

Factors predictive of relapse in variceal upper gastrointestinal bleeding. A prospective study in patients with liver cirrhosis

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Abstract. Aim: The aim of the study was to identify the main predictive factors of relapse in variceal upper gastrointestinal bleeding (UGIB) in cirrhotic patients. Methods: The study was performed on 184 cirrhotic patients who presented for variceal UGIB to the emergency department of a tertiary hospital during a period of 26 months. Clinical, laboratory and endoscopic data were recorded. Results: The rate of failure to control bleeding was 17.9%, of these, 48.5% died in the first 5 days ($p < 0.001$). Two factors proved to be independently associated with failure to control bleeding: the grade of esophageal varices (OR=4.35, 95%CI: 1.23-15.34) ($p=0.022$) and hypoalbuminemia (OR=2.56, 95%CI: 1.08-6.09) ($p=0.033$). Failure to control bleeding was more frequent in patients with an albumin level < 2.9 g/dL. The rebleeding rate at 6 weeks was 16.7%. Two factors were independently associated with rebleeding: failure to control bleeding (OR=6.63, 95%CI: 2.16-20.37) ($p=0.001$) and the INR level (OR=3.87, 95%CI: 1.58-9.45) ($p=0.003$). The risk of rebleeding increased above an INR cut-off of 1.94 ($p=0.011$). Conclusion: Several factors have been identified to correlate with failure to control bleeding and rebleeding in patients with cirrhosis and variceal hemorrhage.

Key Words: varices, rebleeding, cirrhosis, ascites.

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Introduction

Upper gastrointestinal bleeding (UGIB) is one of the most frequent and severe gastroenterological emergencies, with an annual incidence of 50-150 in 100,000 people (Vreeburg et al 1999). Upper gastrointestinal bleeding is characterized by hematemesis (i.e. vomiting of red blood or coffee ground emesis), or melena (black, shiny, tarry and smelly faeces), or both at the same time. Another sign that is less common is hematochezia (the passage of fresh blood through the anus), and can occur if the intestinal transit is accelerated or bleeding is severe (Cappel et al 2008). Severe complications of UGIB may occur. The most important are rebleeding and death. Over the past 10 years, the reported mortality rate has remained between 3% and 14% (Sostres et al 2011). In our previous study (Groza et al 2017) we found a 10-20% six-week mortality rate. Rebleeding is considered to be one of the risk factors for mortality. It occurs between 10% and 30% of the cases considered at first to be successfully treated (Matei et al 2013, Chandra et al 2011, Ahmed et al 2003). Upper gastrointestinal bleeding may occur from either variceal or non-variceal sources. Variceal bleeding is present in 60-65% of patients with liver cirrhosis, and 30% of them bleed in the first year after diagnosis (Garcia-Tsao et al 2007). The incidence of esophageal varices varies from 30% to 70% in patients with liver cirrhosis. Gastric varices are present in 5-33% of patients with portal hypertension (McKay et al 2007; Popovici et al 2013).

Rebleeding occurs in 50-80% of these patients, and in more than half of them, during the first 6 weeks (De Franchis et al 2010; Paunescu et al 2004). Each episode of variceal gastrointestinal bleeding is associated with a 20-35% mortality rate (Cerquiera et al 2009). Variceal rebleeding is a new haemorrhagic episode that occurs later than 5 days from the first one, an interval that defines the acute bleeding episode. There is a higher risk of rebleeding between 5 days and 6 weeks (De Franchis et al 2015). After this period, the risk of rebleeding is the same as in other patients with cirrhosis and without variceal bleeding (Sharma et al 2011). Failure to control bleeding is defined as an impossibility to manage the bleeding, including death, or rebleeding in the interval from the onset of bleeding and day 5 (Herrera 2014; De Franchis et al 2010; De Franchis et al 2015).

Rebleeding can be associated with failure to control bleeding, presence of ascites, hepatic encephalopathy, spontaneous bacterial peritonitis, marked changes in coagulation factors, low platelet counts, extensive esophageal varices, gastric varicose veins as the source of bleeding, or active bleeding during endoscopy (Biecker 2013).

The low survival rate among patients with variceal bleeding and liver cirrhosis is primarily due to the decompensation of liver disease - presence of ascites and hepatic encephalopathy (Kim et al 2014; Garcia-Tsao et al 2007). Other risk factors for mortality in variceal bleeding are: rebleeding, hepatocarcinoma,

renal failure, active bleeding, the grade of esophageal varices, or thrombocytopenia. The Child-Pugh score and the model for end-stage liver disease (MELD) score are useful to assess liver disease severity and to predict survival at 6 weeks in patients with cirrhosis (Krige et al 2014; Laine et al 2012).

There is currently no consensus on the risk factors for rebleeding after variceal bleeding due to variable and contradictory results found in literature: small patients' series, different endoscopic techniques, or differences in the definition of rebleeding (Kraja et al 2017; Waddell 2017).

The objective of this study was to identify the main predictive factors for relapse in variceal UGIB.

Material and methods

We performed an observational, analytical, longitudinal and prospective cohort study.

The study was performed on 206 patients admitted for variceal UGIB to the emergency department of the "Prof Dr. O. Fodor" Regional Institute of Gastroenterology and Hepatology in Cluj-Napoca over a period of 26 months, between November 2012 and January 2015.

All patients signed the informed consent for inclusion in the study. The study was conducted according to the Declaration of Helsinki and was approved by the Ethics committee.

Inclusion criteria

All consecutive patients admitted to our tertiary hospital with hematemesis or coffee ground emesis, melena or hematochezia, and underwent emergency upper gastrointestinal endoscopy during the first 24 hours were considered for inclusion in the study. All patients with variceal UGIB occurring in the context of liver disease, namely cirrhosis, were included.

Exclusion criteria

Patients who refused to undergo upper gastrointestinal endoscopy, patients with unidentified UGIB source or non-variceal bleeding, and patients with secondary (prehepatic) portal hypertension as the cause of variceal bleeding were excluded from the study. Also, the patients that could not be followed, were excluded from the study.

Data collection

The collection of data was initiated with pre-hospital information obtained upon admission in the form of a questionnaire, and the data acquired in hospital was subsequently added.

The pre-hospital information included: age, gender, previous history and number of episodes of variceal upper gastrointestinal bleeding.

The hospital information included: clinical data - mental status, presence of ascites; laboratory parameters - platelet count (normal range [NR] 140-440/mm³), serum creatinine (0.67-1.17mg/dL), albumin (NR 3.5-5.2g/dL), total bilirubin (NR 0.1-1.2mg/dL), sodium (NR 130-145mEq/l) and INR (NR 0.84-1.1); endoscopic data: grade of esophageal varices (grade I - small varices disappearing on insufflation; grade II - varices occupying <50% of the lumen, separated by normal mucosa, not disappearing on insufflation; grade III - varices occupying > 50% of the lumen, sometimes confluent (Tripathi et al 2015, Philips et al 2016).

We also recorded the presence of flattened varices of any grade, red marks, scarring, active bleeding wherever appropriate and the source of bleeding (esophageal or gastric varices)

The MELD and the Child-Pugh scores were also calculated.

The upper gastrointestinal endoscopies were performed using the Olympus Exera 3 endoscope.

All patients received a standard treatment during admission: vasoactive drugs (terlipressin, initial 48 hours: 2 mg intravenously every 4 hours until bleeding was controlled, maintenance: 1 mg intravenously every 4 hours to prevent rebleeding, for a duration of 2-5 days) in combination with endoscopic therapy and antibiotic therapy. For prevention of recurrent variceal hemorrhage, all patients received: first line therapy with a combination of non-selective beta-blockers (NSBB) and endoscopic variceal ligation (EVL). The NSBB (propranolol, nadolol or carvedilol) were dosed using a step-up approach to ensure a 25% reduction in the resting heart rate, while keeping it above 55 beats/min (Garcia-Tsao et al 2017).

Patients were followed up for 6 weeks, in order to monitor for failure to control bleeding and rebleeding. Failure to control bleeding and variceal rebleeding were defined using the Baveno V consensus (De Franchis 2015). Accordingly, failure to control bleeding was defined as the acute bleeding episode occurring within the first 5 days after the initial episode, and rebleeding was defined as bleeding occurring within 5 days-6 weeks after the initial haemorrhagic episode.

Failure to control bleeding was indicated by the occurrence of haematemesis (fresh blood, >100ml) more than 2 hours after vasoactive and endoscopic therapy, a decrease in haemoglobin levels of >3g over a 24-hour period in patients not receiving blood transfusion, hypovolemic shock, death or a decrease in systolic blood pressure below 90mmHg and an increased heart rate above 100beats per minute.

Rebleeding was indicated by the occurrence of haematemesis, melena, hemoglobin depletion, hemorrhagic shock, and the need for endoscopic therapy.

The statistical analysis was performed using the MedCalc Statistical Software version 17.8.5 (MedCalc Software bvba, Ostend, Belgium, <http://www.medcalc.org>, 2017). We characterized nominal variables using frequency and percentage and we expressed quantitative variables using the mean and standard deviation or the median and the 25th and 75th percentiles, when appropriate (we used to assess the normality of the distribution). We used the Mann-Whitney test to compare the continuous variables of both groups. We evaluated frequency differences between nominal variables using the chi-square test. The multivariate analysis was performed using binary logistic regression. We considered parameters with a p value of <0.05 statistical significant; these were included in univariate analysis. The prediction value of the score was assessed by using the area under the ROC (AUROC). We used a cut-off value in defining them. The cut-off value was chosen for maximum specificity and sensitivity. It was determined the cut-off value of the MELD score, creatinine and albumin, to increase the risk of failure to control bleeding.

Results

A total of 206 patients presented to the emergency department during the chosen time-frame. Of these, 21 patients were

Table 1. Characteristics of patients with variceal upper gastrointestinal bleeding and hepatic cirrhosis.

| Variables | | n=184 patients |
|---|--------------------|-------------------|
| Age (years) | | 58.87±11.97 |
| Gender | Women | 57 (31%) |
| | Men | 127 (69%) |
| History of variceal bleeding | | 77 (41.8%) |
| Number of episodes: | 1-3 episodes | 64 (83.1%) |
| | ≥ 4 episodes | 13 (16.9%) |
| Hepatic encephalopathy | | 55 (29.9%) |
| Ascites | | 136 (73.9%) |
| Cause of cirrhosis | Alcohol | 57.10% |
| | Viral infection | 25.50% |
| | Mixed | 10.30% |
| | Another cause | 7.10% |
| Platelets (no./mm ³) | ≤140.000 | 150 (81.5%) |
| | >140.000 | 34 (18.5%) |
| Serum albumin (g/dL) | | 3.2 (2.7; 3.5) |
| Serum bilirubin (mg/dL) | | 2.2 (1.4; 4.2) |
| INR (international normalized ratio) | | 1.66 (1.48; 2) |
| Sodium | | 140 (136; 143) |
| Creatinine (mg/dL) | | 0.75 (0.61; 1.01) |
| Creatinine (mg/dL) | | >1.5mg/dL |
| Child-Pugh classification | Child-Pugh A: | 35 (19%) |
| | Child-Pugh B: | 71 (38.6%) |
| | Child-Pugh C: | 78 (42.4%) |
| MELD score | | 16.5 (13; 21) |
| Source of variceal bleeding | Esophageal varices | 177 (96.2%) |
| | Gastric varices | 7 (3.8%) |
| Cherry red spots | | 142 (77.2%) |
| Scarring | | 21 (11.4%) |
| Active bleeding at upper gastrointestinal endoscopy | | 41 (22.3%) |
| Grade of esophageal varices: | grade I | 2 (1.1%) |
| | grade II | 96 (54.2%) |
| | grade III | 66 (37.3%) |
| | flattened | 13 (7.3%) |

excluded because the cause of variceal bleeding was prehepatic portal hypertension or because of a lack of endoscopic signs of upper gastrointestinal bleeding. As a result, the study included 184 patients.

The basic characteristics of patients with UGIB are presented in Table 1.

Failure to control bleeding occurred in 33 (17.9%) patients. Of these, 16 (48.5%) died in the first 5 days. The clinical and laboratory data of patients with failure to control bleeding are shown in Table 2.

We analysed the clinical and laboratory parameters possibly associated with failure to control bleeding. Hepatic encephalopathy, serum albumin level, creatinine level, INR, MELD score,

and the severity of esophageal varicose veins were significantly correlated with failure to control bleeding.

We found a MELD score cut-off of >25. Higher values increased the likelihood of failure to control bleeding (AUC 0.577, sensitivity 27.27%, specificity 90.07%, positive predictive value 37.45%, and negative predictive value 85.3%) (p=0.017).

For the serum albumin, the cut-off value for failure to control bleeding was <2.9g/dL (AUC 0.68, sensitivity 69.23%, specificity 69.7%, positive predictive value 47.06, negative predictive value 85.08) (p≤0.001).

The cut-off value for creatinine was >1.13mg/dL. Higher values increased the probability of failure (AUC 0.628, sensitivity 36.36%, specificity 85.43%, positive predictive value 35.23% and negative predictive value 86.02%) (p=0.007).

Table 2. Characteristics of patients with failure to control bleeding

| Variables | All patients, n=184 | | P | |
|---|--|------------------------------|--------------|-------|
| | Failure to control bleeding n=33 patients | No failure n=151 patients | | |
| Death | 16 (48.5%) | 0 | <0.001 | |
| Age, (years) | 61.42±10.41 | 58.43±12.22 | 0.194 | |
| Gender | Women | 10 (30.3%) | 47 (31.12%) | 1 |
| | Men | 23 (69.69%) | 104 (68.87%) | |
| History of variceal bleeding | 11 (33.33%) | 66 (43.7%) | 0.247 | |
| Number of episodes: | 1-3 episodes | 10 (90.9%) | 54 (81.81%) | 0.756 |
| | ≥ 4 episodes | 1 (9.09%) | 12 (18.18%) | |
| Hepatic encephalopathy | 17 (51.51%) | 38 (25.16%) | 0.003 | |
| Ascites | 26 (78.78%) | 110 (72.84%) | 0.628 | |
| Platelets(no./mm ³) | ≤140.000 | 24 (72.72%) | 126 (83.44%) | 0.234 |
| | >140.000 | 9 (27.27%) | 25 (16.55%) | |
| Serum albumin (g/dL) | 2.82 (2.4; 3.45) | 3.3 (2.8; 3.5) | 0.002 | |
| Serum bilirubin (mg/dL) | 2.6 (1.35; 5.65) | 2.1 (1.4; 4) | 0.403 | |
| INR (international normalized ratio) | 1.94 (1.51; 2.34) | 1.62 (1.47; 1.92) | 0.034 | |
| Sodium | 137.27±6.15 | 139.01±5.57 | 0.114 | |
| Creatinine (mg/dL) | 1.94 (1.51; 2.34) | 1.62 (1.47; 1.92) | 0.021 | |
| Creatinine (mg/dL) | >1.5mg/dL | 7 (21.21%) | 12 (7.94%) | 0.051 |
| | ≤1.5mg/dL | 26 (78.78%) | 139 (92.05%) | |
| Child-Pugh classification | Child-Pugh A: | 3 (9.09%) | 32 (21.19%) | 0.051 |
| | Child-Pugh B: | 10 (30.3%) | 61 (40.39%) | |
| | Child-Pugh C: | 20 (60.6%) | 58 (38.41%) | |
| MELD score | 19.64±7.79 | 17.22±5.91 | 0.046 | |
| Source of variceal bleeding | Esophageal varices | 33 (100%) | 144 (95.36%) | 0.448 |
| | Gastric varices | 0 | 7 (100%) | |
| Cherry red spots | 22 (66.66%) | 120 (79.47%) | 0.147 | |
| Scarring | 5 (15.15%) | 16 (10.59%) | 0.657 | |
| Active bleeding at upper gastrointestinal endoscopy | | 11 (33.33%) | 30 (19.9%) | 0.146 |
| | grade I | 1 (3.03%) | 1 (0.69%) | |
| | grade II | 13 (39.39%) | 83 (57.63%) | |
| | grade III | 12 (36.36%) | 54 (37.5%) | |
| | flattened | 7 (21.21%) | 6 (4.16%) | |

The Child-Pugh class association with active bleeding was then analysed in patients with failure to control bleeding, in comparison to those without failure, and the following results were obtained: Child A (3.03% vs. 3.11%); Child B (3.03% vs. 6.62%); Child C (4.89% vs. 8.15%) (p=0.081).

Variables showing statistical significance (MELD score, Child-Pugh class, hepatic encephalopathy, the severity of esophageal varices, creatinine, INR and albumin) were introduced in the multivariate analysis. Among these factors, creatinine and INR are included in the MELD score, so the multivariate analysis only included the MELD score. The Child-Pugh class was not used in the multivariate analysis, but some of its components

Table 3. Predictors for failure to control bleeding

| Variables | B | Odds ratio | 95% CI | P |
|------------------------|-------|------------|------------|-------|
| Hepatic encephalopathy | 0.681 | 1.977 | 0.79-4.88 | 0.14 |
| Albumin <2.9 | 0.942 | 2.566 | 1.08-6.09 | 0.033 |
| Esophageal varices | | | | 0.072 |
| Grade (1) | 0.341 | 1.406 | 0.57-3.43 | 0.455 |
| Grade (2) | 1.471 | 4.355 | 1.23-15.34 | 0.022 |
| MELD score >25 | 0.439 | 1.55 | 0.51-4.65 | 0.434 |

Table 4. Characteristics of patients with rebleeding

| Variables | | All patients, n=168 | | P |
|---|--------------------|-----------------------------|---------------------------------|--------|
| | | Rebleeding n=28 patients | No rebleeding n=140 patients | |
| Failure to control bleeding | | 9 (32.14%) | 8 (5.71%) | <0.001 |
| Age, mean \pm SD (years) | | 58.8 \pm 15.7 | 58.8 \pm 11.4 | 0.913 |
| Gender | Women | 7 (25%) | 47 (33.57%) | 0.506 |
| | Men | 21 (75%) | 93 (66.42%) | |
| History of variceal bleeding | | 12 (42.8%) | 60 (42.8%) | 1 |
| 1-3 episodes | | 9 (75%) | 50 (83.33%) | 0.784 |
| \geq 4 episodes | | 3 (25%) | 10 (16.66%) | |
| Hepatic encephalopathy | | 10 (35.71%) | 36 (25.71%) | 0.395 |
| Ascites | | 21 (75%) | 103 (73.51%) | 1 |
| Platelets (no./mm ³) | \leq 140,000 | 21 (75%) | 118 (84.28%) | 0.361 |
| | $>$ 140,000 | 7 (25%) | 22 (15.71%) | |
| Serum albumin (g/dL) | | 3.0 \pm 0.6 | 3.1 \pm 0.56 | 0.2 |
| Serum bilirubin (mg/dL) | | 2.7 (1.5; 5.45) | 2.05 (1.4; 3.97) | 0.295 |
| INR (international normalized ratio) | | 1.97 (1.58; 2.22) | 1.61 (1.46; 1.9) | 0.011 |
| Sodium | | 1.39 \pm 4.6 | 1.39 \pm 5.5 | 1 |
| Creatinine (mg/dL) | | 0.76 (0.6; 0.98) | 0.73 (0.61; 0.97) | 0.803 |
| Creatinine (mg/dL) | $>$ 1.5mg/dL | 2 (7.14%) | 12 (8.57%) | 1 |
| | \leq 1.5mg/dL | 26 (92.85%) | 128 (91.42%) | |
| Child-Pugh classification | Child-Pugh A: | 5 (17.85%) | 29 (20.71%) | 0.045 |
| | Child-Pugh B: | 6 (21.42%) | 60 (42.85%) | |
| | Child-Pugh C: | 17 (60.71%) | 51 (36.42%) | |
| MELD score, mean \pm SD | | 18.21 \pm 6.75 | 17.04 \pm 5.93 | 0.353 |
| Source of variceal bleeding | Esophageal varices | 25 (89.28%) | 136 (97.14%) | 0.167 |
| | Gastric varices | 3 (10.71%) | 4 (2.85%) | |
| Cherry red spots | | 20 (71.42%) | 113 (80.71%) | 0.396 |
| Scarring | | 5 (17.85%) | 13 (9.28%) | 0.315 |
| Active bleeding at the upper gastrointestinal endoscopy | | 5 (17.85%) | 31 (22.14%) | 0.801 |
| Grade of esophageal varices | grade I | 0 | 1 (0.73%) | 0.883 |
| | grade II | 13 (52%) | 78 (57.35%) | |
| | grade III | 10 (40%) | 50 (36.76%) | |
| | flattened | 2 (8%) | 7 (5.14%) | |

were: albumin and encephalopathy. Patients with grade I varicose veins, who experienced rebleeding and those under the age of 18 were also excluded.

Among the parameters studied, (hepatic encephalopathy, albumin, the severity of esophageal varices and MELD score), the severity of esophageal varices and hypoalbuminemia were found to be independent factors associated with failure to control bleeding (table 3).

Rebleeding occurred in 28 (16.7%) patients in the first 6 weeks. The factors influencing rebleeding are presented in Table 4.

The occurrence of rebleeding was analysed taking into account several clinical and lab parameters. Consequently, when comparing patients with rebleeding with patients without, we observed higher rates of rebleeding inpatients with a history of

variceal bleeding, in those with ascites, hepatic encephalopathy, hypoalbuminemia, coagulation disorders, higher Child-Pugh class, gastric varicose veins as the source of bleeding, severe esophageal varicose veins (grade III and flattened) and those with a higher MELD score. Of these, the Child-Pugh class and INR value were statistically significant. In the group of patients with rebleeding, those in Child-Pugh class C had significantly higher rates than those in class B and A (60.71% vs. 21.42% vs. 17.85%) (p=0.045). A cut-off value of 1.94 was calculated for INR, above which the likelihood of rebleeding increases (AUC 0.632, sensitivity 53.57%, specificity 76.92%, positive predictive value 29.38%, negative predictive value 90.23%) (p=0.011). Subsequently, based on these results and on the Child Pugh class, a comparison was made between the patients with active bleeding

Table 5. Predictors for rebleeding

| Variable | B | Odds ratio | 95% CI | P |
|------------------------------------|------|------------|------------|-------|
| Failure to control bleeding | 1.89 | 6.63 | 2.16-20.37 | 0.001 |
| INR>1.94 | 1.35 | 3.87 | 1.58-9.45 | 0.003 |

during endoscopy and those without rebleeding. We found the following results: Child-Pugh class A (3.57% vs. 3.57%), class B (3.57 vs. 7.14%) and class C (10.71% vs. 11.42%, respectively) ($p=0.165$).

Another evaluated parameter was the failure to control bleeding. Its impact on rebleeding was monitored. When compared to rebleeding without previous failure, it was observed that the rate of rebleeding was significantly higher when associated with failure (32.14% vs. 5.71%) ($p<0.001$).

The statistically significant variables were introduced in the multivariate analysis to assess the occurrence of rebleeding (Table 5). We only used the INR value in the multivariate analysis, and not the Child-Pugh score.

Failure to control bleeding and INR are independent factors associated with the likelihood of rebleeding (Table 5).

Discussion

In this study we analysed the clinical and laboratory parameters predicting failure to control bleeding and the occurrence of rebleeding in patients with cirrhosis and variceal UGIB. Many studies have shown the role of these parameters in the outcome of patients with variceal gastrointestinal bleeding. In the current study, failure to control bleeding occurred in 17.9% patients, 48.5% of whom died. In a study on 382 patients conducted in a hospital in India, failure to control bleeding was observed in 10.2% of these patients, and 30.7% of them died. In the same study, the rebleeding rate was 12.8% (Majid et al. 2009), compared to 16.7% in our study. Another study found a 12.4% rate of failure to control bleeding in 291 patients with cirrhosis and variceal haemorrhage in an Italian hospital (D'Amigo et al. 2003). In 1999, a study reported a 42% failure rate (Ben-Ari et al. 1999), and later, in 2003, another study observed a 15% and 16% failure rate, respectively (D'Amigo et al. 2003, Bambha et al. 2008).

In these studies, several prognostic factors were found to be involved in failure to control bleeding, such as hepatic encephalopathy, active bleeding at the time of endoscopy, the Child-Pugh score, platelet count, number of transfusions, or alcohol consumption (Biecker 2013). In our patients, the percentage of failure to control bleeding was slightly higher than in other studies. According to the factors reported in the literature, we also found that the presence of hepatic encephalopathy, the Child-Pugh score and active bleeding were predictive factors associated with failure to control bleeding, however only hepatic encephalopathy was statistically significant. Encephalopathy has been correlated with serum albumin levels, degree of varicose veins and the MELD score and it has a significant influence on the failure to control bleeding. The severity of liver disease, quantified by the MELD score and the Child-Pugh classification, or by their individual components, is acknowledged as a predictive factor for failure to control bleeding (Salvador et al. 2010). Therefore, the mean albumin cut-off associated with the

occurrence of failure might be less important as it is included in the Child-Pugh classification. Some studies, however, have reported that serum albumin levels <2.9 g/dL may increase the risk of failure to control bleeding (Hunter et al. 2013).

A MELD score >18 has been reported as one of the predictors of failure (Bambha et al. 2008). The MELD cut-off value found in our study was >19 . In other studies, involving 100 patients, the failure rate was 15% and one of the risk factors found was a MELD score >18.73 (Hunter et al. 2013, Reverter et al. 2014). In the recent years, few published studies have reached a consensus regarding the predictive factors for failure to control bleeding. On rebleeding, however, several complex studies have been performed lately. A study conducted on 136 patients in Korea over a 2-year period reported a 12.9% rebleeding rate (Lec et al. 2002). A study spanning 9 years, published in 2009, reported a 23% rebleeding rate (Tripathi et al. 2015). The main risk factors were the presence of ascites in 40% of cases and the coagulation anomalies. Of the patients who experienced rebleeding, 60% were in Child-Pugh class B.

A study performed on smaller groups of patients, reported the following factors as predictors of rebleeding: hepatic encephalopathy in 6% of cases, and severity of varicose veins in 36% (Charif et al. 2013). Another study, performed on 101 patients over a 2-year period, mentioned a 20.8% rebleeding rate, and the main risk factors were MELD score >18 , red signs and a hepatic venous pressure gradient (HVPG) >20 mmHg, while the presence of active bleeding at endoscopy, the Child-Pugh score, the number of transfusions performed and the cause of cirrhosis were not correlated with rebleeding (Zhao et al. 2014). The components of the Child-Pugh classification were individually monitored, but only a high INR was found to be a significant cause of rebleeding.

One of the limitations of our study is the relatively small number of patients included, due to the selected exclusion criteria. Also, the HVPG could not be measured in these patients. However, this study provides reliable data on the factors involved in the occurrence of failure to control bleeding and variceal rebleeding.

Conclusion

The predictive factors for failure to control bleeding in our group of patients with variceal bleeding were the presence of hepatic encephalopathy, a high MELD score, low serum albumin level, high serum creatinine and INR, and a higher severity grade of esophageal varices. Furthermore, the Child-Pugh score, a high INR and the failure to control bleeding were the predictors found for rebleeding after variceal haemorrhage.

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