Cellular and Molecular Biology

Journal homepage: www.cellmolbiol.org

Predictive factors for re-bleeding of esophageal varices in hospitalized patients

Han Yaru[1], ZuJin Mei[1], Li Kaixin[1], Chen Ruyue[1], Liu Mingshu[2*]

[1]Department of Vascular Surgery, The First Hospital of Hebei Medical University, Shijiazhuang, Hebei Province, 050000 China

[2]Liverish center, The First Hospital of Hebei Medical University, Shijiazhuang, Hebei Province, 050000, China

ARTICLE INFO

Original paper

Article history:
Received: July 18, 2021
Accepted: January 12, 2022
Published: February 28, 2022

Keywords:
Child Turcotte Pugh, Esophageal Varices, PAI-1, Predictive Factor, Re-bleeding

ABSTRACT

Bleeding due to esophageal varices is associated with high mortality and hospital costs. The incidence of morbidity and mortality can be reduced with appropriate treatment measures by identifying the predictors of re-bleeding at admission. Therefore, this study aimed to determine the risk factors for re-bleeding in hospitalized esophageal varices patients using factors included in the Child Turcotte Pugh (CTP) scoring system. In this cross-sectional study, 100 patients were evaluated for bleeding from esophageal varices. Some characteristics and variables were recorded, including age, gender, cause of disease, CTP classification score, and clinical, endoscopic, and laboratory findings. Patients were divided into two groups with and without bleeding from esophageal varices, and predictive factors were identified in both groups. Besides, a genetic predictor factor, i.e. plasminogen activator inhibitor type I (PAI-1), was evaluated by the Real-time PCR technique. Sixty-eight patients in the non-re-bleeding group with a mean age of 49.88 ± 16.42 years and 32 patients with a mean age of 54.22 ± 19.81 years were in the group with re-bleeding. Varicose vein size, encephalopathy, ascites, and CTP classification had a predictive effect on re-bleeding. Twelve people were in class A, 59 people in class B and 29 people in class C had CTP classification. The sensitivity of CTP, PAI-1 gene expression, and bilirubin in prediction through the ROC chart were calculated to be more than 85%, 61.4%, and 62%, respectively. In general, determining the degree and score of CTP at the time of referral of a patient with varicose hemorrhage provides valuable information on the risk of bleeding. Patients with class B CTP were strongly susceptible to re-bleeding in this study. Also, with increased bilirubin or ascites and more severe encephalopathy, the risk of bleeding is higher, and these people should be followed up.

DOI: http://dx.doi.org/10.14715/cmb/2022.68.2.26 **Copyright:** © 2022 by the C.M.B. Association. All rights reserved.

Introduction

Esophageal varices bleeding is an acute clinical problem with acute gastrointestinal bleeding with manifestations of hematoma (bloody vomiting), with or without melena or hematochezia (bloody stools). Hemodynamic instability is also typical (1). Bleeding from esophageal varices is the major complication of cirrhotic portal hypertension, accounting for 10 to 30% of all cases of upper gastrointestinal bleeding (2). Esophageal varices bleeding is associated with higher mortality and higher hospital costs than other causes of gastrointestinal bleeding. Esophageal varices occur in 30% of cirrhotic patients, responsible for 80 to 90% of their bleeding (3). About 30 to 50 percent of liver cirrhosis patients die within the first six weeks of varicose bleeding. Although the mortality rate has decreased with progress in managing varicose bleeding, it is unacceptably high (4).

Given the above facts, understanding the predictors of pathogenicity and mortality due to esophageal varices bleeding is very important. Many studies have been performed, and researchers have presented several predictive models to determine the risk factors in these patients (4-6). These proposed models are APACHE (Acute Physiology and Chronic Health Assessment), SOFA (Sequential Organ Failure Assessment), and AOSF (Acute Organ Failure Assessment) models (7-9). They are specific to patients admitted to ICU and cirrhotic patients with bleeding esophageal varices. It has been suggested that models such as the Model of End-Stage Liver Disease (MELD) and Child-Turcotte-Pugh (CTP) be used in cirrhotic patients (10). The BLATCHFORD model is another type that considers the upper gastrointestinal tract bleeding as a whole. Another scoring system, Rokal, is designed for upper hemorrhage with subtypes of peptic ulcer and esophageal varices. The NICE National Intensive Care Evaluation Score is another indicator assessed based on patients' clinical status by CTP classification

*Corresponding author. E-mail: liumingshu0817@163.com

and endoscopic profile of esophageal varices (11).

In addition to the mentioned factors, genetic factors are also important in predicting the re-bleeding of esophageal varices today (12). One of these factors is plasminogen activator inhibitor type I (PAI-1) (13). PAI-1 is a glycoprotein that has an inhibitory effect on plasminogen activator, preventing the formation of plasmin and thus preventing hydrolysis of clots in blood vessels (14). On the other hand, studies have shown that increasing the amount of this glycoprotein in the blood prevents sudden bleeding. Therefore, it can be used as a genetic predictor for hemorrhage (13-15).

This study aimed to determine the predictors of the risk of re-bleeding in hospitalized patients due to bleeding from esophageal varices. In this study, the factors involved in the Child-Pugh scoring system have been used. The Child Turcotte Pugh (CTP) scoring system was initially designed to determine emergency and elective surgery mortality in cirrhotic patients. Still, it is now used to determine the prognosis and severity of treatment and the need for liver transplantation (16). Besides, a genetic predictor factor, i.e. PAI-1, was used for more evaluations.

Materials and methods

Studied patients

This study was a cross-sectional study in which 100 patients with gastrointestinal bleeding due to esophageal varices hospitalized were evaluated. Patients were excluded from the study due to non-esophageal bleeding (bleeding from gastric varicose veins), other concomitant lesions such as ulcers and erosions that may be the source of bleeding, a history of previous anticoagulants and antihypertensive drugs, and lack of antihypertensive medications.

These patients underwent endoscopy within 24 hours after hospitalization, and some demographic information of each patient was confirmed along with the initial clinical and laboratory findings of the disease.

Clinical and laboratory evaluations

Clinical findings, including ascites, encephalopathy, hypotension, and shock, were evaluated. A pulse of more than 100 beats per minute and systolic blood pressure of less than 100 mm Hg before endoscopy was considered shocks. Ascites were determined by clinical examination using Ballotman and Shifting Dullness tests. Table 1 was used to classify encephalopathy in the first 6 hours after admission. Hypertension was assessed by repeated measurement of systolic and diastolic pressure during hospitalization before endoscopy and treatment. Systolic pressure less than 100 mm Hg was considered hypotension. Observation of recent bleeding stigmata (black clot on varicose veins) or direct bleeding from the esophagus or blood in the stomach and the absence of any reason for bleeding other than esophageal varices and varicose veins were considered. These patients using Sclerotherapy were treated with a sclerosing agent (rhombus 3% and absolute alcohol of equal volume) or a ligation bandage based on the current condition (possibility of bandaging). The simultaneous presence of gastric varicose veins in patients was also evaluated. In this study, obvious bleeding after initial amputation or hypotension after initial resuscitation, or a decrease in hemoglobin of more than two grams within 24 hours was considered hemorrhage. The size of varicose veins at the time of endoscopy was classified into small and large groups, respectively, based on the grade of 3, 2, 1, or 4, respectively. After endoscopy, the patients underwent an ultrasound of the liver and bile ducts, and the size of the liver was divided into large and small and large (more than the standard size of the liver ultrasound).

Diagnosis of liver cirrhosis in this study was made by clinical and laboratory findings related to cirrhosis, a history of varicose veins or ascites without other etiology, and the presence of at least three individuals less than 5 mg/day. Total more than 2 mg/dl, alkaline phosphatase more than 120 international units per liter, AST and ALT more than 40 international units per liter, and PT elongation at least 4 seconds longer than control.

In this study, the diagnosis of liver cirrhosis was not performed by liver biopsy and was not diagnosed. Finally, laboratory findings were determined, including bilirubin, albumin, platelets, ALT, AST, INR, and the amount of blood transfused in all patients. Information from clinical findings and laboratory findings were used for CTP scoring based on Table 1. The CTP score is calculated by adding the scores of each of the five factors and can vary between 5 and 15. After summing the scores of each

patient, scores 5 and 6 are in Class A, scores 7 to 9 are in Class B, and scores 10 to 15 are in Class C of the CTP classification. Finally, patients with hemorrhage from varicose veins who undergo re-bleeding during hospitalization were treated as a group with re-bleeding. Patients with hemorrhage from varicose veins who did not undergo re-bleeding during hospitalization were considered the control group.

Table 1. Child-Turcotte-Pugh classification of cirrhosis

Factor	1	2	3
Bilirubin (mg/dL)	2.0 >	2.0 – 3.0	3.0 <
Albumin (g/dL)	3.5 <	0.3 – 3.5	0.3 >
Prothrombin time (INR)	1.7 >	1.7 – 2.3	2.3 <
Ascites	None	Medium (drug controlled)	Severe (not well controlled)
Hepatic encephalopathy	None	Medium (drug controlled)	Severe (not well controlled)

Genetics evaluations

In this part, 100 blood samples were taken from patients. 100 µl of whole blood was first placed in a 1.5 ml microtube to extract RNA from the blood. RNA extraction and cDNA synthesis were performed by RNX-Plus kit (Qiagen, South Korea) and Vivantis cDNA synthesis kit (Malaysia). Specific primer pairs were designed to amplify the sequences of Plasminogen Activator Inhibitor 1 (PAI-1) and GAPDH (internal control) genes. The primers were designed using Gene Runner 5 and Primer Express 1.0.3 software. Table 2 shows the sequence of primers for the real-time PCR technique.

Table 2. The Primer sequences of PAI-1 and GAPDH genes for the real-time PCR technique

Gene	Primer Sequence (5'-3')	Product size
PAI-1 (Forward)	TCAGGCTGACTTCACGAGTCTTT	182bp
PAI-1 (Reverse)	CTGCGCGACGTGGAGAG	
GAPDH (Forward)	ATGGAGAAGGCTGGGGCT	121bp
GAPDH (Reverse)	ATCTTGAGGCTGTCATACTTCTC	

The final volume for each reaction was 20µl, including 100ng of Power SYBR® Green PCR Master, 1µl of cDNA, 10µl of Master Mix (Applied Biosystems, USA), 10mmol/µl of primers, and 6µl of nuclease-free water. Temperature protocol was performed as initial denaturation at 95°C for 3 minutes. Subsequently, 45 cycles were performed as denaturation at 95°C for 5 seconds and annealing at 60°C for 30 seconds. Reproduction analysis and melting curve were performed using Applied Biosystems 7500. Then gene expression diagram was drawn using Prism 5 GraphPad software.

Statistical analysis

Descriptive statistical methods (frequency percentage and mean ± standard deviation) were used to analyze the data. The Chi-square test was used to evaluate the relationship between qualitative variables and re-bleeding. The logistic regression model was used to predict the qualitative factors and CTP scoring in re-bleeding. Drawing the ROC curve and calculating the area under the curve were used to determine the sensitivity and specificity of the CTP classification method in predicting re-bleeding (qualitatively dependent variable). P <0.05 and 95% confidence interval were considered in all cases.

Results and discussion

In this study, 100 patients admitted to the gastrointestinal ward were studied. Sixty-seven patients were male, and 33 were female, with a mean age of 51.27 ± 17.59 years. Of the 100 patients admitted, 32 with a mean age of 54.22 ± 19.81 years had recurrent bleeding during hospitalization and 68 patients with a mean age of 49.88 ± 16.42 years had no active gastrointestinal bleeding. Information on clinical, endoscopic, and ultrasound findings and their association with recurrent hemorrhage is summarized in Table 3. Among the studied variables in this table, encephalopathy (P<0.0001), hypotension (p=0.03), ascites (P<0.0001), and varicose size (p=0.046) had a statistically significant relationship.

Among the quantitative laboratory indices, the relationship between bilirubin level [OR = 0.64, CI 95% (0.24-0.9), P = 0.55], INR [OR = 0.62, CI 95% (3.2-1.3), P = 0.34], and albumin [OR=1.31, CI 95% (0.55-2.18), P=0.38] with the incidence of recurrent bleeding from varicose veins was not statistically significant (Table 4).

The Sensitivity results of these three laboratory factors (i.e. bilirubin, albumin, and INR) through ROC, the sensitivity value for albumin were 62%. Albumin was the only laboratory factor with high sensitivity. Encephalopathy and ascites were significantly associated with the incidence of varicose re-bleeding as a predictor. In this study, 12 (12%) were CTP class A, 59 (59%) were CTP class B, and 29 (29%) were CTP class C. There was a very strong correlation between the re-bleeding rate with the CTP classification (P <0.0001). The sensitivity of CTP in predicting re-bleeding by ROC was 58%, indicating

the ability to classify and score in predicting re-bleeding (Figure 1). Also, the highest sensitivity (84%) was found for CTP class B. The area under the ROC curve was 85% in patients with re-bleeding.

Table 3. Clinical, endoscopic, and sonographic findings and their association with re-bleeding

Variable	With re-bleeding	Without re-bleeding	P-value
Gender			
Female	12 (37.5%)	21 (30.9%)	0.51
Male	20 (62.5%)	47 (69.1%)	
Previous bleeding history			
Yes	26 (81.2%)	49 (72.1%)	0.32
No	6 (18.8%)	19 (27.9%)	
Treatment history			
Band	6 (18.8%)	12 (17.6%)	0.89
Sclerotherapy	26 (81.2%)	56 (82.4%)	
Encephalopathy			
Yes	7 (21.9%)	1 (1.5%)	<0.0001
No	25 (78.1%)	67 (98.5%)	
Ascites			
Yes	18 (56.2%)	11 (16.2%)	<0.0001
No	14 (34.8%)	57 (83.8%)	
Hypotension			
Yes	17 (53.1%)	22 (32.4%)	0.03
No	15 (46.9%)	46 (67.6%)	
Port hypertension			
Yes	1 (3.1%)	4 (5.9%)	-
No	31 (96.9%)	64 (94.1%)	
The primary cause of the disease			
HBV	6 (18.8%)	18 (26.5%)	-
HCV	4 (12.5%)	7 (10.3%)	
Other cases	22 (68.8%)	43 (63%)	
Varicose size			
Little	7 (21.9%)	28 (41.2%)	0.046
big	25 (78.1%)	40 (58.8%)	
Simultaneous esophageal and gastric varices			
Yes	6 (18.8%)	15 (22.1%)	-
No	26 (81.2%)	53 (77.8%)	
Red Color Sign			
Yes	14 (43.8%)	18 (26.5%)	-
No	18 (56.2%)	50 (73.5%)	
Liver size on ultrasound			
Little	16 (50%)	20 (29.4%)	-
normal	15 (46.9%)	41 (60.3%)	
big	1 (3.1%)	7 (10.3%)	

Table 4. Results of a regression model based on predictor variables

	With Re-bleeding Group	Without Re-bleeding Group	OR	P-value
Bilirubin	4.69 ± 1.1	3.24 ± 1.7	0.64 (0.24-0.9)	0.55
Albumin	2.70 ± 0.72	2.94 ± 0.67	1.31 (0.55-2.18)	0.38
INR	1.75 ± 0.16	1.5 ± 0.47	0.68 (0.3-2.1)	0.34

According to the results of PAI-1 gene expression, the sensitivity of PAI-1 in predicting re-bleeding by ROC was 61.4%, indicating the ability to classify and score in predicting re-bleeding (Figure 2). The area under the ROC curve was 64.5% in patients with re-bleeding.

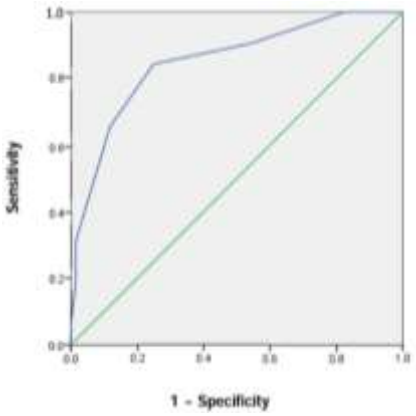

Figure 1. ROC curve according to CT classification

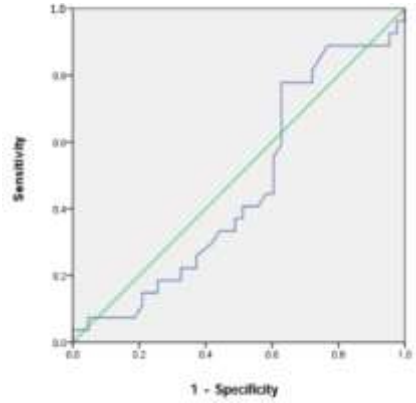

Figure 2. ROC curve according to PAI-1 gene expression classification

Bleeding due to esophageal varices is associated with higher mortality and hospital costs than other causes of gastrointestinal bleeding (1). Suppose the predictors of re-bleeding can be identified as the leading cause of mortality during hospitalization (17). Appropriate treatment measures such as hospitalization in the relevant wards (general, gastrointestinal, and ICU), appropriate treatment measures, pathogenicity, and death are reduced. In the present study, re-bleeding was observed in 6% of patients correlated with encephalopathy, ascites, hypotension, and varicose size. Still, other variables such as the history of previous bleeding, cause of cirrhosis, type of treatment performed, and hypertension were not associated with hypertension. In Schmassmann *et al*. study (18), re-bleeding was reported in 67%. In another study (19), 86.6% of patients had re-bleeding, which is more than our study. However, in Lee *et al*. (20) analysis, the bleeding rate was 12.9%, less than in the present study. In the study of Krige *et al*. (21), bleeding was observed in 36.6% of patients. In this study,

sclerotherapy was evaluated as effective in preventing re-bleeding.

In Schmassmann *et al*. (18) and Varghese *et al*. (22) studies, as in our research, there is no association between the cause of cirrhosis and bleeding. But this relationship has been reported in the study of Tesdal *et al*. (23). Encephalopathy and ascites have a predictive effect on the recurrence of bleeding in the present study, but no such relationship has been reported in the studies of Schmassmann *et al*. (18) and Abraldes *et al*. (24). Among the laboratory variables with the pro-albumin effect, it had more than 62% sensitivity. There was no association between prothrombin time and bilirubin level with re-bleeding. These results are similar to those of Benedeto-Stojanov *et al*. (19). According to the results of this study, the CTP classification was very strongly associated with re-bleeding, which was the most sensitive (more than 84%) to class B CTP.

The CTP score for the case and control groups was 10.06 ± 1.81 and 7.73 ± 1.39, respectively. The sensitivity of CTP in predicting hemorrhage through ROC was calculated to be above 85%, indicating the ability to classify and score in predicting hemorrhage. In another study, the CTP scores in the case and control groups were 7.3 ± 1.39 and 8.5 ± 1.8, respectively (25).

In the study of Schmassmann *et al*. (18), in the case group, the percentage of patients in CTP class A was 50%, CTP class B was 17%, and CTP class C was 33%. The non-bleeding group was 80%, 20%, and 0%, respectively. In this study, no correlation was found between CTP classifications and re-bleeding. Tesdal *et al*. (23) noted that no significant correlation was found between the incidence of re-bleeding and CTP scores and classes. In Tayyem *et al*. (26) study, CTP Class A was 73.7% and 29.1% respectively. Class B was 26.3% and 66.4%, respectively, and class C was 0% and 4.5%, respectively. In this study, CTP class B was effective in determining re-bleeding. In another study, inconsistent with our findings, it was found that the highest risk of re-bleeding was in CTP class C (27). Patch *et al*. (28) stated in a review study that patients with class C CTP had lower-than-expected re-bleeding rates, which is consistent with our findings.

According to the results of PAI-1 gene expression, the sensitivity of PAI-1 in predicting re-bleeding was 61.4%, indicating the ability to classify and score in predicting re-bleeding. But CTP was a better factor in diagnosing re-bleeding than PAI-1 gene expression because it was a cheaper method and had a faster and more accurate answer.

Determining the degree and score of CTP at the time of patient referral with varicose bleeding is very valuable. Our study also showed that patients with class B CTP are prone to re-bleeding. In these patients, appropriate preventive measures should be taken immediately, and continuous observation should be performed. The predictive effect of encephalopathy and ascites on varicose vein re-bleeding has also been observed. More severe ascites and encephalopathy increase the risk of bleeding. Preventive and conservative measures should also be taken for these individuals.

Acknowledgments

The authors are thankful to the higher authorities for the facilities provided.

Authors' contribution

This study was done by the authors named in this article, and the authors accept all liabilities resulting from claims which relate to this article and its contents.

Interest conflict

The authors declare that they have no conflict of interest.

Funding

The study foundered by Hebei Province 2019 Medical Science Research Project No. 20191539.

Availability of data and materials

The data used to support the findings of this study are available from the corresponding author upon request.

Statements and Declarations

The author declares that no conflict of interest is associated with this study.

References

1. Sharma M, Singh S, Desai V et al. Comparison of therapies for primary prevention of esophageal variceal bleeding: a systematic review and network meta-analysis. Hepatology 2019; 69(4): 1657-1675.

2. Garbuzenko DV, Arefyev NO. Primary prevention of bleeding from esophageal varices in patients with liver cirrhosis: An update and review of the literature. J Evid Based Med 2020; 13(4): 313-324.
3. Rodrigues SG, Cárdenas A, Escorsell À, Bosch J. Balloon tamponade and esophageal stenting for esophageal variceal bleeding in cirrhosis: a systematic review and meta-analysis. Semin Liver Dis 2019; 39(02): 178-194.
4. Molleston JP, Bennett Jr WE. Mortality, risk factors and disparities associated with esophageal variceal bleeding in children's hospitals in the US. J Pediatr 2021; 232: 176-182.
5. Dueñas E, Cachero A, Amador A et al. Ulcer bleeding after band ligation of esophageal varices: risk factors and prognosis. Dig Liver Dis 2020; 52(1): 79-83.
6. Aziziaram Z. C3953T genetic variation in interleukin 1β and idiopathic male infertility: a systematic review and meta-analysis. Cent Asian J Med Pharm Sci Innov 2021; 1(6): 242-249.
7. Akavipat P, Thinkhamrop J, Thinkhamrop B, Sriraj W. Acute physiology and chronic health evaluation (APACHE) II score–the clinical predictor in neurosurgical intensive care unit. Acta Clin Croat 2019; 58(1): 50.
8. Jentzer JC, Bennett C, Wiley BM et al. Predictive value of the sequential organ failure assessment score for mortality in a contemporary cardiac intensive care unit population. J Am Heart Assoc 2018; 7(6): e008169.
9. Lee TK, Han MS, Lee SK, Moon BJ, Lee JK. Outcomes of patients undergoing anterior screw fixation for odontoid fracture and analysis of the predictive factors for surgical failure. Neurospine 2020; 17(3): 603.
10. Tseng Y, Li F, Wang J et al. Spleen and liver stiffness for noninvasive assessment of portal hypertension in cirrhotic patients with large esophageal varices. J Clin Ultrasound 2018; 46(7): 442-449.
11. Hegab AM, Luketic VA. Bleeding esophageal varices: how to treat this dreaded complication of portal hypertension. Postgrad Med 2001; 109(2): 75-89.
12. Yang YY, Hou MC, Lin MW et al. Combined platelet count with s CD 163 and genetic variants optimizes esophageal varices prediction in cirrhotic patients. J Gastroenterol Hepatol 2013; 28(1): 112-121.
13. Yun JW, Kim BI, Chun HB et al. Fibrinolytic activities and their relations to esophageal variceal bleeding in patients with liver cirrhosis. Korean J Gastroenterol 2004; 43(6): 349-354.
14. Primignani M, Dell'Era A, Bucciarelli P et al. High-D-dimer plasma levels predict poor outcome in esophageal variceal bleeding. Dig Liver Dis 2008; 40(11): 874-881.
15. D'Amico M, Pasta F, Pasta L. Thrombophilic genetic factors PAI-1 4G-4G and MTHFR 677TT as risk factors of alcohol, cryptogenic liver cirrhosis and portal vein thrombosis, in a Caucasian population. Gene 2015; 568(1): 85-88.
16. Kaplan DE, Dai F, Aytaman A et al. Development and performance of an algorithm to estimate the Child-Turcotte-Pugh score from a national electronic healthcare database. Clin Gastroenterol Hepatol 2015; 13(13): 2333-2341.
17. Al-Obaid LN, Bazarbashi AN, Cohen ME et al. Enteric tube placement in patients with esophageal varices: Risks and predictors of postinsertion gastrointestinal bleeding. JGH Open 2020; 4(2): 256-259.
18. Schmassmann A, Zuber M, Livers M, Jäger K, Jenzer H, Fehr H. Recurrent bleeding after variceal hemorrhage: predictive value of portal venous duplex sonography. Am J Roentgenol 1993; 160(1): 41-47.
19. Benedeto-Stojanov D, Nagorni A, Bjelaković G, Milanović J, Stojanov D. Predictive factors of bleeding from esophageal varices in patients with liver cirrhosis and portal hypertension. Med Biol 2006; 13(3): 164-167.
20. Lee JY, Lee JH, Kim SJ et al. Comparison of predictive factors related to the mortality and rebleeding caused by variceal bleeding: Child-Pugh score, MELD score, and Rockall score. Korean J Hepatol 2002; 8(4): 458-464.
21. Krige J, Bornman P, Goldberg P, Terblanche J. Variceal rebleeding and recurrence after endoscopic injection sclerotherapy: a prospective evaluation in 204 patients. Arch Surg 2000; 135(11): 1315-1322.
22. Varghese J, Cherian J, Solomon R, Jayanthi V. Predictors of variceal bleed among patients with liver cirrhosis in the era of sclerotherapy. Singapore Med J 2008; 49(3): 239.
23. Tesdal IK, Filser T, Weiss C, Holm E, Dueber C, Jaschke W. Transjugular intrahepatic portosystemic shunts: adjunctive embolotherapy of gastroesophageal collateral vessels in the prevention of variceal rebleeding. Radiology 2005; 236(1): 360-367.
24. Abraldes JG, Villanueva C, Bañares R et al. Hepatic venous pressure gradient and prognosis in patients with acute variceal bleeding treated with pharmacologic and endoscopic therapy. J Hepatol 2008; 48(2): 229-236.
25. Chen PH, Chen WC, Hou MC et al. Delayed endoscopy increases re-bleeding and mortality in patients with hematemesis and active esophageal variceal bleeding: a cohort study. J Hepatol 2012; 57(6): 1207-1213.
26. Tayyem O, Bilal M, Samuel R, Merwat SK. Evaluation and management of variceal bleeding. Dis Mon 2018; 64(7): 312-320.
27. Wong MW, Chen MJ, Chen HL et al. Application of chronic liver failure-sequential organ failure assessment score for the predication of mortality after esophageal variceal hemorrhage post endoscopic ligation. PLoS One 2017; 12(8): e0182529.
28. Patch D, Armonis A, Sabin C et al. Single portal pressure measurement predicts survival in cirrhotic patients with recent bleeding. Gut 1999; 44(2): 264-269.