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ORIGINAL ARTICLE

Clinical results of patients with variceal bleeding and risk analysis of scoring systems

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ABSTRACT

Introduction: Gastroesophageal varices are a common complication of chronic liver disease and the associated portal hypertension. Gastroesophageal variceal bleeding is the most important cause of mortality in cirrhotic patients, and the risk of developing varices and bleeding significantly increases when hepatic venous pressure gradient (HVPG) exceeds 10-12 mmHg.

Aim: In this study, we aimed to determine the most useful scoring system to assess patients with gastric and esophageal variceal bleeding to guide treatment according to the type of varices, to predict the risk of rebleeding and mortality, and to determine the relationship between types of varices, comorbidities, and mortality.

Results: We retrospectively analyzed the files of 566 patients who presented to the Emergency Internal Medicine Department with gastrointestinal hemorrhage. Among these, we recruited 117 patients who were diagnosed with varices. Hematemesis and melena were significantly more common in patients with esophageal variceal bleeding compared to patients with gastric variceal bleeding (p=0.025 and p=0.036, respectively) Among the analyzed scoring systems, the Child-Pugh score most successfully predicted mortality with the highest AUC value (AUC: 0.851, 95% CI: 0.770-0.932, p<0.0001)

Conclusion: Assessment with scoring systems upon admission is useful for risk classification and prediction of mortality risk. In this context, the Child-Pugh score can be used to assess acute variceal hemorrhages.

Keywords: variceal bleeding, risk analysis, Child-pugh score

INTRODUCTION

Gastroesophageal varices are a common complication of chronic liver disease and the associated portal hypertension. The incidence of gastroesophageal varices correlates with the severity of chronic liver disease and they occur in approximately 50% of all patients, with an annual risk of approximately 8%. Gastroesophageal varices predominantly result from increased resistance to portal flow secondary to regenerative nodules and fibrosis, intrahepatic vasoconstriction, splanchnic vasodilation, and increased portal flow [1]. Gastroesophageal variceal bleeding is the most important cause of mortality in cirrhotic patients, and the risk of developing varices and bleeding significantly increases when hepatic venous pressure gradient (HVPG) exceeds 10-12 mmHg [2]. The most important risk factors for variceal bleeding are the size of the varices and having decompensated disease, and the annual risk of hemorrhage is approximately 15% per year [3]. The literature reports variable results regarding the diagnostic value of the numerous scoring systems that have been developed to predict mortality due to variceal bleeding in cirrhotic patients, and there currently is no consensus.

In cirrhotic patients, scoring systems are crucial to predict prognosis in order to reduce the risk of varices and variceal bleeding, to determine the appropriate intervention and follow-up method for variceal bleeding, and to reduce the risk of rebleeding to improve survival and quality of life. In this study, we aimed to determine the most useful scoring system to assess patients with gastric and esophageal variceal bleeding to guide treatment according to the type of varices, to predict the risk of rebleeding and mortality, and to determine the relationship between types of varices, comorbidities, and mortality.

MATERIALS and METHODS

We retrospectively analyzed the files of 566 patients who presented to the Emergency Internal Medicine Department with gastrointestinal hemorrhage between October 2020-october 2021. Among these, we recruited 117 patients who were diagnosed with varices. All patients underwent gastroscopy within twenty-four hours. Patients presenting with gastrointestinal bleeding were treated with proton pump inhibitors, and all patients with variceal bleeding were treated with somatostatin analogues. The treatment was reviewed and revised daily. The patients were aged between 19 and 89 years. We excluded patients who were aged below 18 years and patients who were diagnosed and started treatment in a different center and were then referred to our hospital. The data obtained from hospital HBYS

the Hospital Information Management Systems (HIMS) notes. Age, sex, symptoms indicating bleeding, concomitant diseases, endoscopic and/or surgical treatments, and follow-up results were recorded from the patients' files. The Rockall score takes into account age, presence of shock, comorbidities, diagnosis, and the type of lesion that is the cause of the recent bleeding after endoscopy [4]. The Glasgow-Blatchford score is calculated using blood urea nitrogen level, hemoglobin, pulse rate per minute, systolic blood pressure, melena, hepatic disease, syncope, and/or cardiac failure and does not require endoscopic data [5]. AIMS65 is based on the criteria of pre-endoscopy serum albumin and international normalized ratio (INR) levels, altered mental status, age, and systolic blood pressure [6]. The MELD-Na score is a combination of serum sodium (Na) levels and the MELD score, which is calculated based on serum bilirubin, creatinine, and INR levels, and it aims to predict the prognosis of cirrhotic patients [7]. The Child-Pugh classification is used to determine the severity of cirrhosis based on the extent of hepatic encephalopathy, ascites, and serum bilirubin, albumin, and INR levels [8]. Assessment scores were calculated during the patients' hospital stays. We analyzed the diagnostic value of the applied scoring systems. The principles of the Helsinki Declaration were followed throughout the research. Mortality observed during hospitalization was noted.

This study was confirmed by the local ethics board (Number: E1-21-2032) on 20.10.2021, and no written informed consent form was obtained from patients.

Statistical analysis

Data were analyzed using SPSS 25.0. Categorical data were expressed as numbers and percentages,

and continuous data as mean ± standard deviation and median (minimum and maximum, interquartile range). According to endoscopy findings, patients were classified into two groups according to esophageal and gastric varices. The Kolmogorov-Smirnov test was used to analyze whether patient ages were normally distributed for each group. Patient ages did not show normal distribution. Therefore, Pearson's chi-square test was used for the analysis of categorical variables. Receiver operating characteristic (ROC) curves were used to assess and compare the diagnostic value of each scoring system. Subsequently, the area under the curve (AUC), sensitivity, and specificity were calculated. Values of $p<0.05$ were accepted as statistically significant.

RESULTS

The average ages of patients with esophageal and gastric varices were 62.96±14.66 years and 56.52±14.18 years, respectively (Table 1). There were 64 male (54.71%) and 53 female (45.29%) patients. Nine (7.69%) patients were discharged within 24 hours, whereas 42 (35.89%) were admitted to the ward and 66 (56.41%) were admitted to the intensive care unit. Endoscopic procedure could not be performed in the acute period due to clinical instability in 23 (19.65%) of the patients who had variceal bleeding, 2 (1.71%) were treated with argon plasma coagulation, 1 (0.85%) with hemoclip, 59 (71.79%) with band ligation, and 7 (5.98%) with sclerotherapy. Seventy-three (62.40%) patients required endoscopic re-intervention. While 30 (25.64%) patients did not require a blood transfusion, 27 (23.08%) were transfused with 1 unit and 60 (51.28%) with more than 1 unit of blood products. Hematemesis and melena were significantly more common in patients with esophageal variceal bleeding compared to patients with gastric variceal bleeding ($p=0.025$ and $p=0.036$, respectively) (Table 2). In terms of comorbidities, chronic kidney disease was significantly less common in patients with gastric varices ($p=0.036$) (Table 3). In addition, appropriate antibiotic therapy was applied to all patients during their hospitalization.

Among the patients who underwent endoscopic treatment for esophageal varices, 2 (2.17%) underwent transarterial embolization (TAE) and 2 (2.17%) surgery, and among patients with gastric varices, 2 (9.52%) underwent TAE and 1 (4.76%) surgery. Thirty-two (33.34%) patients with esophageal varices and 9 (42.86%) patients with gastric varices developed variceal rebleeding. In long-term follow-up, recurrent variceal bleeding was significantly more common in patients with gastric varices ($p=0.003$). Nineteen (19.79%) patients with esophageal varices and 4 (19.05%) patients with gastric varices died during follow-up (Table 4).

Among the analyzed scoring systems, the Child-Pugh score most successfully predicted mortality with the highest AUC value (AUC: 0.851, 95% CI: 0.770-0.932, $p<0.0001$) (Table 5) (Figure 1).

Table 1. Age distribution

Endoscopic Findings		n	Min.	Median	IQR	Max
Age	Esophageal varices	96	19	65	18	89
	Gastric varices	21	26	61	21	76

Table 2. The incidence of symptoms indicating bleeding

		Endoscopic Findings		p
		Esophageal varices (N: 96)	Gastric varices (N:21)	
Hematemesis	N	77	12	0.025
	%	80,21%	57,14%	
Melena	N	54	17	0.036
	%	56,25%	80,95%	
Hematochezia	N	16	1	0.161
	%	16,67%	4,76%	

Table 3. Other diseases accompanying variceal bleeding

		Endoscopic Findings		p
		Esophageal varices	Gastric varices	
Heart failure	N	5	0	0.285
	%	5,21%	0,00%	
Arrhythmia	N	7	0	0.202
	%	7,29%	0,00%	
Coronary artery disease	N	17	4	0.885
	%	17,71%	19,05%	
Chronic kidney disease	N	3	3	0.036
	%	3,13%	14,29%	
Chronic liver disease	N	87	18	0.502
		0,90625	85,71%	

TAE: Transarterial embolization.

Table 4. Follow-up results of patients who underwent endoscopic treatment

			Endoscopic Findings		p
			Esophageal varices	Gastric varices	
Surgical	TAE	N	2	2	0.177
		%	2,08%	9,52%	
	Surgical	N	2	1	
		%	2,08%	4,76%	
Rebleeding		N	32	9	0.407
		%	33,33%	42,86%	
Long-Term Rebleeding		N	17	10	0.003
		%	17,71%	47,62%	
Mortality		N	19	4	0.938
		%	19,79%	19,05%	

Table 5. AUC values indicating how scoring methods predict mortality

Test Result Variable(s)	Area Under the Curve (AUC)	p	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
Full Rockall Score	0.749	<0.001	0.639	0.860
Blatchford Score	0.782	<0.001	0.675	0.888
Child-Pugh Score	0.851	<0.001	0.770	0.932
MELD-Na Score	0.765	<0.001	0.653	0.877
AIMS65 Score	0.757	<0.001	0.638	0.877

DISCUSSION

Gastrointestinal varices are associated with portal hypertension and chronic liver disease and can potentially cause life-threatening hemorrhage [9]. In the setting of portal hypertension, the incidence of esophageal varices is higher compared to gastric varices. One study reported gastric varices in 25.10% and esophageal varices in 57% of cirrhotic patients [10]. Similarly, our patients predominantly had esophageal varices.

In our study, hematemesis and melena at admission were more common in patients with esophageal varices than in patients with gastric varices. One study reported that hematemesis was associated with increased mortality among cirrhotic patients [11]. The literature reports a higher risk of initial bleeding and long-term rebleeding for esophageal varices [12], similarly to our results.

Without proper treatment, the risk of rebleeding for esophageal varices is about 60%; thus, emergency intervention and appropriate treatment are vital

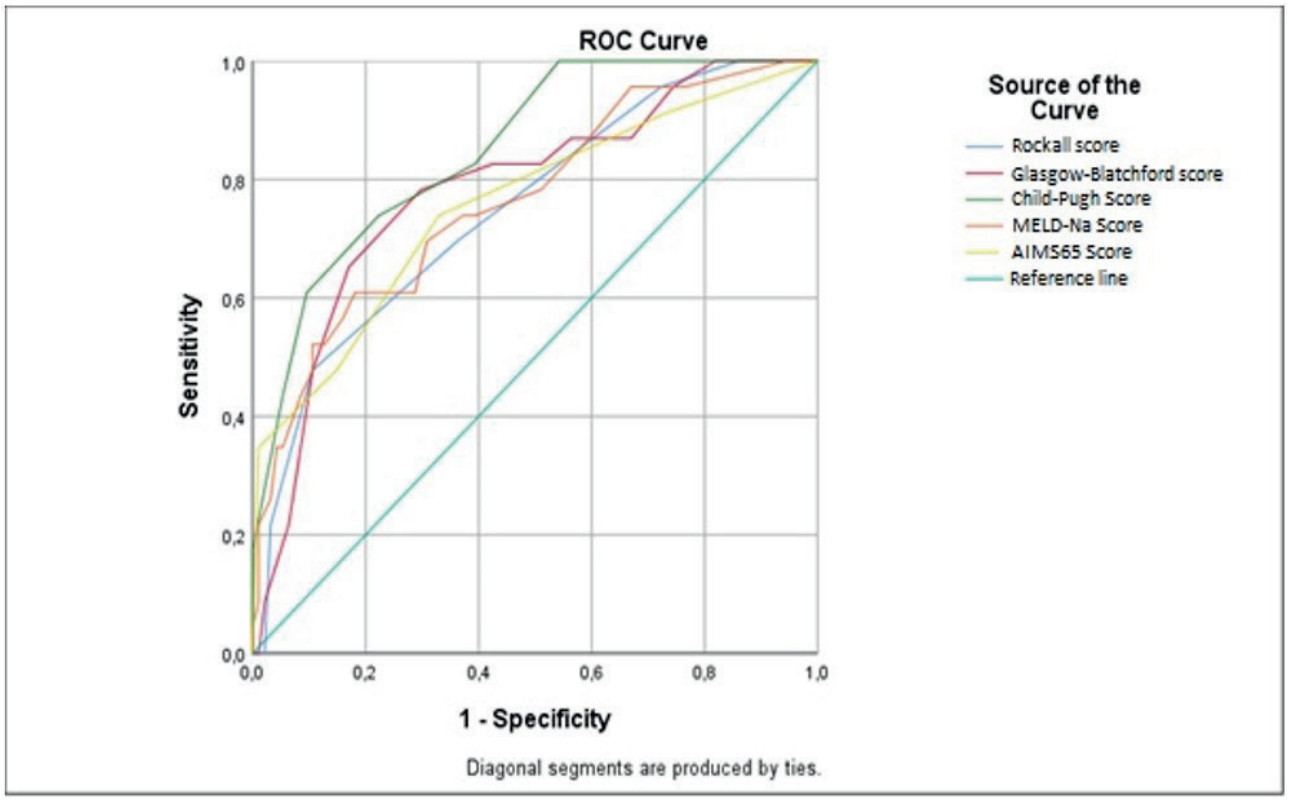

Figure 1. ROC curves indicating how scoring methods predict mortality

when managing variceal bleeding. Apart from endoscopic treatment, the initial interventions should include adequate volume replacement, achieving hemodynamic stability with blood product transfusions if needed, and administering vasoactive drugs to reduce portal blood pressure [13]. For some patients, this treatment approach is sufficient and endoscopic treatment will not be needed. These treatments are applied to patients who cannot undergo emergency endoscopic intervention. Similarly, the rate of patients who could not undergo an emergency endoscopic treatment was 23 (19.65%) in our study. These patients were followed up with vasoactive drug therapy in the acute period. Hemodynamic stability was tried to be achieved. As gastroesophageal varices can potentially cause massive bleeding, a significant number of patients require transfusion of one or more units of blood products, as was the case in our study.

If variceal bleeding is suspected, endoscopic intervention is required and should be performed within the first 12 hours [14]. Delayed endoscopic interventions are associated with a higher mortality risk [15]. Endoscopic band ligation has been demonstrated to be one of the most effective treatments of variceal hemorrhage and to reduce the incidence of rebleeding compared to sclerotherapy [16]. In our study, endoscopic band ligation was the predominant endoscopic intervention and was applied to more than half of all patients with variceal bleeding.

Although gastric varices are rarer and carry a lower risk of initial bleeding compared to esophageal varices, they are more likely to rebleed [17]. Gastric varices tend to be deeper and larger in size; therefore, endoscopic band ligation is less likely to be successful in patients with gastric varices [18,19]. Compared to esophageal varices, gastric varices are more likely to rebleed after band ligation due to exposure to gastric acids and pepsin and gastric peristalsis [20,21]. Consistently, the rebleeding rate was 42.86% vs. 33.34% for gastric versus esophageal varices in our study. Gastric varices carry an increased risk of gastrorenal shunt and therefore an increased risk of migration of the sclerosing substance into the systemic circulation; consequently, sclerotherapy is not an effective or safe approach for the treatment of gastric varices [22]. In our study, the predominant endoscopic treatment method was band ligation, and gastric varicose patients were more likely to require

surgical intervention and TAE due to rebleeding compared to patients with esophageal varices, consistently with the literature.

Gastric varices are observed in approximately 5-33% of cirrhotic patients and are associated with a lower risk of bleeding but higher mortality rates [23]. In our study, the mortality rate was 19.79% for esophageal varices and 19.04% for gastric varices. The fact that the mortality rate was lower in patients with gastric varices compared to esophageal varices in our study may be attributed to the small number of patients with gastric varices.

Large spontaneous gastrorenal shunts are more common in gastric varices than in esophageal veins, which allows for a comparatively lower portal pressure [22,24]. This phenomenon may explain the lower prevalence of chronic kidney disease in the gastric varices group compared to the esophageal varices group.

Predicting the risk of mortality due to variceal bleeding in cirrhotic patients helps guide clinicians in patient management, where patients with a high risk of mortality are followed and treated more closely in the intensive care setting. Numerous scoring systems have been developed to predict mortality in the setting of cirrhosis. It is well known that esophageal variceal bleeding is the most important cause of mortality in cirrhotic patients. One study used the AIMS65, MELD, APACHE II, and Child-Pugh scores to predict mortality in cases of acute variceal hemorrhage in cirrhotic patients and showed that the AIMS65 score had the highest sensitivity and specificity [25]. A different study reported that the AIMS65 and Rockall scores were superior to the other assessed scoring systems in predicting mortality [26]. In our study, the AIMS65 and Rockall scoring systems were less reliable compared to other scoring systems. This discrepancy may be attributed to our sample size and differences in the distribution of disease stages. One study reported that esophageal varices were correlated with the MELD score in cirrhotic patients [27]. A different study compared the Glasgow-Blatchford score, Child-Pugh score, and MELD score in predicting 1- and 6-week mortality in patients with esophageal variceal bleeding. Glasgow-Blatchford scoring was found to be superior to other scores in predicting 1-week mortality, whereas the MELD score was superior in predicting 6-week mortality [28]. One study demonstrated that the Glasgow-Blatchford score was superior in predicting the need for transfusion and additional interventions in patients with esophageal variceal bleeding [26]. Another study indicated that the MELD and Child-Pugh scores were the most valuable in determining 6-week mortality in cirrhotic patients with gastroesophageal varices bleeding [29]. Similarly, we found that the Child-Pugh score was the most valuable scoring system in predicting mortality due to variceal bleeding, followed by the Glasgow-Blatchford and MELD-Na scores. The Child-Pugh score can reliably predict the prognosis of cirrhotic patients together with endoscopic criteria including varices size, red wale sign (an endoscopic sign suggestive of recent hemorrhage), and recent variceal bleedings [3]. In reference to this information, the Child-Pugh score is an important tool for risk classification, treatment, and follow-up of cirrhotic patients with varices.

The limitations of this study were that, since it was evaluated retrospectively, we could not obtain information about long-term mortality and rebleeding rates. Therefore, prospective studies are needed on the relationship between the examined scores and long-term mortality.

CONCLUSION

Esophageal varices are at higher risk for bleeding whereas gastric variceal bleedings are at higher risk for rebleeding, mortality, and secondary intervention after endoscopy. Pre- and post-bleeding management of these patients is of vital importance for prognosis. Assessment with scoring systems upon admission is useful for risk classification and prediction of mortality risk. In this context, the Child-Pugh score can be used to assess acute variceal hemorrhages. Our study is noteworthy for shedding light on differences in the approach to treatment and follow-up in patients with portal hypertension with gastric versus esophageal varices.

Author contribution

Study conception and design: OE, EG, and NYÇ; data collection: EG, RE, BK, MB, NYÇ and OE; analysis and interpretation of results: NYÇ, SK and EG; draft manuscript preparation: NYÇ, EG, OE and SK. All authors reviewed the results and approved the final version of the manuscript.

Ethical approval

This study was confirmed by the local ethics Ankara City Hospital Ethical 1 board (Number: E1-21-2032) on 20.10.2021.

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Conflict of interest

The authors declare that there is no conflict of interest.

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