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Long-term Predictors of Rebleeding and Mortality in Patients with Acute Variceal Hemorrhage

Muhammed Bahaddin Durak[1], Cem Simsek[2], Yavuz Cagir[1], Ilhami Yuksel[1, 3]

[1] *Department of Gastroenterology, Ankara City Hospital, Ankara, Turkey.*

[2] *Department of Gastroenterology, Health Sciences University, Mehmet Akif Inan Training and Research Hospital, Sanliurfa, Turkey.*

[3] *Department of Gastroenterology, Ankara Yildirim Beyazit University School of Medicine, Ankara, Turkey.*

Abstract

This study's objective was to elucidate the predictors of rebleeding and mortality over three and six-month intervals in cirrhotic individuals suffering from Acute Variceal Bleeding.Data encompassing symptoms, clinical and laboratory parameters, endoscopic findings, along with Child-Turcotte-Pugh and Model for End-Stage Liver Disease (MELD) scores were meticulously collected during emergency room presentations. Within the first three months, rebleeding was evident in 32 patients (31.1%), and mortality was recorded in 18 patients (17.5%). At the six-month mark, rebleeding was observed in 43 patients (41.7%), and 31 patients (30.1%) succumbed to their condition. Patients who re-bleeded within six months demonstrated a higher MELD score than their non-rebleeding counterparts (14 versus 11). Notably, individuals who expired within six months compared to survivors exhibited an admission heart rate of ≥100/min, elevated serum urea and INR levels, and diminished albumin levels. The assessment of clinical and laboratory variables such as elevated urea, prolonged INR, reduced platelet count, and low albumin levels, in conjunction with Child-Turcotte-Pugh and MELD scores, are pivotal in predicting long-term mortality in patients presenting with Acute Variceal Bleeding. This study thus underscores the value of these parameters in enhancing prognostic accuracy.

Keywords: *Acute Variceal Bleeding, Child-Turcotte-Pugh Score, Model for End-Stage Liver Disease, Mortality, Rebleeding.*

I. Introduction

Despite advancements in technology and healthcare accessibility, acute variceal bleeding (AVB) continues to be a significant contributor to mortality amongst patients with cirrhosis[1, 2]. Cirrhosis is the most common cause of acute variceal bleeding, and thrombotic disorders and myeloproliferative illnesses can also bring it on[3, 4]. AVB episodes carry a 20% mortality rate, and survivors of an initial bleeding event possess a 70% risk of rebleeding within the ensuing year[5-7].AVB is observed in 25-40% of cirrhotics, highlighting the importance of accurately identifying high-risk individuals for targeted prevention. This strategic identification can prevent unnecessary and potentially harmful preventative measures in the 60-75% of patients who will not experience variceal hemorrhage[8, 9].

The interaction between the flow of portal circulation and the portal vein's (PV) resistance against that circulation determines how portal pressure changes over time. The most frequent etiology leading to portal

hypertension, cirrhosis, increases portal blood pressure in two different ways: Impaired hepatic sinusoids cause greater outflow resistance, while splanchnic vasodilation causes amplified portal inflow [10]. Varices evolve as conduits to alleviate this escalated pressure in the hypertensive PV, effectively delivering blood to the systemic circulation. Patients with lower pressures normally do not have varices or bleeding. They typically arise once the blood pressure disparity among the portal and hepatic veins exceeds 12 mmHg [11].

Active bleeding at the time of the first endoscopy, the CTP and MELD scores, the hepatic venous pressure gradient (HVPG), alcoholic liver illness, serum bilirubin, and albumin levels, and hepatocellular carcinoma have all been identified as indicators of risk for AVB mortality [12-14].Although the Baveno criteria, often employed for variceal rebleeding risk, have demonstrated an association with AVB risk within five days, their utility for long-term rebleeding risk is limited. Moreover, while CTP, MELD scores, and other indicators have been utilized to forecast AVB, comparative evaluations of these scoring systems have revealed their inadequacies in predicting long-term rebleeding and mortality. Our study intends to develop predictive models for rebleeding and mortality at three- and six-month intervals in cirrhotics presenting with AVB.

II. Materials - methods

2.1. Study Population

The study population comprised cirrhotic patients diagnosed with AVB endoscopically (esophageal, gastric, or both). Exclusion criteria incorporated patients unable or unwilling to undergo endoscopy, those refusing to participate in the research, noncirrhotic patients, and those with insufficient data. The Scientific Assessment and Ethics Board accepted the project (Approval No: E1/1051/2020). Study subjects were informed and written consent was obtained.

2.2. Data Collection

Data collection was conducted prospectively between February 2019 and September 2020, and included symptomatology, medical history, hemodynamic condition, laboratory variables, and endoscopic findings, recorded at the point of emergency room admission. The CTP and MELD scoring systems were calculated using a globally recognized calculator application. Hospitalization data, blood transfusion, medical treatment, endoscopic procedures, and 3-6months rebleeding and mortality were prospectively recorded through the hospital's electronic civil medical registration system.

2.3. Patient Management

Initial assessment of all AVB patients was conducted at the Ankara City Hospital's emergency department, Turkey. Patients were administered either somatostatin (250 micg/h after a 250 micg bolus) or terlipressin (1mg bolus followed by administration every 4-6 hours) based on availability. Duration of vasopressor therapy (3-5 days) was determined by the patient's clinical status. Additionally, antibiotic prophylaxis was administered as intravenous ceftriaxone (1.0 g/day) for five days. Blood transfusions were carried out in patients with hemoglobin levels below 7.0 g/dl, aiming to maintain serum hemoglobin levels within the 7-8 g/dl range.

Endoscopic procedures were performed within the first 12 or 24 hours, guided by the patient's hemodynamic status, hemoglobin level drop despite transfusion, and evidence of active bleeding. Therapeutic options included endoscopic band ligation or cyanoacrylate sclerotherapy. Should endoscopic therapy fail, a Sengstaken-Blackmore tube or transhepatic intrajugular portosystemic shunt (TIPS) procedure was implemented to halt bleeding.

In cases of rebleeding during hospitalization, endoscopic procedures were repeated. Upon discharge, barring contraindications, propranolol dosage titration was initiated. Patients demonstrating clinical improvement post-discharge were monitored for six months. All patients underwent endoscopic procedures for variceal eradication 1-6 weeks post-index endoscopy, with treatments continuing until variceal eradication was achieved.

2.4. Study Outcomes

Rebleeding and mortality over 3-6 months served as clinical outcome measures. Rebleeding was defined as a hemoglobin decrease exceeding 2.0 g/dl, coupled with hemorrhagic symptoms (hematemesis or melena). In case of reduced hemoglobin and bleeding symptoms, a second endoscopy was undertaken to confirm rebleeding. Death from any reason, including death during hospitalization and death within six months, was referred to as mortality. The correlation between clinical characteristics, laboratory variables, follow-up details, in-hospital treatment, rebleeding, and mortality was investigated.

2.5. Statistic assessment

The Kolmogorov-Smirnov test was used to assess the homogeneity of the distribution of the numerical variable. The student's t-test was used to compare ordinarily dispersed quantitative data given as mean standard deviation (SD). The Mann-Whitney U test evaluated the distribution of non-normal numerical parameters reported as median (interquartile range [IQR]). As applicable, the Chi-Square test or the Fisher's Exact test was used to compare categorical variables expressed as frequency (%).Variables that were statistically significant or clinically relevant for rebleeding within six months were analyzed via univariate logistic regression analysis. By taking into account factors having a p-value of < 0.1 in univariate analyses, multiple variate logistic regression analysis (entry technique) was used to examine distinct indicators of rebleeding within six months. The odds ratio (OR), 95% confidence interval (CI), and p-value were used to present the results. Similarly, univariate and multivariate Cox regression analyses were used to examine clinically or statistically significant factors for death within six months. Results have been given using the hazard ratio (HR), 95 percent confidence interval (CI), and p-value. The six-month mortality in connection to the rebleeding status within eight weeks and six months was examined using the Kaplan-Meier analysis and log-rank test. The mortality rate (frequency and percentage), overall survival days (mean SD and 95% CI), log-rank Chi-Square value, and p-value were used to present the data. The IBM SPSS Statistics for Windows was used to perform the statistical calculations. The significance threshold was defined as a two-sided p-value of 0.05 or less.

III. Results

The median age of the study population was 64 years (interquartile spectrum, IQR: 53-73) and 53.4% of the population was male (n=55). In 64.1% (n=66) of the patients, variceal hemorrhage had previously occurred. The MELD score was 12 (IQR: 9-16), whereas the median Child-Turcotte-Pugh (CTP) score was 7 (IQR: 6-9). In the first 12 hours after admission, 63.1% of patients (n=65) underwent endoscopy, with a significant 96.1% (n=99) receiving subsequent endoscopic intervention. Endoscopic band ligation was performed in 78.6% (n=81) of these patients. Blood transfusion was required for approximately 72.8% (n=75) of the patients. The median hospital stay spanned 8 days (IQR: 4-11). Within the initial six months, rebleeding was recorded in 41.7% (n=43) of the patients, with mortality observed in 30.1% (n=31).

Patients were stratified into three cohorts: those who experienced rebleeding, those who did not, and the total patient pool, as outlined in Table I. Male patients had a significantly increased incidence of rebleeding, according to a comparison study (67.4% vs. 43.3%, p=0.016). Rebleeding patients had a statistically significant higher MELD score than non-rebleeding patients (14, IQR:11-16 vs. 11, IQR:8-16, p=0.023). The number of patients who received Transjugular Intrahepatic Portosystemic Shunt (TIPS) operations was higher in the rebleeding group (p=0.011). Other parameters did not show any change that was statistically significant (p>0.05 for all).

Table II provides a comparison of patient characteristics, laboratory data, and medication information across two groups: those who survived within six months and those who did not. A tachycardic heart rate (>100 beats/min) on presentation was significantly associated with higher mortality (22.6% vs. 6.9%, p= 0.040). At admission, the mortality group had statistically higher urea levels (75, IQR:47-92 mg/dL vs. 50, IQR:40.25-75.5 mg/dL, p=

0.013), and International Normalized Ratio (INR) levels (1.5, IQR:1.3-1.8 vs. 1.5, IQR:1.3-1.8), along with significantly lower albumin levels (27 g/L, IQR:20-31 vs. 32 g/L, IQR:28.25-36, p<0.001).

Between the mortality and surviving groups, there were substantial variations in CTP scores and CTP categorization distributions (p 0.001). Similarly, MELD scores in the mortality group were substantially higher (17, IQR:12-26 vs. 11, IQR:8-14, p0.001) than in the control group. In addition, more patients in the mortality group (12.9% vs. 1.4%, p=0.028) had undergone TIPS. For the mortality group, the hospital stay was considerably longer (11 vs. 6.5, p=0.017). Other parameters did not differ significantly (p>0.005 for all) from one another. In addition, 32 patients (31.1%) experienced rebleeding within 3 months after the research, and 18 patients (17.5%) passed away (Table III).

Logistic regression analysis of the factors that influence rebleeding following six months (Table IV) only revealed gender as a significant variable (univariate analysis: OR:2.709, 95% CI:1.197-6.132, p= 0.017; multivariate analysis: OR:2.837, 95% CI:1.230-6.547, p= 0.014).

Table V outlines the Cox regression analysis for six-month mortality predictors. In univariate analyses, heart rate >100 beats/min (HR:2.828, 95% CI:1.214-6.584, p= 0.016), systolic blood pressure <90 mmHg (HR:2.642, 95% CI:1.012-6.901, p= 0.047), urea level (HR:1.009, 95% CI:1.003-1.015, p= 0.002), INR value (HR:1.637, 95% CI:1.196-2.241, p= 0.002), albumin value (HR:0.869, 95% CI:0.820-0.921, p< 0.001), platelet value (HR:1.001 95% CI:1.001-1.002, p= 0.007), CTP classification (HR:5.222, 95% CI:2.472-11.030, p< 0.001), MELD score (HR:6.825, 95% CI:3.330-13.990, p< 0.001), history of TIPS (HR:4.244, 95% CI:1.479-12.180, p= 0.007), length of stay in hospital (HR:1.077, 95% CI:1.037-1.119, p< 0.001), and rebleeding within 3 and 6 months (HR:3.036, 95% CI:1.499-6.151, p= 0.002, and HR:2.240, 95% CI: 1.097-4.573, p= 0.027) were strongly related to mortality. Multivariate analyses revealed platelet value (HR:1.001 95% CI:1.001-1.002, p= 0.004) and rebleeding within 3 months (HR:2.362, 95% CI:1.012-5.515, p= 0.047) as statistically significant predictors.

The Kaplan-Meier survival analysis (Table VI) indicates statistically significant differences in 6-month mortality based on rebleeding status at 3 and 6 months (Log-rank Chi-Square: 10.581, p= 0.001 and Log-rank Chi-Square: 5.204, p= 0.023, respectively) (Figure I). At 3 months, mortality occurred at a rate of 15 (21.1%) in the group without bleeding, compared to 16 (50%) in the group with rebleeding. At six months, mortality rates in the groups with and without rebleeding were (41.9%, n=18) versus 13 (21.7%) respectively.

IV. Discussion

The prognostic determination of survival in cirrhotic with AVB remains an elusive consensus in the medical community. This complexity arises from the multifaceted nature of the disease, where the severity of bleeding does not necessarily correspond to the prognosis. In contrast, factors such as cirrhosis etiology and disease progression carry substantial prognostic implications [15, 16]. Consequently, establishing a comprehensive prognostic model becomes challenging, necessitating consideration of advanced disease signs.

In developing a robust and clinically useful prognostic model, the potential role of indirect laboratory markers of disease progression should not be overlooked. Indicators such as serum bilirubin, albumin, INR, platelet count, and urea may offer valuable insights and could be integral components of a future prognostic model. Ultimately, the ability to identify high-risk patients is crucial, aiding in the development of innovative risk-reduction strategies and identifying suitable candidates for protective measures.

Currently, however, there are no widely accepted risk models for patients with AVB. The Rockall and Glasgow Blatchford scores, frequently used in Upper Gastrointestinal Bleeding (UGIB), have been validated primarily for non-variceal UGIB patients and demonstrate limited efficacy in prognosticating outcomes in AVB patients [17, 18]. Recent investigations have shown potential promise in the CTP and MELD scores for AVB prognosis, but their predictive superiority remains debatable [19-21].

Our prospective study reports a 31.1% rebleeding rate and 17.5% mortality within the first three months. By the six-month mark, these figures rose to 41.7% and 30.1%, respectively. A noteworthy observation was that rebleeding patients within six months had a higher MELD score (14 vs. 11), indicating a potential relationship between this score and the risk of rebleeding. Furthermore, patients who succumbed within the six-month period had an admission heart rate of ≥100/min, elevated serum urea and INR levels, and reduced albumin levels compared to survivors. Likewise, these patients had higher CTP (9 vs. 6) and MELD scores (17 vs. 11), hinting at the utility of these scores in prognostic considerations.

In our Cox univariate regression analysis, several variables, including admission heart rate >100 beats/min, urea level, INR value, albumin value, platelet value, CTP score, MELD score, and rebleeding incidence within three and six months, emerged as potential predictors of six-month mortality. The multivariate analysis further refined this to admission platelet value and three-month rebleeding incidence for predicting three-month mortality, with platelet value alone predicting six-month mortality. This finding emphasizes the prognostic value of platelet count in this patient population.

Previous studies predominantly focused on short-term clinical outcomes and employed the CTP and MELD scores for evaluation [12, 22, 23]. Bambha and colleagues [15]while comparing clinical parameters along with the MELD score, limited their investigation to 5-day rebleeding and 6-week mortality without examining the CTP score. Our study stands out by assessing long-term rebleeding and mortality, incorporating clinical, laboratory, and scoring systems in the evaluation process.

In the current study, high CTP and MELD scores correlated with increased six-month mortality. The MELD score additionally predicted six-month rebleeding, affirming the contribution of these scoring systems to AVB risk stratification. We explored the association of simple laboratory parameters and vital signs with rebleeding and mortality, evaluating their individual impact on poor clinical outcomes in AVB patients. Developing a future scoring system based on these parameters might enhance prognostic accuracy in AVB patients.

Each AVB episode carries a mortality risk of up to 20%, which escalates in patients experiencing rebleeding [6, 12]. In our cohort, half of the patients with rebleeding within three months died, with half of those occurring within the first week post-bleeding episode. Hence, effective primary and secondary prophylactic treatment strategies may potentially increase patient survival.

Our study, however, was not without limitations. As a tertiary care center, our patient population was skewed towards those with a high-risk profile, potentially introducing bias. We also did not distinguish between esophageal and gastric varices, nor did we measure the hepatic venous pressure gradient, known for its predictive value in variceal bleeding outcomes. Furthermore, the inclusion of hepatocellular carcinoma-related deaths in our mortality group may have inadvertently inflated our mortality rate. Nonetheless, the prospective design of our study, standardized medical treatment approach, and early endoscopic intervention in all patients constitute its strengths. Additionally, we examined the long-term (3-6 months) clinical outcomes, further enriching the field's understanding of AVB prognosis.

V. Conclusion

In patients with acute variceal bleeding (AVB), the evaluation of laboratory and clinical factors, such as high urea, protracted INR, low platelet count, and low albumin levels, emerges as important indicators of six-month death. CTP and MELD scores can also significantly improve prognostic accuracy in this patient population. Therefore, considering these parameters in conjunction with long-term clinical outcomes paves the way for the development of an optimal prognostic model for AVB patients, thus facilitating improved risk stratification and patient management.

Conflict of Interest Statement:

The authors have no conflicts of interest to declare.

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Table 1. Patients' characteristics, laboratory variables, and treatment details of the study group, and subgroups according to rebleeding status within 6 months[x].

	Study group (n=103)	Non-rebleeding group (n=60)	Rebleeding group (n=43)	*P*
Age, years	64 (53-73)	64.5 (46.5-73)	64 (55-72)	0.891
Gender, male, n (%)	55 (53.4)	26 (43.3)	29 (67.4)	**0.016**
Previous episode of variceal bleeding, n (%)	66 (64.1)	34 (56.7)	32 (74.4)	0.064
Pulse, > 100 beats/min, n (%)	12 (11.7)	8 (13.3)	4 (9.3)	0.529
Systolic blood pressure, < 90mmHg, n (%)	9 (8.7)	6 (10)	3 (7)	0.731
Hemoglobin level on admission (g/dL)	9.03 ± 2.08	9.06 ± 2.17	8.98 ± 1.99	0.839
Urea level on admission (mg/dL)	58 (43-81)	56.5 (43-79)	58 (43-88)	0.740
INR on admission	1.38 (1.2-1.61)	1.38 (1.2-1.67)	1.4 (1.24-1.55)	0.531
Albumin level on admission (g/L)	31 (27-36)	31.5 (28-36)	30 (26-34)	0.139
Platelet level on admission (10^9/L)	124 (89-176)	124 (89.75-178.5)	128 (83-176)	0.857
Child-Pugh score	7 (6-9)	7 (6-8)	7 (6-9)	0.066
Child-Pugh class, n (%)				0.347
A	42 (40.8)	28 (46.7)	14 (32.6)	
B	45 (43.7)	24 (40)	21 (48.8)	
C	16 (15.5)	8 (13.3)	8 (18.6)	
MELD score	12 (9-16)	11 (8-16)	14 (11-16)	**0.023**
Medical therapy, n (%)				0.414
Somatostatin	48 (46.6)	30 (50)	18 (41.9)	
Terlipressin	55 (53.4)	30 (50)	25 (58.1)	
Endoscopic intervention, n (%)				0.361
None	4 (3.9)	3 (5)	1 (2.3)	
Band ligation	81 (78.6)	49 (81.7)	32 (74.4)	
Sclerotherapy	18 (17.5)	8 (13.3)	10 (23.3)	
TIPS, n (%)	5 (4.9)	-	5 (11.6)	**0.011**
Blood transfusion within 24 hours, n (%)				0.131
None	28 (27.2)	20 (33.3)	8 (18.6)	
	23 (22.3)	10 (16.7)	13 (30.2)	

One unit	52 (50.5)	30 (50)	22 (51.2)	
More than one unit				
Index endoscopy time, n (%)				0.440
≤12 hours	65 (63.1)	36 (60)	29 (67.4)	
>12-24 hours	38 (36.9)	24 (40)	14 (32.6)	
Length of stay, days	8 (4-11)	8 (3.25-11)	7 (5-11)	0.720

[x] Results are expressed as: mean ± standard deviation, median (interquartile range), or frequency (%). Significant P values are in bold.
INR: International normalized ratio, MELD: Model for End-Stage Liver Disease, TIPS: Transjugular intrahepatic portosystemic shunt.

Table 2. Patients' characteristics, laboratory variables, and treatment details of the subgroups according to mortality status within 6 months[x].

	Survival group (n=72)	Mortality group (n=31)	*P*
Age, years	63.5 (50-71)	66 (55-81)	0.139
Gender, male, n (%)	39 (54.2)	16 (51.6)	0.812
Previous episode of variceal bleeding, n (%)	47 (65.3)	19 (61.3)	0.699
Pulse, > 100 beats/min, n (%)	5 (6.9)	7 (22.6)	**0.040**
Systolic blood pressure, < 90mmHg, n (%)	4 (5.6)	5 (16.1)	0.124
Hemoglobin level on admission (g/dL)	9.21 ± 2.17	8.6 ± 1.85	0.177
Urea level on admission (mg/dL)	50 (40.25-75.5)	75 (47-92)	**0.013**
INR on admission	1.35 (1.2-1.5)	1.5 (1.3-1.8)	**0.019**
Albumin level on admission (g/L)	32 (28.25-36)	27 (20-31)	**<0.001**
Platelet level on admission (10^9/L)	117.5 (89-159)	156 (91-216)	0.053
Child-Pugh score	6 (6-8)	9 (7-10)	**<0.001**
Child-Pugh class, n (%)			**<0.001**
A	40 (55.6)	2 (6.5)	
B	27 (37.5)	18 (58.1)	
C	5 (6.9)	11 (35.5)	
MELD score	11 (8-14)	17 (12-26)	**<0.001**
Medical therapy, n (%)			0.292
Somatostatin	36 (50)	12 (38.7)	
Terlipressin	36 (50)	19 (61.3)	
Endoscopic intervention, n (%)			0.663
None	3 (4.2)	1 (3.2)	
Band ligation	58 (80.6)	23 (74.2)	

Sclerotherapy	11 (15.3)	7 (22.6)	
TIPS, n (%)	1 (1.4)	4 (12.9)	**0.028**
Blood transfusion within 24 hours, n (%)			0.830
None	20 (27.8)	8 (25.8)	
One unit	17 (23.6)	6 (19.4)	
More than one unit	35 (48.6)	17 (54.8)	
Index endoscopy time, n (%)			0.846
≤12 hours	45 (62.5)	20 (64.5)	
>12-24 hours	27 (37.5)	11 (35.5)	
Length of stay, days	6.5 (4-10)	11 (5-17)	**0.017**

[x] Results are expressed as: mean ± standard deviation, median (interquartile range), or frequency (%). Significant P values are in bold.
INR: International normalized ratio, MELD: Model for End-Stage Liver Disease, TIPS: Transjugular intrahepatic portosystemic shunt.

Table 3. Clinical outcomes[x].

Rebleeding, within 3 months, n (%)	32 (31.1)
Rebleeding, within 6 months, n (%)	43 (41.7)
Mortality, within 3 months, n (%)	18 (17.5)
Mortality, within 6 months, n (%)	31 (30.1)

[x] Results are expressed as frequency (%).

Table 4. Logistic regression analysis of predictors for rebleeding within 6 months.

	Univariate analysis			Multiple variate analysis		
	OR	95% CI	*P*	OR	95% CI	*P*
Age, years	1.006	0.979-1.034	0.662	-	-	-
Gender, male	2.709	1.197-6.132	**0.017**	2.837	1.230-6.547	**0.014**
Previous episode of variceal bleeding	2.225	0.947-5.228	0.067	2.365	0.977-5.723	0.056
Pulse, > 100 beats/min,	0.667	0.187-2.374	0.531	-	-	-
Systolic blood pressure, < 90mmHg	0.675	0.159-2.863	0.594	-	-	-
Hemoglobin level on admission (g/dL)	0.980	0.812-1.184	0.837	-	-	-
Urea level on admission (mg/dL)	1.004	0.995-1.013	0.397	-	-	-
INR on admission	0.699	0.318-1.533	0.371	-	-	-
Albumin level on admission (g/L)	0.964	0.908-1.023	0.226	-	-	-
Platelet level on	1	1-1	0.996	-	-	-

admission (10^9/L)						
Child-Pugh class						
A, B	1	-	-	-	-	-
C	1.486	0.510-4.330	0.468			
MELD score						
≤18	1	-	-	-	-	-
>18	1.500	0.540-4.163	0.436			
Medical therapy						
Somatostatin	1	-	-	-	-	-
Terlipressin	1.389	0.631-3.058	0.415			
Endoscopic intervention	2.211	0.222-22.004	0.499	-	-	-
TIPS	>100	-	0.999	-	-	-
Blood transfusion within 24 hours	2.187	0.857-5.583	0.102	-	-	-
Index endoscopy time						
≤12 hours	1	-	-	-	-	-
>12 hours	0.724	0.319-1.645	0.441			

Significant P values are in bold
OR: Odds ratio, CI: Confidence interval, INR: International normalized ratio, MELD: Model for End-Stage Liver Disease, TIPS: Transjugular intrahepatic portosystemic shunt.

Table 5. Cox regression analysis of predictors for mortality within 6 months.

	Univariate analysis			Multiple variate analysis*			Multiple variate analysis**		
	HR	95% CI	*P*	HR	95% CI	*P*	HR	95% CI	*P*
Age, years	1.022	0.995-1.050	0.115	-	-	-	-	-	-
Gender, male	0.976	0.483-1.975	0.947	-	-	-	-	-	-
Previous episode of variceal bleeding	0.836	0.406-1.723	0.628	-	-	-	-	-	-
Pulse, > 100 beats/min,	2.828	1.214-6.584	**0.016**	-	-	-	-	-	-
Systolic blood pressure, < 90mmHg	2.642	1.012-6.901	**0.047**	-	-	-	-	-	-
Hemoglobin level on admission (g/dL)	0.891	0.754-1.054	0.178	-	-	-	-	-	-
Urea level on admission (mg/dL)	1.009	1.003-1.015	**0.002**	-	-	-	-	-	-
INR on admission	1.637	1.196-2.241	**0.002**	-	-	-	-	-	-
Albumin level on admission (g/L)	0.869	0.820-0.921	**<0.001**	-	-	-	-	-	-
Platelet level on admission (10^9/L)	1.001	1.001-1.002	**0.007**	1.001	1.001-1.002	**0.004**	1.001	1.001-1.002	**0.002**
Child-Pugh class									
A, B	1	-	-	-	-	-	-	-	-
C	5.222	2.472-11.030	**<0.001**						
MELD score									
≤18	1	-	-	-	-	-	-	-	-
>18	6.825	3.330-13.990	**<0.001**						
Medical therapy									
Somatostatin	1	-	-	-	-	-	-	-	-
Terlipressin	1.556	0.755-3.207	0.231						

Endoscopic intervention	1.098	0.150-8.052	0.927	-	-	-	-	-	-
TIPS	4.244	1.479-12.180	**0.007**	-	-	-	-	-	-
Blood transfusion within 24 hours	1.120	0.501-2.503	0.783	-	-	-	-	-	-
Index endoscopy time *≤12 hours* *>12 hours*	 1 0.855	 - 0.409-1.784	 - 0.676	-	-	-	-	-	-
Length of stay, days	1.077	1.037-1.119	**<0.001**	-	-	-	-	-	-
Rebleeding within 3 months	3.036	1.499-6.151	**0.002**	2.362	1.012-5.515	**0.047**	-	-	-
Rebleeding within 6 months	2.240	1.097-4.573	**0.027**	-	-	-	-	-	-

* The column shows the results of multiple variate analysis, including the variates with a p-value <0.1 in univariate analyses and rebleeding within 3 months. The results were given for only those with statistically significant (p<0.05).

** The column shows the results of multiple variate analysis, including the variates with a p-value <0.1 in univariate analyses and rebleeding within 6 months. The results were given for only those with statistically significant (p<0.05).

Significant P values are in bold

HR: Hazard ratio, CI: Confidence interval, INR: International normalized ratio, MELD: Model for End-Stage Liver Disease, TIPS: Transjugular intrahepatic portosystemic shunt.

Table 6. Results of Kaplan-Meier survival analysis of mortality within 6 months according to the rebleeding status within 3 months and rebleeding status within 6 months.

	Mortality rate within 6 months, n (%)	Overall survival, days		Log-rank Chi-Square	*P*
		Mean ± SD	95% CI		
Rebleeding within 3 months					
Yes (n=32)	16 (50)	111.22 ± 13.83	84.122-138.315	10.581	**0.001**
No (n=71)	15 (21.1)	155.13 ± 6.45	142.493-167.760		
Rebleeding within 6 months					
Yes (n=43)	18 (41.9)	125.60 ± 11.30	103.467-147.743	5.204	**0.023**
No (n=60)	13 (21.7)	152.87 ± 7.33	138.510-167.224		

Significant P values are in bold.
SD: Standard deviation, CI: Confidence interval.

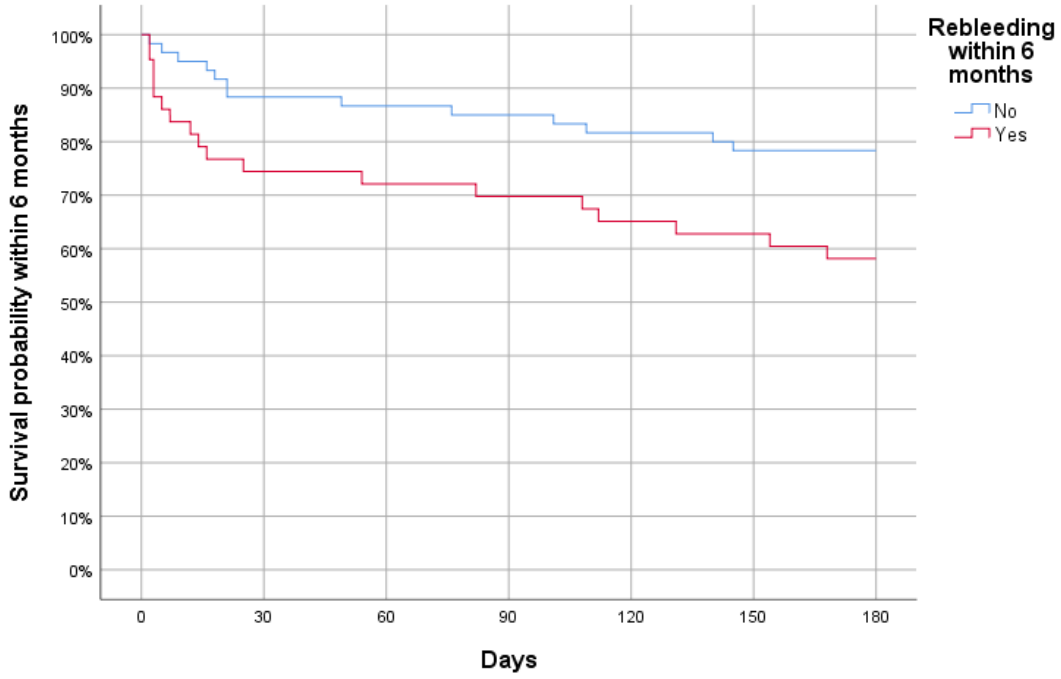

Figure 1. Kaplan-Meier survival analysis of mortality within 6 months according to the rebleeding status within 6 months.