Original Article
Safety and efficacy of endoscopic treatment for elderly and younger patients with esophageal varices

Xin Ma[1,2*], Fei Pan[1*], Yichao Shi[1], Xi Luo[1], Zhiyuan Guo[1], Hui Mao[3], Wenjie Xi[1], Gang Sun[1], Yunsheng Yang[1]

Departments of [1]Gastroenterology and Hepatology, [3]Oncology, Chinese PLA General Hospital, Beijing, P. R. China; [2]Department of Gastroenterology and Hepatology, The Affiliated Hospital of Xuzhou Medical College, Xuzhou, Jiangsu, P. R. China. *Equal contributors.

Abstract: This study aimed to investigate the safety and efficacy of endoscopic treatment for elderly patients with cirrhosis and esophageal varices (EV). Here, this retrospective study included patients with cirrhosis who underwent endoscopic treatment for esophageal varices at Chinese PLA General Hospital from December 2013 to May 2015. Three hundred and thirty four patients were enrolled and sequentially assigned to two groups: elderly group (A: age ≥60, n = 116) and non-elderly group (B: age <60, n = 218). Of these patients, 303 underwent 3-month gastroscopy review in our hospital: 106 in group A and 197 in group B. The rates of re-bleeding, complications and mortality were compared between the two groups. Clinical characteristics and biochemical parameters were compared to evaluate the risk factors for re-bleeding of different populations. There were no significant differences between the elderly and non-elderly groups in the re-bleeding rate within 7 days after endoscopy (elderly vs. non-elderly: 6.03% vs. 3.21%, P = 0.22) and the 3-month re-bleeding rate (elderly vs. non-elderly: 3.77% vs. 3.55%, P = 0.92). The distributions of adverse events were similar in the two groups (elderly vs. non-elderly: 45.69% vs. 47.71%, P = 0.73). Logistic regression analysis demonstrated that greater ascites volume and larger EV size were independent risk factors for 7-day re-bleeding in elderly patients. Meanwhile, higher Child-Pugh score was independent risk factors for 3-month re-bleeding in elderly patients. Similarly, the significant risk factors for complication in elderly patients were the severity of last bleeding and larger EV size. Taken together, endoscopic therapy is safe and efficacious for elderly patients with esophageal varices. Based on the risk factors analyzed here, effective measures should be adopted before elderly patients undergo endoscopic therapies.

Keywords: Esophageal varices, endoscopy, elderly patients, safety, efficacy
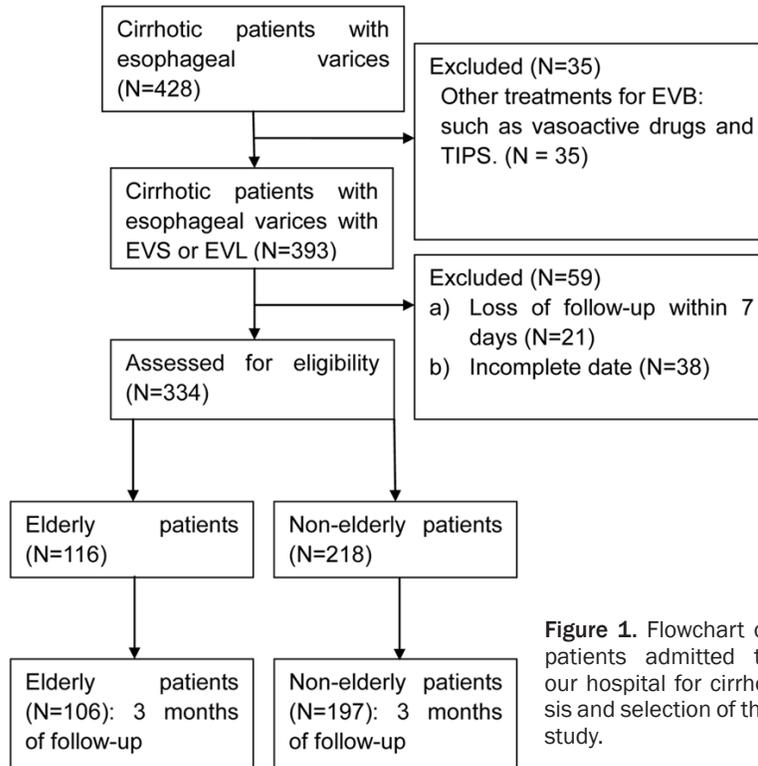
Introduction

Esophageal varices (EV) occur in more than half of patients with decompensated cirrhosis and in about one third of patients with compensated cirrhosis [1]. Esophageal variceal bleeding (EVB) is a serious, life-threatening complication of cirrhosis, with a high rate of mortality (≥20%) and a rate of recurrent bleeding (60%) within one year [2]. Evaluating bleeding risk and effective management of EVB are key issues for clinicians to treat portal hypertension [3]. EVB management has improved greatly in the past few years [4, 5]. The variety of therapies used to treat EVB includes drugs, endoscopic treatments and treatments such as transjugular intrahepatic portosystemic shunts (TIPSs) and surgery [6-9]. Post-operative mortality continues to decrease as treatment methods are updated and improved, and improvements in endoscopic treatment have contributed greatly to these increased survival rates [6]. Endoscopic treatment mainly includes endoscopic variceal sclerotherapy (EVS) and endoscopic variceal ligation (EVL). EVS and EVL are widely used in the clinic and can be used to prevent or stanch EVB for emergency treatment, primary prophylaxis, or secondary prophylaxis [7]. However, endoscopy is associated with inherent risks, particularly in elderly patients with poor liver function.

The global population is aging. According to the United Nations Population Division, China became an Old Age society in 2000. As one of China's biggest hospitals, the proportion of

Figure 1. Flowchart of patients admitted to our hospital for cirrhosis and selection of the study.

Materials and methods

General information

A single-center retrospective study was conducted in 334 patients with cirrhosis, including 236 males and 98 females, with a median age of 54.67±12.44 years at baseline and an age range of 18 to 87 years. The patients were admitted to our department due to EVs from December 2013 to May 2015 (**Figure 1**). All enrollees were followed post discharge after undergoing endoscopic treatment in the form of EVS or EVL. The subjects were classified into the elderly group (group A, age ≥60 years, n = 116) and the non-elderly group (group B, age <60 years, n = 218). Various clinical parameters of the inpatients were collected from medical records and the endoscopic database, such as sex, age, Child-Pugh score, the cause of cirrhosis, underlying diseases, history of bleeding, the data of endoscopic findings, and so on. Only 303 of 334 patients underwent the three-month follow-up evaluation and gastroscopy review in our hospital: 106 cases in group A and 197 patients in group B (**Figure 1**). All patients underwent endoscopic therapy in our department. Major parameters were compared between the two groups including the 7-day re-bleeding rate, 3-month re-bleeding rate, all events of side effects, and the mortality rate. This study was reviewed and approved by the Medical Ethics Committee of PLA General Hospital.

Efficacy was evaluated based on the 7-day and 3-month re-bleeding rates; re-bleeding was defined as melena or hematemesis after 24 hours that was confirmed and treated by rescue endoscopic therapy or conservative treatment. Safety was evaluated based on the incidence of complications. Treatment failure was defined as continuous EVB or EVB leading to death after EVS or EVL.

inpatients over the age of 60 in our hospital is increasing annually, and the number of elderly patients undergoing endoscopic treatment with poor physical condition and a variety of underlying diseases is also increasing. As an initial therapy for acute bleeding, compared to gastroscopic examination, endoscopic therapy requires longer time and is associated with certain hazards due to its invasive nature, including potential life-threatening complications. Therefore, for elderly patients with EVs, it is necessary to consider the risk of the endoscopic therapies themselves, how well elderly patients tolerate these procedures, and, obviously, the effectiveness of these treatments. Many prognostic studies of endoscopic treatment for cirrhosis were performed without differentiating adult and elderly patients. Therefore, in the present study, we conducted a single-center, cross-sectional study of cirrhosis patients admitted to our department due to EVs to gain further insight into the safety and efficacy of endoscopic interventional treatment in this patient population and to evaluate predictors of efficacy and safety in elderly patients.

Table 1. Baseline characteristics of cirrhotic patients

	Group A (n = 116)	Group B (n = 218)	P-value
Age (mean ± SD)	68.22±6.66	47.45±7.98	<0.0001*
Sex (male, %)	69 (59.50%)	167 (76.60%)	0.001*
Child-Pugh score (n, %)			0.29
A	59 (50.86%)	130 (59.63%)	
B	39 (33.62%)	62 (28.44%)	
C	18 (15.52%)	26 (11.93%)	
Ascites			0.58
None or mild	89 (76.72%)	173 (79.36%)	
Moderate or severe	27 (23.28%)	45 (20.64%)	
Cause of cirrhosis (n, %)			<0.001*
Hepatitis B	41 (35.34%)	129 (59.17%)	
Hepatitis C	10 (8.62%)	9 (4.13%)	
Alcoholic	17 (14.66%)	31 (14.22%)	
Primary biliary hepatitis	14 (12.07%)	9 (4.13%)	
Autoimmune hepatitis	10 (8.62%)	3 (1.38%)	
Drug induced hepatitis	3 (2.59%)	0	
Cryptogenic cirrhosis	21 (18.10%)	37 (16.97%)	
Hepatocellular carcinoma (n, %)	29 (25.00%)	40 (18.35%)	0.16
Chronic disease (n, %)			<0.05*
Hypertension	32 (27.59%)	18 (8.26%)	
Coronary heart disease	4 (3.45%)	1 (0.46%)	
Diabetes	31 (26.72%)	43 (19.72%)	
Cerebrovascular disease	6 (5.17%)	4 (1.83%)	
Cardiovascular disease	5 (4.31%)	4 (1.83%)	
Pulmonary disease	12 (10.34%)	5 (2.29%)	
Immune diseases	5 (4.31%)	1 (0.46%)	
The severity of last bleeding (n, %)			0.39
Light <200 ml	38 (32.76%)	91 (41.74%)	
Moderate 200-1000 ml	45 (38.79%)	81 (37.16%)	
Severe >1000 ml	29 (25.44%)	42 (19.27%)	
History of endoscopic treatment (n, %)			0.95
None	66 (56.90%)	117 (53.67%)	
EVS	28 (24.14%)	57 (26.15%)	
EVL	16 (13.79%)	31 (14.22%)	
EVS+EVL	6 (5.17%)	13 (5.96%)	
With beta blockers	110 (94.8%)	210 (96.3%)	0.53
Time of operation			0.43
Emergency	9 (7.76%)	12 (5.50%)	
Selective	107 (92.24%)	206 (94.50%)	

P-values are two-tailed and *is denoted as P<0.05, and of statistical significance.

immediately in patients with postoperative bleeding necessary. Antibiotics were routinely used for 3 days after each endoscopic sclerotherapy and were used longer if transient fever occurred. All endoscopic images were interpreted by two veteran doctors who were double blinded. All medical records were collected by two researchers who were also double blinded.

Statistical method

Category analysis was employed to analyze qualitative data, and quantitative data were analyzed mainly by statistical description. Descriptive analysis and difference significance tests were adopted in the final result analysis. The χ^2 test was used to compare the baseline characteristics of subjects (categorical variables), efficacy and safety outcomes (7-day or 3-month re-bleeding rate or adverse events from treatment or the mortality rate) in the two groups. To explore the association of the re-bleeding rate and the incidence of complications with the characteristics of elderly patients with EV, univariate and multivariate logistic regression were performed to calculate adjusted odds ratios (ORs) and 95% confidence intervals (CIs). For all analyses, SPSS software version 13 (Chicago, IL, USA) was used; $P<0.05$ was accepted as statistically significant.

Each patient underwent endoscopic treatment by an experienced doctor using standard endoscopes and standard techniques. EVL or EVB was used as appropriate for the form of varicose veins as judged by the individual operator. Rescue endoscopic therapy was performed

Table 2. Endoscopic features and related data

	Group A (n = 116)	Group B (n = 218)	P-value
With gastric varix	37 (31.9%)	96 (44.0%)	0.03*
Endoscopic therapies			0.26
EVL	41 (35.34%)	64 (29.36%)	
EVS	75 (64.66%)	154 (70.64%)	
The number of sessions			0.37
1	92 (79.3%)	164 (75.2%)	
2	24 (20.7%)	51 (23.4%)	
>2	0	3 (1.4%)	
EV Grade			0.1
I	0	6 (2.75%)	
II	5 (4.31%)	16 (7.34%)	
III	111 (95.69%)	196 (89.91%)	
Esophageal erosion (n, %)	9 (7.76%)	11 (5.05%)	0.33
Red thrombosis	2 (1.72%)	7 (3.21%)	0.41
+			
-			
White thrombosis	11 (9.48%)	12 (5.50%)	0.18
+			
-			
Active bleeding	4 (3.45%)	5 (2.29%)	0.54
+			
-			
Rf			0.81
0	6 (5.17%)	8 (3.67%)	
1	94 (81.03%)	179 (82.11%)	
2	16 (13.79%)	31 (14.22%)	
D of EV (n, %)			0.68
D0.3	15 (12.93%)	21 (9.63%)	
D1	43 (37.07%)	87 (39.91%)	
D1.5	46 (39.66%)	79 (36.24%)	
D2	11 (9.48%)	29 (13.30%)	
D3	1 (0.86%)	2 (0.92%)	

D = the maximum diameter of the varices, D0: no varices; D0.3: variceal diameter ≤0.3 cm; D1: variceal diameter 0.4-1.0 cm; D1.5: variceal diameter 1.1-1.5 cm; D2: variceal diameter 1.6-2.0 cm; D3: variceal diameter from 2.1-3.0 cm. Rf = Risk factor, it represented the risk index for variceal bleeding. Rf1: red color signs + or hepatic venous pressure gradient >12 mmHg; Rf2: varices with erosion, thrombus, active bleeding, or a lot of fresh blood excluded from the non-variceal bleeding. P-values are two-tailed and based on the Pearson χ^2 test. *is denoted as $P<0.05$, and of statistical significance.

Results

Demographic and clinical features of the patients in the elderly and non-elderly groups

The two groups were comparable for some parameters; as shown in **Table 1**, there were no significant differences in the Child-Pugh scores of the patients in the elderly and non-elderly groups (P = 0.29). The volume of ascites did not differ significantly between the groups (P = 0.58). The causes of cirrhosis differed significantly between the two groups ($P<0.001$); chronic viral hepatitis was the most common cause of cirrhosis (43.96% in group A *vs.* 63.31% in group B), followed by cryptogenic cirrhosis, alcoholism primary biliary hepatitis, autoimmune hepatitis and drug-induced hepatitis. The prevalence of hepatocellular carcinoma was slightly higher in group A than in group B, but this difference was not statistically significant (29, 25.00% *vs.* 40, 18.35%, P = 0.16). This difference may reflect the progression of chronic liver disease; elderly patients have a longer disease course, with subsequent development of cirrhosis or liver cancer. The incidence of chronic diseases was higher in group A than group B ($P<0.05$). In group A, hypertension was most prevalent (27.59%), followed by diabetes (26.72%) and pulmonary disease (10.34%). By contrast, diabetes was the most prevalent chronic disease in group B (19.72%), followed by hypertension (8.26%) and pulmonary disease (2.29%). The severity of last bleeding and histories of endoscopic treatment and operation were similar between the two groups, with P values of 0.39, 0.95, and 0.33, respectively. The indicator of severity of last bleeding was slightly greater in group A than in group B, but this difference was not significant (29 (25.44%) *vs.* 42 (19.09%), $P>0.05$). Prior treatment with EVS or EVL was slightly more common in group B than in group A, but this difference was not significant (50 (43.1%) *vs.* 101 (46.33%) $P>0.05$). Twenty-two patients in group A had previously undergone surgery for reduce portal hypertension. The majority of the operations were elective. The routine drug treatment for prevention of re-bleeding (beta blockers) used in our hospital for these patients is Carvedilol. Most patients (98.8%) received the

Table 3. The outcome of endoscopic therapy

	Group A	Group B	P value
Early re-bleeding rate (7 days) (n, %)	7 (6.03%)	7 (3.21%)	0.22
Short-term re-bleeding rate (3 months) (n, %)	4 (3.77%)	7 (3.55%)	0.92
Death within 3 months (n, %)	2 (1.72%)	2 (0.92)	0.52
Complications (n, %)			
None	63 (54.31%)	114 (52.29%)	0.73
Transient fever	18 (15.52%)	26 (11.93%)	0.356
Retrosternal pain	24 (20.69%)	55 (25.23%)	0.22
Difficulty in swallowing	10 (8.62%)	21 (9.63%)	0.761
Nausea and vomiting	7 (6.03%)	12 (5.50%)	0.841
Esophageal stenosis	7 (6.03%)	9 (4.13%)	0.437
Pneumonia	4 (3.45%)	0	0.006*

P-values are two-tailed and based on the Pearson χ^2 test. *is denoted as *P*<0.05, and of statistical significance.

beta blockers for prevention of re-bleeding with 94.8% (110/116) in group A and 96.3% (210/218) in group B. The rate of emergency operations was slightly higher in group A than in group B. A total of 21 of the 334 patients underwent emergency endoscopic therapy to treat active EVB (9 in group A, 12 in group B) and the other patients were treated after an episode of EVB (92.24% *vs.* 94.50%, *P*>0.05).

The differences between EV grading under endoscopy and related indicators were also not statistically significant, as shown in **Table 2**. 37 of 116 patients in group A were combined with gastric varix and in group B, 96 of 218 patients were combined with gastric varix. Results showed that patients combined with gastric varix were higher in elderly group than in non-elderly group. And we reviewed our data, and found that all the re-bleeding patients were from the non- gastric varix. This is very interesting. EVL and EVS were performed in 35.34% (41/116) and 64.66% (75/116) of patients in group A and 29.36% (64/218) and 70.64% (154/218) of patients in group B. Furthermore, the number of sessions of endoscopy to eradicate EVs was 92 in group A and 164 in group B at 1, 24 in group A and 51 in group B at 2, and none in group A and 3 in group B at >2. There were no significant differences in EV grade, EV risk factors (Rf), or EV diameter, with *P* values of 0.1, 0.81, and 0.68, respectively.

Outcomes of endoscopic therapy in the elderly and non-elderly groups

The main outcomes of endoscopic therapy are presented in **Table 3**. The evaluation of effectiveness and safety mainly focused on the performance and included the 7-day re-bleeding rate, 3-month re-bleeding rate and complication rate. There were no significant differences in the 7-day re-bleeding rate and 3-month re-bleeding rate between the two groups. After endoscopic therapy, the re-bleeding rates within 7 days after index endoscopy were similar in the two groups (group A *vs.* B: 6.03% (7/116) *vs.* 3.21% (7/218), *P* = 0.22). At the follow-up interview, only 4 of 106 patients (3.77%) in group A and 7 of 197 patients (3.55%) in group B experienced recurrent bleeding within 3 months (*P* = 0.92). Furthermore, only 2 patients in each group died within 3 months; three died of failure of endoscopic hemostasis, and one died of cancer and multiple organ failure. The death rate was not obviously different between group A and group B (*P* = 0.52). The complications after endoscopic treatments are listed in **Table 3**. Some mild complications were reported and only four patients in group A developed pneumonia. Seven patients in group A and nine patients in group B developed esophageal stenosis, and no other severe complications were reported. These adverse events were distributed similarly in the two groups (*P* = 0.73).

Logistic regression analysis on risk factors for effectiveness and safety of treatments in all patients

To investigate the risk factors for effectiveness of treatments in all patients, we performed the univariate and multiple logistic regression analysis on the 7-day re-bleeding. Univariate logistic regression analysis showed that ascites, active bleeding, EV size, Rf and the severity of last bleeding were associated with the 7-day re-bleeding. ORs and 95% CIs were 7.343 (2.378-22.672), 14.273 (3.151-64.653), 2.373 (1.31-4.296), 6.815 (2.31-20.106) and 2.049 (1.021-4.113), respectively. However, age, sex and the number of sessions of endoscopy to eradicate EVs are of no relation to the 7-day re-

Table 4. Univariate and multiple logistic regression models to identify risk factors for effectiveness of treatments in all patients (7-day rebleeding)

	Univariate analysis				Multivariate analysis			
	P value	OR	95% CI		*P* value	OR	95% CI	
Age	0.288	1.936	0.662	5.66				
Sex	0.594	0.737	0.241	2.259				
Ascites	0.001*	7.343	2.378	22.672	0.002*	6.841	2.07	22.609
Active bleeding	0.001*	14.273	3.151	64.653	0.004*	14.976	2.393	93.712
EV size	0.004*	2.373	1.31	4.296	0.009*	2.502	1.252	5.002
Rf	0.001*	6.815	2.31	20.106				
The severity of last bleeding	0.044*	2.049	1.021	4.113				
The number of sessions	0.714	1.234	0.402	3.784				

CI = confidence interval, EV = esophageal varices, OR = odds ratio, Rf = Risk factor, it represented the risk index for variceal bleeding. Rf1: red color signs + or hepatic venous pressure gradient >12 mmHg; Rf2: varices with erosion, thrombus, active bleeding, or a lot of fresh blood excluded from the non-variceal bleeding. *is denoted as *P*<0.05, and of statistical significance.

Table 5. Univariate and multiple logistic regression model to identify risk factors for safety of treatments in all patients

	Univariate analysis				Multivariate analysis			
	P value	OR	95% CI		*P* value	OR	95% CI	
Age	0.725	0.922	0.587	1.449				
Sex	0.480	0.844	0.527	1.352				
Active bleeding	0.082	4.083	0.836	19.954	0.041*	5.496	1.068	28.275
EV size	<0.001*	1.871	1.43	2.449	<0.001*	1.897	1.44	2.499
The number of sessions	0.009*	1.937	1.184	3.169				

CI = confidence interval, EV = esophageal varices. OR = odds ratios. *is denoted as *P*<0.05, and of statistical significance.

bleeding (**Table 4**). Furthermore, multiple logistic regression analysis demonstrated that ascites, active bleeding and EV size were independent risk factors for the 7-day re-bleeding. The adjusted ORs and 95% CIs were 6.841 (2.07-22.609), 14.976 (2.393-93.712) and 2.502 (1.252-5.002), respectively (**Table 4**).

To investigate the risk factors for safety of treatments in all patients, we performed the univariate and multiple logistic regression analysis on complications of endoscopic treatment. Univariate logistic regression analysis showed that EV size and the number of sessions of endoscopy to eradicate EVs are related to safety of these treatments in all patients. ORs and 95% CIs were 1.871 (1.43-2.449) and 1.937 (1.184-3.169), respectively. However, age, sex and active bleeding are of no correlations with safety of these treatments (**Table 5**). Moreover, multiple logistic regression analysis demonstrated that Active bleeding and EV size are independent risk factors for the safety of these treat-

ments in all patients. The adjusted ORs and 95% CIs were 5.496 (1.068-28.275) and 1.897 (1.44-2.499), respectively (**Table 5**).

Logistic regression analysis on risk factors for effectiveness and safety of treatments in elderly patients

To investigate the risk factors for effectiveness of treatments in elderly patients, we performed the univariate and multiple logistic regression analysis on the 7-day and 3-month re-bleeding. Univariate logistic regression analysis indicated that ascites, EV size and Rf were associated with the 7-day re-bleeding. ORs and 95% CIs were 25.143 (2.871-220.18), 3.352 (1.241-9.052) and 5.429 (1.141-25.836), respectively (**Table 6**). Furthermore, multiple logistic regression analysis demonstrated that greater ascites volume and larger EV size were independent risk factors for the 7-day re-bleeding with the adjusted ORs and 95% CIs being 21.779 (2.243-205.66) and 3.573 (1.132-13.122),

Table 6. Univariate and multiple logistic regression models to identify risk factors for effectiveness of treatments in elderly patients (7-day rebleeding)

	Univariate analysis				Multivariate analysis			
	P value	OR	95% CI		P value	OR	95% CI	
Ascites	0.004*	25.143	2.871	220.18	0.007*	21.779	2.243	205.66
EV size	0.017*	3.352	1.241	9.052	0.045*	3.573	1.132	13.122
Red thrombosis	0.05	18	0.999	324.25				
Rf	0.034*	5.429	1.141	25.836				
The number of sessions	0.669	0.623	0.071	5.439				

CI = confidence interval, EV = esophageal varices, OR = odds ratio, Rf = Risk factor, it represented the risk index for variceal bleeding. Rf1: red color signs + or hepatic venous pressure gradient >12 mmHg; Rf2: varices with erosion, thrombus, active bleeding, or a lot of fresh blood excluded from the non-variceal bleeding. *is denoted as $P<0.05$, and of statistical significance.

Table 7. Univariate and multiple logistic regression models to identify risk factors for effectiveness of treatments in elderly patients (3-month rebleeding)

	Univariate analysis				Multivariate analysis			
	P value	OR	95% CI		P value	OR	95% CI	
Child-Pugh score	0.03*	5.586	1.177	26.508	0.03*	5.586	1.177	26.508
Ascites	0.183	3.667	0.542	24.807				
The number of sessions	0.304	0.327	0.039	2.764				

CI = confidence interval, OR = odds ratios. *is denoted as $P<0.05$, and of statistical significance.

Table 8. Univariate and multiple logistic regression models to identify risk factors for safety of treatments in elderly patients

	Univariate analysis				Multivariate analysis			
	P value	OR	95% CI		P value	OR	95% CI	
History of endoscopic treatment	0.029*	0.429	0.201	0.918				
The severity of last bleeding	0.018*	1.75	1.101	2.781	0.044*	1.645	1.015	2.667
EV size	0.048*	1.944	1.219	3.099	0.011*	1.846	1.148	2.969
The number of sessions	0.351	1.536	0.623	3.789				

CI = confidence interval, EV = esophageal varices, OR = odds ratio, *is denoted as $P<0.05$, and of statistical significance.

respectively (**Table 6**). Then same analysis on 3-month re-bleeding proved that higher Child-Pugh score was positively correlated with 3-month re-bleeding. And higher Child-Pugh score was the independent risk factor for the 3-month re-bleeding with the adjusted ORs and 95% CIs being 5.586 (1.177-26.508) (**Table 7**).

Similarly, to investigate the risk factors for safety of treatments in elderly patients, univariate and multiple logistic regression analysis on complications of endoscopic treatment were conducted. Univariate logistic regression analysis showed that History of endoscopic treatment, the severity of last bleeding and EV size are related to safety of these treatments for elderly patients, with ORs and 95% CIs being

0.429 (0.201-0.918), 1.75 (1.101-2.781) and 1.944 (1.219-3.099), respectively (**Table 8**). However, the number of sessions of endoscopy to eradicate EVs is of no correlations with safety of these treatments for elderly patients, (**Table 8**). Moreover, multiple logistic regression analysis demonstrated that the severity of last bleeding and EV size are independent risk factors for the safety of these treatments. The adjusted ORs and 95% CIs were 1.645 (1.015-2.667) and 1.846 (1.148-2.969), respectively (**Table 8**).

Discussion

China is an aging society in which many senior citizens suffer from a combination of chronic

diseases. Elderly patients with cirrhosis are particularly susceptible to chronic disease due to longer disease course, poor liver function and additional complications. In addition, hepatitis B is a major health problem in China. According to Chinese Ministry of Health statistics, approximately 120 million people carry hepatitis B virus in China, indicating that every tenth Chinese person is a hepatitis B virus carrier. Every year, hundreds of thousands of people die of chronic hepatitis B (CHB)-related diseases, and one of the major causes is cirrhosis and its complications. EVs from portal hypertension often result in gastrointestinal bleeding, a life-threatening complication of cirrhosis [10]. EVB may be the first manifestation of cirrhosis. About one-third of the patients with cirrhosis and EVs experience EVB during the course of the disease, with a 20-30% mortality rate [11, 12].

Re-bleeding occurs in approximately 60% of patients after an initial bleeding event from EV. Consequently, all cirrhotic patients who survive a bleeding event must undergo secondary prophylaxis to prevent rebleeding [13, 14]. In recent years, endoscopic interventional treatment has proven to be an efficacious therapeutic option for EVB. Due in part to the increasing age of the population as well as increasing acceptance of the benefits of endoscopic therapy for elderly patients, older patients are increasingly inclined to choose endoscopic therapy [15]. Urgent endoscopy significantly reduces the need for emergency surgery, thus improving the survival of elderly bleeding patients and preventing rebleeding [16]. Ohta *et al.* [17] demonstrated that the efficacy of endoscopy is similar between adult and elderly patients. However, there was insufficient evidence to compare the safety and efficacy of endoscopic therapies for elderly patients with cirrhosis and EVs and controls. In this study, we reviewed medical records to identify essential patient characteristics, to define the efficacy and safety of endoscopic treatment for elderly patients and to explore the clinical risk factors of short term rebleeding and complications during treatment intervals of endoscopic therapy in elderly patients with EVs.

Our study revealed that the 7-day and 3-month re-bleeding rates after endoscopic therapy were similar between elderly patients (group A) and non-elderly patients (group B) (6.03% *vs.* 3.21%, $P = 0.22$; 3.77% *vs.* 3.55%, $P = 0.92$, respectively). The effectiveness of endoscopic therapy was not correlated with advanced age. Our results differ from those of previous studies due to differences in the definitions used for short-term re-bleeding. In our department, nearly all patients underwent medical observation for at least 7 days after the endoscopic procedure, and we requested that they undergo reevaluation at our hospital after 3 months. We defined early re-bleeding as occurring within 7 days and defined short-term bleeding as occurring within 3 months. However, many previous studies have used different definitions and reported different results. For example, Krige et al. [18] reported that seventy-seven (24.8%) patients died, 29 (9.3%) patients experienced re-bleeding within 5 days after the initial treatment, and 48 (15.4%) experienced re-bleeding between 6 and 42 days after the initial treatment. Amitrano et al. [19] observed that 4.3% of liver cirrhotic patients experienced re-bleeding within 5 days after endoscopic treatment. D'Amico et al. [20] observed that 3.9% of variceal bleeding patients experienced re-bleeding within 5 days after endoscopic treatment.

Numerous recent studies have investigated risk factors for predicting the efficacy of endoscopic treatment [18, 20-22]. However, few studies have predicted efficacy and safety specifically in elderly patients. Our results revealed four significant factors that were closely related to the efficacy of endoscopic treatment among all patient characteristics. The first risk factor was a greater ascites volume, which reflects worse liver function. The second risk factor was the severity of last bleeding, which often indicates severe liver function damage and larger EV size. The third risk factor was the size of the varices. Variceal size may determine variceal tension. At equal pressure, larger varices will rupture, whereas smaller varices will not [12]. The fourth risk factor was active bleeding observed during endoscopy. Active bleeding observed during endoscopy requires immediate endoscopic hemostasis, resulting in a plateauing of the Rf level and a high risk of re-bleeding in these EV patients. These results are consistent with previous research; Amitrano et al. [19] determined that Child-Pugh class C was an independent predictor of the 5-day re-bleeding rate after endoscopic treatment.

D'Amico *et al.* [20] identified active bleeding on endoscopy, Child-Pugh class, and so on as significant predictors of 5-day failure for bleeding from varices. In our group of elderly patients, the efficacy of endoscopic treatment was strongly associated with the ascites volume, varix size and Child-Pugh class. These results for elderly patients were also consistent with the aggregate data.

Mortality of upper gastrointestinal bleeding (UGIB) is significantly associated with the presence of comorbid pulmonary [23] and cardiovascular [24] disease in the elderly compared with younger patients with UGIB [25-28]. The prognosis of patients presenting with acute bleeding is dictated by the presence of medical co-morbidities and by the severity of liver disease in patients with varices. We evaluated chronic disease morbidity before we analyzed the safety and effectiveness of endoscopy treatment to understand the risks to elderly patients with regards to the cardiac, cerebrovascular and pulmonary systems. As expected, the incidence of complications was significantly higher in elderly patients. Although the incidence of chronic disease morbidities and age-related physiological problems increases with age and might increase the adverse effects of treatment, there was no significant difference between the two groups in the incidence of adverse events caused by endoscopic treatments. Although the complication rate appeared high, serious complications were rare, and most of the complications were mild and temporary, such as transient fever, retrosternal pain and nausea, difficulty in swallowing and vomiting. All symptoms were treated and disappeared within 3 days. Two significant factors were identified that were closely related to the safety of endoscopic treatment. Last bleeding severity was identified as a risk factor; heavy bleeding often indicates severe liver function damage and larger EV size, which explain the relatively high rate of post-surgical discomfort. The second risk factor was the size of the varices; larger varices might require a greater volume of sclerotherapy, more ligations, and additional sessions of endoscopic therapy. Thus, the strong correlation between the size of varices and the complication rate is reasonable. Our data demonstrated that the safety for younger and older populations was similar to those reported in clinical trials. This finding provides further evidence that age is not significantly associated with adverse effects, which are consistent with the findings of previous studies. Al-Ebrahim *et al.* [29] observed that patients who received endoscopic treatment after a recent MI exhibited higher rates of serious complications (acute coronary syndrome, arrhythmia, respiratory failure and aspiration pneumonia). However, they also noted that age, hemoglobin level and timing of endoscopy were not able to predict complications.

In the present study, we observed no relationship between age and re-bleeding rate or complication rates, further demonstrating that age does not affect the safety and efficacy of endoscopic treatment. However, liver function-related indexes and endoscopic indexes do influence the safety and efficacy of endoscopic treatment.

There are still several limitations to our study. First, this is a retrospective single-center trial. There are many inevitable statistical biases in a retrospective study. Second, some important clinical laboratory data and imaging data were not available in the database. We omitted these data to obtain a more precise analysis. Third, in our study, we defined elderly patients as patients over the age of 60, as reported by the World Health Organization; however, the definition of elderly patients varies among studies. We did not determine a cut-off age between the younger and older populations for statistical analysis. Additional research may be required to determine the appropriate definition of elderly patients.

In conclusion, there is no unique method applicable to the treatment of bleeding EVs based on patient age; endoscopic therapy is considered effective, safe and repeatable in experienced hands. Endoscopic treatment of varices and variceal hemorrhage should be decided based on clinical manifestations and endoscopic characteristics in old or young patients, such as the Child-Pugh score, ascites volume and size of varices.

Acknowledgements

Disclosure of conflict of interest

None.

Address correspondence to: Drs. Yunsheng Yang and Gang Sun, Chinese PLA General Hospital & Chinese PLA Medical School, 28 Fuxing Road, Beijing, P. R. China. Tel: 86 (10) 66499005; E-mail: sunny301ddc@126.com (YSY); Tel: 86-13501078679; E-mail: sunok301@126.com (GS)

References

[1] D'Amico G, Pagliaro L and Bosch J. The treatment of portal hypertension: a meta-analytic review. Hepatology 1995; 22: 332-354.

[2] Triantos C and Kalafateli M. Endoscopic treatment of esophageal varices in patients with liver cirrhosis. World J Gastroenterol 2014; 20: 13015-13026.

[3] Xu XD, Dai JJ, Qian JQ, Pin X and Wang WJ. New index to predict esophageal variceal bleeding in cirrhotic patients. World J Gastroenterol 2014; 20: 6989-6994.

[4] Hwang JH, Shergill AK, Acosta RD, Chandrasekhara V, Chathadi KV, Decker GA, Early DS, Evans JA, Fanelli RD, Fisher DA, Foley KQ, Fonkalsrud L, Jue T, Khashab MA, Lightdale JR, Muthusamy VR, Pasha SF, Saltzman JR, Sharaf R, Cash BD; American Society for Gastrointestinal Endoscopy. The role of endoscopy in the management of variceal hemorrhage. Gastrointest Endosc 2014; 80: 221-227.

[5] Peck-Radosavljevic M, Angeli P, Cordoba J, Farges O and Valla D. Managing complications in cirrhotic patients. United European Gastroenterol J 2015; 3: 80-94.

[6] Sharara AI and Rockey DC. Gastroesophageal variceal hemorrhage. N Engl J Med 2001; 345: 669-681.

[7] Cardenas A, Baiges A, Hernandez-Gea V and Garcia-Pagan JC. Endoscopic hemostasis in acute esophageal variceal bleeding. Gastroenterol Clin North Am 2014; 43: 795-806.

[8] Sonnenberg A. Timing of endoscopy in gastrointestinal bleeding. United European Gastroenterol J 2014; 2: 5-9.

[9] Koziel S, Kobryn K, Paluszkiewicz R, Krawczyk M and Wroblewski T. Endoscopic treatment of gastric varices bleeding with the use of n-butyl-2 cyanoacrylate. Prz Gastroenterol 2015; 10: 239-243.

[10] Tripathi D, Stanley AJ, Hayes PC, Patch D, Millson C, Mehrzad H, Austin A, Ferguson JW, Olliff SP, Hudson M and Christie JM. UK guidelines on the management of variceal haemorrhage

in cirrhotic patients. Gut 2015; 64: 1680-1704.

[11] Carbonell N, Pauwels A, Serfaty L, Fourdan O, Levy VG and Poupon R. Improved survival after variceal bleeding in patients with cirrhosis over the past two decades. Hepatology 2004; 40: 652-659.

[12] Garcia-Tsao G, Sanyal AJ, Grace ND, Carey W; Practice Guidelines Committee of the American Association for the Study of Liver Diseases; Practice Parameters Committee of the American College of Gastroenterology. Prevention and management of gastroesophageal varices and variceal hemorrhage in cirrhosis. Am J Gastroenterol 2007; 102: 2086-2102.

[13] Bosch J and Garcia-Pagan JC. Prevention of variceal rebleeding. Lancet 2003; 361: 952-954.

[14] D'Amico G, Pagliaro L and Bosch J. Pharmacological treatment of portal hypertension: an evidence-based approach. Semin Liver Dis 1999; 19: 475-505.

[15] Nahon S, Nouel O, Hagège H, Cassan P, Pariente A, Combes R, Kerjean A, Doumet S, Cocq-Vezilier P, Tielman G, Paupard T, Janicki E, Bernardini D, Antoni M, Haioun J, Pillon D, Bretagnolle P; Groupe des Hémorragies Digestives Hautes de l'Association Nationale des Hépatogastroentérologues des hôpitaux Généraux. Favorable prognosis of upper-gastrointestinal bleeding in 1041 older patients: results of a prospective multicenter study. Clin Gastroenterol Hepatol 2008; 6: 886-892.

[16] Kravetz D. Prevention of recurrent esophageal variceal hemorrhage: review and current recommendations. J Clin Gastroenterol 2007; 41 Suppl 3: S318-22.

[17] Ohta M, Hashizume M, Kamakura T, Ueno K, Tomikawa M, Tanoue K, Kitano S and Sugimachi K. Endoscopic injection sclerotherapy for esophageal varices in the elderly. World J Surg 1994; 18: 764-768.

[18] Krige JE, Kotze UK, Distiller G, Shaw JM and Bornman PC. Predictive factors for rebleeding and death in alcoholic cirrhotic patients with acute variceal bleeding: a multivariate analysis. World J Surg 2009; 33: 2127-2135.

[19] Amitrano L, Guardascione MA, Manguso F, Bennato R, Bove A, DeNucci C, Lombardi G, Martino R, Menchise A, Orsini L, Picascia S and Riccio E. The effectiveness of current acute variceal bleed treatments in unselected cirrhotic patients: refining short-term prognosis and risk factors. Am J Gastroenterol 2012; 107: 1872-1878.

[20] D'Amico G, De Franchis R; Cooperative Study Group. Upper digestive bleeding in cirrhosis. Post-therapeutic outcome and prognostic indicators. Hepatology 2003; 38: 599-612.

[21] Wakatsuki T, Obara K, Irisawa A, Sakamoto H, Kuwana T, Takiguchi F, Saito A, Shishido H, Hikichi T, Oyama H, Shibukawa G, Takagi T, Yamamoto G, Imamura H, Takahashi Y, Sato A, Sato M, Kasukawa R and Ohira H. Analysis of prognostic factors in patients with gastric varices after endoscopic treatment. Dig Endosc 2009; 21: 232-238.

[22] Hori S, Takaki A, Okada H, Fujiwara A, Takenaka R, Makidono C and Shiratori Y. Endoscopic therapy for bleeding esophageal varices improves the outcome of Child C cirrhotic patients. J Gastroenterol Hepatol 2006; 21: 1704-1709.

[23] Cappell MS and Nadler SC. Increased mortality of acute upper gastrointestinal bleeding in patients with chronic obstructive pulmonary disease. A case controlled, multiyear study of 53 consecutive patients. Dig Dis Sci 1995; 40: 256-262.

[24] Yamaguchi Y, Yamato T, Katsumi N, Morozumi K, Abe T, Ishida H and Takahashi S. Endoscopic hemostasis: safe treatment for peptic ulcer patients aged 80 years or older? J Gastroenterol Hepatol 2003; 18: 521-525.

[25] Thomopoulos KC, Vagenas KA, Vagianos CE, Margaritis VG, Blikas AP, Katsakoulis EC and Nikolopoulou VN. Changes in aetiology and clinical outcome of acute upper gastrointestinal bleeding during the last 15 years. Eur J Gastroenterol Hepatol 2004; 16: 177-182.

[26] Rockall TA, Logan RF, Devlin HB and Northfield TC. Incidence of and mortality from acute upper gastrointestinal haemorrhage in the United Kingdom. Steering committee and members of the national audit of acute upper gastrointestinal haemorrhage. BMJ 1995; 311: 222-226.

[27] Katschinski B, Logan R, Davies J, Faulkner G, Pearson J and Langman M. Prognostic factors in upper gastrointestinal bleeding. Dig Dis Sci 1994; 39: 706-712.

[28] Clason AE, Macleod DA and Elton RA. Clinical factors in the prediction of further haemorrhage or mortality in acute upper gastrointestinal haemorrhage. Br J Surg 1986; 73: 985-987.

[29] Al-Ebrahim F, Khan KJ, Alhazzani W, Alnemer A, Alzahrani A, Marshall J and Armstrong D. Safety of esophagogastroduodenoscopy within 30 days of myocardial infarction: a retrospective cohort study from a Canadian tertiary centre. Can J Gastroenterol 2012; 26: 151-154.