Received: 3 September 2020 | Revised: 16 December 2020 | Accepted: 17 December 2020

DOI: 10.1002/jcla.23694

RESEARCH ARTICLE

WILEY

The value of platelet parameters and related scoring system in predicting esophageal varices and collateral veins in patients with liver cirrhosis

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Abstract

Objective: To explore the value of platelet parameters and related scoring system in predicting esophageal varices and collateral veins in patients with liver cirrhosis.

Method: A total of 94 patients with liver cirrhosis diagnosed in our hospital from March 2017 to July 2018 were divided into without esophageal varices group (NEV) and esophageal varices group (EV) into mild, moderate, and severe subgroups according to the results of general gastroscopy. The differences of biological indexes among different degrees of esophageal varices and collateral veins were analyzed, and the related factors of esophageal varices and collateral veins were analyzed.

Results: PLT count and PCT decreased gradually with the increase of esophageal varices in EV group. There were significant differences in PLT count and PCT, which were negatively correlated with the degree of collateral vein in esophageal collateral vein group. The maximum cross-sectional diameter and mean diameter of esophageal collateral veins in EV group were wider than those in NEV group. Further study showed that the maximum cross-sectional total diameter and mean diameter of esophageal collateral veins in severe esophageal varices group were wider than those in NEV group and mild esophageal varices group. Sequential Logistic regression analysis showed that PCT could effectively predict the existence of esophageal varices. Platelet parameters had no significant diagnostic value in predicting peri-ECV and Para-ECV. For platelet-related FI, APRI, FIB-4, King, Lok, GUCI, and FibroQ scoring systems, multivariate Logistic regression showed that FI, FIB-4, Lok and FibroQ scoring systems could effectively predict the presence of EV and Para-ECV ($P<0.05$), and its Lok Index is better than other rating systems, with AUROC values of 0.773 and 0.747, respectively. There is no significant predictive value for above scoring systems of peri-ECV.

Conclusions: PCT and LOK index can effectively predict the existence of esophageal varices and para-esophageal veins in patients with liver cirrhosis, and can be used as an effective filling method for common gastroscopy and endoscopic ultrasonography to detect EV and ECV in liver cirrhosis.

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KEYWORDS
esophageal varices, liver cirrhosis, non-invasive, platelets

1 | INTRODUCTION

Esophageal varices are one of the most common complications of liver cirrhosis, and its rupture and bleeding is an urgent medical emergency. According to statistics, nearly 1% of patients with liver cirrhosis died of esophageal and gastric varices bleeding caused by portal hypertension.[1] Therefore, if esophageal varices and their degree can be identified as early as possible, it is of positive significance for the long-term prognosis of patients with liver cirrhosis. Esophageal varices and their degrees are commonly found by endoscopic examination, but they are invasive and difficult to be accepted by medical equipment, personnel, and repeated examinations. Therefore, in recent years, non-invasive examination to predict esophageal varices has become a research hotspot. The purpose of this study is to explore the value of non-invasive index platelet parameters and related scoring system in predicting the degree of esophageal varices and collateral veins, so as to guide clinical diagnosis and treatment.

2 | MATERIALS AND METHODS

2.1 | Case selection

A total of 94 patients with liver cirrhosis treated in Tianjin second people's Hospital from March 2017 to July 2018 were selected, including 49 males and 45 females, aged from 25 to 84 years old. The causes of liver cirrhosis were hepatitis B cirrhosis (n = 55), autoimmune cirrhosis (n = 4), hepatitis C cirrhosis (n = 14), alcoholic cirrhosis (n = 9), unknown cause cirrhosis (n = 11) and fatty cirrhosis (n = 1). The patients were divided into two groups according to the degree of esophageal varices under general gastroscopy: non-varicose group (NEV group, n = 25) and (EV) group (n = 69), including mild varicose group (n = 38), moderate varicose group (n = 17) and severe 3/19 degree varicose group (n = 14). In EV group, there were 27 cases of Child-Pugh A, 28 cases of, Child-Pugh B, 14 cases of Child-Pugh C; 16 cases of Child-Pugh A, 9 cases of Child-Pugh B, and 0 cases of Child-Pugh C in NEV group; 31 cases (33%) were complicated with ascites, including 28 cases in EV group (3 cases in 90%), NEV group).

2.2 | Case selection and exclusion criteria

Inclusion criteria: patients with liver cirrhosis meet the diagnostic criteria of liver cirrhosis, that is, diagnosis is made according to the patient's history, physical examination, laboratory examination, ultrasound scan, and liver biopsy. General gastroscopy was performed to determine the presence of esophageal varices and the degree of esophageal varices. According to the 2019 expert consensus on diagnosis and treatment of esophageal and gastric varices in patients with liver cirrhosis and portal hypertension,[2] esophageal varices were classified as mild (G1): esophageal varices were linear or slightly circuitous, without red sign. Moderate (G2): esophageal varices were linear or slightly tortuous, with red sign or serpentine protuberance but no red sign. Severe (G3): esophageal varices were serpentine and tortuous, with red sign or esophageal varices in beads, nodules, or tumors (with or without red sign). The patients in the group were examined by endoscopic ultrasonography at the same time, the scanning range was from the middle and lower segment of the incisor 25 cm to the door of the cardia, and the main content of the examination was the para-esophageal collateral veins (para-ECV), which refers to the thick collateral vein located outside the esophageal wall without contact with the muscular layer, and the peri-esophageal collateral veins, (peri-ECV) refers to the small collateral vein directly adjacent to the surface of the muscular layer of the esophageal wall. The maximum diameters of the two types of veins were recorded by scanning different levels. Para-ECV was divided into mild (internal diameter <5 mm) and severe (internal diameter ≥5 mm), and peri-ECV was also divided into mild (internal diameter <2 mm) and severe (internal diameter ≥2 mm).[3] Exclusion criteria: patients with liver cancer and other malignant tumors, patients with liver failure, patients with thrombocytopenia and splenomegaly caused by hematological diseases, splenectomy, ligation of esophageal varices or use of propranolol and other vasoactive drugs to reduce portal hypertension, patients with portal vein thrombosis who underwent jugular intrahepatic portosystemic shunt, ALT >10 times the normal upper limit of (ULN) patients, patients with infection, patients with other factors affecting the level of PLT. All patients have signed informed consent.

2.3 | Observation indicators

The data of all subjects were collected, including the following: (1) basic information: age, sex, and etiology of liver cirrhosis; (2) laboratory indicators: blood biochemistry, blood routine, and blood coagulation function; (3) imaging indicators: abdominal ultrasound, including the shape and structure of the liver, the diameter of the portal vein, the size of the spleen, the presence of fluid dark areas in the abdominal and pelvic cavity and the depth of effusion, etc.; (4) endoscopic indicators: detection of esophageal varices under general gastroscopy; and (5) the maximum cross-sectional diameter of para-esophageal and peri-esophageal collateral veins was measured by endoscopic ultrasonography.

2.4 | Methods

Blood test: blood biochemistry was detected by HITACHI automatic biochemical analyzer-7180 produced by Japan Co., Ltd. Alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin (TBIL), blood urea nitrogen (BUN), creatinine (Cr), uric acid (UA) kit provided by Fuji Film and Optical Pharma Co., Ltd. Albumin (ALB), prealbumin (pALB), β_2-microglobulin (β_2-MG) kit provided by Mike Biological Co., Ltd. Beijing Century Ward Biotechnology Co., Ltd. provides homocysteine (HCY) kit, and Orson Clinical Diagnostics (USA) Co., Ltd. provides sodium ion (Na) determination kit. Blood routine was detected by Sysmex XN-2000 blood analyzer produced by Sysmex Company of Japan, and the matching reagent, quality control liquid of Sysmex Company of Japan, CX21 optical microscope (Olympus, Japan) and Ruiji dye solution (Zhuhai Beso Biotechnology Co., Ltd.) were used. The coagulation function was detected by SysmexCS-5100 automatic blood coagulation analyzer, and the original matching reagent and quality control liquid of Sysmex Company of Japan were used. The indexes of liver fibrosis were detected by AUTOBIO A2000Plus automatic chemiluminescence detector, detection kits of laminin, hyaluronic acid, N-terminal peptide of type III procollagen, and IV type collagen were provided by Zhengzhou AUTO Biological Diagnostics Co., Ltd. (AUTOBIO DIAGNOSTICS. CO, LTD). Abdominal color ultrasound: detected by Acuson S3000 color ultrasound instrument produced by German Ximen subsidiary. General gastroscope: the Japanese Olympus CV-260SL electronic gastroscope was used for examination. Endoscopic ultrasonography: Japanese Olympus GF-UE260 type endoscopic ultrasonography was used for examination. The ultrasonic frequency is 20 MHz, the maximum axial resolution is 0.2 mm, and the detection depth is 10 cm.

2.5 | Calculation formulas of different liver fibrosis scoring systems related to platelets[4-7]:

APRI = [(AST/ULN) × 100]/PLT (The ULN of this study is 40U/L);

FIB-4 = (Age × AST)/(PLT×$ALT^{1/2}$);

FI = 8–0.01 × PLT–ALB;

King = Age × AST × INR/PLT;

Lok = −5.56–0.0089 × PLT + 1.26 × AST/ALT + 5.27 × INR;

FibroQ (10 x age x AST x PT INR)/(PLT x ALT)

GUCI (Goteborg University Cirrhosis Index) (AST/ULN) × PT-INR×100/PLT(10^9/L)

2.6 | Statistical analysis The data were analyzed by SPSS 21.0

The measurement data in accordance with normal distribution were described by mean ±standard deviation, and the differences were compared by t-test. The measurement data of non-normal distribution were expressed by median and upper and lower quartile M (P25, P75). Mann–Whitney U test was used to compare the differences, and the classified variables were compared by Mann–Whitney U test. The (ROC) analysis of the working characteristic curve of the subjects was performed by MedCalc (15.2.2), and the diagnostic efficacy of each index in the diagnosis of esophageal varices and collateral veins in patients with liver cirrhosis was compared. Youden index was used to determine the best decision point, and multivariate Logistic and ordered Logistic regression were used to analyze the relationship between each index and esophageal varices and collateral veins. The difference was statistically significant if the test level was $\alpha = 0.05$ ($p < 0.05$).

3 | RESULTS

3.1 | Differences of general data and scoring systems between groups with or without esophageal varices

According to the results of gastroscopy, 94 patients with liver cirrhosis were divided into (NEV) group without esophageal varices (13 males and 12 females, mean age 51.16 ± 13.15 years) and 69 patients with esophageal varices ((EV) group, 36 males and 33 females, mean age 55.87 ± 10.64 years). The results showed that there was no significant difference in age and sex between the two groups ($p > 0.05$.The levels of ALT, pALB, HGB, and FIB in); EV group was significantly lower than those in NEV group ($p < 0.05$). The levels of TBIL, β-MG, HA, and LN in EV group were significantly higher than those in NEV group, and the levels of RDW-CV and RDW-SD in EV group were significantly higher than those in NEV group, which were 14.50% (13.45)% VS 13.00% and 49.50% (45.50) fL VS 42.30). PLT count and PCT in EV group were lower than those in NEV group, which were 81.00 (55.50127.00) ×10 9 VS 122.00 (94.00150.50) ×10 9 shock L and 0.10 (0.07) VS 0.15% (0.11 0.17)%, respectively, and the difference was statistically significant ($p < 0.05$). PT and INR in EV group were significantly higher than those in NEV group (14.20) s VS 17.25) s (P 6/19 14.50). The general characteristics of the two groups are shown in Table 1.

3.2 | Differences of platelet-related scoring system between EV and NEV groups

There was no significant difference in APRI, King, and GUCI score system between the two groups ($p > 0.05$), FI, FIB, Lok, and FibroQ score system (Table 2).

3.3 | Differences of platelet parameters and related scoring system between groups with different degrees of esophageal varices

There were significant differences in PLT count and PCT among different degrees of esophageal varices. With the aggravation of esophageal varices, PLT count and PCT decreased gradually. Among the platelet-related FI, APRI, FIB-4, King, Lok, GUCI, and FibroQ

TABLE 1 differences of general characteristics between NEV and EV groups

Factors	Without esophageal varices (n = 25)	Esophageal varices (n = 69)	*p* value
Gender (male/female)	13/12	36/33	0.988
Age (years)	51.16 ± 13.15	55.87 ± 10.64	0.079
ALT(U/L)	68.00 (31.50,138.50)	40.00 (25.00,63.00)	0.016
AST(U/L)	58.00 (34.50,123.00)	54.00 (35.50,84.00)	0.499
ALB(g/L)	43.00 (30.80,44.55)	34.20 (29.90,41.25)	0.055
TBIL(μmol/L)	17.70 (12.15,33.80)	25.70 (17.30,45.70)	0.044
pALB (mg/L)	148.40 ± 64.58	114.27 ± 59.15	0.018
β-MG(mg/L)	1.20 (0.95,1.95)	1.70 (1.40,2.00)	0.036
BUN (mmol/L)	5.10 (4.05,6.85)	4.70 (4.00,6.05)	0.360
Cr(μmol/L)	65.00 (57.00,77.50)	59.00 (51.00,57.00)	0.082
UA(μmol/L)	289.00 (229.00,345.50)	277.00 (199.00,352.50)	0.414
eGFR(ml/min)	106.33 (92.93,116.79)	100.57 (92.13,113.31)	0.663
Hcy(μmol/L)	10.70 (6.95,15.55)	12.20 (9.30,15.00)	0.202
Na(mmol/L)	141.60 (139.95,143.40)	141.10 (138.85,143.20)	0.742
WBC(*10^9/L)	4.32 (3.08,5.56)	4.28 (3.02,5.60)	0.827
Ne(*10^9/L)	2.34 (1.63,3.66)	2.51 (1.82,3.57)	0.524
LYM(*10^9/L)	1.42 (0.94,1.62)	1.06 (0.67,1.60)	0.082
N/L	1.93 (1.32,2.50)	2.11 (1.55,3.65)	0.102
HGB(g/L)	134.48 ± 25.08	119.26 ± 25.41	0.012
RDW-CV (%)	13.00 (12.10,14.55)	14.50 (13.45,15.80)	0.004
RDW-SD (fL)	42.30 (39.70,48.80)	49.50 (45.50,53.10)	0.001
PLT(*10^9/L)	122.00 (94.00,150.50)	81.00 (55.50,127.00)	0.002
MPV (fL)	11.42 ± 1.07	11.39 ± 0.98	0.894
P-LCR (%)	36.31 ± 8.58	35.82 ± 7.61	0.792
PDW (fL)	14.00 (12.30,16.20)	13.80 (12.15,15.45)	0.662
PCT (%)	0.15 (0.11,0.17)	0.10 (0.07,0.15)	0.001
PT(s)	14.50 (13.55,15.30)	15.40 (14.20,17.25)	0.004
INR	1.14 (1.04,1.21)	1.23 (1.10,1.43)	0.004
FIB(g/L)	2.47 (2.16,3.30)	2.14 (1.74,2.77)	0.027
HA (ng/ml)	128.00 (79.50,342.50)	256.00 (128.00,560.50)	0.016
LN (ng/ml)	106.00 (79.00,157.00)	141.00 (101.00,175.00)	0.043
IV-C (ng/ml)	94.00 (57.50,142.50)	117.00 (77.50,184.00)	0.080
PC III (ng/ml)	10.00 (6.00,13.50)	11.00 (8.00,16.00)	0.075

Abbreviations: HA, hyaluronic acid; HA: III, type III procollagen N-terminal peptide; Hcy, homocysteine; IV-C, IV collagen; LN, laminin; MPV, mean platelet volume; pALB, prealbumin; PCT, platelet specific volume; PDW, platelet distribution width; P-LCR, large platelet ratio; RDW-CV, erythrocyte distribution width variants; RDW-SD, erythrocyte distribution width standard deviation; β 2-MG, β 2-microglobulin.

scoring systems, only FIB-4, Lok, and FibroQ scoring systems were significantly different between the two groups (Table 3).

3.4 | Differences of platelet parameters and related scoring system in different degrees of para-esophagus and peri-esophageal collateral veins

Among the platelet parameters, only PLT count and PCT were significantly different among different degrees of peri-esophageal collateral vein groups, and PLT count and PCT decreased gradually with the aggravation of collateral vein degree. Among the FI, APRI, FIB-4, King, Lok, and FibroQ scoring systems related to platelets, only FIB-4, Lok, and FibroQ scoring systems showed significant differences between the two groups (Table 4).

With the aggravation of the degree of collateral veins of esophagus, the PLT count and PCT decreased gradually, and there was significant difference between the two groups ($p < 0.05$). There were significant differences in FI, APRI, FIB-4, King, Lok, and GUCI scores related to platelets among different degrees of collateral veins of esophagus (Table 4).

TABLE 2 difference of platelet-related scoring system with or without esophageal varices

Score system	Without esophageal varices (n = 25)	Esophageal varices (n = 69)	*p* value
APRI	1.61 (0.75,2.73)	1.68 (0.80,2.92)	0.546
FIB−4	3.69 (1.77,5.77)	5.88 (4.04,9.26)	0.003
FI	−35.86 (−37.75,−24.80)	−28.63 (−34.42,−23.41)	0.036
King	43.34 (15.72,70.90)	48.25 (29.72,99.30)	0.122
Lok	0.55 (−0.09,1.38)	1.88 (0.93,3.42)	0.000
GUCI	1.64 (0.89,3.29)	2.57 (1.22,4.18)	0.142
FibroQ	4.98 (2.63,8.35)	10.27 (7.15,21.95)	<0.001

TABLE 3 differences of platelet parameters and related scoring system among groups with different degrees of esophageal varices

Factors	Without esophageal varices (n = 25)	Mild esophageal varices (n = 38)	Moderate esophageal varices (n = 17)	Severe esophageal varices (n = 14)	*p* value
Gender (male/female)	13/12	23/15	10/7	3/11	0.082
Age (years)	51.16 ± 13.15	55.39 ± 9.55	56.59 ± 13.55	56.29 ± 10.25	0.360
PLT	122.00 (94.00,150.50)	93.50 (62.50,134.25)	79.00 (48.50,109.50)	65.00 (46.75,102.75)	0.004
MPV	11.42 ± 1.07	11.46 ± 0.95	11.14 ± 0.71	11.54 ± 1.29	0.669
P-LCR	36.31 ± 8.58	36.09 ± 7.24	33.68 ± 5.98	37.69 ± 9.97	0.541
PDW	14.00 (12.30,16.20)	14.00 (12.38,15.55)	12.70 (10.90,15.10)	13.75 (13.13,15.15)	0.714
PCT	0.15 (0.11,0.17)	0.12 (0.09,0.15)	0.08 (0.06,0.14)	0.07 (0.04,0.11)	0.001
APRI	1.61 (0.75,2.73)	1.72 (0.93,2.41)	1.41 (0.79,3.18)	1.66 (0.78,3.58)	0.940
FIB−4	3.69 (1.77,5.77)	5.68 (3.72,8.39)	6.34 (4.26,9.96)	5.76 (4.66,11.65)	0.022
FI	−35.86 (−37.75,−24.80)	−29.38 (−34.91,−23.78)	−25.88 (−32.02,−21.24)	−27.37 (−31.59,−21.92)	0.118
King	43.34 (15.72,70.90)	48.64 (29.92,71.09)	45.77 (26.85,106.06)	56.50 (27.19,114.22)	0.474
Lok	0.55 (−0.09,1.38)	1.49 (0.86,3.32)	2.35 (1.22,5.27)	2.26 (0.71,3.32)	0.000
GUCI	1.64 (0.89,3.29)	2.58 (1.40,3.91)	2.23 (1.13,4.85)	2.55 (1.10,5.35)	0.525
FibroQ	4.98 (2.63,8.35)	9.34 (6.13,14.01)	11.26 (8.92,31.19)	13.32 (8.10,21.56)	<0.001

TABLE 4 Differences of platelet parameters and related scoring system among different degrees of para-esophageal collateral vein groups

Factors	No (n = 52)	Mild (n = 27)	Severe (n = 15)	*p* value
Gender (male/female)	28/24	17/10	4/11	0.073
Age (years)	54.81 ± 12.72	53.11 ± 9.89	56.67 ± 9.72	0.624
PLT	120.00 (83.25,157.25)	83.00 (56.00,112.00)	54.00 (32.00,73.00)	<0.001
MPV	11.30 ± 0.97	11.34 ± 1.01	11.85 ± 1.01	0.166
P-LCR	35.18 ± 7.51	35.29 ± 7.97	39.81 ± 8.10	0.115
PDW	13.70 (12.13,15.28)	13.60 (11.30,15.50)	14.60 (13.10,16.10)	0.481
PCT	0.15 (0.10,0.17)	0.10 (0.07,0.14)	0.07 (0.04,0.08)	<0.001
APRI	1.34 (0.75,2.74)	1.68 (0.79,2.19)	2.49 (1.50,4.21)	0.033
FIB−4	4.54 (2.78,7.16)	5.88 (4.24,8.15)	11.58 (5.35,16.77)	<0.001
FI	−32.04 (−37.13,−25.09)	−26.92 (−33.44,−23.50)	−25.41 (−28.72,−21.26)	0.019
King	43.23 (19.12,74.39)	47.84 (29.32,61.94)	108.88 (45.83,145.35)	0.006
Lok	0.89 (0.31,1.83)	2.30 (1.30,2.92)	3.18 (1.00,5.82)	<0.001
GUCI	1.88 (0.88,3.40)	1.98 (1.21,2.98)	3.86 (2.05,6.73)	0.012
FibroQ	6.36 (3.33,9.98)	11.01 (8.29,21.08)	20.38 (10.27,32.78)	<0.001

TABLE 5 Comparison of the maximum cross-sectional total diameter and mean diameter of para-esophageal and peri-esophageal collateral veins among groups with different degrees of esophageal varices

Factors	Without esophageal varices (n = 25)	Mild esophageal varices (n = 38)	Moderate esophageal varices (n = 17)	Severe esophageal varices (n = 14)	*p* value
Gender (male/female)	13/12	23/15	10/7	3/11	0.082
Detection of collateral veins	13 (25)	34 (38)	17 (17)	14 (14)	**<0.001**
Total diameter of collateral veins	3.31 (1.90,4.55)	4.86 (2.70,6.02)	5.51 (3.40,6.95)*	9.96 (6.1,11.20)*#	**<0.001**
Average diameter of collateral veins	2.27 (1.90,2.50)	2.76 (1.71,3.09)	3.28 (2.43,3.75)*	5.16 (3.73,5.60)*#	**<0.001**

Note: compared with non-esophageal varices group, $^{*}p < 0.05$; compared with mild esophageal varices group, $^{\#}p < 0.05$.

TABLE 6 correlation analysis of platelet parameters and related scoring system with the degree of esophageal varices and collateral veins

Factors	EV (*r*)	*p*	peri-ECV (*r*)	*p*	para-ECV(r)	*p*
PLT	−0.374	0.000	−0.357	<0.001	−0.527	<0.001
MPV	−0.014	0.892	0.037	0.724	0.186	0.072
P-LCR	−0.025	0.809	0.046	0.661	0.199	0.054
PDW	−0.058	0.581	0.045	0.664	0.084	0.423
PCT	−0.426	0.000	−0.346	0.001	−0.500	<0.001
APRI	0.059	0.570	0.127	0.223	0.200	0.053
FIB−4	0.304	0.003	0.352	0.001	0.392	<0.001
FI	0.248	0.016	0.217	0.036	0.291	0.004
King	0.149	0.151	0.220	0.033	0.255	0.013
Lok	0.392	0.000	0.310	0.002	0.421	<0.001
GUCI	0.138	0.184	0.174	0.094	0.263	0.011
FibroQ	0.378	<0.001	0.214	0.038	0.469	<0.001

3.5 | Comparison of the maximum cross-sectional total diameter and mean diameter of para-esophageal and peri-esophageal collateral veins among groups with different degrees of esophageal varices

In the 25 cases of NEV group, endoscopic ultrasonography detected a total of 13 cases (52%) of the para-esophageal and/or peri-esophageal collateral veins. In the 38 cases of mild esophageal varices group, 34 cases of the para-esophageal and/or peri-esophageal side were detected The detection rate of branch veins (89.5%), para-esophageal and/or peri-esophageal collateral veins in the moderate and severe esophageal varices groups was 100%. Endoscopic ultrasonography showed that there were significant differences in the maximum cross-sectional total diameter and average diameter of esophageal collateral veins among different degrees of esophageal varices ($p < 0.05$). Further study showed that the maximum cross-sectional total diameter and mean diameter of esophageal collateral veins in severe esophageal varices group were wider than those in non-esophageal varices group and mild esophageal varices group ($p < 0.05$). Details were shown in Table 5.

3.6 | Correlation analysis of platelet parameters and related scoring system with the degree of esophageal varices and collateral veins

PLT count and PCT were negatively correlated with the degree of esophageal varices (r = 0.374, r = 0.426, $p < 0.05$), while FIB-4, FI, Lok and FibroQ were positively correlated with the degree of esophageal varices (rang 0.304, r = 0.248, r = 0.392, r = 0.378, $p < 0.05$). There was no significant correlation among APRI, king, and GUCI score system and the degree of esophageal varices. Correlation analysis with esophageal collateral veins (peri-ECV and para-ECV) showed that PLT count and PCT were significantly negatively correlated with them, and only APRI had no significant correlation with collateral circulation in FI, APRI, FIB-4, King, Lok, GUCI, and FibroQ scoring system (Table 6).

3.7 | Multivariate regression analysis of platelet parameters in cirrhotic patients with esophageal varices

Sequential Logistic regression analysis showed that among the platelet parameters, only PCT could effectively predict esophageal

varices (p = 0.013) (Table 7). There was no significant predictive value of platelet parameters for peri-esophageal and para-esophageal collateral veins (p > 0.05).

TABLE 7 multivariate ordered Logistic regression analysis of platelet parameters in cirrhotic patients with esophageal varices

	Regression coefficients (β)	OR (95%CI)	p
Gender			
Male	−0.195	0.82 (0.37,1.83)	0.633
Female	0	—	—
Age	0.021	1.02 (0.99,1.06)	0.235
PLT	0.004	1.00 (0.99,1.02)	0.539
MPV	−0.516	0.60 (0.08,4.43)	0.614
P-LCR	0.074	1.08 (0.82,1.41)	0.590
PDW	−0.054	0.95 (0.70,1.28)	0.728
PCT	−15.628	1.63×10^{-7}(6.80×10^{-13},0.04)	0.013

Note: 0 is the reference. OR=1.63 10^{-7}, indicating that PCT is a protective factor for varicose veins. The higher the PCT, the lower the degree of varicose veins. Ordered logistic, OR cannot be simply used to represent multiples at this time.

3.8 | The value of FI, APRI, FIB-4, King, Lok, GUCI, and FibroQ scoring system in the diagnosis of esophageal varices and collateral vein

Taking different platelet-related scoring systems as test variables and diagnostic results as state variables, the working characteristic curves of subjects were drawn. ROC, results showed that the AUROC values of FI, APRI, FIB-4, King, Lok, GUCI, and FibroQ scoring system for the diagnosis of esophageal varices were 0.642, 0.541, 0.698, 0.605, 0.773, 0.599, and 0.770, respectively, and the AUROC value of Lok for the diagnosis of esophageal varices was the highest. Multivariate Logistic regression analysis showed that among the platelet-related scoring systems, only FI, FIB-4, Lok, and FibroQ scoring system could effectively predict esophageal varices (Table 8, Figure 1A). Among the above scoring systems, Lok scoring system AUROC has the highest diagnostic efficiency of esophageal collateral veins (peri-ECV and para-ECV), which is 0.680 and 0.747, respectively. Multivariate Logistic regression analysis showed that none of the six scoring systems could effectively predict the collateral veins around the esophagus, and the FI, FIB-4, Lok, and FibroQ scoring systems could effectively predict the existence of the collateral veins around the esophagus. For details, see (Table 9, Figure 1B; Table 10, Figure 1C).

TABLE 8 diagnostic efficiency of each scoring system on the degree of esophageal varices and multivariate Logistic regression analysis

Score system	OR (95%CI)	p	AUC (95%CI)	Cutoff	Sensitivity (%)	Specificity (%)
FI	**1.07 (1.00,1.15)**	**0.043**	0.642 (0.537,0.739)	−35.18	81.16	56.00
APRI	1.06 (0.90,1.26)	0.471	0.541 (0.435,0.644)	1.04	71.01	44.00
FIB−4	**1.18 (1.02,1.37**	**0.024**	0.698 (0.595,0.788)	3.82	79.71	56.00
King	1.00 (1.00,1.01)	0.473	0.605 (0.498,0.704)	25.87	78.26	44.00
Lok	**1.53 (1.12,2.11)**	**0.008**	0.773 (0.675,0.853)	0.86	78.26	68.00
GUCI	1.08 (0.93,1.25)	0.299	0.599 (0.493–0.699)	1.18	76.81	44.00
FibroQ	1.075 (1.010,1.144)	0.024	0.770 (0.676–0.865)	6.99	87.23	57.45

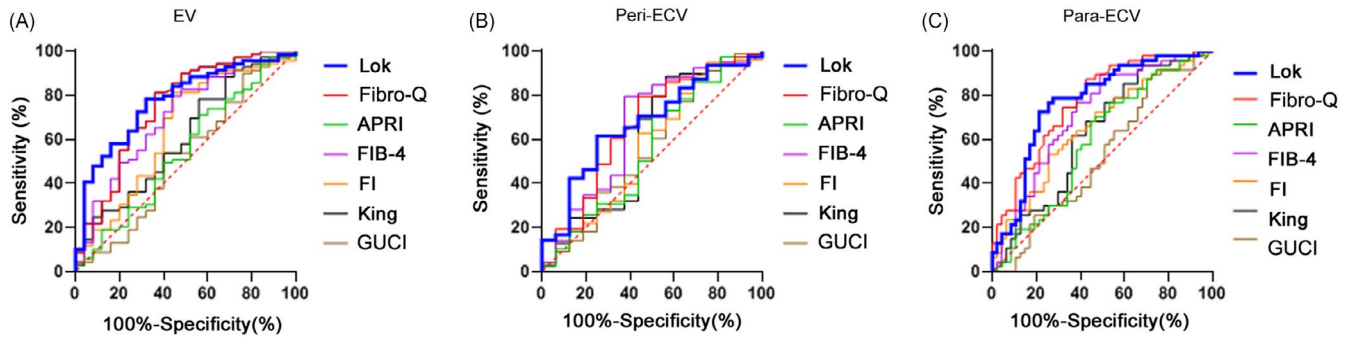

FIGURE 1 The diagnosis efficacy of platelet parameters and related scoring system in predicting esophageal varices and collateral veins. (A) ROC curve of esophageal varices predicted by scoring system; (B) ROC curve of peri-ECV vein degree predicted by scoring system; (C) ROC curve of para-ECV vein degree predicted by scoring system.

TABLE 9 the diagnostic efficiency of each scoring system for the venous degree of peri-ECV (distinguishing whether it is present or not) and multivariate Logistic regression analysis

Score system	OR (95%CI)	*p*	AUC (95%CI)	Cutoff	Sensitivity	Specificity
APRI	1.03 (0.86,1.24)	0.720	0.561 (0.455,0.663)	1.04	71.79%	50.00%
FI	1.03 (0.958,1.12)	0.398	0.567 (0.461,0.669)	−39.40	94.87%	25.00%
FIB−4	1.09 (0.95,1.25)	0.203	0.667 (0.563,0.761)	3.70	80.77%	62.50%
King	1.00 (1.00,1.01)	0.855	0.605 (0.499,0.704)	19.09	89.74%	43.75%
Lok	1.27 (0.94,1.66)	0.090	0.680 (0.579,0.773)	1.16	62.82%	75.00%
GUCI	1.04 (0.90,1.19)	0.618	0.579 (0.473,0.680)	1.18	75.64%	50.00%
FibroQ	1.042 (0.983,1.104)	0.165	0.664 (0.510,0.819)	6.12	79.50%	56.25%

TABLE 10 the diagnostic efficiency of each scoring system for the venous degree of para-ECV (distinguishing whether it is present or not) and multivariate Logistic regression analysis

Score system	OR(95%CI)	*p*	AUC (95%CI)	Cutoff	Sensitivity	Specificity
APRI	1.05 (0.93,1.18)	0.472	0.582 (0.476,0.683)	1.33	71.43%	50.00%
FI	1.08 (1.02,1.15)	**0.010**	0.658 (0.552,0.752)	−29.21	66.67%	61.54%
FIB−4	1.11 (1.02,1.21)	**0.020**	0.696 (0.593,0.787)	3.83	90.48%	46.15%
King	1.00 (1.00,1.00)	0.859	0.609 (0.502,0.708)	19.38	95.24%	28.25%
Lok	1.41 (1.13,1.75)	**0.002**	0.747 (0.647,0.831)	1.62	71.43%	73.08%
GUCI	1.04 (0.95,1.13)	0.383	0.621 (0.515,0.719)	1.18	83.33%	38.46%
FibroQ	1.082 (1.032, 1.136)	0.003	0.742 (0.676–0.865)	6.99	87.20%	57.45%

4 | DISCUSSION

Liver cirrhosis is an important stage in the development of chronic liver disease. its common complications include esophageal and gastric varices bleeding, hypersplenism, ascites, hepatorenal syndrome, hepatopulmonary syndrome 14/19 syndrome, and so on. Some patients may develop into liver cancer. Among them, esophagogastric varices is one of the most common concomitant diseases, and more patients die because of its bleeding every year, so if we can identify the degree and degree of esophageal and gastric varices as early as possible, and then carry out preventive intervention, the mortality can be significantly reduced.[8-10] Clinically, gastroscopy is the gold standard for screening esophageal and gastric varices. However, in recent years, non-invasive index prediction of esophageal and gastric varices and its degree has become a hot topic in academic circles.

Decreased platelet count is a common manifestation of patients with liver cirrhosis. According to statistics, about 84% of patients with liver cirrhosis are complicated with low platelet blood, and a number of studies have shown that its level can predict esophageal varices.[5,11-13] Baveno VI recommendation also points out that gastroscopy can be exempted from gastroscopy in cirrhotic patients with LSM <20 kPa and PLT >150 × 10 9xL.[14] In this study, it was found that the PLT count in EV group was significantly lower than that in NEV group, and the PLT count decreased gradually with the aggravation of esophageal varices. There was also a significant difference in PLT count between different degrees of esophageal collateral veins (peri-ECV and para-ECV), which was negatively correlated with the degree of esophageal collateral veins. Kumar et al.[15] also found that PLT count was significantly correlated with moderate and severe esophageal varices ((large esophageal varices, LEV), which was basically consistent with the conclusions of this study. Zhang et al.[16] compared the blood cell count in patients with peptic ulcer bleeding (PUB) and esophagogastric variceal bleeding (EGVB). It was found that platelet count in EGVB group was significantly lower than that in PUB group. It is an effective and potential biomarker to distinguish PUB from EGVB, and has more accurate and reliable diagnostic value. Therefore, the PLT count level can be used to predict the degree of esophageal varices and collateral veins.

Platelet parameters include mean platelet volume (MPV), large platelet ratio (PLCR), platelet distribution width (PDW), and platelet-specific volume (PCT). PCT refers to the percentage of platelets in the blood and the total volume of reactive platelets, which is positively correlated with the number and size of platelets. Wang et al.[17] studied patients with newly diagnosed chronic hepatitis B who underwent liver biopsy and found that PCT was an independent predictor of liver fibrosis in patients with chronic hepatitis B. The areas under the ROC curve for predicting significant fibrosis, advanced fibrosis and cirrhosis were 0.645, 0.709, and 0.714, respectively. The diagnostic efficiency of PCT in predicting the staging of liver fibrosis is better than that of APRI. In this study, it was also found that PCT in EV group was significantly lower than that in NEV group, and PCT decreased gradually with the aggravation of esophageal varices. The PCT in severe esophageal collateral veins (peri-ECV and para-ECV) was significantly lower than that in mild esophageal collateral veins

and no esophageal collateral veins, and it was negatively correlated with the degree of esophageal collateral veins. Further Sequential Logistic regression analysis showed that PCT could orderly predict esophageal varices, which was a protective factor of varices. The higher the PCT, the lower the degree of varices. This conclusion has a certain guiding significance in the clinical evaluation of esophageal varices and collateral veins.

Gastroscopy is the gold standard for the detection of esophageal varices, but endoscopic ultrasonography is needed to detect peri-esophageal and para-esophageal collateral veins which cannot be detected by ordinary gastroscope. Endoscopic ultrasonography is superior to ordinary endoscopy in finding the rate and accuracy of esophageal and gastric varices.[18,19] In addition, endoscopic ultrasonography can also predict the recurrence of esophageal varices after EVL by observing the degree of veins around the esophagus and the collateral veins of the esophagus.[20] In this study, it was found that the more serious the degree of esophageal varices, the wider the diameter of esophageal collateral veins, and there was a significant positive correlation between them. Therefore, when esophageal varices were detected, esophageal collateral veins should be injected at the same time to guide the next step of diagnosis and treatment.

Ascites is one of the common complications of decompensated cirrhosis. In this study, the proportion of ascites in EV group (41%) was higher than that in NEV group (12%), but there was no significant difference. There is no significant correlation between ascites and esophageal varices, which is consistent with the results of Kumar et al.,[15] Hong et al.[21] and Cherian et al.[22] found that the incidence of esophageal varices in patients with advanced liver cirrhosis (Child-Pugh B and Child-Pugh C) was significantly higher than that in Child-Pugh A patients. To some extent, patients with Child-Pugh B and Child-Pugh C liver function could predict the existence of moderate and severe esophageal varices. And the reasons for the analysis may be related to the number of subjects included, the etiology of liver cirrhosis, the distribution of cases, the detection methods and the operator's determination of the degree of esophageal varices. Therefore, it is necessary to further exclude the relevant influencing factors to analyze and verify the above conclusions.

In addition, in recent years, a number of platelet-related scoring systems have been pre-tested and verified for liver cirrhosis, including APRI, Fibrosis-4 (FIB-4), FI, King, Lok, GUCI, and so on. However, there are few comparative studies on the predictive efficacy of the above-mentioned non-invasive indexes in predicting the degree of esophageal varices and its collateral veins (peri-ECV and para-ECV). This study compares the diagnostic efficacy of the above non-invasive indexes and it was found that the value of Lok index in predicting esophageal varices was higher than that of other scoring systems (the area under the ROC curve was 0.773). Many studies at home and abroad suggest that when predicting the degree of esophageal varices, the AUROC value of Lok score is about 0.8,[4] which is basically consistent with this conclusion. In addition, Zhou et al.[23] studied 132 patients with compensatory cirrhosis associated with hepatitis B who did not meet the Baveno VI criteria. The results showed that in the prediction of varicose veins, only the AUROC value of Lok was higher than 0.7 in the APRI, FIB-4, Lok, and FibroQ scoring system, and the conclusion was similar to this conclusion. Gao et al.[24] evaluated the predictive value of four scoring systems (APRI), aspartate aminotransferase alanine transaminase ratio (AAR), FIB-4 and S index (1000 GGT/ (PLT varices albumin 2)) in predicting esophageal varices. The results showed that in the ROC curve for predicting esophageal varices, the ROC values of APRI, FIB-4, and S index for predicting esophageal varices were 0.681, 0.642, and 0.673, respectively. Multivariate logistic regression analysis showed that APRI and FIB-4 were predictors of disease progression. Said et al[25] analyzed the predictive value of FIB-4 and APRI in liver cirrhosis and esophageal varices in a large-scale interdisciplinary study of patients with HCV-4 genotype in Egypt. The results suggest that FIB-4 and APRI are reliable methods for predicting liver cirrhosis in large-scale HCV therapy, but they do not play a significant role in predicting gastroesophageal varices (AUROC value of FIB-4 and APRI are 0.65 and 0.62, respectively). In this study, multivariate logistic regression analysis showed that FI, FIB-4, Lok, and FibroQ scoring system could effectively predict esophageal varices (AUROC value was 0.642, 0.698, 0.773, and 0.770), and the predictive value of APRI was lower (AUROC value was 0.541), which was slightly different from that of Gao and Said, which may be related to different regions and different enrollment conditions of patients. Farid et al.[26] compared 8 common liver fibrosis scoring systems and found that the AUROC value of AAR, APRI, GUCI, BRC, Fabro-Alfa, FIB-4, Lok, and Fibro-Q were 0.58, 0.63, 0.66, 0.68, 0.72, 0.70, 0.72, and 0.77, respectively, and through further analysis established a new predictive scoring system (PAP score), which predicts moderate to severe esophageal varices in patients with liver cirrhosis caused by HCV, with an AUROC value of 0.85. Due to the small number of cases included in this study, it is not possible to establish a model for predicting the degree of esophageal varices, which needs to be further expanded in the future to verify the above conclusions.

The establishment of esophageal collateral circulation is a manifestation of portal hypertension. Studies have shown that patients with peri-esophageal collateral veins and perforating veins will affect the progression of EV and have a greater risk of EV rupture and bleeding.[27,28] In addition, studies have shown that the diameter of para-esophageal veins is related to a higher recurrence rate of varices.[29,30] However, at present, there are few studies on the prediction of esophageal collateral veins. Through further analysis, it is found that Lok index, FI, FIB-4 and FibroQ scores can predict the existence of esophageal collateral veins, and the predictive value of LOK index is higher than other scores (AUROC values was 0.747). This plays a guiding role in advance prevention for patients with high risk of EV rupture and bleeding.

To sum up, platelet parameters and related scoring systems such as PAP scores, AAR, APRI, GUCI, BRC score, Fibro-Alfa, FIB4, Lok, and Fibro-Q, have a certain value in predicting the degree of esophageal varices and collateral veins in patients with liver cirrhosis.[26,31,32] In many scoring systems, the predictive value of Lok index is better than other scoring systems, but because of its low AUROC value, it cannot replace the gold standard endoscopy, so we need to further

expand the sample size to verify it. At same time, we will validate the conclusion with more sample number in further research due to the low number of sample in this study.

CONFLICTS OF INTEREST

The remaining authors have no conflicts of interest to report.

DATA AVAILABILITY STATEMENT

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

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How to cite this article: Liu H, Chen P, Jiang B, Li F, Han T. The value of platelet parameters and related scoring system in predicting esophageal varices and collateral veins in patients with liver cirrhosis. *J Clin Lab Anal*. 2021;35:e23694. https://doi.org/10.1002/jcla.23694