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Predictors of early rebleeding after endoscopic therapy of first variceal bleeding in liver cirrhosis

Maha Salah Abu Alia¹, Abdallah Ahmed Elsayw^{1*} , Reda Abdelsamaie Elarabawy² and Hegazy Mohamed Hegazy¹

Abstract

Background: Despite the great advancement in therapeutic modalities for esophageal varices, early variceal rebleeding still occurs at high rates leading to an exaggeration of the morbidity and mortality for cirrhotic patients, so meticulous follow-up with optimum prediction and proper preventive measures for early variceal rebleeding are mandatory for increasing survival of those patients. In this respect, we evaluated the clinical, laboratory, abdominal ultrasound, and endoscopic criteria of variceal cirrhotic patients as possible risk predictors of early variceal rebleeding after endoscopic control of first variceal bleeding. All included patients were followed up blindly for 12 weeks after endoscopic control of bleeding for ascertainment of first variceal rebleeding. The demographic, clinical, laboratory, abdominal ultrasound, and upper gastrointestinal endoscopic criteria were evaluated for all patients at first admission.

Results: By univariate regression analysis, the statistically significant predictors for early variceal rebleeding were serum albumin, serum bilirubin, prothrombin concentration, Child-Pugh score, platelet count, spleen diameter, ascites, portal vein diameter and velocity, variceal size, variceal location, and red color sign. By using multivariate regression analysis, the most independent significant predictors were Child-Pugh score (sig: 0.001 and OR: 1.661), platelets count (sig: 0.000 and OR: 0.956), portal vein velocity (sig: 0.000 and OR: 0.664), variceal grading (sig: 0.000 and OR: 3.964), and variceal red color sign (sig: 0.000 and OR: 4.964). We used the multivariate regression coefficients for the significant predictors to build up early variceal rebleeding risk (EVRR) score with a significant discriminatory performance (AUC: 0.965 and sig: 0.000).

Conclusion: Child-Pugh score, platelet count, portal vein velocity, variceal grading, and variceal red color sign are independent risk predictors for early variceal rebleeding after successful control of first variceal bleeding in cirrhotic patients. Our proposed EVRR score could be helpful for the prediction of early variceal rebleeding in cirrhotic patients after endoscopic control of acute variceal bleeding; however, it should be externally validated in large prospective studies.

Keywords: Variceal rebleeding, Predictors, Risk, Cirrhosis, Variceal bleeding

Background

Despite the recent great advancement in therapeutic modalities for bleeding esophageal varices (EV) in cirrhotic patients, early variceal rebleeding still occurs at higher rates that may reach up to 30–40% of cases in some reports. This high variceal rebleeding rate could exaggerate its attributed morbidity and mortality burden

for those cirrhotic patients [1–4], so meticulous follow-up with an optimum prediction of early rebleeding and proper preventive measures are mandatory for increasing survival of those patients [5–7].

Many predictive risk factors for variceal rebleeding were previously reported with high degree of variability as regards their methodological design, sample size, and results [8–13]. In this respect, we evaluated the most relevant demographic, routine laboratory, and abdomen ultrasound features that are closely related to the pathogenesis and development of esophageal varices (EV) in

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liver cirrhosis and at the same time the endoscopic variceal criteria as well as the type of endoscopic modality of variceal bleeding control either endoscopic band ligation (EBL) or endoscopic injection therapy (EIT) as possible risk predictors of early rebleeding after endoscopic control of first variceal bleeding. In our study, we tried to derive a new prediction score for variceal rebleeding in our cirrhotic patients.

Methods

Study design and source of data

This is a prospective predictor cohort study that was conducted in accordance to the TRIPOD Statement (Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis) [14]. It was conducted at the emergency endoscopic unit of the internal medicine department at our university hospitals (a tertiary hospital). All participants were consecutively enrolled in the period from August 2019 to April 2020, and they were followed up for 12 weeks after endoscopic successful bleeding control.

Participants

Five hundred and sixty-two patients were consecutively presented to our emergency endoscopic unit by upper gastrointestinal bleeding (hematemesis and/or melena); all patients were resuscitated and evaluated using upper gastrointestinal endoscopy for the study eligibility criteria before enrollment. These eligibility criteria included proved cirrhotic patients who were consecutively presented by first variceal bleeding that was controlled well by esophagogastroduodenoscopy (EGD).

The eligibility criteria were fulfilled in 412 patients who were consecutively presented by cirrhosis and first variceal bleeding that was successfully controlled either by endoscopic band ligation (EBL) or endoscopic injection therapy (EIT). One hundred and fifty patients were excluded before enrollment, 30 patients were excluded due to non-variceal upper GIT bleeding, 20 patients were excluded as they were non-cirrhotic, 60 patients were excluded as they had a history of endoscopic treatment for esophageal varices (EV), 10 patients were excluded due to hepatocellular carcinomas (HCC) or malignant liver metastasis, 10 patients were excluded due to portal vein thrombosis, 6 patients were excluded due to history of splenectomy, 10 patients were excluded as the bleeding source was isolated gastric varices, and 4 patients were excluded as the bleeding was failed to be controlled endoscopically.

All included patients were blindly followed up for 12 weeks after endoscopic control of bleeding for ascertainment of possible variceal rebleeding as our endpoint; the variceal rebleeding was diagnosed according to Baveno criteria by reappearance of hematemesis and/or melena

or requirement for > 2 units of packed red blood cells within 24 h with hemodynamic instability and was confirmed by upper gastrointestinal (GIT) endoscopy [15]. All these are illustrated in the participant's flowchart (Fig. 1).

Evaluated predictors

The following base-line criteria were evaluated for all included patients at first admission: demographic criteria (age and sex), clinical presentations (hematemesis and/or melena), abdominal ultrasound criteria (spleen diameter, portal vein diameter (PVD), portal vein velocity (PVV) and ascites), routine laboratory criteria (AST, ALT, serum albumin, serum bilirubin, prothrombin concentration (PC), serum creatinine, platelet count, and hemoglobin), and upper GIT endoscopic criteria which were graded according to the Japanese Research Society for Portal Hypertension (variceal form, variceal location, and red color signs) [16], as well as endoscopic modality of variceal bleeding control (EBL or EIT).

Sample size estimation

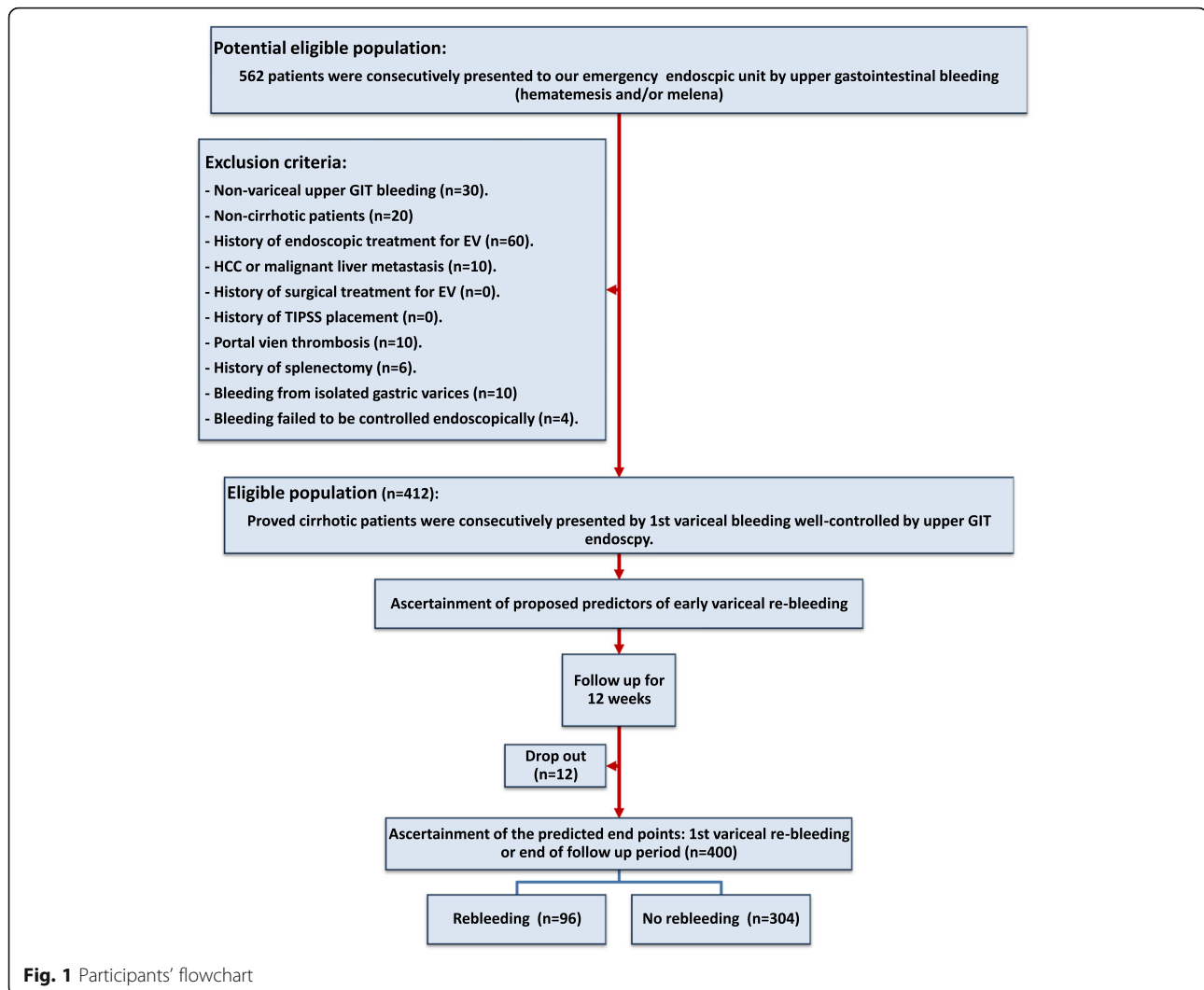
Sample size estimation was statistically based on the previously reported incidence rate of early variceal rebleeding that ranges from 30 to 40%, the sample size calculation assumed that the confidence interval was 95% and the estimation error was 0.05.

Statistical analysis methods

We used IBM SPSS, version 23 statistic software (IBM, NY, USA) for both summarization and statistical analysis of our collected data. The median with (minimum to maximum) was calculated for all quantitative data as it was abnormally distributed; however, all qualitative data were tabulated as frequency and relative frequency.

The pre-selection of our predictors was based on well-conducted previous reports, clinical reasoning, and on univariate logistic regression analysis of our evaluated predictors. Logistic regression analysis was performed to find out the best predictors of early variceal rebleeding. Univariate logistic regression analysis was done first for each predictor to identify the significant predictor with its unadjusted hazard ratio (OR), and then the most independent significant predictors were evaluated using the multivariable logistic regression analysis by entering all the previously identified significant predictors simultaneously with a stepwise backward strategy.

The regression coefficients of the most independent significant predictors—that were identified in multivariate regression analysis—were used to derive our predicted risk score. Receiver operating characteristic (ROC) curves were calculated for our predictor score and the area under the ROC curve (AUC) was computed. The new predictor score was graded to 3 risk



groups: low, medium, and high risk by using cutoff points along its scale; the 1st cutoff point was selected to rule in the outcome with the highest specificity and highest LR+, the 2nd cutoff point was selected to rule out the outcome with the highest sensitivity and lowest LR-, and then the hazard distribution in-between different grades was illustrated using Kaplan-Meier method and was analyzed using log-rank test. P values less than 0.05 were considered statistically significant.

Results

Table 1 of our results shows participants' demographic criteria, the different clinical presentations of acute upper GIT bleeding, the most relevant, laboratory and abdomen ultrasound features that are closely related to pathogenesis and development of EV in liver cirrhosis, the endoscopic variceal criteria, and the type of endoscopic modality of variceal bleeding control. The rebleeding was ascertained in 96 (24%) of our patients

during the 12-week follow-up period after control of the first variceal bleeding.

Table 2 of our results shows the univariate logistic regression analysis for our studied proposed predictors for early variceal rebleeding. The statistically significant laboratory predictors were serum albumin, serum bilirubin, PC, Child-Pugh score, and platelets. The statistically significant abdominal ultrasound parameters were spleen diameter, ascites, PVD, and PVV. The statistically significant endoscopic variceal criteria were variceal form, variceal location, and red color sign.

All the previously significant predictors were evaluated simultaneously using multivariate logistic regression analysis to identify the most independent significant predictors for early variceal rebleeding as illustrated in Table 3. The most independent significant predictors were Child-Pugh score, platelets, PVV, variceal form, and variceal red color sign. We used the multivariate logistic regression coefficients that are illustrated in Table

Table 1 Main evaluated participants' criteria

Participants' criteria			Total n=400		Rebleeding n=96		No rebleeding n=304		Sig.
Demographic criteria									
• Age (years)		Mean (SD)	56	(8.1)	56.8	8.2	56	7.9	0.367
• Sex	• Male	Count (%)	268	67%	59	61.5%	209	68.8%	0.185
	• Female	Count (%)	132	33%	37	38.5%	95	31.2%	
Patients clinical presentation									
• Hematemesis		Count (%)	178	44.5%	55	57.3%	123	40.5%	0.007
• Melena		Count (%)	102	25.5%	15	15.6%	87	28.6%	
• Combined hematemesis and melena		Count (%)	120	30%	26	27.1%	94	30.9%	
Liver functions									
• ALT (IU/L)		Mean (SD)	39	(11.7)	41.1	10.6	38.6	11.9	0.052
• AST (IU/L)		Mean (SD)	44	(13.8)	44.8	13	44.3	14.2	0.739
• Serum albumin (gm/dl)		Mean (SD)	3.32	(0.26)	3.12	0.23	3.33	0.25	< 0.0001
• Serum bilirubin (mg/dl)		Median (IQR)	1.5	(0.6)	1.6	0.4	1.45	0.6	< 0.0001
• Prothrombin concentration (%)		Median (IQR)	71	(9)	68	6	71	9	< 0.0001
• Child-Pugh score		Median (QR)	7	(2)	8	1	7	2	< 0.0001
• Child-Pugh grade	• Child A	Count (%)	136	34%	10		126		< 0.0001
	• Child B	Count (%)	247	61.75%	87		169		
	• Child C	Count (%)	17	4.25%	8		9		
Radiological parameters									
• Spleen diameter (cm)		Median (IQR)	16.3	(2.6)	17	2	16	2.2	< 0.0001
• Ascites	• No ascites	Count (%)	148	37%	11	11.5%	137	45.1%	< 0.0001
	• Easy to treat	Count (%)	228	57%	70	72.9%	158	52%	
	• Difficult to treat	Count (%)	24	6%	15	15.6%	9	3%	
• PVD (mm)		Median (IQR)	13.5	(4.8)	15.7	4.1	12.3	4.1	< 0.0001
• PVV (cm/s)		Median (IQR)	14	(7)	11	6	16	6	< 0.0001
Other laboratory parameters									
• Serum creatinine (mg/dl)		Median (IQR)	1.2	(0.2)	1.2	0.2	1.2	0.2	0.292
• Platelets ($\times 10^3/\text{mm}^3$)		Median (IQR)	145	(54)	95	36	154	37	< 0.0001
• Hemoglobin (g/dl)		Median (IQR)	9.8	(0.9)	9.6	1	9.8	0.9	0.501
Endoscopic parameters									
• Variceal form (F)	• F1	Count (%)	131	32.75%	9	9.4%	122	40.1%	< 0.0001
	• F2	Count (%)	150	37.5%	34	35.4%	116	38.2%	
	• F3	Count (%)	119	29.75%	53	55.2%	66	21.7%	
• Variceal location (L)	• L1	Count (%)	246	61.5%	47	49%	199	65.5%	0.013
	• L2	Count (%)	141	35.25%	44	45.8%	97	31.9%	
	• L3	Count (%)	13	3.25%	5	5.2%	8	2.6%	
• Red color signs	• Absent	Count (%)	196	49%	25	26%	171	56.3%	< 0.0001
	• Not extensive	Count (%)	160	40%	36	37.5%	124	40.8%	
	• Extensive	Count (%)	44	11%	35	36.5%	9	3%	
• Gastric extension		Count (%)	116	29%	34	29.3%	82	70.7%	0.112
• Modality of bleeding control	• EBL	Count (%)	185	46.25%	42	43.8%	143	47%	0.573
	• EIT	Count (%)	215	53.75%	54	56.2%	161	53%	

ALT alanine aminotransferase, AST aspartate aminotransferase, PVD portal vein diameter, PVV portal vein velocity, EBL endoscopic band ligation, EIT endoscopic injection therapy

Table 2 Univariate logistic regression analysis for the evaluated predictors

Participants' criteria	Constant	B	SE	Wald	Sig.	EXP(B)	95% CI	
							Lower	Upper
Demographic criteria								
• Age (years)	- 1.901	0.13	0.015	0.817	0.366	1.013	0.985	1.043
• Sex	0.943	- 0.322	0.243	1.747	0.186	0.725	0.515	1.171
Liver functions								
• ALT (IU/L)	- 1.850	0.018	0.010	3.286	0.07	1.018	0.999	1.037
• AST (IU/L)	0.003	0.002	0.008	0.102	0.749	1.003	0.986	1.019
• Serum albumin (gm/dl)	9.496	- 3.292	0.530	38.585	< 0.0001	0.037	0.013	0.105
• Serum bilirubin (mg/dl)	- 2.175	0.635	0.222	8.199	0.004	1.887	1.222	2.914
• Prothrombin concentration (%)	8.908	- 0.145	0.024	36.851	< 0.0001	0.865	0.825	0.907
• Child-Pugh score	- 4.451	0.455	0.089	26.242	< 0.0001	1.577	1.325	1.877
Radiological parameters								
• Spleen diameter (cm)	- 4.904	0.225	0.067	11.315	0.001	1.253	1.099	1.428
• Ascites	- 3.986	1.564	0.251	38.806	< 0.0001	4.776	2.920	7.811
• PVD (mm)	- 6.596	0.378	0.051	55.551	< 0.0001	1.459	1.321	1.612
• PVV (cm/s)	4.612	- 0.449	0.050	79.876	< 0.0001	0.638	0.578	0.704
Other laboratory parameters								
• Serum creatinine (mg/dl)	- 1.874	0.598	0.787	0.578	0.447	1.819	0.389	8.514
• Platelets ($\times 10^3/\text{mm}^3$)	5.216	- 0.051	0.005	94.666	< 0.0001	0.950	0.940	0.960
• Hemoglobin (g/dl)	- 0.140	- 0.103	0.178	0.338	0.502	0.561	0.636	1.278
Endoscopic parameters								
• Variceal form (F)	- 3.614	1.146	0.175	42.816	< 0.0001	3.144	2.231	4.431
• Variceal Location (L)	- 2.013	0.588	0.203	8.384	0.004	1.801	1.209	2.681
• Red color sign	- 2.258	1.436	0.196	53.780	< 0.0001	4.205	2.865	6.173
• Gastric extension	- 1.276	0.395	0.249	2.509	0.113	1.485	0.910	2.421
• Modality of bleeding control	- 1.225	0.133	0.236	0.317	0.573	1.142	0.720	1.812

ALT alanine aminotransferase, AST aspartate aminotransferase, PVD portal vein diameter, PVV portal vein velocity

3 for the most independent significant predictors to build up a predictor model for early variceal rebleeding using the following equation of the predicted probability: $\exp [1.826 + 0.508 \cdot \text{Child-Pugh score} - 0.045 \cdot \text{PLT} - 0.409 \cdot \text{PVV} + 1.242 \cdot \text{variceal form} + 1.602 \cdot \text{variceal red color sign}] / (1 + \exp [1.826 + 0.508 \cdot \text{Child-Pugh score} - 0.045 \cdot \text{PLT} - 0.409 \cdot \text{PVV} + 1.242 \cdot \text{variceal form} + 1.602 \cdot \text{variceal red color sign}])$, where PLT count was in $10^3/\text{ml}$ and PVV was in cm/s . We named this predictor model as early variceal rebleeding risk score (EVRR score).

color sign)/(1 + exp [1.826 + 0.508*Child-Pugh score - 0.045*PLT - 0.409*PVV + 1.242*variceal form + 1.602*variceal red color sign]), where PLT count was in $10^3/\text{ml}$ and PVV was in cm/s . We named this predictor model as early variceal rebleeding risk score (EVRR score).

Table 3 Multivariable regression analysis for the evaluated predictors

Participants' criteria	B	SE	Wald	Sig.	EXP(B)	95% CI	
						Lower	Upper
• Child-Pugh score	0.508	0.159	10.226	0.001	1.661	1.2117	2.268
• Platelets ($\times 10^3/\text{mm}^3$)	- 0.045	0.008	33.362	< 0.0001	0.956	0.941	0.970
• PVV (cm/s)	- 0.409	0.080	26.108	< 0.0001	0.664	0.568	0.777
• Variceal form	1.242	0.287	18.728	< 0.0001	3.964	1.973	6.077
• Red color sign	1.602	0.309	26.950	< 0.0001	4.964	2.711	9.089
Constant	1.826						

PVV portal vein velocity

The predicted probability = $\exp [1.826 + 0.508 \cdot \text{Child-Pugh score} - 0.045 \cdot \text{PLT} - 0.409 \cdot \text{PVV} + 1.242 \cdot \text{variceal form} + 1.602 \cdot \text{variceal red color sign}] / (1 + \exp [1.826 + 0.508 \cdot \text{Child-Pugh score} - 0.045 \cdot \text{PLT} - 0.409 \cdot \text{PVV} + 1.242 \cdot \text{variceal form} + 1.602 \cdot \text{variceal red color sign}])$

Variceal forms were numerically coded (1 for F1, 2 for F2, and 3 for F3) and red color signs were numerically coded (0 for absent, 1 for non-extensive, and 2 for extensive)

Table 4 and Fig. 2 of our results illustrate the discriminatory performance of our proposed EVRR score using the receiver operating characteristics that identified two cutoff points (≤ 0.10 and ≥ 0.90); the 1st cutoff point was selected to rule out the possibility of occurrence of early variceal rebleeding for values equal or below it with its sensitivity, specificity, LR+, and LR- were 98%, 80%, 4.96, and 0.03, respectively, and the 2nd cutoff point was selected to rule in the possibility of occurrence of early variceal rebleeding for values equal or above it with its sensitivity, specificity, LR+, and LR- were 43%, 99.7%, 129.8, and 0.57, respectively (AUC:0.965 and sig < 0.0001).

We graded the EVRR score to 3 grades using the previous two cutoff points for risk stratification: values ≤ 0.10 to identify EVRR grade 1 with mild risk, values ≥ 0.90 to identify EVRR grade 3 with high risk, and EVRR grade 2 with moderate risk for the remaining values. The crosstabulation between different risk scores and rebleeding distribution was illustrated in Table 5, the rebleeding free survival function of the different risk grades of EVRR score was illustrated using the Kaplan-Meier curve, and their pairwise comparisons were analyzed using log-rank test as illustrated in Fig. 3, with statistically significant difference between the different risk grades (sig < 0.0001).

Discussion

The high variceal rebleeding rate could exaggerate the morbidity and mortality burden on cirrhotic patients, so meticulous follow-up with an optimum prediction of rebleeding with proper preventive measures are mandatory for those patients to mitigate this devastating complication and increase survival [1–7]. This assumption of the deleterious effects of variceal rebleeding was taken as a rationale by many studies for the exploration of the possible predictor factors for this risk with wide variable results [8–13]. In this respect, we tried searching for the most independent predictor factors that may increase the hazard of early variceal rebleeding in cirrhotic patients after successful endoscopic control of the first episode of variceal bleeding. In our study, we took into consideration the most relevant routine laboratory and radiological criteria that are closely related to pathogenesis and development of EV in liver cirrhosis, as well as the endoscopic variceal criteria as regards its severity

and bleeding risk signs and at the same time the type of endoscopic modality of variceal bleeding control.

As regards the underlying baseline liver functions, we found that higher Child-Pugh score, hypo-albuminemia, hyper-bilirubinemia, and lower levels of prothrombin concentration were significant predictors for early variceal rebleeding; however, the Child-Pugh score was found to be the most independent significant predictor factor using multivariate analysis (sig = 0.001 and OR = 1.661.). In accordance with our results, many reports identified that early variceal rebleeding rate significantly increases in higher Child-Pugh scores than lower scores [17, 18]. We could explain this finding, as the Child-Pugh score is a surrogate parameter for the underlying liver cell functions that are deteriorated in accordance to the progression of the underlying liver cirrhosis which is considered as the leading cause of portal hypertension [5, 7].

After multivariate analysis of other laboratory criteria for our participants, we found that thrombocytopenia was the only independent significant predictor for variceal rebleeding. This finding is confirmed by the results of previous reports that identified the possible role of thrombocytopenia in the prediction of portal hypertension and esophageal varices in patients with liver cirrhosis [19, 20].

The univariate regression analysis of the baseline radiological criteria of our participants identified that splenomegaly, increased ascites, increased PVD, and decreased PVV were significantly associated with increased risk of early variceal rebleeding. However, by multivariate analysis, we found that PVV was the only independent significant predictor for the risk of variceal rebleeding. The reliability of PVV as a non-invasive tool for the prediction of esophageal varices in cirrhotic patients was confirmed previously in many reports [21, 22]. Consequently, we could suggest that PVV may be used not only in the prediction of esophageal varices in cirrhotic patients but also in the prediction of early variceal rebleeding in those patients. However, to our knowledge, there were no studies that discussed the correlation between PVV and the risk of early variceal rebleeding of esophageal varices.

As regards the endoscopic variceal criteria of our participants, the univariate regression analysis showed that

Table 4 Receiver operating characteristics of the proposed prediction model

	Role	Cutoff	Sensitivity	Specificity	LR+	LR-	AUC		
							Value	(95%CI)	Sig.
Proposed model	Rule out	≤ 0.10	98%	80%	4.96	0.03	0.965	(0.948–0.981)	< 0.0001
	Rule in	≥ 0.90	43%	99.7%	129.8	0.57			

LR likelihood ratio, AUC area under the curve

Risk grading of the proposed prediction model: grade 1 (Low risk) if the predicted probability $\leq 10\%$; grade 3 (high risk) if the predicted probability $\geq 90\%$, and grade 2 (moderate risk) for other values

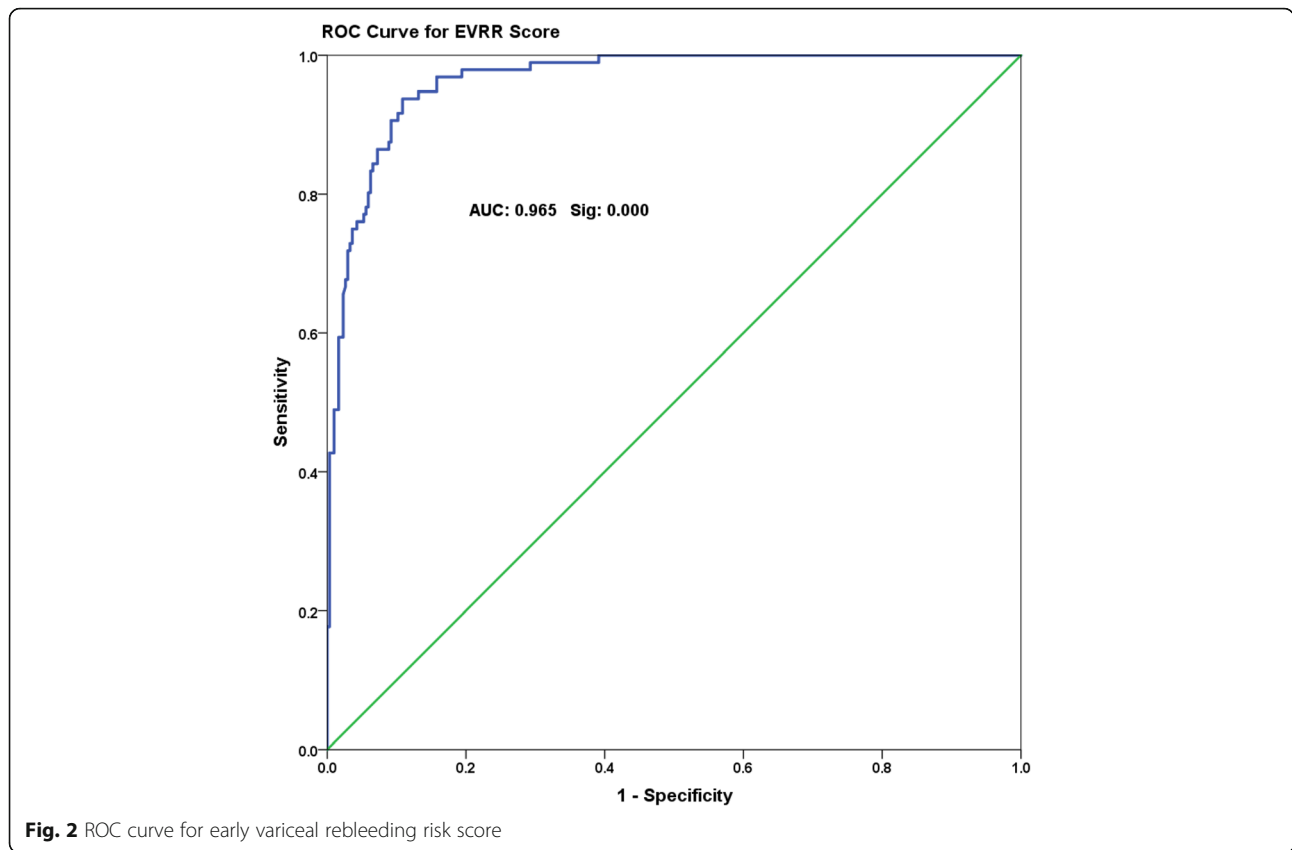


Fig. 2 ROC curve for early variceal rebleeding risk score

variceal grading, variceal location, and red color signs were significantly associated with the risk of rebleeding. However, the multivariate regression analysis identified that the most independent significant endoscopic variceal criteria were EV grading and variceal red color sign. These results are in agreement with many previous reports that found a significant association of variceal rebleeding with variceal size [23–25] and variceal red color sign or nipple sign [24–26].

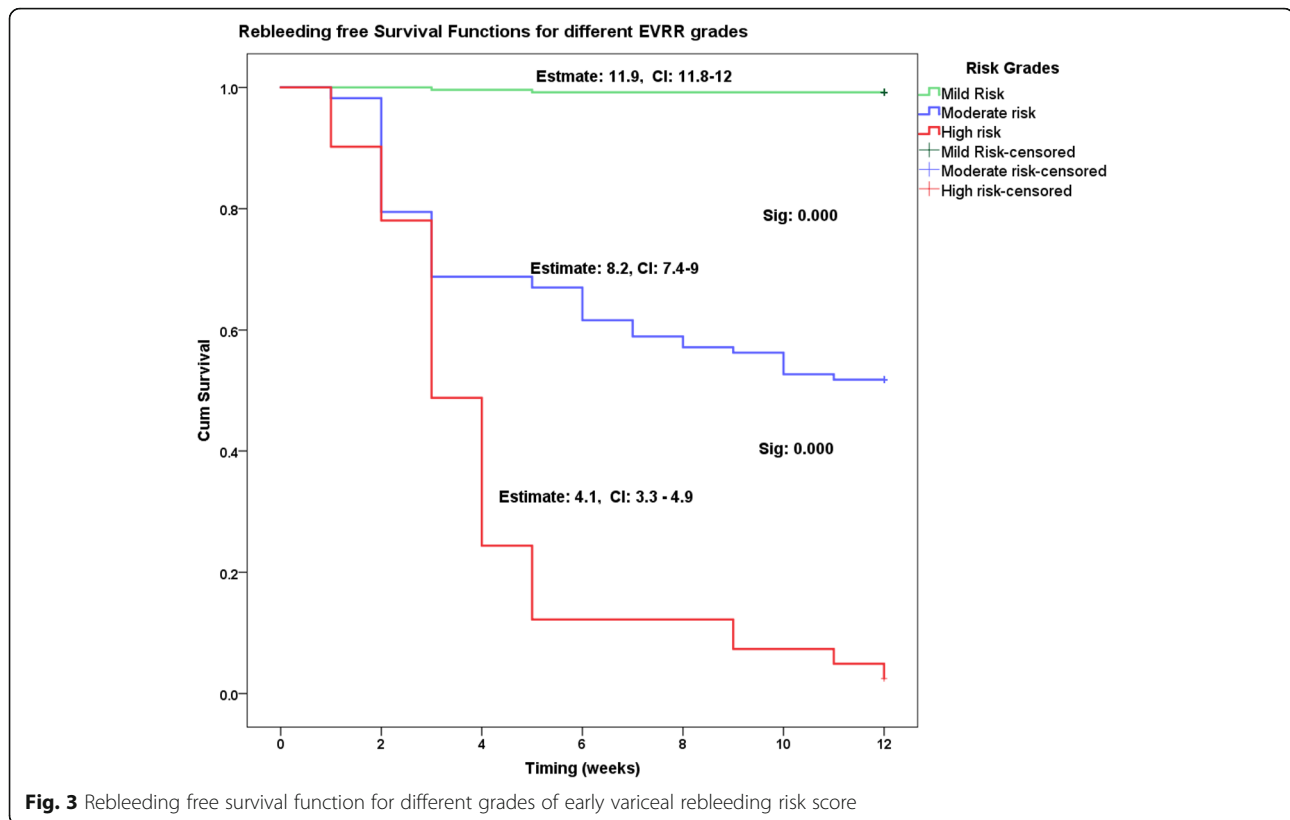
In summary, after univariate and multivariate analysis of all our potential predictors for variceal rebleeding, we found that the only independent significant predictors were higher

levels of the Child-Pugh score, thrombocytopenia, decreased PVV, larger variceal size, and the presence of variceal red color risk sign. All of these five independent significant predictors are related to pathophysiology or the complications of portal hypertension and EV in cirrhotic patients [7, 27].

We used the multivariate regression coefficients of those five independent significant predictors to derive a new early variceal rebleeding risk (EVRR) score that revealed a significant discriminatory performance, and two cutoff points (≤ 0.10 and ≥ 0.90) were identified; the 1st cutoff point was selected to rule out the possibility of

Table 5 Variceal rebleeding distribution in accordance to a risk score of the proposed model

Risk group		Count	Rebleeding		Total
			Absent	Present	
Mild Risk	Count	245	2	247	
	% within Risk_group	99.2%	0.8%	100.0%	
Moderate risk	Count	58	54	112	
	% within Risk_group	51.8%	48.2%	100.0%	
High risk	Count	1	40	41	
	% within Risk_group	2.4%	97.6%	100.0%	
Total	Count	304	96	400	
	% within Risk_group	76.0%	24.0%	100.0%	



occurrence of early variceal rebleeding for values equal or below it and the 2nd cutoff point was selected to rule in the possibility of occurrence of early variceal rebleeding for values equal or above it. We graded the EVRR score to 3 grades using those two cutoff points for risk stratification: values ≤ 0.10 to identify EVRR grade 1 with mild risk, values ≥ 0.90 to identify EVRR grade 3 with high risk, and EVRR grade 2 with moderate risk for remaining values, the pairwise comparisons of rebleeding free survival function between the different risk grades of EVRR identified statistically significant difference. However, this proposed score should be externally validated later in large prospective studies.

We found some aspects of limitations in our study, one of them is the single center enrollment that may limit the study generalizability, and the presence of more than one operator for both endoscopy and abdomen ultrasound that may increase the inter-observer variability in values of predictors; however, this limitation was mitigated through their highly trained experience and using of advanced equipment. Other aspects of limitations, as we did not take into consideration the medical treatment that may be prescribed for variceal patients after endoscopy and during the follow-up data like non-selective beta-blockers and proton pump inhibitors, however, these medical treatments were prescribed to most of our patients.

Conclusion

We concluded that the Child-Pugh score, platelet count, PVV, EV grading, and variceal red color sign are the most independent significant risk predictors for early variceal rebleeding after endoscopic control of first variceal bleeding in cirrhotic patients. Our proposed EVRR score could be helpful for the prediction of early variceal rebleeding in cirrhotic patients after endoscopic control of acute variceal bleeding; however, it should be externally validated in large prospective studies.

Abbreviations

ALT: Aspartate aminotransferase; AST: Alanine aminotransferase; AUC: Area under the curve; EBL: Endoscopic band ligation; EIT: Endoscopic injection therapy; EV: Esophageal varices; EVRR: Early variceal rebleeding risk; GIT: Gastrointestinal tract; HCC: Hepatocellular carcinoma; LR: Likelihood ratio; OR: Odds ratio; PC: Prothrombin concentration; PLT: Platelets; PVD: Portal vein diameter; PVV: Portal vein velocity; Sig: Significance; TRIPOD: Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis

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Authors' contributions

All authors read and approved the final manuscript, according to the following respective roles of each author. MSA shared in study conception and design, data collection, and data interpretation. AAE shared in study conception and design, data collection, data analysis, data interpretation, and as a corresponding author. RAE shared in study conception and design,

data collection, and data interpretation. HMH shared in study conception and design, data collection, and data interpretation.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The present study was conducted in accordance with the Declaration of Helsinki. The study protocol was approved by the ethics committee of the Tanta Faculty of Medicine (No: 33264/07/19). All patients provided written informed consent. The results of the research were used only in scientific purposes and not in any other aims.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

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