Predictors of endoscopic prophylaxis for rebleeding in esophageal varices combined type 2 gastroesophageal varices

Mei-Chun Jiang
Nanchang Number 9 Hospital
Yuan Nie
First Affiliated Hospital of Nanchang University https://orcid.org/0000-0001-7367-2359
Yue Zhang
First Affiliated Hospital of Nanchang University
Si-Zhe Wan
First Affiliated Hospital of Nanchang University
Cong Liu
First Affiliated Hospital of Nanchang University
An-jiang wang
First Affiliated Hospital of Nanchang University
Xuan Zhu (waiyongtg@163.com)
https://orcid.org/0000-0002-1240-0947

Research article

Keywords: gastroesophageal varices, endoscopic treatment, secondary prophylaxis, rebleeding

DOI: https://doi.org/10.21203/rs.2.18037/v2

Abstract

Background: Patients with decompensated cirrhosis and esophageal varices (EVs) combined with type 2 gastroesophageal varices (GOV2) are at risk of rebleeding after endoscopic prophylaxis. This study was performed to evaluate the preventive efficacy of endoscopic treatment in patients with EVs combined with GOV2, and to identify the risk factor of rebleeding.

Methods: We performed a single-center, observational, retrospective study of hospitalized patients with EVs combined with GOV2. The biochemical examination results, demographics, endoscopic performance measures and treatment methods of patients undergoing endoscopic treatment were collected. All patients were observed for 1-year, or were loss to follow-up. The predictors of rebleeding were analyzed by logistic regression analysis.

Results: A total of 124 patients underwent endoscopic treatment, including 2 (1.6%) patients in whom bleeding failed to cease and 19 (15.3%) patients who were lost to follow-up. A total of 103 patients were observed until 1 year, including 11 (10.7%) patients who experienced rebleeding. The results indicated that EVs+GOV2 with GOV1, age, prothrombin time (PT), bilirubin level, platelet count, Child-Pugh grade, and model for end-stage liver disease (MELD) score were associated with rebleeding at 1 year in patients with EVs combined with GOV2. Multivariate logistic analysis revealed that age, EVs+GOV2 with GOV1, bilirubin level, and PT were independent risk factors for rebleeding.

Conclusion: Endoscopic treatment is effective as a preventive treatment in patients with EVs combined with GOV2. EVs combined with GOV1, older age, coagulation failure, and increased bilirubin levels should be given close attention due to their associations with rebleeding after endoscopic prophylaxis. GOV1 may have a negative effect in patients with EVs +GOV2.

Background

Bleeding from varices is a common and severe complication of liver cirrhosis and portal hypertension. It occurs in ~50% of patients with cirrhosis with an incidence of 5~15% each year (1,2). Although the proportion of gastric varices (GVs) is lower than esophageal varices (EVs), the rebleeding and mortality of GVs is higher than EVs (3-5). The most common type of GV is GOV type 1 (GOV1), which accounts for approximately 70%, followed by GOV type 2 (GOV2) at 21%, isolated gastric varices 1 type (IGV1) at 7%, and isolated gastric varices 2 type (IGV2) at 2% (6). However, the type most strongly associated with the rebleeding of GVs is IGV1, with a bleeding rate of 78%, followed by GOV2, with a bleeding rate of 55%, and GOV1 and IGV2, with a bleeding rate of 10% (6).

Prognosis is an essential part of the assessment of any disease. A previous study indicated the risk of bleeding of GVs (1-year risk:10-16%; 5-year risk:44%) is connected with many factors, such as the subtype of GVs, Child Pugh score, hepatocellular carcinoma (HCC), red spots (6-8). These studies on the prognosis of rebleeding in GOV patients is mostly concentrated on IGV1, however, the study in GOV2 is limited (3). At present, endoscopic treatment, including endoscopic variceal sclerotherapy (EVS),

endoscopic band ligation (EBL), endoscopic variceal obturation (EVO), and combined therapy (9), is optimal for preventing the rebleeding of GOVs. GOV2 is a type that more prone to bleeding, but studies about the treatment effect and prognosis of rebleeding in GOV2 patients after endoscopic secondary prophylaxis treatment is uncertain. Due to the high mortality rate in GOV1 patients (3), it is necessary to explore whether GOV2 patients with GOV1 have a high risk of rebleeding. Therefore, we performed this study with the purpose of identifying the risk factors for rebleeding in GOV2 patients after endoscopic secondary prophylaxis treatment to guide clinical practice.

Methods

Study design

This was a single-center retrospective observational cohort conducted at a large tertiary level public hospital in South China between January 2009 and December 2018. The study protocol was approved by the Institutional Ethics Committee of the First Affiliated Hospital of Nanchang University. Informed written consent was obtained from all the study participants.

Study population and setting

The study cohort included all hospitalized patients aged ≥ 18 years with EVs combined with GOV2 based on gastroscopic diagnosis with endoscopic secondary prophylaxis treatment. Exclusion criteria were as follows: no bleeding history; malignant tumors of extrahepatic origin; varices caused by noncirrhotic causes such as cavernous transformation of the portal vein; patients with a transjugular intrahepatic portosystemic shunt (TIPS); patients who underwent balloon-occluded retrograde transvenous obliteration (BRTO); surgical pericardial devascularization; other patients with a shunt and devascularization; and incomplete clinical data. All patients were treated following accepted recommendations and guidelines after admission to the hospital, and they were followed up until death or 1 year.

Definitions

The presence of liver cirrhosis was diagnosed according to clinical, biochemical, and radiological parameters; the presence of ascites, hepatic encephalopathy (HE), and/or signs of portal hypertension; ultrasonography; variceal bleeding; and even histology at hospital admission. Active bleeding was defined as follows: spurting at the variceal veins or active oozing; varicose veins showing signs of recent bleeding (white/red thrombus or varicose veins covered with clots); or in the absence of other sources of bleeding, blood is visible in the stomach (10). Hemostasis failed was defined as follows: death occurring within 5 days of intervention, hematemesis ≥2 hours after endoscopic treatment, hemoglobin decreased by >3 g/dl at 24 hours without blood transfusion, and hemorrhagic shock (11). Rebleeding was defined as follows: hematemesis and/or the reappearance of melena after 5 days of active bleeding (11). Renal impairment was defined as follows: creatinine levels > 1.5 mg/dL in patients with no kidney disease or > 50% in patients with previous kidney disease (12). The Child-Pugh score was calculated according to the

total bilirubin (TBIL) and albumin levels, international normalized ratio (INR), ascites status, and degree of HE. The MELD score was calculated using the following formula: 3.78 x Ln (TBIL μmol/L) + 11.2 x Ln (INR) + 9.57 x Ln (creatinine μmol/L) + 6.43 × (constant for liver disease etiology =0, if cholestatic or alcoholic, otherwise =1) (13). The count of MELD-Na was performed by using MELD+1.59 × [135-Na (mmol/l)] (14).

Study protocol

Patients with EVs combined with GOV2 based on gastroscopic diagnosis with endoscopic secondary prophylaxis treatment were enrolled in the current study. During hospitalization, data regarding the demographic profile, history, clinical features, presence of other comorbidities, etiology of cirrhosis, type of decompensation and number of complications, endoscopic performance, and blood laboratory parameters at admission were collected and compiled. Patients were followed up for 1 year to determine survival. Patients with incomplete follow-up at 1 year were not included in the final analysis.

Statistical analysis

Statistical analyses were performed using SPSS software version 23.0 (SPSS Inc., Chicago, IL). Continuous variables were tested by the Kolmogorov-Smirnova method for normality testing. Continuous data with normal distribution are described by the mean ± standard deviation, and compared by using Student's t-test. Continuous data without normal distribution are described by the median (interquartile range [IQR]), and compared by using Mann–Whitney U-test. Categorical variables are described as frequency (percentage [%]), and were compared by using Chi-squared analysis or Fisher's exact test. Logistic regression analysis was employed to demonstrate the predictors for the rebleeding rate of patients with EVs combined with GOV2. All variables that were found to be associated with rebleeding ($P<0.10$) were included as candidate variables in forward conditional stepwise logistic regression analysis to identify independent predictors for rebleeding in patients with EVs combined with GOV2. All statistical tests were two-sided, and a value of $P < 0.05$ was considered statistically significant.

Results

Baseline characteristics

As shown in Figure 1, 228 patients with EVs combined with GOV2 who were hospitalized between January 2009 and December 2018 were included in this retrospective study.22 patients were excluded:6 patients received a TIPS, 12 patients received a surgical shunt, 4 patients experienced cavernous transformation of the portal vein, 2 patients had Budd-Chiari syndrome, and 1 patient had gastric cancer.. Of the 124 patients, 76 were EV+GOV2, and 48 patients were EV+GOV1+GOV2. Considering GOV2 often combines with GOV1, therefore, the clinical features of 124 patients were also divided into EV+GOV2 without GOV1 groups, and EV+GOV2 with GOV1. Of the 124 patients, 76 were EVs+GOV2 without GOV1, and 48 were EVs+GOV2 with GOV1. A total of 124 patients, median (interquartile range): 49 (42.25-57.50). The majority of the patients were male (95/124, 76.6%). The demographic and biochemical

characteristics of the study population are outlined in Table 1. The main cause of disease was hepatitis virus-associated cirrhosis (64.5%). There were no significant differences in age, sex, creatinine, albumin, PT, INR, bilirubin, hemoglobin, platelet counts, MELD score, MELD-Na score, Child-Pugh score, HCC, ascites, HE, splenectomy between the EVs+GOV2 with GOV1 groups and EVs+GOV2 without GOV1 (all P values >0.05).

Endoscopic features of endoscopic prophylaxis in patients with EVs combined with GOV2

The majority of patients with EVs combined with GOV2 had red spots (111/124, 89.5%), and communicating branches (107/124, 86.3%). EBL was performed mainly in patients with EVs combined with GOV2 (95/124, 76.6%), followed by EVS+EVO (11/123 8.9%), EBL+EVS+EVO (6/124 4.8%), EBL+EVO, EBL+EVS (3/124 2.4%), EVO (1/124 0.8%), and EVS (6/124 4.8%). There was no significant difference between the EVs+GOV2 with GOV1 and EVs+GOV2 without GOV1 groups regarding endoscopic erythema, traffic branch, active bleeding, thrombus, variceal diameter, and distance from the incisors (all P values >0.05).

Comparison between the rebleeding group and the non-rebleeding group in patients with EVs combined with GOV2

A total of 124 patients underwent endoscopic treatment for secondary prophylaxis, including 2 patients with hemostasis failure and 19 patients who were lost to follow-up. Therefore, a total of 103 patients was enrolled in the final study. According to whether there was bleeding within 1-year, 103 patients were divided into the non bleeding group (n=92) and the bleeding group (n=11). The analysis showed that EV+GOV2 combined with GOV1 (P=0.043) and age (P=0.039), PT (P=0.019), bilirubin (P=0.033), Child-Pugh grade (P=0.009), and MELD score (P=0.044) were associated with rebleeding in patients with EVs combined with GOV2. By multivariate logistic regression analysis, age (OR:1.186, 95% CI: 1.050–1.340, P=0.006), the variceal classification of EV+GOV2 with GOV1(OR: 3.063, 95% CI: 1.560–6.184, P =0.024), bilirubin (OR:1.088, 95% CI: 1.022–1.158, P =0.009) , and PT ((OR:1.109, 95% CI: 1.043–1.288, P =0.038) were independent risk factors for rebleeding within 1-year. Among them, variceal classification had the most significant effect, and EV+GOV1+GOV2 were the independent predictive factors for rebleeding within 1-year.

Discussion

Variceal bleeding is still one of the most common serious complications in patients with liver cirrhosis. Even with developments in medicine and endoscopic therapy, acute variceal bleeding has a high rate of mortality (15%-20%) (15-17). According to the Sarin classification, although the frequency of GOV2 is lower than GOV1, the rebleeding risk of GOV2 is significantly higher than GOV1. Prognosis is an essential part of the assessment of rebleeding; it is the basis not only for the information that a physician provides to the patient, but also for any decision-making process. EVs combined with GOV1 has a high detection rate and are widely studied, but there is limited study on EVs combined with GOV2 (18, 19). This study intended to analyze the endoscopic treatment effect and risk factors for rebleeding at 1-year to identify

high-risk patients with rebleeding and take corresponding treatment measures to improve their prognosis. Considering that EVs+ GOV2 is often accompanied by GOV1 in the clinic, patients were divided into two groups based on their clinical and endoscopic features, EVs+GOV2 without GOV1 and EVs+GOV2 with GOV1, and compared because no studies have directly compared the clinical and endoscopic features between patients with EVs+GOV2 without GOV1 and those with EVs+GOV2 with GOV1.

In our study, the cause of both groups was mainly hepatitis virus related cirrhosis, which is consistent with the epidemiological characteristics of cirrhosis in China. A total of 124 patients underwent secondary prophylaxis, among whom 2 (1.6%) experienced hemostasis failure, 19 (15.3%) were lost to follow-up, 11 (10.7%) experienced rebleeding within 1-year. As expected, the rebleeding incidence in patients who underwent endoscopic prophylaxis was similar with other study (16, 17). In Dong XJ's study on 29 patients with EVs+GOV2, 3 patients (10.3%) experienced hemostatic failure, and 7 patients (24.1%) experienced rebleeding within 6 weeks after undergoing EBL. The incidence of rebleeding in the patients in Dong XJ's study is higher than our study, which may be caused by the severity of liver disease in patients in Dong XJ's study (20). No significant differences were found in endoscopic characteristics or clinical features were found between EVs+GOV2 without GOV1 group and EVs+GOV2 with GOV1 groups. Multivariate logistic regression analysis identified age, EVs+GOV2 with GOV1, bilirubin, and PT as risk factors for 1-years rebleeding in patients with EVs +GOV2. An increasing number of studies have been focused in predict esophageal and gastric variceal bleeding. Xu L's study showed that PTA>18s (OR=62.83, 95% CI:9.39-420.56) and moderate/severe ascites (OR=11.35,95% CI:1.93-66.7) were independent risk factors for early rebleeding after endoscopic treatment (21). Kim SJ's study indicated that Child-Pugh grade C was an independent risk factor for rebleeding in GV patients (22). Our study showed that the Child-Pugh score was associated with rebleeding in patients with EVs+GOV2, but the Child-Pugh score was not associated with rebleeding in the multivariate logistic regression. This inconsistent conclusion may be related to the small number of Child-Pugh C patients, the influence of albumin infusion on the degree of ascites degree and level of albumin in some patients in our study during treatment. The blood provision of GOV1 and GOV2 is different, suggesting elevated portal vein pressure when present at the same time. Our study found that patients with EVs+ GOV2 with GOV1 had an increased risk of rebleeding at 1 year, and EVs+ GOV2 with GOV1 was identified as an independent risk factor (OR=31.063, 95% CI: 1.560-618.4).Kang EJ et al reported the incidence of rebleeding incident of in patients with liver cancer (P<0.001) and GOV2 (P=0.009) was significantly increased at 1-year when comparing the prognosis of 127 GV patients (GOV1:GOV2: IGV=56:61:10) who had been treated with tissue glue for preventing rebleeding(23). Jun CH et al retrospectively analyzed reported 455 GVs patients after endoscopic treatment showed that no different in rebleeding for 1-year between the GOV1 and GOV2 (24), however, the comparing between EV+GOV2 without GOV1 group and EV+GOV2 with GOV1 group was not complete. We found a significant difference in the incidence of rebleeding at 1-year between EV+GOV2 without GOV1 group and EV+GOV2 with GOV1 group. Our results indicate that EVs combined with GOV1 may had influence in GOV2 of rebleeding. Mishra et al reported that a MELD score > 18 and active bleeding at endoscopy are risk factors for 6-week rebleeding and morbidity in GOV2 patients (25). Chen WT et al recently reported that the MELD score was associated with rebleeding in patients with GVs

at 1 month (OR=1.2, 95% CI: 1.1-1.4) after endoscopic treatment (26). We showed that the MELD score was associated with rebleeding in patients with EVs+ GOV2, but it was not an independent risk factor and may be related to the low MELD score of patients in this study. In this study, factors such as age, EV+GOV2 with GOV1, bilirubin, and PT were identified as independent risk factors for rebleeding in EVs combined with GOV2 after endoscopic prophylaxis, therefore it is necessary to identify the patients with high risk of rebleeding. Any patient with persistent bleeding or severe rebleeding should be considered for TIPS.

The platelet count could serve as a noninvasive index to predict the severity of varices, and a decrease in the platelets can indirectly reflect increased portal pressure (27, 28). In this study, the platelet count in the rebleeding group was significantly lower than non-rebleeding group; however, no significant correlation was found in multivariate analyses. One patient in the rebleeding group had underwent splenectomy, which may have affected this result.

This study also has several limitations. First, as a single-center retrospective cohort study, the analysis may have a hereditary limitation and some patients were lost to follow-up, which may have resulted result in the selection bias. Second, the hepatic venous pressure gradient (HVPG) was not measured in all patients all patients due to limitations such as economic status and the acceptance of invasive examinations. Last, our study focused mainly on EBL treatment, and different endoscopic treatment methods were not considered.

Conclusions

Endoscopic treatment is effective treatment of EVs combined with GOV2. Age, EV+GOV2 with GOV1, bilirubin, and PT were revealed as independent risk factors for rebleeding in patients with EVs combined with GOV2 after endoscopic prophylaxis. GOV1 may have a negative effect in patients with EVs +GOV2.

Declarations

Ethics approval and consent to participate

Study protocol was approved by the institutional ethics committee of First Affiliated Hospital of Nanchang University. Written informed consent was obtained from all the study participants.

Consent for publication

Not applicable

Availability of data and material

All data generated or analyzed during this study are included in this published article.

Competing interests

The authors declare that there are no competing interest.

Funding

The study design, data collection, analysis and interpretation of data, writing manuscript were funded by the National Natural Science Foundation of China (No. 81960120) and the “Gan-Po Talent 555 Project of Jiangxi Province.

Authors' Contributions

MCJ, YN and YZ contributed equally to this study. MCJ, and YN designed and wrote the manuscript, YZ collected the data, SZW and CL analysed the data, XZ and AJW critically revised the manuscript. All of the authors have read and approved the final manuscript.

Author details

[1] Department of Gastroenterology, The First Affiliated Hospital of Nanchang University, Nanchang, Jiangxi, China

Acknowledgements

We would like to thanks the National Natural Science Foundation of China and the “Gan-Po Talent 555” Project of Jiangxi Province for the economic support.

Abbreviations

EVs: esophageal varices; GOV2: type 2 gastroesophageal varices; GOV1: type 1 gastroesophageal varices; GVs: gastric varices; IGV1: gastric varices 1 type; IGV1: gastric varices 2 type; PT: prothrombin time; MELD: model for end-stage liver disease; HCC: hepatocellular carcinoma; EVS: endoscopic variceal sclerotherapy; EBL: endoscopic band ligation; EVO: endoscopic variceal obturation (EVO); TIPS: transjugular intrahepatic portosystemic shunt; BRTO balloon-occluded retrograde transvenous obliteration; TBIL: total bilirubin; INR: international normalized ratio; IQR: interquartile range; HVPG: hepatic venous pressure gradient.

References

1. Garcia-Tsao G, Abraldes JG, Berzigotti A, Bosch J. Portal hypertensive bleeding in cirrhosis: Risk stratification, diagnosis, and management: 2016 practice guidance by the American Association for the study of liver diseases. Hepatology. 2017;65(1):310-35.
2. Ibrahim M, Mostafa I, Deviere J. New Developments in Managing Variceal Bleeding. Gastroenterology. 2018;154(7):1964-9.
3. Kovacs TOG, Jensen DM. Varices: Esophageal, Gastric, and Rectal. Clinics in liver disease. 2019;23(4):625-42.

4. Lee EW, Shahrouki P, Alanis L, Ding P, Kee ST. Management Options for Gastric Variceal Hemorrhage. JAMA surgery. 2019;154(6):540-8.
5. Jakab SS, Garcia-Tsao G. Screening and Surveillance of Varices in Patients With Cirrhosis. Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association. 2019;17(1):26-9.
6. Haq I, Tripathi D. Recent advances in the management of variceal bleeding. Gastroenterology report. 2017;5(2):113-26.
7. Ma L, Tseng Y, Luo T, et al. Risk stratification for secondary prophylaxis of gastric varices due to portal hypertension[J]. Dig Liver Dis, 2019,51(12):1678-1684.
8. Sarin SK, Kumar A. Endoscopic treatment of gastric varices. Clinics in liver disease. 2014;18(4):809-27.
9. Mansour L, El-Kalla F, El-Bassat H, Abd-Elsalam S, El-Bedewy M, Kobtan A, et al. Randomized controlled trial of scleroligation versus band ligation alone for eradication of gastroesophageal varices. Gastrointestinal endoscopy. 2017;86(2):307-15.
10. Sarin SK, Kumar A, Angus PW, Baijal SS, Baik SK, Bayraktar Y, et al. Diagnosis and management of acute variceal bleeding: Asian Pacific Association for Study of the Liver recommendations. Hepatology international. 2011;5(2):607-24.
11. de Franchis R, Baveno VIF. Expanding consensus in portal hypertension: Report of the Baveno VI Consensus Workshop: Stratifying risk and individualizing care for portal hypertension. Journal of hepatology. 2015;63(3):743-52.
12. Terg R, Gadano A, Cartier M, Casciato P, Lucero R, Munoz A, et al. Serum creatinine and bilirubin predict renal failure and mortality in patients with spontaneous bacterial peritonitis: a retrospective study. Liver international : official journal of the International Association for the Study of the Liver. 2009;29(3):415-9.
13. Malinchoc M, Kamath PS, Gordon FD, Peine CJ, Rank J, ter Borg PC. A model to predict poor survival in patients undergoing transjugular intrahepatic portosystemic shunts. Hepatology. 2000;31(4):864-71.
14. Biggins SW, Kim WR, Terrault NA, Saab S, Balan V, Schiano T, et al. Evidence-based incorporation of serum sodium concentration into MELD. Gastroenterology. 2006;130(6):1652-60.
15. Reverter E, Tandon P, Augustin S, Turon F, Casu S, Bastiampillai R, et al. A MELD-based model to determine risk of mortality among patients with acute variceal bleeding. Gastroenterology. 2014;146(2):412-19 e3.
16. Seo YS. Prevention and management of gastroesophageal varices. Clinical and molecular hepatology. 2018;24(1):20-42.
17. Seo YS, Park SY, Kim MY, Kim JH, Park JY, Yim HJ, et al. Lack of difference among terlipressin, somatostatin, and octreotide in the control of acute gastroesophageal variceal hemorrhage. Hepatology. 2014;60(3):954-63.

18. Bosch J. Prevention of variceal rebleeding: endoscopes, drugs, and more. Hepatology. 2000;32(3):660-2.
19. Sung JJ, Tsoi KK, Lai LH, Wu JC, Lau JY. Endoscopic clipping versus injection and thermo-coagulation in the treatment of non-variceal upper gastrointestinal bleeding: a meta-analysis. Gut. 2007;56(10):1364-73.
20. Dong XJ, Chen WQ. [Therapeutic efficacy of endoscopic variceal ligation to treat gastric varices: a study of 63 consecutive cases]. Zhonghua gan zang bing za zhi = Zhonghua ganzangbing zazhi = Chinese journal of hepatology. 2013;21(9):692-6.
21. Xu L, Ji F, Xu QW, Zhang MQ. Risk factors for predicting early variceal rebleeding after endoscopic variceal ligation. World journal of gastroenterology. 2011;17(28):3347-52.
22. Kim SJ, Choi CW, Kang DH, Kim HW, Park SB, Hong YM, et al. Emergency endoscopic variceal ligation in cirrhotic patients with blood clots in the stomach but no active bleeding or stigmata increases the risk of rebleeding. Clinical and molecular hepatology. 2016;22(4):466-76.
23. Kang EJ, Jeong SW, Jang JY, Cho JY, Lee SH, Kim HG, et al. Long-term result of endoscopic Histoacryl (N-butyl-2-cyanoacrylate) injection for treatment of gastric varices. World journal of gastroenterology. 2011;17(11):1494-500.
24. Jun CH, Kim KR, Yoon JH, Koh HR, Choi WS, Cho KM, et al. Clinical outcomes of gastric variceal obliteration using N-butyl-2-cyanoacrylate in patients with acute gastric variceal hemorrhage. The Korean journal of internal medicine. 2014;29(4):437-44.
25. Mishra SR, Sharma BC, Kumar A, Sarin SK. Primary prophylaxis of gastric variceal bleeding comparing cyanoacrylate injection and beta-blockers: a randomized controlled trial. Journal of hepatology. 2011;54(6):1161-7.
26. Chen WT, Lin CY, Sheen IS, Huang CW, Lin TN, Lin CJ, et al. MELD score can predict early mortality in patients with rebleeding after band ligation for variceal bleeding. World journal of gastroenterology. 2011;17(16):2120-5.
27. Elalfy H, Elsherbiny W, Abdel Rahman A, Elhammady D, Shaltout SW, Elsamanoudy AZ, et al. Diagnostic non-invasive model of large risky esophageal varices in cirrhotic hepatitis C virus patients. World journal of hepatology. 2016;8(24):1028-37.
28. Ying L, Lin X, Xie ZL, Hu YP, Shi KQ. Performance of platelet count/spleen diameter ratio for diagnosis of esophageal varices in cirrhosis: a meta-analysis. Digestive diseases and sciences. 2012;57(6):1672-81.

Tables

Table 1 The clinical features of endoscopic prophylaxis in patients with EVs combined GOV2.

Characteristic	EVs+GOV2 (n=124)	EVs+GOV2 without GOV1(n=76)	EVs+GOV2with GOV1(n=48)	P-value
Etiology, n (%)				0.182
Hepatitis Viral	80 (64.5%)	51 (67.1%)	29 (60.4%)	
Autoimmune	6 (4.8%)	4 (5.3%)	2 (4.2%)	
Alcoholic	10 (8.1%)	8 (10.5%)	2 (4.2%)	
Other	20 (16.2%)	9 (11.8%)	11 (23.0%)	
Age, median (IQR)	49 (42.25-57.50)	48 (41.25-59)	52 (43.25-55.75)	0.719
Sex, Male (%)	95 (76.6%)	60 (78.9%)	35 (72.9%)	0.515
Creatinine (μmol/L)	75.75 (62.25-89.75)	67.95 (59-81.38)	90 (73.25-100.75)	0.300
Bilirubin (g/L) (±SD)	34.10±6.48	33.30±6.64	35.02±6.25	0.156
PT (IQR)	13.95 (12.75-15.67)	14.15 (12.9-15.73)	13.7 (12.5-14.9)	0.125
INR (IQR)	1.21 (1.11-1.35)	1.21 (1.11-1.39)	1.21 (1.10-1.30)	0.355
Albumin (μmol/L) (IQR)	16.85 (11.53-24.69)	16.65 (11.72-25.93)	18.15(11.32-22.95)	0.949
Hemoglobin (g/L) (±SD)	87.89±23.53	88.41±25.63	86.40±21.30	0.651
Platelet count ($\times 10^9$ /L) (IQR)	69.6 (43.25-99.25)	66.5 (42-96.75)	73.5 (44.75-102)	0.416
MELD (IQR)	9.15 (7.54-10.87)	9.28 (7.62-11.18)	8.82 (7.47-10.7)	0.376
MELD-Na (IQR)	9.34 (7.72-11.75)	9.97 (7.96-12.50)	8.86 (7.53-10.90)	0.238
Child-Pugh (A/B/C)	49/63/12	26/42/8	23/21/4	0.315
HE, n (%)	5 (4.0%)	3 (3.9%)	2(4.2%)	0.998
HCC, n (%)	13 (10.4%)	9 (11.8%)	4 (8.4%)	0.765
Ascites (no/mild/severe)	56/31/37	32/21/23	24/10/14	0.618
Renal impairments, n (%)	2 (1.6%)	1 (1.3%)	1(2.1%)	0.994
Splenectomy, n (%)	16 (12.9%)	10 (13.2%)	6 (12.6%)	0.893
SBP, n (%)	3 (2.4%)	1 (1.3%)	2 (4.2%)	0.320

IQR: Interquartile range; SD: Standard deviation; EVs: esophageal varices; GOV1: type 1 of gastric varices; GOV2: type 2 of gastric varices; IQR: interquartile range; PT: prothrombin time, INR: international normalized ratio; MELD: model for end-stage liver disease; MELD-Na: MELD combined with serum sodium concentration; HE: hepatic encephalopathy; HCC: Hepatocellular carcinoma; SBP: spontaneous peritonitis.

Table 2 The endoscopic features and treatment details of endoscopic prophylaxis in patients with EVs combined GOV2

Characteristics	EVs+GOV2 (n=124)	EVs+GOV2 without GOV1(n=76)	EVs+GOV2 with GOV1 (n=48)	P-value
Red spot, n (%)	111 (89.5%)	65 (85.5%)	46 (95.8%)	0.079
Communicating branch, n (%)	107 (86.3%)	63 (82.9%)	44 (91.7%)	0.192
Active bleeding at endoscopy, n (%)	32 (25.8%)	19 (25%)	13 (27.1%)	0.796
Blood clots, n (%)	25 (20.2%)	17 (22.4%)	8 (16.7%)	0.441
variceal diameter (cm) (IQR)	1.23 (1.05-1.62)	1.2 (1.2-1.5)	1.25 (0.85-1.75)	0.103
Varices distance from the incisors (cm)	20.16±5.93	20.01±6.00	20.27±5.86	0.815
EBL, n (%)	95 (76.6%)	62 (81.6%)	33(68.8%)	
Use 2 pairs of legators, n (%)	30 (24.2%)	22 (35.5%)	8(24.2%)	0.203
Number of rubber bands, (±SD)	8.1±2.9	8.6±3	7.6±2.7	0.109
EVS+EVO, n (%)	11 (8.9%)	5 (6.6%)	6 (12.5%)	
Injection sessions (IQR)	4 (2.6-6)	4 (3-5)	4 (1.5-7)	0.968
Sclerotherapy dose (mL) (IQR)	34 (25-60)	34 (25-60)	30 (17.5-54)	0.537
Cyanoacrylate dose (mL) (IQR)	3 (2-2.5)	3 (2-2.5)	2.75 (1.37-4)	0.989
EBL+EVS+EVO, n (%)	6 (4.8%)	2 (2.6%)	4(8.3%)	
EBL+EVO, n (%)	3 (2.4%)	1 (1.3%)	2(4.2%)	
EBL+EVS, n (%)	1 (0.8%)	0	1(2.1%)	
EVO, n (%)	2 (2.6%)	1(1.3%)	1(2.1%)	
EVS, n (%)	6 (4.8%)	5(6.7%)	1(2.1%)	

IQR: interquartile range; EVs: endoscopic variceal sclerotherapy; EBL: endoscopic band ligation; EVO: endoscopic variceal obturation.

Table 3 Comparing clinical features, endoscopic features and treatment details of endoscopic prophylaxis between rebleeding and non-bleeding groups.

Characteristics at enrollment	Rebleeding within 1-year (n=11)	Non-rebleeding within 1-year (n=92)	P-value
EVs+GOV2 with GOV1, n (%)	7 (55.6%)	30 (37.5%)	**0.043**
Red spot, n (%)	72 (78.2%)	8 (72.7%)	0.677
communicating branch, n (%)	79 (85.8 %)	8 (72.7%)	0.255
Active bleeding at endoscopy, n (%)	6 (54.5%)	28 (30.4%)	0.108
Blood clots, n (%)	3(27.3%)	20 (21.7 %)	0.677
Variceal diameter (cm) (IQR)	1.2(0.8-1.5)	1.2(0.85-1.75)	0.814
Varices distance from the incisors (cm) (±SD)	22.11±5.56	19.78±5.88	0.255
Endoscopic treatment, n (%)			0.182
EBL	72 (78.2%)	9 (81.8%)	
EVS+EVO	6 (6.5%)	2 (18.2%)	
Others	14 (15.2%)	0	
Etiology (%)			0.796
Hepatitis Viral, n (%)	67 (72.8%)	8 (72.7%)	
Autoimmune, n (%)	6 (6.5%)	0	
Alcoholic, n (%)	8 (8.7 %)	1 (9.1%)	
Other, n (%)	11 (11.9%)	2 (18.2%)	
Age, median (IQR)	64(47-72)	48.5(42-56)	**0.039**
Sex, Male (%)	72 (78.3%)	7 (63.6%)	0.278
Na (mmol/L) (IQR)	139.1(137-141)	139(136.95-140.95)	0.718
Creatinine (μmol/L) (IQR)	67.35(56.55-78.15)	57.5(50.4-73.3)	0.311
Albumin (g/L) (±SD)	31.07±7.75	34.49±6.31	0.128
PT (IQR)	15.6(13.7-20.45)	13.9(12.52-14.97)	**0.019**
INR (IQR)	1.3(1.17-1.56)	1.21(1.11-1.33)	0.132
Bilirubin (μmol/L) (IQR)	36.2 (13.75-64.4)	16.4 (11.23-22.35)	**0.033**
Hemoglobin (g/l) (IQR)	88.41±25.63	80.11±25.26	0.297
Platelet count ($\times 10^9$ /L) (IQR)	65 (42.25-96)	80 (40-106.5)	**0.041**
Child-Pugh A/B/C	30/52/10	2/4/5	**0.009**
MELD (IQR)	13.47(7.77-15.93)	8.85(7.68-10.64)	**0.044**
MELD-Na (IQR)	13.47(7.77-17.22)	9.16 (7.96-11.23)	0.090
HE, n (%)	2 (18.2%)	3 (3.3%)	0.197
HCC, n (%)	11 (12.0%)	1 (9.1%)	0.799
Ascites (no/mild/severe）	37/31/24	4/2/5	0.353
Renal impairment, n (%)	2 (2.2%)	0	0.621
Splenectomy, n (%)	2 (18.2%)	13(14.1%)	0.719
SBP, n (%)	1 (9.1%)	2 (2.2%)	0.197

IQR: Interquartile range; SD: Standard deviation; EVs: esophageal varices; GOV1: type 1 of gastric varices; GOV2: type 2 of gastric varices; IQR: interquartile range; EVs: endoscopic variceal sclerotherapy; EBL: endoscopic band ligation; EVO: endoscopic variceal obturation; PT: prothrombin time, INR: international normalized ratio; MELD: model for end-stage liver disease; MELD-Na: MELD combined with serum sodium concentration; HE: hepatic encephalopathy; SBP: spontaneous peritonitis

Table 4 Multivariate analyses of risk factors associated with rebleeding for 1-year

Characteristics	β	SE	P	OR	95%CI
Age, (years)	0.170	0.062	0.006	1.186	1.050-1.340
Variceal classification (EVs+GOV2 with GOV1)	3.436	1.526	0.024	3.063	1.560-6.184
Bilirubin, (μmol/L)	0.084	0.032	0.009	1.088	1.022-1.158
PT	0.103	0.077	0.038	1.109	1.042-1.288

SE: Standard error; OR: odds ratio; CI: confidence interval; EVs: esophageal varices; GOV1: type 1 of gastric varices; GOV2: type 2 of gastric varices; PT: prothrombin time.

Figures

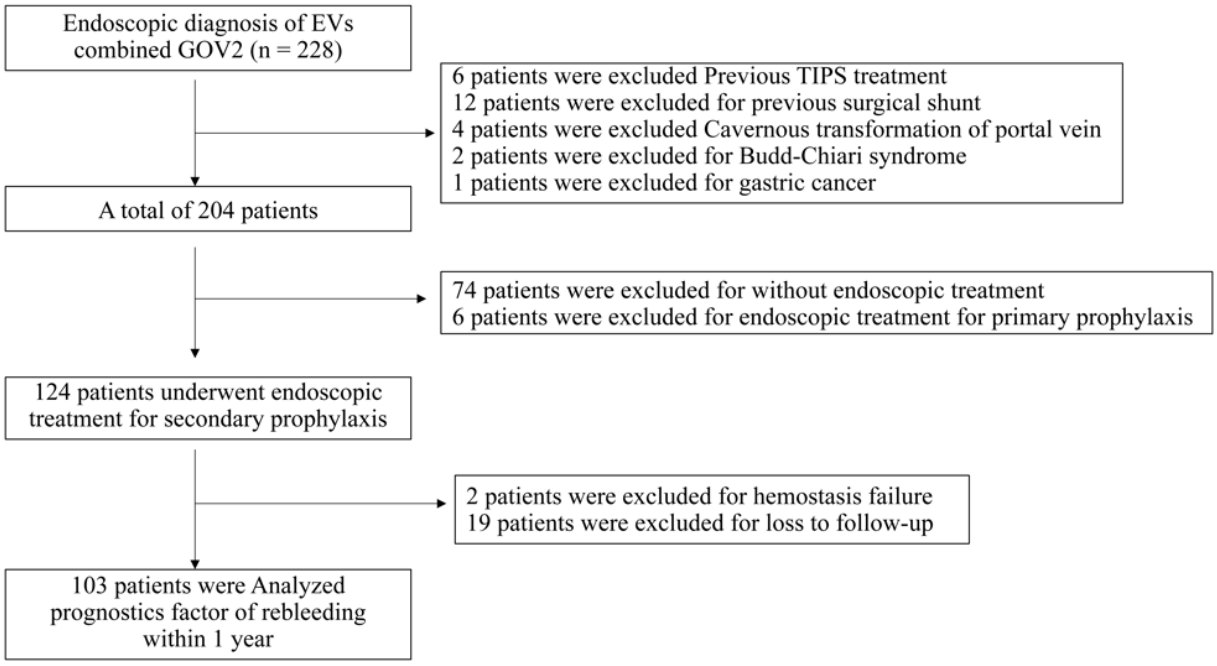

Figure 1

Study flow diagram showing each stage of inclusion, exclusion, and loss to follow-up of patients in our study.