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Second urgent endoscopy within 48-hour benefits cirrhosis patients with acute esophageal variceal bleeding

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Abstract

Urgent endoscopy (UE) is important to the diagnosis and treatment of liver cirrhosis patients with esophageal variceal bleeding (EVB). It was reported that a second-look endoscopy may benefit acute upper gastrointestinal bleeding (UGIB) caused by peptic ulcer, while whether it could improve UGIB caused by liver cirrhosis associated EVB remains unclear. This study aimed to investigate the characteristics of second UE for liver cirrhosis with EVB and further examined the potential prognostic factors.

Patients aged ≥18 years who underwent UE for EVB within 2 hours after the admission were included and divided into scheduled second-look group (n = 245) and uncontrolled bleeding group (n = 352) based on the indications for second UE within 48 hours after initial endoscopy. Demographic and clinical data were collected and analyzed. Univariate and multivariate analysis were used to identify the risk factors for prognosis. The value of different scoring system was compared.

Statistical differences were found on history of bleeding and hepatocellular carcinoma, ascites, endoscopic type of bleeding, between scheduled second-look group and uncontrolled bleeding group. Univariate and multivariate logistic regression analysis confirmed that ascites, hemoglobin <60 g/L, AIMS65 score and failure to identify in initial UE were independent risk factors for bleeding uncontrolled after initial UE, and age, bilirubin level, initial unsatisfactory UE hemostasis, failure to identify bleeding on initial UE and tube/urgent TIPS suggested in initial UE were independent risk factors for 42-day mortality.

A second-look UE could bring benefit for liver cirrhosis patients with EVB without increasing the complication rate.

Abbreviations: AUROC = area under the receiver operating characteristic curve, CI = confidence interval, EVB = esophageal variceal bleeding, GOV2 = gastroesophageal varices type 2, IGV = isolated gastric varices, INR = international normalized ratio, OR = odds ratio, PT = prothrombin time, TIPS = transjugular intrahepatic portosystemic shunt, UE = Urgent endoscopy, UGIB = upper gastrointestinal bleeding.

Keywords: esophagogastric varices, liver cirrhosis, upper gastrointestinal bleeding, urgent endoscopy

1. Introduction

Esophagogastric variceal bleeding (EVB) is a fatal complication of liver cirrhosis. In patients with decompensated liver cirrhosis accompanied by ascites or hepatic encephalopathy, acute EVB has a high mortality. Variceal bleeding is a severe medical emergency and despite recent improvements on therapy, its 6-week mortality remains high up to 10% to 20%.[1–3] The treatment of acute EVB mainly includes conservative drug administration, endoscopic treatment, balloon tamponade, transjugular intrahepatic portosystemic shunt (TIPS) and surgery.[4–7] Drug treatment combined with endoscopic treatment is currently the main method for treating acute EVB, which can improve the success rate of hemostasis.[8]

To control acute active bleeding as soon as possible can reduce the incidence of complications such as ascites, infection, hepatic encephalopathy and electrolyte imbalance after acute hemorrhage, and start treatment for preventing re-bleeding early. Uncontrolled bleeding is one of the major causes for death[1–2,9] and the most critical period for successful treatment outcome and bleeding control is the first 5 days.[10] Active bleeding at urgent endoscopy (UE) was a significant prognostic indicator of failure to control bleeding.[11] Whether acute EVB is controlled is mainly determined based on patient's symptoms, signs and laboratory test results. However, due to various factors like bleeding amount, bleeding rate, body compensatory

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ZL and XS contributed equally to this work.

All procedures performed in studies involving human participants were in accordance with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent was obtained from all individual participants included in the study.

The authors have no conflicts of interests to disclose.

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response, individual differences and treatment response, it is difficult to make timely and accurate judgment of re-bleeding based on clinical manifestations. Endoscopy as the gold standard can confirm active bleeding. Patients with uncontrolled bleeding could receive endoscopic treatment again if necessary. Several randomized controlled clinical trials have confirmed that a scheduled second-look endoscopy and application of appropriate therapy when necessary can significantly reduce the risk of recurrent bleeding and hence improve clinical outcome in non-variceal upper gastrointestinal bleeding (UGIB) and endoscopic submucosal dissection.[12–17] However, for variceal hemorrhage, there were few reports of the efficacy of second UE. Thus, in this study we aimed to determine predictors of uncontrolled bleeding in acute EVB and indicators of uncontrolled independent risk factors for EVB endoscopic treatment, analyze the causes and purposes of second UE and further evaluate the clinical application of second UE in treating cirrhosis with acute UGIB. Our results also examined and compared the role of commonly used scoring systems for UGIB in facilitating earlier triage and goal-directed treatment when endoscopic data are unavailable.

2. Methods

2.1. Study design

Medical records were retrospectively evaluated from July 2012 to May 2018 in the Fifth Medical Center of Chinese PLA General Hospital. All the outpatients or inpatients diagnosed as cirrhosis with EVB received UE within 2 hours of admission and second UE within 48 hours. Clinical data of all patients were complete. This study was approved by the Fifth Medical Center of Chinese PLA General Hospital.

2.2. Patients

We included patients aged ≥18 years who underwent UE for EVB within 2 hours after admission. Patients with histologically proven cirrhosis or clinical and ultrasonographic data compatible with the diagnosis of cirrhosis admitted because of hematemesis and/or melena were considered eligible for this study (Fig. 1). Inclusion criteria were:

(1) age 18 to 80 years;
(2) clinical evidence of bleeding (hematemesis and/or melena) during the previous 24 hours;
(3) treatment with drug therapy at least 0.5 hour before UE;
(4) EVB as shown by the finding on initial UE, performed within 2 hours at admittance to emergency room or in the general ward from the initial evaluation to the start of endoscopy within 2 hours of active bleeding from a varix, stigmata of recent hemorrhage, or fresh blood in stomach and esophageal varices as the only potential source of bleeding;
(5) signed informed consent to participate in the study.

Patients referred from other hospitals were included only if they fulfilled all the above-mentioned criteria. The protocol and all the procedures scheduled conformed to the guidelines and rules of Good Clinical Practice in clinical trials.

Exclusion criteria were:

(1) unfit for resuscitation;
(2) received initial UE in the ICU;
(3) band ligation within 2 weeks or sclerotherapy within 1 week; previous (7-day period) earlier TIPS to treat previous episodes of variceal hemorrhage; history of severe cardiovascular disease; known hypersensitivity to terlipressin or sclerosing agents; pregnancy; chronic renal failure;

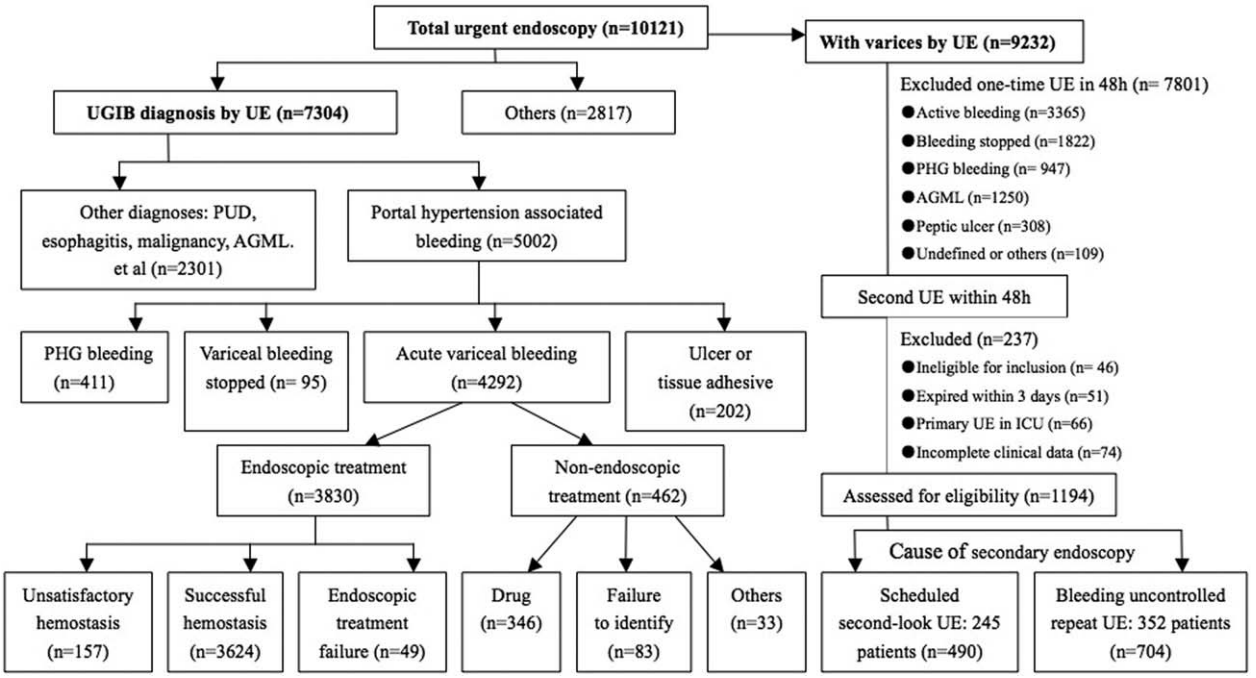

Figure 1. Patients inclusions. (UE: urgent endoscopy).

(4) those whose bleeding started while already hospitalized with another illness or those who bled from known gastric carcinoma or non-ulcerative lesions such as Dieulafoy's lesion, portal hypertensive gastropathy, peptic ulcer bleeding, UGIB and patients with rare varicose veins such as duodenal varices.

Before initial UE, clinical history, physical examination, ultrasonographic data and laboratory tests were obtained. Patients were closely monitored. Blood pressure (BP), heart rate, and central venous pressure were recorded every 2 to 4 hours, meanwhile, Blood routine, liver and renal function, prothrombin time (PT), international normalized ratio (INR) were monitored. Patients were subjected to second UE within 48 hours after initial UE. Variables included demographic factors (age, sex), medical history, vital signs (pulse, systolic BP, diastolic BP, temperature, and respiratory rate), mental status, results of laboratory tests, and underlying comorbid conditions. Baseline characteristics including complete Child-Pugh score, MELD score, AIMS65 score, Rockall score, Glasgow-Blatch-ford score, the reason of second UE, and second UE characteristics, endoscopic hemostasis overall procedure were evaluated in all enrolled patients.

2.3. Variceal hemorrhage and UE

UE was performed for the emergency patients within 2 hours after admission, and patients in the ward or intensive care unit within 2 hours at diagnosis of UGIB. All patients received drug treatment before UE. The patients were conscious and could cooperate with endoscopic examination. The patients with hepatic encephalopathy, coma or unable to cooperate with the endoscopy examination underwent sedation and airway protection if necessary. Urgent endoscopic hemostasis was performed according to the bleeding type, location and patients' willingness. The whole urgent endoscopic procedures were performed by expert endoscopists who had experience of more than 200 urgent endoscopic hemostasis. The endoscope used was either a GIF-260 or a GIF-290 gastroscope (Olympus, Tokyo, Japan). The methods of endoscopic hemostasis included variceal band ligation, endoscopic injection sclerotherapy or tissue adhesive injection therapy. Ligation or sclerotherapy is the recommended endoscopic therapy for acute EVB,[6–7] and endoscopic therapy with tissue adhesive is recommended for acute bleeding from isolated gastric varices (IGV) and those gastroesophageal varices type 2 (GOV2) that extend beyond the cardia. The ligature is 6 bursts of ligatures (COOK, USA), the sclerotherapy (either 10 ml/ branch, lauromacrogel Shanxi Tianyu, China or 2 ml/branch, sodium smorrhuate injection Xinyi, China) using a combined intravariceal and paravariceal technique, the injection site is located at the cardia end of the varicose vein where the bleeding is local or hemorrhage. A maximum total volume of 20 ml lauromacrogel and 3 ml sodium smorrhuate was injected at any single bleeding vessel. The injection of tissue adhesive is based on the "sandwich" method. The injection needle is MTW 23-25G disposable hardening needle, and the Histoacryl was from Braun (0.5 ml/ branch, Germany) and the iodinated oil injection was produced by the China company (10 ml/ branch).

Successful hemostasis is defined as confirmed stop of active bleeding from rupture varices after endoscopic procedures. Unsatisfactory hemostasis means the cessation of bleeding but not confirmed after endoscopic treatment, and endoscopic treatment failure is defined as active bleeding still seen after endoscopic treatment. Uncontrolled bleeding is defined by one of the following criteria (UK guidelines 2015)[4]:

(1) Fresh hematemesis or nasogastric aspiration of ≥100 mL of fresh blood ≥2 hours after the start of a specific drug treatment or therapeutic endoscopy.
(2) Development of hypovolemic shock.
(3) 30 g/L drop in hemoglobin (9% drop of hematocrit) within any 24 hours period if no transfusion is given.

Variceal rebleeding is defined as the occurrence of a single episode of clinically significant rebleeding from portal hypertensive sources from day 5.

2.4. Grouping

The decision to perform second UE is taken by the physician responsible of the bleeding unit based on clinical judgment. Criteria decision was whether active bleeding controlled. Patients were divided into 2 groups based on the indications for second UE within 48 hours after initial endoscopy. Scheduled second-look group was patients with stable conditions, considering bleeding controlled, intended to scheduled second-look endoscopy, in order to open up the diet as early as possible (Fig. 2). Uncontrolled bleeding group was patients to consider active bleeding uncontrolled, performed the repeat UE to confirm the condition, endoscopic treatment again if necessary. Additionally, patients (n = 3033) who only underwent UE in the study period were also enrolled as control group for the comparison on the influence of second-look endoscopy on the morality.

2.5. Outcome definitions

Patients were monitored for closely duration in the hospitalization stay with a final follow-up on day 42. A record of active bleeding signs was maintained (maximum interval 6 hours). Hemoglobin and hematocrit were measured before and after endoscopic treatment, at least once daily on days 2 to 5. Evaluation parameters included the number of balloon tamponade performed, the number of urgent TIPS performed, amount of blood transfusions given, changes in radiological and serum related parameters (measured using standard methods). The primary endpoint was rebleeding rate, 5-day and 42-day mortality. Secondary endpoints were length of hospitalization stay (LOS) and cost.

2.6. Statistical analysis

All statistical analyses were performed using SPSS Statistics (version 23; IBM Corp, Armonk, NY). Data are presented as mean ± SD, unless otherwise stated. Differences in categorical variables were evaluated using Pearson's $\chi 2$ test. Differences in continuous variables were evaluated using T test for independent samples, after verifying homogeneity of variance with Levene test. Multiple logistic regression analysis using selection of variables significant at the 0.10 level in univariate analysis was applied to assess independent risk factors related to outcomes. The odds ratio (OR) and its 95% confidence interval (CI) was estimated to assess the predicted individual probabilities. $P < .05$ was considered to be statistically significant. The ability of a variety score to predict the outcome of 42-day mortality was determined by calculating the area under the receiver operating characteristic curve (AUROC).

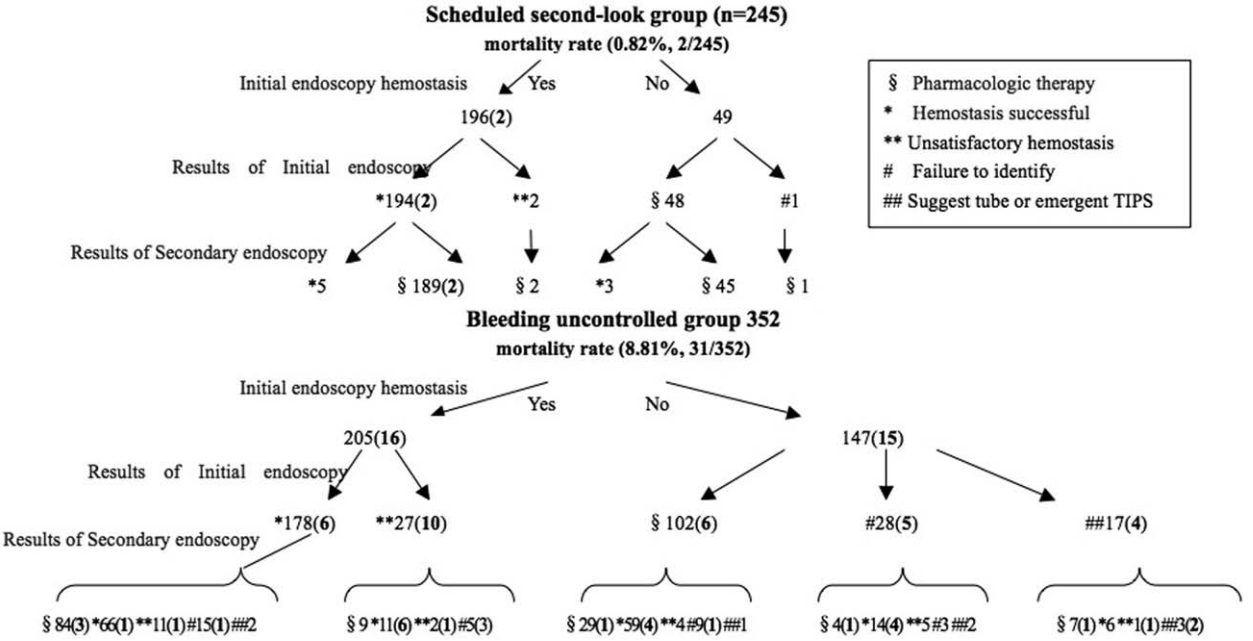

Figure 2. Treatment of scheduled second-look endoscopy.

3. Results

As a specialized hospital for liver diseases, the Fifth Medical Center of Chinese PLA general hospital has developed "on-call" UE since January 2010. From July 2012 to May 2018, a total of 10,121 cirrhosis patients with acute UGIB received UE. There were 7304 cases diagnosed as UGIB, including 4292 cases of EVB. Among them, 597 EVB patients received second UE within 48 hours of admission.

3.1. Demographic and clinical characteristics

There were no significant differences between scheduled second-look group and uncontrolled bleeding group on mean age (52.72 ± 10.56 vs 53.88 ± 12.12), the male-to-female ratio (2.31:1 vs 3.24:1), admission status (emergency department/general ward), liver cirrhosis etiology, presentation and intervals from symptom onset to initial endoscopy, overall duration of initial endoscopic hemostasis procedure. The bleeding history in the scheduled second-look group with 139 (56.73%) patients was much higher in the uncontrolled bleeding group with 157 (44.60%) patients ($P < .01$). The incidence of hepatocellular cancer in uncontrolled bleeding group was significantly higher than that in scheduled second-look group ($P < .01$) (Table 1). The ratio of heart rate over 100/minute in uncontrolled bleeding group was significantly higher than that in scheduled second-look group. The level of albumin was significantly higher in the scheduled second-look group (30.67 ± 5.11 vs 28.01 ± 5.59, $P < .01$). There were significant differences on mean levels of bilirubin, creatinine, PT and INR between the 2 groups. It is important that the serum levels tended to be higher in uncontrolled bleeding group patients than in those scheduled second-look group patients ($P < .05$). Similarly, ascites and portal thrombosis were more frequent in the uncontrolled bleeding group than in the scheduled second-look group. The collateral circulation was more common in the scheduled second-look group than in the uncontrolled bleeding group. There was no significant difference in the opening of para umbilical vein between the 2 groups, but the gastric renal shunt was significantly higher in the scheduled second-look group than in the uncontrolled bleeding group (Table 1). More patients with very high pre-endoscopy Child-Pugh score were in uncontrolled bleeding group, compared with those in scheduled second-look group (8.20 ± 1.68 vs 7.39 ± 1.73, $P < .01$). Pre-endoscopy median score of MELD, AIMS65, Rockall risk score and Glasgow-Blatch-ford score were significantly higher in the uncontrolled bleeding group than the scheduled second-look group ($P < .05$, Table 1).

3.2. Findings at initial UE

Among the endoscopic diagnoses, 399 cases had EVB with endoscopic stigmata of acute bleeding, fresh thrombus (40 vs 52), oozing (29 vs 34), or spurting (121 vs 123) in scheduled second-look group and uncontrolled bleeding group, respectively. Patients in uncontrolled bleeding group were significantly more likely to have outmoded blood or clot than in scheduled second-look group [33.81% (n = 119) vs 20.00% (n = 49); $P < .01$]. Moreover, more patients in the uncontrolled bleeding group had unclear vision during the initial UE [6.82% (n = 24) vs 2.45% (n = 6); $P < .01$]. Uncertain bleeding location was more common in the uncontrolled bleeding group than in the scheduled second-look group ($P < .01$). The initial endoscopic treatment rate of scheduled second-look group was significantly higher than that of uncontrolled bleeding group (79.18% vs 50.57%; $P < .01$). In addition, nearly 7.67% patients (n = 27) of the uncontrolled bleeding group were unsatisfied with the initial endoscopic hemostasis, and no definite bleeding stopped was observed after endoscopic treatment, which was significantly higher than that of the scheduled second-look group (0.82%, n = 2). 20.00% and 41.76% of the patients in the two groups did not receive initial endoscopic treatment ($P < .01$). In uncontrolled bleeding group,

Table 1

Characteristics of 597 cirrhosis patients with acute EVB received primary and secondary urgent endoscopy within 48 hours. Baseline characteristics at admission or as recorded at time of inpatient presentation, findings at initial urgent Endoscopy, comparison of initial urgent endoscopic characteristics and mandatory therapy were listed.

Characteristics	Scheduled second-look group (n = 245)	Bleeding uncontrolled group (n = 352)	*P* value
Age (yr), mean ± SD	52.72 ± 10.56.	53.88 ± 12.12	.270
Sex, M/F	171/74 (2.31:1)	269/83 (3.24:1)	.073
Emergency department/General ward, n/n	138/107 (1.29:1)	177/175 (1.01:1)	.123
Liver cirrhosis etiology, n (%)			
Hepatitis B	156 (63.67)	214 (60.80)	.308
Hepatitis C	23 (9.39)	30 (8.52)	
Alcohol	22 (8.98)	41 (11.65)	
Drugs or toxins	8 (3.27)	5 (1.42)	
Primary biliary cirrhosis	15 (5.95)	14 (3.98)	
Autoimmune cirrhosis	6 (2.45)	15 (4.26)	
Overlapping infections	10 (4.08)	20 (5.68)	
Others	5 (2.04)	13 (3.69)	
Presentation, n (%)			
Red blood emesis &Coffee grouds	157 (64.08)	238 (67.61)	.230
Melena	73 (29.80)	88 (25.00)	
Bloody stool	15 (6.12)	22 (6.25)	
Other	0 (0)	4 (1.14)	
History of bleeding, n (%)	139 (56.73)	157 (44.60)	<.01
History of bleeding treatment, n (%)			
Pharmacologic therapy	41/139 (29.50)	18/157 (11.46)	<.01
Emergency endoscopic therapy	27/139 (19.42)	53/157 (33.76)	
Endoscopic preventive therapy	20/139 (14.39)	22/157 (14.01)	
Emergency and preventive therapy	15/139 (10.79)	7/157 (4.46)	
TIPPS	4/139 (2.88)	6/157 (3.82)	
Splenectomy (or +endoscopic therapy)	28/139 (20.14)	51/157 (32.48)	
Gastric coronary/splenic embolization	3/139 (2.16)	5/157 (3.18)	
History of Hepatocellular carcinoma, n (%)	51 (20.82)	164 (46.59)	<.01
Vital signs, n (%)			
SBP < 90mmHg	22 (8.98)	24 (6.82)	.193
SBP 90–100 mmHg	165 (67.35)	218 (61.93)	
SBP >100 mmHg	58 (23.67)	110 (31.25)	
Heart rate >100/min	84 (34.29)	213 (60.51)	<.01
Lab test results, mean ± SD			
Hemoglobin (131–172 g/dl)	82.23 ± 24.24	81.65 ± 21.87	.762
Platelets (100–300 x 10^9/l)	95.74 ± 65.43	101.23 ± 67.72	.324
Albumin (35–55 g/l)	30.67 ± 5.11	28.01 ± 5.59	<.01
Bilirubin (3.4–20.5 umol/l)	37.60 ± 58.00	52.77 ± 86.87	.017
Creatinine (62–115 umol/l)	78.91 ± 33.67	92.91 ± 76.80	<.01
Prothrombin time (11–14.3s)	14.82 ± 2.76	15.65 ± 4.90	.017
INR (0.8–1.2%)	1.30 ± 0.23	1.40 ± 0.75	.041
Medium-large ascites, n (%)	71 (28.98)	154 (43.75)	<.01
Portal vein branch/trunk thrombosis, n (%)	66 (26.94)	145 (41.19)	<.01
Collateral circulation, n (%)			
None	129 (52.65)	222 (63.07)	<.01
Gastric-renal or spleen-renal shunt	36 (14.69)	27 (7.67)	
Para umbilical vein	80 (32.65)	103 (29.26)	
Child-Pugh score, mean ± SD	7.39 ± 1.73	8.20 ± 1.68	<.01
Child-Pugh grade (A/B/C), n/n/n	95/132/25	65/252/72	
MELD score, mean ± SD	8.20 ± 6.36	10.22 ± 7.25	<.01
AIMS65 score, mean ± SD	0.76 ± 0.82	1.39 ± 1.00	<.01
Rockall score, mean ± SD	4.25 ± 1.35	4.58 ± 1.88	.021
Glasgow-Blatch-ford, mean ± SD	12.82 ± 3.37	13.64 ± 2.31	<.01
Type of bleeding, n (%)			
Outmoded blood or clot	49 (20.00)	119 (33.81)	<.01
Fresh thrombus	40 (16.33)	52 (14.77)	
Oozing	29 (11.84)	34 (9.66)	
Spurting	121 (49.39)	123 (34.94)	
Unclear vision	6 (2.45)	24 (6.82)	
Location of bleeding, n (%)			

(*continued*)

Table 1

(continued).

Characteristics	Scheduled second-look group (n = 245)	Bleeding uncontrolled group (n = 352)	*P* value
Uncertain	43 (17.55)	138 (39.20)	<.01
Esophageal varices	100 (40.82)	108 (30.68)	
Cardiac part	65 (26.53)	73 (20.74)	
Gastric fundus and body	30 (12.24)	34 (9.66)	
IGV	3 (1.22)	4 (1.14)	
Esophageal and Gastric varices	4 (1.63)	5 (1.42)	
Initial endoscopic therapy, n (%)	194 (79.18)	178 (50.57)	<.01
Unsatisfactory endoscopic hemostasis, n (%)	2 (0.82)	27 (7.67)	<.01
No initial endoscopic therapy, n (%)	49 (20.00)	147 (41.76)	
Drug suggested	48 (19.59)	102 (28.98)	<.01
Failure to identify	1 (0.41)	28 (7.95)	
Tube suggested or emergent TIPS	0 (0)	17 (4.83)	

7.95% (n = 28) patients had no endoscopic treatment favorite conditions because the bleeding site could not be identified. 4.83% (n = 17) patients were suggested receiving Sengstaken-Blackmore tube, radiologic intervention or operation instead, which was significantly higher than the scheduled second-look group ($P < .01$) (Table 1). Overall medical treatment characteristics were similar between groups. Selection and switching of vasoactive drugs was based on the investigator's judgment. Intravenous proton pump inhibitor was used in 2 group without statistical difference.

3.3. Second UE

According to the decision taken by the physician responsible of the bleeding unit based on clinical judgment, the aim of second UE in scheduled second-look group was to reexamination, to decide to open up the diet or not (Table 2). With respect to the characteristics of the lab test results at second endoscopy, the level of albumin was significantly higher in the scheduled second-look group than the uncontrolled bleeding group (29.27 ± 4.81 vs 27.56 ± 4.71, $P < .01$). The level of bilirubin and creatinine were significantly different between the 2 groups ($P = .045$ and .019, respectively). PT tended to be longer in patients with bleeding uncontrolled than in those with scheduled second-look (16.14 ± 5.81 seconds vs 14.57 ± 2.67 seconds, $P < .01$). The incidence of ascites in uncontrolled bleeding group was significantly higher than that in scheduled second-look group, which were more severe. Among 352 patients who underwent repeated UE because of uncontrolled bleeding, a total of 228 (64.77%) patients had rebleeding endoscopic stigmata with thrombus or oozing (80 cases, 22.73%), active rebleeding (142 cases, 40.34%), or clot (6 cases, 2.84%). The proportion of patients with rebleeding in scheduled second-look group was rare, and 237 (96.73%) patients were confirmed that the bleeding had stopped. Patients in

Table 2

Outcomes in the repeated endoscopy including primary and secondary end points.

Characteristics	Scheduled second-look Group (n = 245)	Bleeding uncontrolled Group (n = 352)	*P* value
The reason of repeated endoscopy, n (%)			
Open up the diet	243 (99.18)	0 (0)	–
Symptoms of rebleeding	0 (0)	229 (65.06)	
Hemoglobin reduction	0 (0)	88 (25.00)	
Symptoms and hemoglobin reduction	0 (0)	25 (7.10)	
Prepare to remove Sengstaken tube	2 (0.82)	10 (2.84)	
Lab test results at secondary endoscopy, mean ± SD			
Hemoglobin (131–172 g/dl)	73.48 ± 18.16	70.13 ± 18.05	.059
Platelets (100–300 10^9/l)	77.63 ± 62.49	83.98 ± 59.11	.213
Albumin (35–55 g/l)	29.27 ± 4.81	27.56 ± 4.71	<.01
Bilirubin (3.4–20.5 umol/l)	36.62 ± 52.60	48.09 ± 76.80	.045
Creatinine (62–115 umol/l)	77.84 ± 42.58	94.29 ± 92.13	.019
Prothrombin time (11–14.3s)	14.57 ± 2.67	16.14 ± 5.81	<.01
INR (0.8–1.2%)	1.26 ± 0.22	1.42 ± 0.49	<.01
Ascites, n (%)			
None	141 (57.55)	138 (39.20)	<.01
Small amount	60 (24.49)	77 (21.88)	
Medium-large amount	44 (17.96)	137 (38.92)	
Secondary endoscopy rebleeding, n (%)	8 (3.27)	228 (64.77)	
Outmoded blood or clot	0 (0)	6 (2.84)	<.01

(*continued*)

Table 2

(continued).

Characteristics	Scheduled second-look Group (n = 245)	Bleeding uncontrolled Group (n = 352)	*P* value
Fresh thrombus	7 (2.86)	80 (22.73)	
Active rebleeding	1 (0.41)	142 (40.34)	
Location of bleeding, n (%)	8 (3.27)	228 (64.77)	
Uncertain	0/8 (0)	24/228 (10.53)	–
Esophageal varices	3/8 (37.50)	73/228 (32.02)	
Cardiac part	3/8 (37.50)	85/228 (37.28)	
Gastric fundus and body	2/8 (25.00)	38/228 (16.67)	
IGV	0/8 (0)	2/228 (0.88)	
Esophageal and Gastric varices	0/8 (0)	6/228 (2.63)	
Secondary endoscopic therapy, n (%)	8 (3.27)	156 (44.32)	<.01
Unsatisfactory hemostasis, n (%)	0 (0)	23 (6.53)	–
No secondary endoscopic therapy, n (%)	237 (96.73)	173 (49.15)	
Suggest drug	237 (96.73)	132 (37.50)	<.01
Failure to identify	0 (0)	33 (9.38)	
Suggest tube or emergent TIPS	0 (0)	8 (2.27)	
Rebleeding, n (%)			
Within 7 days	2 (0.82)	23 (6.53)	<.01
8–42 days	10 (4.08)	27 (7.67)	<.01
Mean day of open diet, d, mean ± SD	2.59 ± 1.38	5.50 ± 2.22	<.01
Mean time of stool color normal, d, mean ± SD	4.10 ± 2.64	6.40 ± 2.96	<.01
Mean time of stool occult blood tests negative, d, mean ± SD	4.37 ± 2.72	6.81 ± 2.93	<.01
Patients transfused red blood cells, n (%)	154 (61.11)	303 (86.08)	<.01
units, mean ± SD	3.62 ± 4.71	7.41 ± 7.46	<.01
Patients transfused plasma, n (%)	55 (21.83)	158 (44.89)	<.01
units, mean ± SD	1.94 ± 6.25	5.65 ± 14.73	<.01
Patients transfused platelet, n (%)	16 (6.35)	46 (11.83)	.028
units, mean ± SD	0.23 ± 1.10	0.22 ± 0.85	.871
Balloon tamponade, n/n (initial endoscopy/ second endoscopy)	2/0	10/24	.136
TIPS shunt, n/n (initial endoscopy/ second endoscopy)	0/0	2/4	–
Prevent recurrent bleeding (within 42 d), n (%)			
endoscopic treatment	36 (14.69)	26 (7.39)	<.01
endoscopy and pharmacology	12 (4.90)	5 (1.42)	.014
surgical	6 (2.45)	14 (3.98)	.362
TIPS	13 (5.31)	25 (7.10)	.610
liver transplantation	0 (0)	2 (0.57)	–
Mortality within 42 d, n (%)	2 (0.82)	31 (8.81)	<.01
Mortality within 5 d, n (%)	1 (0.41)	17 (4.83)	<.01
Mortality within 6–42 d, n (%)	1 (0.41)	14 (3.98)	<.01
Cause of death, n (%)			
Bleeding	2 (0.82)	19 (5.40)	<.01
Infection	0 (0)	3 (0.85)	–
MSOF	0 (0)	9 (2.56)	–
LOS, d, mean ± SD	18.42 ± 12.70	21.65 ± 15.64	<.01
Costs, Yuan, mean ± SD	67581.83 ± 66545.09	94846.72 ± 77903.32	<.01

uncontrolled bleeding group showed significant differences with bleeding location in initial and second UE, because more bleeding sites were found on second endoscopy. The proportion of uncertain bleeding location in the second endoscopy was lower than in the initial UE (10.53% vs 39.20%, $P < .01$). At the second UE, endoscopic hemostasis was achieved in 156 patients of uncontrolled bleeding group, 23 patients had endoscopic treatment unsatisfactory. Then, the bleeding site could not be identified in 33 patients (9.38%), who had no favorite conditions for endoscopic treatment. Eight patients in scheduled second-look group who did not have clinical rebleeding received endoscopic therapy during second UE because the characteristics of EVB were diagnosed as high risk for rebleeding.

3.4. Outcomes of endoscopic treatment

The 7-day and 6-week rebleeding incidence was significantly lower in scheduled second-look group than those in uncontrolled bleeding group patients ($P < .01$) (Table 2). The mean day of open diet in patients of scheduled second-look group was 2.59 ± 1.38 days, significantly shorter than the 5.50 ± 2.22 days in uncontrolled bleeding group. The mean time of stool with normal color and negative stool occult blood tests were significantly prolonged in the uncontrolled bleeding group than the scheduled second-look group. The number of patients whose supplement of red blood cells, plasma or platelet in uncontrolled bleeding group were significantly more than in scheduled second-look group ($P < .01$). The transfused units of

red blood cells and plasma of the uncontrolled bleeding group were 7.41 ± 7.46 and 5.65 ± 14.73, whereas the transfused for the scheduled second-look group were 3.62 ± 4.71 and 1.94 ± 6.25. Because of endoscopic hemostasis failure, 12 patients received balloon tamponade for varices after the initial endoscopy; among them, there were 10 patients in uncontrolled bleeding group. After the second endoscopy, 24 patients received balloon tamponade again in this group. Obviously, the incidence of emergency TIPS was significantly higher in uncontrolled bleeding group than in scheduled second-look group. After the controlled bleeding, most patients in scheduled second-look group underwent elective therapy to prevent recurrent bleeding within 42 days. Overall, there were no significant differences between the 2 groups regarding the surgery or TIPS. However, more patients in scheduled second-look group received preventive endoscopic treatment than in the uncontrolled bleeding group.

None died suddenly during the endoscopy in all patients. During the 42-day follow-up, the mortality within 5 days and 6 to 42 days were significantly higher in the uncontrolled bleeding group compared with scheduled second-look group, respectively. The main cause of death was bleeding, followed by multiple system organ failure (MSOF), and the most common was hepatic function failure and respiratory failure. Patients (n = 3033) who only underwent UE in the study period were also enrolled as control group. The mortality was compared. The results showed that the 5-day mortality was 0.41% (1/245), 4.83% (17/352), and 5.28% (160/3033) in scheduled second-look group, uncontrolled bleeding group and control group, which within 6 to 42 days was 0.41% (1/245), 3.98% (14/352), and 8.61% (261/3033). The overall mortality in scheduled second-look group was lower than that in uncontrolled bleeding group and control group, respectively [0.82% (2/245) vs 8.81% (31/352) and 13.88% (421/3033), $P < .01$], indicating that second-look endoscopy can obviously decrease 42-day mortality.

Median duration of hospitalization stay was significantly different between the 2 groups (18.42 ± 12.70 days in scheduled second-look group vs 21.65 ± 15.64 days in uncontrolled bleeding group, $P < .01$). Moreover, the costs of uncontrolled bleeding group (94846.72 ± 77903.32 Yuan) were significantly higher than the scheduled second-look group (67581.83 ± 66545.09 Yuan) ($P < .01$) (Table 2).

3.5. Side effects and complications

The 199 patients in scheduled second-look group received 204 urgent endoscopic injection treatments, and 294 patients in uncontrolled bleeding group received 384 urgent endoscopic injection treatments during a total of initial and second UE sessions. 29 (11.84%) and 69 (19.60%) complication events were documented in 2 groups during surveillance, respectively. Compared with 3360 patients undergoing single urgent endoscopic treatment in the same period, there were no differences considering the total numbers of side effects between the single urgent group and the scheduled second-look group. Meanwhile, the total numbers of side effects in uncontrolled bleeding group was significant higher than 2 groups above (Table 3). Mucosal ulceration at the injection site was found at follow-up endoscopy on 6 patients in scheduled second-look group and 10 patients in uncontrolled bleeding group. The incidence of ulcer related with endoscopic treatment has a trend towards being higher in the second group than in the single UE group (2.84% vs 2.45% vs 1.88%). Fortunately, severe complications were not observed in second UE groups; meanwhile, there were no differences when considering the serious events among the uncontrolled bleeding group, scheduled second-look group and single UE group. Considering the minor side effects, the incidence of transient fever in the uncontrolled bleeding group was higher the other 2 groups.

3.6. Predictors of uncontrolled bleeding after initial UE

According to the second urgent endoscopic characteristics, 597 patients were divided into 2 groups: bleeding stopped group (360 cases) and active bleeding group (237 cases). Table 4 shows univariate and multivariate analysis of early clinical-related rebleeding. In our univariate analysis, hepatocellular carcinoma and ascites were more common in patients with active bleeding. Hemoglobin <60 g/L and albumin <28 g/L were risk factors for bleeding uncontrolled. Although PT prolong ≥6 seconds was not identified as a risk factor for bleeding uncontrolled ($P = .053$), patients with PT prolong ≥6 seconds had a higher risk of rebleeding. MELD score, AIMS65 score, MELD score (≥15) and AIMS65 score (≥2) were risk factors for bleeding uncontrolled ($P < .05$). The univariable logistic regression analysis showed that unsatisfactory hemostasis and failure to identify in initial UE were also risk factors

Table 3

Side effects and complications related to endoscopic therapy.

Complications, n (%)	Single urgent endoscopy group (n = 3360)	Scheduled second-look group (n = 245)	Bleeding uncontrolled group (n = 352)
Total	427 (12.71)	29 (11.84)	69 (19.60)
Major	88 (2.62)	8 (3.27)	14 (3.98)
Aspiration	2 (0.06)	0 (0)	0 (0)
Aspiration pneumonia	21 (0.63)	2 (0.82)	4 (1.14)
Septic shock	1 (0.03)	0 (0)	0 (0)
Ulcer	63 (1.88)	6 (2.45)	10 (2.84)
Abnormal embolization	1 (0.03)	0 (0)	0 (0)
Minor	339 (10.09)	21 (8.57)	55 (15.63)
Thoracic pain	117 (3.48)	8 (3.22)	19 (5.40)
Transient fever	211 (6.28)	13 (5.31)	33 (9.38)
Transient dysphagia	8 (0.24)	0 (0)	3 (0.85)
Esophageal hematoma	3 (0.09)	0 (0)	1 (0.28)

Table 4

Univariable analysis and multivariable logistic regression to determine factors associated with uncontrolled bleeding.

Variables, n (%)	Bleeding stop in secondary UE (n = 360)	Active bleeding in secondary UE (n = 237)	Univariable *P* value	Multivariable		
				P value	OR	95% CI
Sex, M/F, n/n	2.87:1	2.70:1	.659			
Age, y, mean ± SD	52.87 ± 10.80	54.14 ± 12.57	.398			
History of bleeding, %	51.11%	49.79%	.997			
Hepatocellular carcinoma, %	31.67%	43.04%	.008	.954		
Collateral circulation, %	43.33%	38.82%	.626			
Portal thrombosis, %	33.89%	37.55%	.799			
Ascites (medium to large), %	14.17%	45.99%	<.001	<.001	4.103	2.671–6.302
Hemoglobin <60 g/L, n	43	56	.007	.018	1.850	1.109–3.087
Albumin <28 g/L, n	108	112	.004	.470		
Bilirubin > 34 umol/l, n	96	77	.685			
Creatinine >115 μmol/l, n	38	30	.607			
PT prolong ≥6 s, n	13	29	.053	.077		
INR >1.5%, n	46	57	.289			
Child-Pugh score, mean ± SD	7.62 ± 1.67	8.24 ± 1.80	.949			
Child-Pugh score ≥10, n	40	52	.144			
MELD score, mean ± SD	8.33 ± 6.71	10.76 ± 7.46	.029	.917		
MELD score ≥15, n	48	57	.040	.459		
AIMS65 score, mean ± SD	0.94 ± 0.91	1.42 ± 1.00	<.001	.038	1.560	1.0243–2.375
AIMS65 score ≥2, n	87	94	.001	.440		
Rockall score, mean ± SD	4.39 ± 1.50	4.52 ± 1.93	.340			
Rockall score ≥5, n	130	98	.084	.133		
Glasgow-Blatch-ford score, mean ± SD	13.17 ± 3.04	13.49 ± 2.47	.889			
Unsatisfactory of initial UE therapy, n	9	21	.004	.061		
Failure to identify in initial UE, n	6	23	<.001	.001	4.888	1.859–12.853
Tube/urgent TIPS suggested in initial UE, n	8	9	.438			

for bleeding uncontrolled. Multivariate logistic regression analysis confirmed that ascites, hemoglobin <60 g/L, AIMS65 score, failure to identify in initial UE were independent risk factors for bleeding uncontrolled after initial UE.

3.7. Predictors of 42-day mortality

In patients of bleeding uncontrolled UE group, the mean age of the dead patients was 60.90 + 14.64 years, which was significantly higher than that of the survivors (Table 5). In univariate analysis, other variables significantly associated with mortality within 42 days in bleeding uncontrolled UE group included albumin level at initial UE, bilirubin level at initial UE, PT at initial UE, MELD score, initial unsatisfactory UE hemostasis, failure to identify in initial UE, tube/urgent TIPS suggested in initial UE, units of transfused red blood cells and units of plasma. By multivariate analysis, only age, bilirubin level, initial unsatisfactory hemostasis, failure to identify in initial UE, tube/urgent TIPS suggested in initial UE were independent risk factors for 42-day mortality.

For all 597 patients who underwent second UE within 48 hours, the univariate factors associated with 42-day mortality included gender, Hepatocellular carcinoma and AIMS 65 score, in addition to the factors mentioned above. Surprisingly, in the multivariate logistic analysis, the variables associated with 42-day mortality were identical to those in the uncontrolled bleeding group. The OR values of independent risk factors such as initial unsatisfactory hemostasis, failure to identify in initial UE, tube/urgent TIPS suggested in initial UE were higher (Table 5).

3.8. Sensitivity and specificity by score cutoff point for second UE in 48 hours

We verified the relationship between scoring system and mortality in all the patients received second UE. MELD score, AIMS65 score and Child-Pugh score were more meaningful to predict 42-day mortality compared with Glasgow-Blatch-ford score and Rockall score. The score of AIMS65 is calculated by summing the number of risk factors present: albumin level less than 3.0 g/dL, INR ≥ 1.5, altered mental status, systolic BP 90 mm Hg or lower, and age older than 65 years. AUROC of the AIMS65 score was 0.705 (95% CI 0.610–0.799), 0.742 (95% CI 0.661–0.824) in bleeding uncontrolled UE group and all patients receiving second UE, respectively. ROC curve of the AIMS65 score showed the optimal value to be AIMS65 scores ≥1.5 had a sensitivity of 67.7% and a specificity of 64.2% for predicting 42-day mortality in bleeding uncontrolled UE group. According to the all second UE patients, MELD score and Child-Pugh score showed a good value in predicting 42-day mortality, and the AUROC were 0.737 and 0.719, respectively. The ROC curve of the MELD score showed the optimal value to be MELD scores ≥12.5 have a sensitivity of 60.6% and a specificity of 79.6%; meanwhile, ROC curve of the Child score showed the optimal value to be Child scores ≥8.5 had a sensitivity of 69.7% and a specificity of 69.2% (Fig. 3).

4. Discussion

EVB can be seen in about 50% of cirrhosis patients. Nearly one third of cirrhosis patients died of EVB caused by portal hypertension. In this study, 9232 cases (91.2%) of 10121 UE

Table 5

Analysis of possible variables associated with 42-day mortality in all secondary UE patients and uncontrolled bleeding group patients. (*P Univariable analysis).**

Variables, n (%)	All secondary UE patients (n = 597)				Bleeding uncontrolled UE group patients (n = 352)			
	Alive (n = 564)	Dead (n = 33)	*P** value	Multivariable *P* value/OR (95%CI)	Alive (n = 321)	Dead (n = 31)	*P** value	Multivariable *P* value/OR/95%CI
Age, y, mean ± SD	52.97 ± 11.62	60.76 ± 14.25	**<.01**	0.010/1.054 (1.013–1.097)	53.20 ± 11.67	60.90 ± 14.64	.01	0.014/1.052 (1.010–1.095)
Male, %	73.05%	84.85%	**.027**	0.396	75.70%	83.87%	.116	0.639
History of bleeding, %	49.82%	45.45%	.919		44.55%	45.16%	.995	
Hepatocellular carcinoma, %	34.57%	60.60%	**.004**	0.081	45.48%	58.06%	.266	0.274
Collateral circulation, %	42.02%	27.27%	.107		38.01%	25.81%	.637	
Portal thrombosis, %	35.11%	36.36%	.435		41.43%	35.48%	.520	
Ascites (Medium-Large amount), %	37.41%	42.42%	.998		43.61%	45.16%	.982	
Hemoglobin at initial UE, mean ± SD	82.30 ± 22.96	74.00 ± 21.03	.430		82.42 ± 21.82	72.77 ± 21.02	.204	
Platelets at initial UE, mean ± SD	98.56 ± 66.59	110.12 ± 60.63	.144		100.73 ± 68.26	107.74 ± 61.80	.309	
Albumin at initial UE, mean ± SD	29.27 ± 5.62	25.61 ± 4.09	**.037**	0.269	28.18 ± 5.62	25.58 ± 4.23	.014	0.458
Bilirubin at initial UE, mean ± SD	43.08 ± 76.58	104.47 ± 129.02	**.036**	0.013/1.006 (1.001–1.010)	47.22 ± 79.32	108.78 ± 132.03	<.01	0.010/1.006 (1.001–1.011)
Creatinine at initial UE, mean ± SD	86.14 ± 63.02	106.36 ± 42.82	.850		91.72 ± 79.11	106.90 ± 44.00	.760	
PT at initial UE, mean ± SD	15.08 ± 4.40	20.76 ± 10.95	**.004**	0.448	15.24 ± 3.95	21.11 ± 11.24	.012	0.645
INR at initial UE at initial UE, mean ± SD	1.34 ± 0.61	1.80 ± 0.96	.616		1.37 ± 0.74	1.83 ± 0.98	.595	
Child-Pugh score, mean ± SD	7.78 ± 1.76	9.39 ± 1.85	.367		8.09 ± 1.62	9.39 ± 1.91	.556	
MELD score, mean ± SD	8.89 ± 7.10	16.22 ± 9.02	**.015**	0.361	9.61 ± 6.78	16.42 ± 9.25	.011	0.366
AIMS65 score, mean ± SD	1.08 ± 0.97	2.03 ± 1.02	**.017**	0.206	1.33 ± 0.96	2.10 ± 1.01	.096	0.270
Rockall score, mean ± SD	4.37 ± 1.69	5.64 ± 1.88	.814		4.47 ± 1.84	5.71 ± 1.92	.975	
Glasgow-Blatch-ford score	13.25 ± 2.85	14.30 ± 2.31	.651		13.57 ± 2.31	14.42 ± 2.25	.484	
Initial unsatisfactory UE hemostasis, n	19	10	**<.01**	<0.01/9.793 (3.035–31.60)	17	10	<.01	<0.01/8.625 (2.528–29.422)
Failure to identify in initial UE, n	24	5	**<.01**	0.012/5.372 (1.445–19.965)	23	5	.013	0.027/4.483 (1.182–17.006)
Tube/ TIPS suggested in initial UE, n	13	4	**<.01**	0.011/6.847 (1.555–30.149)	13	4	.006	0.025/5.726 (1.251–26.198)
Second hemostasis successfully, n	70	1	.520		65	1	.258	
Balloon tamponade or TIPS, n	34	8	.649		32	8	.617	
Rebleeding in 7 days, n	22	3	.177		20	3	.356	
Rebleeding in 8–42 days, n	34	3	.774		24	3	.690	
Units of transfused red blood cells, mean ± SD	5.43 ± 6.73	13.05 ± 13.72	**.006**	0.191	6.79 ± 6.23	13.82 ± 13.80	<.01	0.199
Units of transfused plasma, mean ± SD	3.61 ± 12.17	12.97 ± 32.65	**.003**	0.526	4.88 ± 11.21	13.61 ± 33.61	.014	0.841

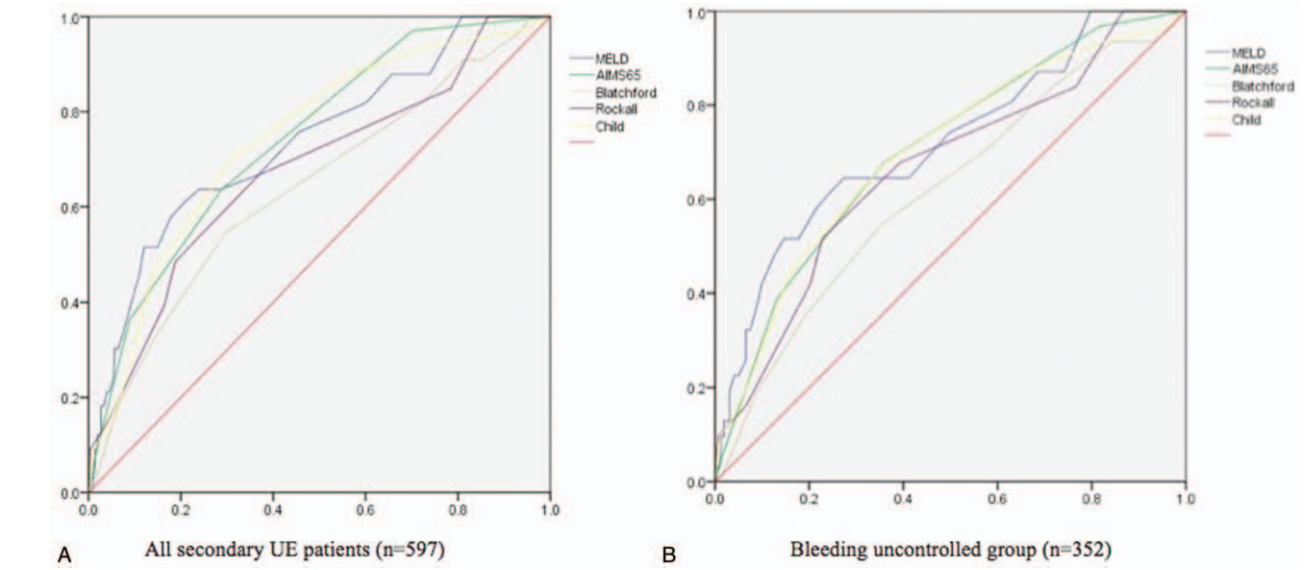

Figure 3. Receiver operator characteristic curves for MELD score, AIMS65 score, Glasgow-Blatch-ford score, Rockall score and Child-Pugh score to predict 42-day mortality. The data point was the measured index value.

examinations of UGIB with cirrhosis were found to have varicose veins. Nearly half (n = 5002) were definitely diagnosed as portal hypertension associated bleeding, and the proportion of acute EVB was 42.4%. Guidelines for the prevention and treatment of variceal bleeding in cirrhosis, published by the Guidelines Research Group of the British Society of Gastroenterology, point out that endoscopy should be performed within 24 hours of admission, and even earlier if the amount of bleeding is large.[4] Many guidelines and reviews suggest that endoscopy should be performed within 12 hours. According to the actual situation in China, the Chinese guidelines point out that esophagogastroscopy within 12 to 24 hours of bleeding is a reliable method for the diagnosis of EVB.[18] After adequate resuscitation and medication, UE was performed within 2 hours after admission or symptoms of UGIB in 10,121 patients with cirrhosis in our institution. Considering 4291 cases of acute variceal bleeding, 3830 cases (89.3%) received emergency endoscopic treatment and 461 cases (10.7%) did not receive emergency endoscopic treatment, of which 100 cases had no definite bleeding site and 31 cases had unclear vision of massive hemorrhage in the lumen. It was suggested that other methods should be used to stop bleeding immediately and twice during examination. Hematemesis, aspiration and sudden change of illness occurred. Literature reports showed that the late rebleeding rate of untreated patients was about 60%, and the 6-week mortality rate caused by variceal bleeding was 15% to 20%. The 6-week mortality rate due to variceal bleeding is 15% to 20%, and in patients with severe decompensated liver cirrhosis with Child-Pugh grade C or even higher grade, the mortality rate increases up to 30%.[19–21] The effective rate of endoscopic hemostasis for variceal bleeding in this group was 94.62% in our study, and the 42-day mortality rate was 4.44%, which was much lower than that reported in the literature.[1,5] The 42-day mortality of failure group and unsatisfactory endoscopic hemostasis group was significantly higher than that of successful endoscopic hemostasis group. It is suggested that patients with cirrhosis complicated with hemorrhage should be diagnosed early and treated by endoscopy as soon as possible. Our results showed that UE was generally safe when adequate preparation was made and indications were fully determined.

The value of second endoscopy for peptic ulcer bleeding has been studied in many previous literatures. Park et al[12] demonstrated that a single endoscopy with complete endoscopic hemostasis was not inferior to scheduled second-look endoscopy for repeat endoscopy would be helpful in patients with unsatisfactory initial endoscopic hemostasis measured by expert endoscopists. El Ouali et al published[22] a meta-analysis of 8 randomized controlled trials (4 fully published papers and 4 in abstract form) published between 1994 and 2011 that evaluated scheduled second-look endoscopy in 938 patients with acute UGIB. In that meta-analysis, scheduled second-look endoscopy appeared to significantly reduce the rebleeding rate (OR 0.55; 95% CI 0.37–0.81) and the need for surgery (OR 0.43; 95% CI 0.19–0.96), but not mortality (OR 0.65; 95% CI 0.26–1.62). The European Society of Gastrointestinal Endoscopy recommends second-look esophagogastrodeuodenoscopy (EGD) with hemostasis in patients with clinical evidence of rebleeding followed by successful initial endoscopic hemostasis.[23] Moreover, the recommendations of various guidelines or meta-analyses regarding the effectiveness of second-look EGD were not consistent. Until now, it is acceptable that second-look EGD may be useful in selected high-risk patients but is not routinely recommended. Furthermore, there are no large-scale clinical studies or guidelines to suggest the significance and value of second UE in patients with cirrhosis and UGIB so far. Thus, we analyzed the data of patients with second UE in our center. According to the indications for second UE, they were divided into 2 groups: scheduled second-look UE group and bleeding uncontrolled repeat UE group. There was no significant difference in condition monitoring and drug treatment between the 2 groups. The results showed that men with a history of hepatocellular carcinoma and moderate to large ascites were more likely to undergo second UE because of uncontrolled bleeding. Hemoglobin <60 g/L and albumin <28 g/L were uncontrolled risk factors for emergency post-endoscopic hemorrhage. Multivariate logistic regression analysis showed that hemoglobin <60 g/L and AIMS65 score were independent risk factors for rebleeding.

The first UE without visual field, unable to determine the location of bleeding, no first endoscopic treatment is an independent risk factor for uncontrolled bleeding. In a prospective multicenter study, failed primary endoscopic treatment and rebleeding showed increased mortality in patients with non-variceal UGIB. Literature reports indicate that failed primary endoscopic treatment and rebleeding were significantly associated with increased mortality (15 times and 2.8 times, respectively).[24–25] In our hospital, the mortality rate of unsatisfactory hemostasis, failure to identify and tube/urgent TIPS suggested in initial UE increased significantly (9.793, 5.372, and 6.847 times, respectively). The results suggest that during the first UE, careful observation, raising the head of the bed and changing the body position when necessary can help to find the bleeding site and implement treatment as far as possible, which will help to improve the success rate of hemostasis. The advantages of a scheduled second-look endoscopy in patients with successful initial endoscopic hemostasis are as follows:

(1) to clearly determine the cessation of bleeding; 237 out of 245 patients in this study were diagnosed as cessation of bleeding. The successful rate of hemostasis was 96.73%.
(2) For the cases with non-stop bleeding, the etiology can be judged again and endoscopic treatment can be taken as appropriate. In this study, 8 cases (3.2%) were diagnosed as high-risk re-bleeding because of the characteristics of EVB. All patients were treated by endoscopy again.
(3) It can guide the time of opening up diet.

Eating as early as possible and rehydrating reasonably can effectively reduce the occurrence of adverse reactions mentioned above. When to open the diet, there is no the consensus. Some suggest all patients should intake diet at the time of yellow stool, while some recommend after the stop of bleeding according to clinical manifestations and some after 8 to 24 hours of endoscopic treatment. In this study, the second gastroscopy of 245 patients confirmed that the bleeding was stopped in 96.8% of the patients, while the time of yellow stool was 1 to 7 days and the time of negative stool occult test was 1 to 13 days. It can be seen that the time of an open diet mentioned above cannot be accurate either sooner or later. It accords with the stop time of bleeding. The patients in this group were given an open diet based on the results of the second endoscopy. The average fasting time was 2.59 ± 1.38 days. This study suggested that it was more reasonable to give an open diet after the second gastroscopy which showed that the bleeding stopped.

Repeated endoscopy is reserved for cases whose still have clinical evidence for recurrent bleeding, because poor visualiza-

tion at the initial endoscopy precluded a thorough and complete examination and failed to identify a clear source of hemorrhage, or at index endoscopy the endoscopist was concerned that the applied hemostasis was inadequate. In this study, the safety of second UE within 48 hours was confirmed in this study. In the single UE group, hemostasis group and uncontrolled bleeding group, there was no difference in the incidence of serious adverse events. The incidence of ulcer after second endoscopy treatment was higher than that of single UE group. This result may be related to 2 factors. First, the 2 UE groups received more endoscopic injections. Secondly, in the 2 UE groups, a large proportion of patients underwent follow-up endoscopy after previous variceal injection.

Previous studies have investigated several scoring models for predicting UGIB,[26–28] and shown that hypoproteinemia <3.0 g/dL is an important independent risk factor for early peptic ulcer bleeding. In variceal rupture bleeding, the value of albumin is also important. In univariable analysis, albumin was a risk factor for evaluating bleeding and death, but it was not an independent risk factor. The possible reason was that the serum albumin level was disease-specific, which can indirectly reflect the nutritional status of patients with acute and chronic diseases. For patients with variceal bleeding, the difference on albumin level was not as large as that in patients with peptic ulcer bleeding. Through retrospective analysis, this study assessed the clinical commonly used scoring system to determine the predictive value of mortality in patients with variceal rupture and hemorrhage. The results showed that MELD score, AIMS 65 score and Child-Pugh score were more meaningful to predict 42-day mortality compared with Glasgow-Blatch-ford score and Rockall score. For patients with score greater than cutoff point value, it was often suggested that the 42-day mortality rate was higher.

Our research also had some limitations. First, our data were primitive, because it was a retrospective analysis in a single center. Secondly, sclerotherapy was the main treatment for esophageal rupture hemorrhage, but current guideline recommends endoscopic variceal ligation for esophageal variceal rupture hemorrhage. Thirdly, 2 emergency endoscopes within 48 hours cannot be completed by the same endoscopist. Different endoscopists cannot completely agree on the evaluation criteria of unsatisfactory endoscopy effect.

In conclusion, for patients with stable condition, the implementation of scheduled second-look UE to assess the cessation of bleeding could help reduce the incidence of complications and start second prevention as soon as possible. For patients with hepatocellular carcinoma, uncontrolled bleeding or re-bleeding should be included in the high-risk group of re-bleeding. Repeated UE can be used for second observation, and appropriate endoscopy should be continued. On the basis of current research, we will carry out a prospective randomized multicenter trial to study the effects of second endoscopy.

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