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

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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
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 esophagogastroduodenoscope (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 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...
| Participants’ criteria                          | Total n=400 | Rebleeding n=96 | No rebleeding n=304 | Sig.  |
|------------------------------------------------|-------------|-----------------|---------------------|-------|
| Demographic criteria                           |             |                 |                     |       |
| • Age (years) Mean (SD)                         | 56 (8.1)    | 59.8            | 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            | 38.6 11.9           | 0.052 |
| • AST (IU/L) Mean (SD)                         | 44 (13.8)   | 44.8            | 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 (QQR)                | 7 (2)       | 8 1             | 7 2                 | < 0.0001 |
| • Child-Pugh grade Count (%)                   | 136 34%     | 10 126          | < 0.0001            |       |
| • Child A Count (%)                            | 148 37%     | 11 11.5%        | 137 45.1%           |       |
| • Child B Count (%)                            | 247 61.75%  | 87 169          | < 0.0001            |       |
| • Child C Count (%)                            | 17 4.25%    | 9               |                     |       |
| Radiological parameters                        |             |                 |                     |       |
| • Spleen diameter (cm) Median (IQR)            | 16.3 (2.6)  | 17 2            | 16 22               | < 0.0001 |
| • 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 (× 10^3/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) Count (%)                  | 131 32.75%  | 9 9.4%          | 122 40.1%           | < 0.0001 |
| • Variceal location (L) Count (%)              | 246 61.5%   | 47 49%          | 199 65.5%           | 0.013 |
| • Red color signs Count (%)                    | 196 49%     | 25 26%          | 171 56.3%           | < 0.0001 |
| • 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.
For the most independent significant predictors to build up a predictor model for early variceal rebleeding using the following equation of the predicted probability:

$$\text{exp} \left[ 1.826 + 0.508 \times \text{Child-Pugh score} - 0.045 \times \text{PLT} - 0.409 \times \text{PVV} + 1.242 \times \text{variceal form} + 1.602 \times \text{variceal red color sign} \right]/(1 + \text{exp} \left[ 1.826 + 0.508 \times \text{Child-Pugh score} - 0.045 \times \text{PLT} - 0.409 \times \text{PVV} + 1.242 \times \text{variceal form} + 1.602 \times \text{variceal red color sign} \right]),$$

where PLT count was in $10^3$/ml and PVV was in cm/s. We named this predictor model as early variceal rebleeding risk score (EVRR score).

### 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 (x 10^3/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 6.737    |
| • 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

### 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 2.628   |
| • Platelets (x 10^3/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 = \( \text{exp} \left[ 1.826 + 0.508 \times \text{Child-Pugh score} - 0.045 \times \text{PLT} - 0.409 \times \text{PVV} + 1.242 \times \text{variceal form} + 1.602 \times \text{variceal red color sign} \right]/(1 + \text{exp} \left[ 1.826 + 0.508 \times \text{Child-Pugh score} - 0.045 \times \text{PLT} - 0.409 \times \text{PVV} + 1.242 \times \text{variceal form} + 1.602 \times \text{variceal red color sign} \right]),\)

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

| 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 ≤ 10%; grade 3 (high risk) if the predicted probability ≥ 90%, and grade 2 (moderate risk) for other values

Table 4 Receiver operating characteristics of the proposed prediction model
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 rebleeding.

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

| Risk group     | Mild Risk | Moderate risk | High risk |
|----------------|-----------|---------------|-----------|
| Count          | 245       | 58            | 1         |
| % within Risk_group | 99.2%     | 51.8%         | 2.4%      |
| Count          | 2         | 54            | 40        |
| % within Risk_group | 0.8%     | 48.2%         | 97.6%     |
| Count          | 4         | 41            | 41        |
| % within Risk_group | 100.0%   | 100.0%        | 100.0%    |

| Rebleeding | Absent | Present | Total |
|------------|--------|---------|-------|
| Mild Risk  | 245    | 2       | 247   |
| Moderate risk | 58   | 54      | 112   |
| High risk  | 1      | 40      | 41    |
| Total      | 304    | 96      | 400   |

| Rebleeding | Absent | Present | Total |
|------------|--------|---------|-------|
| Mild Risk  | 99.2%  | 0.8%    | 100.0%|
| Moderate risk | 51.8% | 48.2%   | 100.0%|
| High risk  | 2.4%   | 97.6%   | 100.0%|
| Total      | 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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