moderately severe	0	0		0	0	
Severe	1 (3.57)	4 (13.33)		2 (6.67)	6 (20.00)	
No	2 (7.14)	1 (3.33)		7 (23.33)	1 (3.33)	
Diameter	0.40±0.16	0.39±0.24	0.299	0.32±0.20	0.40±0.21	**0.068**
Rc (+)	10 (40.00)	20 (68.97)	0.054	3 (11.11)	8 (34.78)	**0.044**
Gastric fundal varices						
Severity			0.104			0.102
Mild	8 (29.63)	6 (20.00)		5 (16.67)	6 (20.00)	
Moderate	0	4 (13.33)		1 (3.33)	5 (16.67)	
Severe	0	2 (6.67)		0	2 (6.67)	
No	19 (70.37)	18 (60.00)		24 (80.00)	17 (56.67)	
Classification			>0.999			0.383
GOV1	7 (23.33)	9 (30.00)		5 (16.67)	11 (36.67)	

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Table 3 continued. Postoperative results at 1-, 3-, 6-, and 12-month follow-up for group A (district tertiary hospital) and group B (provincial tertiary hospital).

Indexes	Six-month follow-up			Twelve-month follow-up		
	Group A (n=30)	Group B (n=30)	*P* value	Group A (n=30)	Group B (n=30)	*P* value
GOV2	0	0		0	0	
IGV1	0	1 (3.33)		1 (3.33)	0	
GOV1+GOV2	1 (3.33)	2 (6.67)		0	2 (6.67)	
No	22 (73.33)	18 (60.00)		24 (80.00)	17 (56.67)	
Diameter	0.26±0.07	0.40±0.20	0.136	0.25±0.08	0.39±0.16	**0.029**
Rc (+)	18 (85.71)	23 (100.00)	0.100	1 (4.35)	2 (8.70)	>0.999
Rectal varices	0	1 (3.33)	>0.999	0	1 (3.33)	>0.999
Endoscopic treatment						
EVL (rings)	10 (35.71)	13 (43.33)	0.600	0	17 (56.67)	**<0.001**
EIS (injection points)	7 (25.00)	2 (6.67)	0.075	2 (7.14)	1 (3.33)	0.605
Sclerotherapy agent volume	25.71±5.35	16.50±2.12	**0.043**	17.00±9.90	1.00	–
Gastric fundus						
ECI (injection points)	4 (14.29)	7 (23.33)	0.508	1 (3.57)	10 (34.48)	**0.005**
Tissue adhesive (glue) volume	1.50±1.22	1.50±0.71	0.771	1.50	1.05±0.60	–
Complications						
Infection	0	0	–	0	0	–
Fever	0	0	–	0	0	–
Liver failure	0	0	–	0	0	–
Pain	0	0	–	0	0	–
Bleeding	4 (14.29)	2 (6.67)	0.415	2 (7.14)	3(10.00)	>0.999

AST, aspartate aminotransferase; ALB, serum albumin; ALP, alkaline phosphatase; BUN, blood urea nitrogen; WBC, white blood cell count; NEU, neutrophil count; LYM, lymphocyte count; PT, prothrombin Time; INR, international normalized ratio; APTT, activated partial thromboplastin time; Rc, red color sign; EVL, endoscopic variceal ligation; EIS, endoscopic injection sclerotherapy; ECI, endoscopic cyanoacrylate injection.

visit (34.61% vs 0%, *P*<0.001). For gastric varices, the number of tissue adhesive (glue) injection points was significantly higher in group B at 12 months (34.48% vs 3.57%, *P*=0.005) (**Table 3**).

During the follow-up period, the specific sources of rebleeding were also identified: in group A, rebleeding originated from esophageal (n=1) and gastric varices (n=1), primarily triggered by poor dietary compliance and persistent portal hypertension; in group B, rebleeding occurred from esophageal (n=1) and gastric varices (n=2), largely associated with portal vein thrombosis and elevated portal pressure.

Regarding rebleeding events occurring after 12 months of treatment, 2 cases occurred in group A (1 from esophageal varices and 1 from gastric varices), while 3 cases occurred in group B (1 from esophageal varices and 2 from gastric varices).

Preoperative and Postoperative Comparison

Representative endoscopic images demonstrating the sequential treatment of esophageal and gastric varices are shown in **Figures 1 and 2**, respectively. Both groups exhibited marked reduction in esophageal variceal severity (*P*<0.001 for both). In group A, severe cases decreased from 73.33% to 6.67%, with 70.00% transitioning to mild severity. Group B showed a

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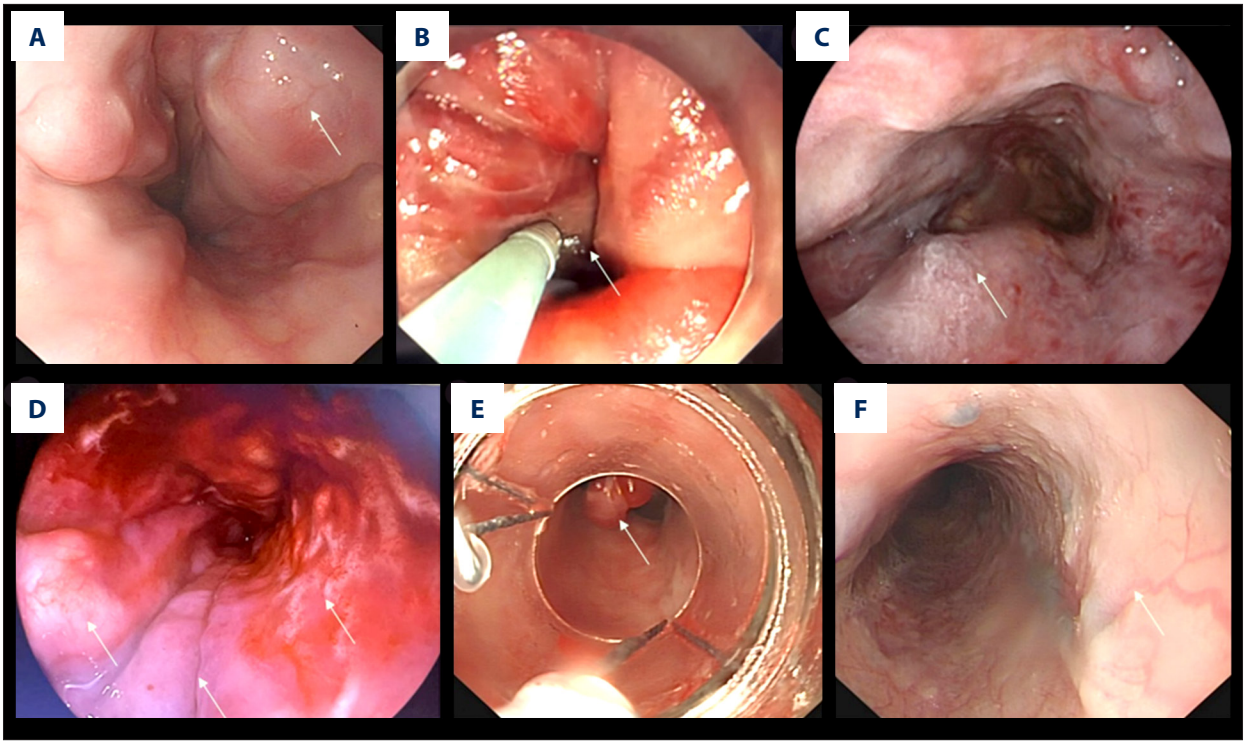

Figure 1. Sequential endoscopic therapy for severe esophageal varices (EV). Representative endoscopic sequence from a single patient (group B). (**A**) Pre-treatment baseline: white arrows indicate significant severe esophageal varices and positive red color sign (Rc+). (**B**) Initial treatment: white arrow indicates endoscopic injection sclerotherapy (EIS) in progress. (**C**) 1-month follow-up: partial relief of varices; white arrow indicates residual varices (supplementary EIS was subsequently performed). (**D**) 3-month follow-up: white arrow indicates residual varices (supplementary endoscopic variceal ligation [EVL was later performed) and upward migration of tissue adhesive from previous gastric variceal injection. (**E**) 6-month follow-up: white arrow indicates supplementary EVL in progress. (**F**) 1-year follow-up: significant improvement; white arrow indicates visible sclerosant retention.

decrease from 83.33% to 20.00% severe cases, with 43.33% becoming mild. Variceal diameter decreased significantly in both groups (group A: 0.90±0.23 cm to 0.32±0.20 cm, $P<0.001$; group B: 1.03±0.43 cm to 0.40±0.21 cm, $P<0.001$). The prevalence of Rc+ also decreased markedly (group A: 96.43% to 11.11%, $P<0.001$; group B: 93.10% to 34.78%, $P<0.001$).

Pain was significantly reduced in group A (30.00% to 0%, $P=0.002$). Bleeding events were comparable between groups (group A: 10.00% to 7.14%, $P\geq0.999$; group B: 6.67% to 10.00%, $P\geq0.999$). No infections, fever, or liver failure occurred in either group (**Table 4**).

Discussion

The advantage of repeated endoscopic treatment is that, in addition to providing emergency hemostasis, it allows for the assessment of variceal severity through regular and standardized follow-up until the varices are eradicated [16]. Our findings demonstrate that a structured, sequential endoscopic protocol combining EVL, EIS, and ECI is a highly effective strategy for the secondary prophylaxis of EGV, this is consistent with previous studies, which have shown that sequential endoscopic therapy may significantly reduce mortality and rebleeding rates in patients with EGVB, compared with other conventional treatment strategies [9,17].

The most striking finding of our study is that long-term effectiveness was achieved in both the district tertiary hospital (group A) and provincial tertiary hospital (group B) settings, despite stark differences in baseline patient characteristics. Specifically, patients in group A demonstrated excellent long-term outcomes, with significant improvement in EGV observed during the 12-month follow-up period. Similarly, patients in group B demonstrated excellent long-term (12-month) outcomes in terms of symptomatic and endoscopic improvement, evidenced by significant reductions in ascites and the dramatic amelioration of esophageal and gastric variceal severity. Despite comparable initial variceal severity, group B exhibited more advanced disease markers, including larger portal vein diameter and spleen size, suggesting a more severe underlying portal

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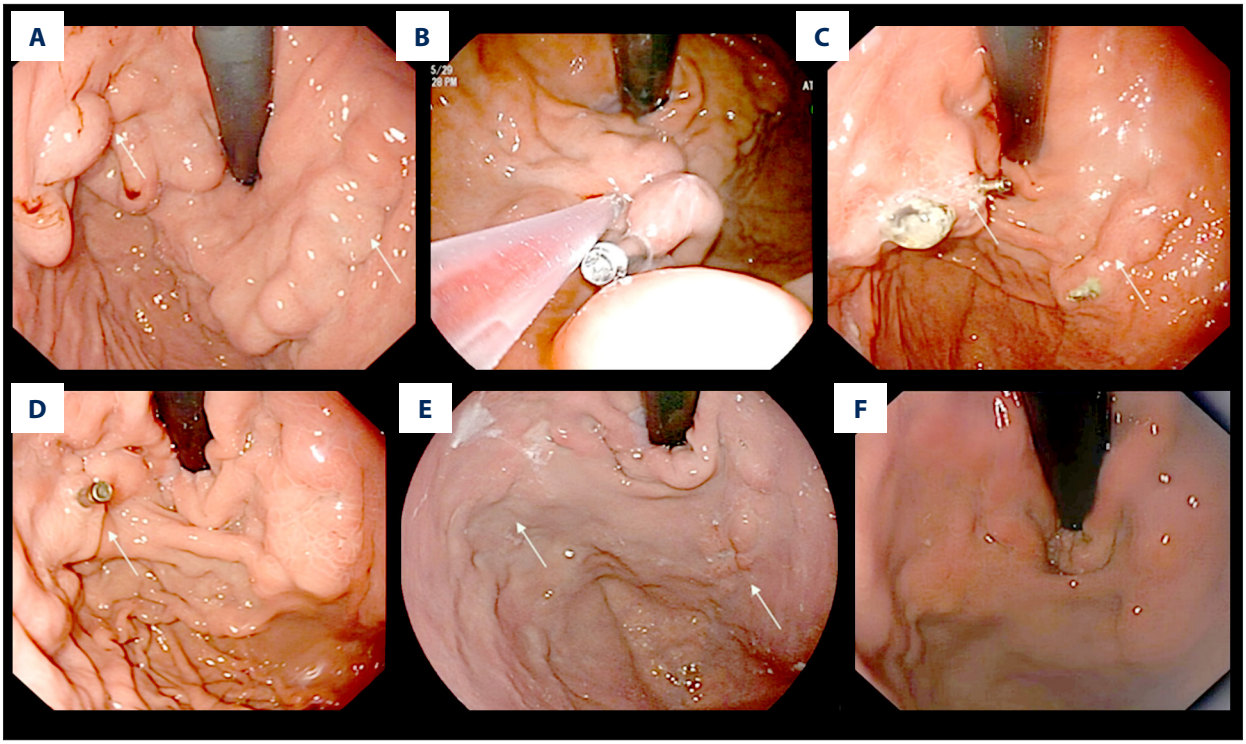

Figure 2. Sequential endoscopic therapy for severe gastric varices (GV). Representative endoscopic sequence from a single patient (group A). (**A**) Pre-treatment baseline: white arrows indicate severe gastric fundal varices. (**B**) Initial treatment: multi-point endoscopic cyanoacrylate injection (ECI) in progress. (**C**) One-month follow-up: significant relief; white arrows indicate a glue extrusion ulcer and small residual varices, followed by supplementary endoscopic injection sclerotherapy (EIS). (**D**) Three-month follow-up: white arrow indicates that varices have largely disappeared and the extrusion ulcer has healed. (**E**) Six-month follow-up: white arrows indicate non-prominent varices. (**F**) One-year follow-up: no varices visible.

hypertensive state at baseline. This is expected, as provincial tertiary centers typically receive referrals for the most complex cases [18]. Additionally, the long-term data reveal interesting patterns in variceal recurrence and management. During the initial treatment phase, group B utilized EIS more frequently, which may be attributed to the generally more severe clinical presentation of patients at baseline. While EVL remains the standard approach, recent studies have revealed its limitations in achieving complete variceal eradication [19]. In such complex cases, EIS, although it carries higher risks, can provide potent intervention by obliterating deep perforating feeders under well-supported conditions. Owing to superior comprehensive management resources and greater procedural proficiency among its medical staff, group B achieved favorable outcomes with EIS, leading to a subsequent shift toward EVL as patients' variceal severity decreased during follow-up. In contrast, group A primarily used EVL initially, as it is technically less demanding and thus more feasible in settings with limited operational experience or resources. In later stages, group A increased the use of EIS to address residual or recurrent varices. Specifically, for smaller vessels that are less amenable to ligation, EIS was used to obliterate deep perforating feeders and achieve complete eradication, consistent with the Chinese Society of Digestive Endoscopy Guidelines [14]. Notably, the incidence of major complications, including rebleeding, was similar between the 2 groups at the 12-month follow-up, suggesting that both methods can achieve comparable efficacy and safety when applied appropriately.

A pivotal aspect of our protocol's success was the adherence to a strict, timed schedule for repeat endoscopic assessments and treatments [20]. Variceal management is not a single event but a process [21]. Liver cirrhosis and portal hypertension are progressive conditions. Even after successful initial eradication, new varices can form, and small residual vessels can repopulate under persistent pressure. Our protocol of scheduled surveillance endoscopies allowed for the timely detection and treatment of residual or recurrent varices before they reached a high-risk stage [9]. There is no standard time limit or number of sessions required for variceal eradication, although most studies report a mean of 3 to 6 sessions [11,22], and the optimal interval remains debated [23]. In this study, endoscopic examinations and treatment was performed every 2 to 6 months to reduce variceal severity until the varices were eradicated. The follow-up completion rate was significantly higher in group B than in group A (78.59% vs 54.32%), indicating better patient

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Table 4. Preoperative and postoperative comparison of group A (district tertiary hospital) and group B (provincial tertiary hospital).

Indexes	Group A			Group B		
	Preoperative (n=30)	Postoperative (n=30)	*P* value	Preoperative (n=30)	Postoperative (n=30)	*P* value
Ascites	3.06±3.54	2.05±2.82	0.355	3.50±3.08	1.89±2.68	**0.009**
Main portal vein diameter	1.33±0.20	1.36±0.30	0.835	1.55±0.30	1.63±0.31	0.285
Spleen size	5.18±1.07	5.48±0.97	0.162	5.81±0.74	5.75±0.62	0.941
AST (u/L)	34.20±15.47	44.27±30.01	0.149	53.63±21.05	49.27±20.95	0.534
ALB (g/L)	33.46±6.59	38.32±5.95	**0.003**	34.33±4.30	35.00±6.07	0.723
ALP (U/L)	102.70±59.69	121.17±62.32	**0.024**	143.97±78.24	141.17±67.37	0.965
TBIL (umol/l)	21.47±11.17	27.91±18.16	**0.048**	32.07±22.58	31.44±21.86	0.668
DBIL (umol/L)	8.49±4.80	12.39±10.15	0.056	14.07±13.13	14.74±15.81	0.767
BUN (mmol/L)	7.56±3.68	8.56±11.49	0.429	5.25±2.78	8.38±14.82	0.717
WBC (10^9/L)	6.25±4.62	5.11±2.98	0.584	3.89±2.64	3.67±2.87	0.487
NEU	4.70±4.09	3.51±2.43	0.433	2.42±1.62	2.63±2.70	0.559
LYM	1.08±0.74	1.05±0.72	0.723	0.68±0.35	0.65±0.22	0.790
HGB	81.67±28.08	105.53±30.95	**0.004**	89.57±28.10	98.63±31.93	0.325
PT	14.11±2.34	15.96±2.84	**0.009**	14.11±2.00	14.08±1.95	0.894
PT-INR	1.23±0.21	1.17±0.25	0.462	1.28±0.19	1.27±0.18	0.888
APTT	33.11±7.15	34.32±8.18	0.467	27.75±2.69	28.62±3.56	0.451
Esophageal varices						
Severity			**<0.001**			**<0.001**
Mild	1 (3.33)	21 (70.00)		0	13 (43.33)	
Moderate	5 (16.67)	0		3 (10.00)	10 (33.33)	
Severe	22 (73.33)	2 (6.67)		25 (83.33)	6 (20.00)	
No	2 (6.67)	7 (23.33)		2 (6.67)	1 (3.33)	
Diameter	0.90±0.23	0.32±0.20	**<0.001**	1.03±0.43	0.40±0.21	**<0.001**
Rc (+)	27 (96.43)	3 (11.11)	**<0.001**	27 (93.10)	8 (34.78)	**<0.001**
Gastric fundal varices						
Severity			**<0.001**			**<0.001**
Mild	11 (36.67)	5 (16.67)		4 (13.33)	6 (20.00)	
Moderate	8 (26.67)	1 (3.33)		6 (20.00)	5 (16.67)	
Severe	8 (26.67)	0		18 (60.00)	2 (6.67)	
No	3 (10.00)	24 (80.00)		2 (6.67)	17 (56.67)	
Diameter	1.04±1.24	0.25±0.08	**0.001**	0.90±0.56	0.39±0.16	**<0.001**
Rc (+)	18 (62.07)	1 (4.35)	**<0.001**	13 (43.33)	2 (8.70)	**0.006**
Rectal varices	0	0	–	1 (3.33)	1 (3.33)	>0.999

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Table 4 continued. Preoperative and postoperative comparison of group A (district tertiary hospital) and group B (provincial tertiary hospital).

Indexes	Group A			Group B		
	Preoperative (n=30)	Postoperative (n=30)	*P* value	Preoperative (n=30)	Postoperative (n=30)	*P* value
Endoscopic treatment						
EVL (rings)	9 (33.33)	0	**0.001**	20 (66.67)	17 (56.67)	0.596
EIS (injection points)	16 (55.17)	2 (7.14)	**<0.001**	8 (26.67)	1 (3.33)	**0.026**
Sclerotherapy agent volume	26.63±4.94	17.00±9.90	0.103	24.00±7.11	1.00	0.173
Gastric fundus						
ECI (injection points)	26 (86.67)	1 (3.57)	**<0.001**	23 (76.67)	10 (34.48)	**0.001**
Tissue adhesive (glue) volume	1.97±1.66	1.5	–	1.87±1.06	1.05±0.60	**0.033**
Complications						
Infection	0	0	–	0	0	–
Fever	0	0	–	0	0	–
Liver Failure	0	0	–	0	0	–
Pain	9 (30.00)	0	**0.002**	0	0	–
Bleeding	3 (10.00)	2 (7.14)	>0.999	2 (6.67)	3 (10.00)	>0.999

AST, aspartate aminotransferase; ALB, serum albumin; ALP, alkaline phosphatase; BUN, blood urea nitrogen; WBC, white blood cell count; NEU, neutrophil count; LYM, lymphocyte count; PT, prothrombin Time; INR, international normalized ratio; APTT, activated partial thromboplastin time; Rc, red color sign; EVL, endoscopic variceal ligation; EIS, endoscopic injection sclerotherapy; ECI, endoscopic cyanoacrylate injection.

compliance in group B. This higher adherence likely contributed to the improved outcomes observed in group B, despite its patients' more severe baseline conditions. Therefore, strengthening dedicated follow-up systems in district tertiary hospitals to enhance patient compliance may improve the management of large cohorts of patients with cirrhosis and help reduce the clinical burden on provincial tertiary centers.

Our study demonstrates that decentralization of care, with district tertiary hospitals handling appropriate cases, is feasible. This requires standardized training programs for endoscopists and nurses in district tertiary hospitals to build and maintain technical proficiency in EVL, EIS, and ECI. Furthermore, the implementation of clear, step-by-step institutional protocols for patient selection, treatment sequences, and follow-up schedules ensures consistency in treatment outcomes across different settings. Equally important is that the establishment of efficient referral pathways to provincial tertiary centers is crucial for managing complications or patients who do not respond to primary care management.

This study has limitations. Its retrospective design and small sample size can introduce selection bias, which warrants larger, prospective validation. Extended follow-up is needed to assess the very long-term durability of variceal eradication and its effect on mortality and transplant-free survival across both cohorts. Furthermore, an inherent selection bias arising from the natural referral of more severe cases to the provincial hospital (group B) influenced baseline characteristics and subsequent efficacy comparisons, while incomplete follow-up in group A resulted in missing statistical data. Additionally, noninvasive elastographic measurements (eg, liver stiffness) were not routinely collected during the study period and were therefore not included in this retrospective analysis. Finally, as the treatment requires comprehensive multidisciplinary support, including nursing, anesthesiology, and even ICU care, all of which can influence outcomes, comparing the integrated management capabilities across different healthcare settings represents a valuable direction for future research.

Conclusions

A standardized sequential endoscopic protocol including EVL, EIS and ECI achieved high effectiveness for secondary

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prophylaxis of EGV across district tertiary and provincial tertiary hospitals, with a similar incidence of 12-month safety profiles, despite differences in baseline characteristics and compliance. Clinically, we recommend the broader adoption of this protocol to facilitate the safe decentralization of EGV management, thereby optimizing healthcare resource allocation and alleviating the burden on provincial centers. Furthermore, future initiatives should focus on enhancing patient adherence systems and unifying technical training to bridge the observed disparities in follow-up compliance and treatment modality selection.

Data Availability Statement

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

Acknowledgements

During the preparation of this work, the authors used Gemini (Google) to improve the English language, grammar, readability, and overall phrasing of the manuscript. After using this tool, the authors carefully reviewed and edited the content as needed and take full responsibility for the final content of the publication. The AI tool was not used for data analysis, interpretation, or generating scientific conclusions.

Institution Where Work Was Done

PiDu District People's Hospital and Sichuan Provincial People's Hospital, Chegdu, Sichuan, PR China.

Ethics Statement

The study protocol was reviewed and approved by the Ethics Committee of Sichuan Provincial People's Hospital. Final approval was obtained from the Ethics Committee of PiDu District People's Hospital (approval No. 2025-52). Written informed consent was obtained from all participants for both treatment and procedures.

Declaration of Figures' Authenticity

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