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A study on two kinds of scoring models in predicting the degree of esophageal varices and bleeding

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Abstract. – OBJECTIVE: This study aims to investigate the value and determine the accuracy of two kinds of scoring models in predicting the degree of esophageal varices (EV) and esophageal variceal bleeding (EVB) in patients with liver cirrhosis (LC).

PATIENTS AND METHODS: A total of 189 patients with LC, who underwent esophagogastroduodenoscopy (EGD), color Doppler ultrasound (CDU), and computed tomography (CT), were retrospectively analyzed. Then, the routine blood examination, liver function test, M-index of the spleen in CT, EGD, and CDU results were recorded. According to the EGD result, these patients were divided into five groups: varicose bleeding group, severe varices group, moderate varices group, mild varices group, and no varices group. Then, the receiver operating characteristic curves of all predicting parameters studied were respectively drawn, the area under the receiver operating characteristic curves were calculated, and the predictive value of EV and EVB was evaluated.

RESULTS: The area under the receiver operating characteristic curve of the VAP score model and Plt/S-D score model was 0.901 and 0.835, respectively. The VAP score model cut-off value of 461.5 for predicting moderate esophageal varices (MoEV), severe esophageal varices (SEV), and EVB has a specificity and sensitivity of 100% and 68.7%, respectively, while the Plt/S-D score model cut-off value of 835.5 for predicting MoEV, SEV, and EVB has a specificity and sensitivity of 95.1% and 58.2%, respectively.

CONCLUSIONS: These two kinds of scoring models can predict the degree of esophageal varices and bleeding in liver cirrhosis patients and has good predictive accuracy.

Key Words:
Scoring models, Esophageal varices, Varicose bleeding, Cirrhosis.

Introduction

In liver cirrhosis (LC) patients, portal hypertension mainly manifests as esophagogastric varices (EGVs), hypersplenism, and ascites. Among these, EGVs are the main manifestation of portal hypertension, and the main cause of death. According to statistics, EGVs can be observed in approximately 50% of LC patients. Patients without varicose veins develop varicose veins at a rate of 5% a year. The varicose vein of the venule (≤5 mm in diameter of the varicose vein) also develops from 5% to 12% per year to the middle or varicose veins of the vena cava (the diameter of the varicose vein is >5 mm). The annual incidence of varicose veins is 5-15%. Esophageal variceal bleeding (EVB) can spontaneously stop in 40% of patients. Although the treatment of EGV bleeding and the prevention of EGV hemorrhage have significantly improved in recent years, the mortality rate in six weeks can still reach up to 20%, and the re-bleeding rate of untreated patients remains at approximately 60%[1,2]. Although esophagogastroduodenoscopy (EGD) is the gold standard for diagnosing EGVs, in recent years, non-invasive methods to diagnose EGVs can reduce the cost and discomfort of some patients, and many scholars have begun to research on more accurate EGV prediction non-invasive methods. Therefore, it is of great clinical value to develop an accurate, practical, and repeatable non-invasive examination method for predicting the degrees of EGVs and bleeding in LC that allow for the good compliance of patients. The present study mainly uses two kinds of scoring models to predict the degree of esophageal varices (EV) and risk of hemorrhage and to evaluate the accuracy of the prediction.

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Patients and Methods

Main Materials

The materials used were: EGD purchased from Olympus 260 (Olympus, Tokyo, Japan); computed tomography (CT); Brilliant 16 (Philips, Amsterdam, The Netherlands); Color Doppler Ultrasound (CDU); HI Vision Preirus (Hitachi, Tokyo, Japan).

Subject of the Study

There were 189 patients with LC. Among these patients, 151 patients were male, and 38 patients were female. Furthermore, among these patients, 25 patients had EVB, 50 patients had severe esophageal varices (SEV), 47 patients had moderate esophageal varices (MoEV), 28 patients had mild esophageal varices (MiEV), and 39 patients had no esophageal varices (NEV). A total of 189 patients with LC underwent EGD and received CDU and CT examinations during their hospitalization in Dalian Sixth People's Hospital from January 1, 2012 to November 1, 2017. The age, gender, degree of EV, level of albumina, blood platelet count (BPC), m-index of the spleen, m-index, and EGD EV diagnosis were determined.

The present study was approved by the Ethics Committee of Dalian Sixth People's Hospital. A written informed consent was obtained from each participant.

Inclusion Criteria

The inclusion criteria were as follows: patients diagnosed with LC, that is, patients with a history that led to LC, such as viral hepatitis and long-term heavy drinking; patients with a clinical manifestation of liver dysfunction or portal hypertension, and had a chemical index of liver function decompensation, such as decreased serum albumin, increased bilirubin, and prolonged prothrombin time; patients with LC according to CDU or CT, and EV revealed by EGD, excluding pre-hepatic portal hypertension and post-hepatic portal hypertension (the gold standard for diagnosing this disease is liver biopsy examination, which presents as a form of pseudo lobule); patients who were admitted to the hospital within 48 hours after onset, underwent EGD, and were evaluated using the endoscopic EV diagnostic criteria based on the endoscopic diagnosis and treatment for gastrointestinal varices and bleeding[3]; patients diagnosed according to the diagnostic criteria of EGV rupture hemorrhage; patients who underwent an emergency endoscopic examination within 48 hours of bleeding; patients whose esophageal varicose hemorrhage (blood seepage) could be observed through an endoscope, patients who had a white thrombus in the hemorrhage of EV, or patients with who had blood clots on the surface, or thrombosis or scab formation. Patients with other potential bleeding sites and other bleeding lesions were excluded.

Exclusion Criteria

Patients with the following symptoms were excluded: patients who were previously administered with beta-blockers medication or blood transfusion, non-cirrhosis patients who had EV rupture hemorrhage, patients with isolated gastric varices and hemorrhage, patients with liver cancer and other malignant tumors, patients with other non-liver diseases that can cause platelet abnormalities, patients who underwent a liver or spleen intervention operation, and patients who received a trans jugular intrahepatic portosystemic shunt (TIPS).

Laboratory Observation Parameters

The diagnosis of patients, and the relevant results of the blood routine test, liver function, EGD, CDU, and CT were recorded. On the basis of the above laboratory examinations and special examinations, the following indexes were calculated: varices and portal hypertensive gastropathy scoring system: VAP=[A(g/dl)×BPC(/mm^3)]/[m-index(cm^3)]; M-index: the splenic multidimensional index, or spleen volume, which is the length, width and thickness of the spleen measured under CT scan; platelet count and spleen diameter ratio: (Plt/S-D)=BPC(/mm^3)/spleen diameter (cm); the diameter of the spleen: the ratio of the maximum length of the spleen to the two levels measured by abdominal CDU.

Statistical Analysis

Categorical variables were compared using X^2-test. The man variables between two groups were compared using Student's *t*-test, the mean variables among multi-groups were compared using one-way analysis of variance, and the post-hoc test of Bonferroni; Duncan test was used to validate ANOVA. The area under the receiver operating characteristic curve (AUROC) was used to select the parameter that revealed a good discriminative power for predicting the presence of EV. In addition, the receiver operating characteristic (ROC) curve was used to determine the cut-off value with the best sensitivity and specificity.

Data were presented as mean ± standard deviation (SD), and each odds ratio (OR) and AUROC curve were presented together with its 95% confidence interval (95% CI). A two-sided $p<0.05$ was considered statistically significant for all analyses. When AUC<0.5 was not in accordance with the real situation, it was rarely observed in the actual situation[4], and the AUC was compared with the z-test. $p<0.05$ was considered statistically significant. The data were analyzed using Statistical Product and Service Solution (SPSS 13.0, Chicago, IL, USA).

Results

Comparison of all Parameters Among all Groups

Table I presents the comparison of groups in each parameter, according to the EV degree. The statistical analysis revealed that there was a significant difference among groups, while age and gender were not statistically significant. The comparison of BPC variables between groups revealed significant differences between the EVB group and the SEV group, NEV group, and the other four groups. In each group, albumin was detected, and the difference in albumin between the NEV group and MiEV group was not statistically significant ($p=0.192$). When compared with the other three groups, there were significant differences between MiEV and MoEV in the SEV group, and the comparison between the EVB groups also had a significant difference ($p<0.05$). There was no significant difference between the SEV group and EVB group ($p=0.938$), and there was no statistically significant difference between the MoEV group and SEV group ($p=0.766$) in m-index variables. However, there was a significant difference between the other groups ($p<0.05$). There was no statistically significant difference among the EVB group, MoEV group, and SEV group ($p>0.05$), but there was a significant difference between the other groups ($p<0.05$). The VAP scoring model had no statistically significant difference among each group in the EVB group, MoEV group, and SEV group ($p>0.05$). However, there was a statistically significant difference when compared to the other groups ($p<0.05$) (Table I).

Comparison of Prediction Models Among the Recombined Groups

There were no significant statistical differences among the five groups above. Hence, the Plt/S-D model and VAP scoring models were divided into two groups, namely, the MoEV+SEV+EVB group and NEV+MiEV group. By further statistically analyzing these parameters, it was found that there were statistically significant differences among groups ($p<0.05$). Furthermore, the difference between the Plt/S-D scoring model and VAP score model was statistically significant ($p<0.05$, 95% CI: 633.7998-405.9910). The Plt/S-D scoring model and VAP scoring model were significantly lower in the MoEV+SEV+EVB group than in the NEV +MiEV group (Table II).

Comparison of ROCs in Predicting Models from MoEV and SEV to EVB

In the ROC curve (Figure 1), the AUROC of the VAP scoring model for predicting MoEV, SEV, and EVB was 0.901 (Table III; 95% CI: 0.853-0.949) in the present study population, which was higher than that for the Plt/S-D model (AUROC=0.838;

Table I. The comparison of all parameters among all groups ($\bar{x}\pm s$).

	Varicose bleeding group	Severe varicose group	Moderate varicose group	Mild varicose group	No varicose group
Gender (male, %)[a]	21 (84.0)	40 (80.0)	39 (83.0)	23 (82.1)	28 (71.8)
Age (year)[a]	57±10.6	55.5±9.4	52.6±9.0	52.3±10.2	45.3±12.1
BPC (10^3/mm^3)	87.8±35.9[b]	61.3±21.2	65.0±27.4	81.5±33.5	138.1±51.9
A (g/L)	30.9±5.8[c]	32.5±5.8	36.8±6.6	37.4±6.3	40.9±5.8
M-Index (cm^3)	2329.2±696.3	1745.4±1028.0[d]	1451.0±916.2	931.8±309.6	440.4±287.2
Plt/S-D	550.5±248.5	391.7±168.5[e]	447.5±214.9	620.3±273.5	1232.9±537.8
VAP scoring system	133.3±83.1	159.4±103.4[f]	211.8±116.6	377.3±224.3	1734.3±1073.4

NOTE: compared with the each group, [a]$p>0.05$; compared with moderate varicose group and mild varicose group, [b]$p>0.05$; compared among the rest of each groups, $p<0.05$; compared with Severe varicose group, [c]$p>0.05$; compared among the rest of each groups, $p<0.05$; compared with moderate varicose group, [d]$p=0.766$; compared among the rest of each groups, $p<0.05$; compared with moderate varicose group and varicose bleeding group, [e]$p>0.05$; compared among the rest of each groups, $p<0.05$; compared with moderate varicose group and varicose bleeding group, [f]$p>0.05$; compared with moderate varicose group and varicose bleeding group, $p<0.05$.

Table II. The comparison of Plt/S-D and VAP scoring system between the recombined groups.

Prediction models	MoEV+SEV+EVB group	NEV+MiEV group	*p*-value
Plt/S-D	446.3±212.2	977.5±538.7	<0.05
VAP scoring system	174.24±108.87	1167.12±1067.12	<0.05

Table III. The comparison of ROC of prediction models prediction from moderate and severe varices to varices bleeding groups.

Prediction models	AUC	95% CI	Z statistic	Criterion	Sensitivity (%)	95% CI	Specificity (%)	95% CI	+LR	-LR
VAP scoring stytem	0.901	0.853-0.949	16.352	≤461.5	100.00	97.0-100.0	68.66	56.2-79.4	3.19	0.00
Plt/S-D	0.838	0.777-0.899	10.863	≤835.5	95.10	89.6-98.2	58.21	45.5-70.2	2.28	0.084

95% CI: 95% CI 0.777-0.899). Therefore, the VAP scoring model has a better discriminative power for predicting the presence of MoEV, SEV and EVB, when compared to the Plt/S-D scoring model, in the present study population. Finally, ROC curves were used to assess the cut-off values for the VAP scoring model and Plt/S-D scoring model with the best sensitivity and specificity for predicting the presence of EVB. A cut-off value of 461.5 had a sensitivity of 100%, a specificity of 68.7%, a positive likelihood ratio of 3.19, and a negative likelihood ratio of 0.00. A cut-off value of 835.5 had a sensitivity of 95.1%, a specificity of 58.2%, a positive likelihood ratio of 2.28, and a negative likelihood ratio of 0.08 (Table III).

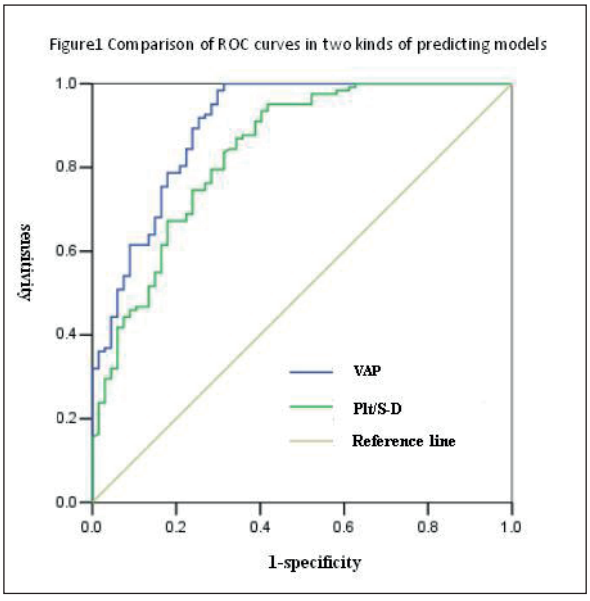

Figure 1. Comparison of ROC curves in the two kinds of predicting models.

Discussion

Thrombocytopenia may occur in hypersplenism caused by portal hypertension, and this is partly because platelets are stored in the enlarged spleen[5]. Some scholars have found that BPC may be correlated with the EGV degree[6,7]. The hypersplenism of LC patients may be associated with multiple factors, such as the shortened life expectancy of platelets, the reduced generation of thrombopoietin, and the alcohol or bone marrow disease caused by the hepatitis B virus itself. A longitudinal study revealed that BPC is associated with the portal hypertension of LC, but it does not accurately identify the occurrence of EGV. Hence, it is not sufficient to solely apply BPC and mean platelet volume to predict the varicosity[8-10]. In order to improve the predictive value of BPC, the investigators attempted to combine other parameters. Plt/S-D refers to the ratio of platelet count (dl) to the maximum length of the spleen diameter (mm) measured by abdominal CDU. According to the study conducted by Giannini et al[11], when the Plt/S-D cut-off value was 909.0, the positive predictive value and negative predictive value of EGVs was 76.6% and 87%, respectively, and the area under the ROC curve was 0.981. Unfortunately, a cut-off value of 909.0 only had a positive predictive value of 76.6% and a negative predictive value of 587% in the multicenter international verification trial, which did not reach the experimental results of the above research[12]. Baig et al[13] found that the cut-off value of Plt/S-D was 1,014, the sensitivity was 98.1%, the specificity was 88.6%, and the area under the ROC curve was 0.942 (95% CI: 0.890-0.995). Schwarzenberger et al[14] also verified that this method has better predictive accuracy. In addition, some scholars also insisted that

Plt/S-D could be used to estimate the emergence of EGV, but this cannot completely replace invasive EGD. However, it is likely to be a useful parameter system to screen for patients with portal hypertension, who underwent primary prevention endoscopy[15]. The present study revealed that when the cut-off value of Plt/S-D was 835.5, the AUC was 0.838, the sensitivity and specificity to predict the emergence of MoEV, SEV, and EVB were 95.10% and 58.21%, respectively, the +likelihood ratio (LR) was 2.28, and the -LR was 0.084. The present model for predicting moderate to above EV patients has good prediction accuracy. Ogasawara et al[16] reported that liver volume and weight are as important as the child Pugh grading. Since the spleen volume of LC patients may significantly increase, there was no significant difference between the liver volume of LC patients and normal liver volume. Therefore, it would be bias to determine the degree of LC by only depending on the changes in liver volume alone[17]. Min et al[18] reported that BPC, albumin, and the M-index were correlated to the emergence of EGV, and that the VAP model was designed to accurately predict the risk of varices and bleeding. It was also found that the score model predicted more accurately than each parameter alone (95% CI: 0.801-0.899). It has been considered that the VAP scoring system can predict the emergence of EGV and bleeding, is superior to other scoring systems, and is more accurate than any of these. At present, few studies abroad have investigated the non-invasive approaches for predicting the occurrence and development of EVG and hemorrhage. Hence, it remains controversial[19-25], especially through the VAP scoring model, making it highly creative and feasible. The deterioration of LC would result to collateral circulations that manifest with EGV, peritoneal varicose and hemorrhoid varices, and it was observed that some patients did not present with EV through a gastroscope. However, the CT scan or abdominal ultrasound was able to reveal the varicose veins in the anterior region of the splenic portal region or varicose veins in the peritoneal cavity. Therefore, it has been considered that it is not very effective to predict EV by simply measuring the data of the spleen or liver. The VAP scoring model is not only a non-invasive examination, but has good repeatability, and it can more accurately predict the emergence and deterioration of EV. Hence, wide clinical application is recommended. In addition, the parameters of the model can be routinely obtained from patients with cirrhosis, its application is simple, flexible, convenient, and applicable for inpatients and outpatients, and it does not incur additional cost. Hence, this would benefit both patients who could not tolerate a gastroscopy and patients who could not bear the cost of a gastroscopy. The present study reveals that the VAP score model can predict the MoEV, SEV, and EVB of LC patients. The AUROC for the VAP scoring model for MoEV, SEV to EVB was 0.901 (95% CI: 0.853-0.949) in the present study. The cut-off value of 461.5 has a sensitivity of 100%, a specificity of 68.7%, a positive likelihood ratio of 3.19, and a negative likelihood ratio of 0.00, showing good prediction accuracy. The VAP scores were not good predictors for the varicose bleeding group, and had a certain insufficiency, when compared to SS. The Plt/S-D scoring model has the best sensitivity and specificity for predicting the presence of EVB. The cut-off value of 835.5 has a sensitivity of 95.1%, a specificity of 58.2%, a positive likelihood ratio of 2.28, and a negative likelihood ratio of 0.08. Due to the relatively small research sample size and the study deviation of the sample selection, further large-sample multicenter studies are needed.

Conclusions

These two kinds of scoring models can be utilized to predict the risk of moderate or severe EV and EV bleeding in patients with cirrhosis, which has high predictive accuracy. Therefore, the application of these two kinds of scoring models should be recommend for predicting the degree of EV and EV bleeding in LC patients. Furthermore, those should be used as a screening tool, especially for patients who cannot tolerate EGD and low-income patients, in the long-term and frequent follow-up of hepatocirrhosis outpatients, and in-patents with portal hypertension.

Conflict of Interests

All authors have contributed significantly to the manuscript and declare that the work is original and has not been submitted or published elsewhere. None of the authors have any financial disclosure or conflict of interest.

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