# Modification of the ALBI-PLT Score for the Prediction of High-risk Varices

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**Abstract.** Background/Aim: A new scoring system [albuminbilirubin-platelet (ALBI-PLT) score] was reported for identifying cirrhotic patients without high-risk varices (HRV), and patients with ALBI grade 1 ( $\leq$ -2.60) and a platelet count over  $150 \times 10^9$ /l were shown to have a low risk of having HRV. The present study modified the cut-off values of the variables in the ALBI-PLT score. Patients and Methods: Among a total of 338 patients with chronic liver diseases, possible cut-off values of the ALBI score and the platelet count were determined by analyzing the first-half group (training cohort: N=169) with the receiver operating characteristic (ROC) method. The utility of the determined values was evaluated in the second-half group (validation cohort: N=169) and total cohort (N=338). In addition, the utility of the modified cut-off values was evaluated in patients with compensated cirrhosis (cirrhotic cohort: N=87). Results: Possible cut-off values of the ALBI score and platelet count were found to be -2.36 and  $114\times10^9$ /l, respectively. In the training cohort, these cut-off values provided a higher ratio of avoiding esophagogastroduodenoscopy than the original ALBI-PLT score (53.3% vs. 25.4%, p<0.01). Consistent results were

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observed in the validation cohort (28.4% vs. 15.4%, p<0.01), total cohort (40.8% vs. 20.4%, p<0.01), and cirrhotic cohort (32.2% vs. 11.5%, p<0.01). However, the missing ratio of patients with the HRV was not significantly increased in any cohort studied. Conclusion: Modification of the ALBI-PLT score may be useful for predicting patients without HRV.

Gastroesophageal varices (GEV) are a major complication in patients with chronic liver diseases (CLDs) (1-3). Esophagogastroduodenoscopy (EGD) is the gold-standard method of precisely evaluating the presence of high-risk varices (HRV) (4-6). However, as EGD is an expensive and burdensome examination, noninvasive methods of predicting the presence of HRV have been explored (7-9).

In the Baveno VI consensus, a criterion based on transient elastography (TE) findings (<20 kPa) and the platelet count (>150×10<sup>9</sup>/l) was shown to successfully identify patients who were unlikely to have HRV (10). The recently reported Baveno VII consensus also recommends the criterion (11). However, TE is available in limited institutions, therefore blood tests to identify patients who can avoid EGD are warranted.

The albumin-bilirubin (ALBI) score is a new index that can categorize the liver reserve function into three grades (ALBI grades 1-3) (12). In 2018, Chen *et al.* evaluated compensated cirrhotic patients and proposed a new scoring system (ALBI-platelet score: ALBI-PLT score) (13). They reported that patients with ALBI grade 1 (≤−2.60) and a platelet count over 150×10<sup>9</sup>/l had a markedly low risk of developing HRV. Those cut-off values were determined according to previously reported papers concerning the ALBI score/grade (12) and the Baveno VI criteria (10); however, the ALBI score and platelet count are continuous variables, therefore, we suspected that different cut-off values could also prove useful.

The present study explored better cut-off values of the ALBI score and platelet count for predicting patients who can avoid EGD.

#### **Patients and Methods**

The current retrospective study included the CLD-patients who received a percutaneous liver biopsy from October 2008 to December 2015 according to the ultrasound-guided standard procedures (14, 15). Liver fibrosis stages were determined according to the METAVIR fibrosis score (16). The etiologies of CLDs were determined according to the classifications, as described previously (17). The blood data, including the albumin level, total bilirubin level, and platelet count, were measured on the same day as the liver biopsy was conducted. The ALBI scores, ALBI grades, and ALBI-PLT scores of the patients were determined according to the following calculations:

[ALBI score]: [log10 bilirubin ( $\mu$ mol/l) ×0.66] – [albumin (g/l) × 0.085] (12)

[ALBI grade]: Grade 1:  $\leq$ -2.60; 2: >-2.60 to -1.39; 3: >-1.39; these grades were classified according to the ALBI scores, and the increased grade number was associated with the poorer liver function (12).

[ALBI-PLT score]: Points obtained by adding the ALBI grade (1-3 points) and the platelet count (1 point: >150×10<sup>9</sup>/l; 2 points: ≤150×10<sup>9</sup>/l), thus the lowest and highest ALBI-PLT scores were 2 and 5, respectively (13).

The endoscopic findings of GEV were assessed using a routine EGD method, and the detected GEV were categorized into three grades (F1, F2, or F3), as described previously (18, 19). The presence of red signs on varices was also evaluated, and the patients with F3 varices or F2 varices with red signs were defined as having HRV (19). In addition, patients with previous endoscopic treatment for varices were classified as those with HRV. Patients whose GEV findings were not determined within six months of the liver biopsy were excluded from the study. Patients who had received the splenectomy or partial splenic arterial embolization were also excluded from the study.

The current research was approved by the Ethics Committee of the Institutional Review Board of our institution (Nos. Hi-92 and 3431).

Statistical analyses. The cut-off values of the ALBI score and the platelet count were determined with receiver operating characteristic (ROC) curves. Frequencies between two groups were compared by the chi-squared test or the Fisher's exact probability test. Differences with a *p*-value of less than 0.05 were determined to be statistically significant.

#### Results

Basic clinical characteristics of patients with CLDs. Based on the criteria described in the Patients and Methods section, a total of 338 patients with CLDs were included in the current study. The basic clinical data are shown in Table I. Among the enrolled patients, 55 had HRV.

Determining the cut-off values and evaluating the predictive performance. In the current study, we divided the patients into the first-half group (liver biopsy conducted from October 2008 to March 2011) and second-half group (liver biopsy conducted from April 2011 to December 2015) (N=169 in each group).

We first assessed the first-half group (training cohort) and determined the potential cut-off values for predicting the presence/absence of HRV. The characteristics of the patients in the first-half group are shown in Table II. The ROC curves determined the candidate cut-off values of the ALBI score and the platelet count to be –2.36 (Figure 1A) and 114×10<sup>9</sup>/I (Figure 1B), respectively. Thus, patients with a lower ALBI score (<–2.36) and a higher platelet count (>114×10<sup>9</sup>/I) were considered to have a low risk of developing HRV.

In the first-half group, the original ALBI-PLT score was considered useful for avoiding EGD in 43 patients, with 1 patient who had HRV missing. Our new criterion spared 90 patients from undergoing EGD, with 1 patient who had HRV missing. Our criterion provided a significantly higher ratio of avoiding EGD (90/169: 53.3% vs. 43/169: 25.4%, p<0.01) without an increase in the ratio of patients with HRV missing (Table III).

We further assessed the second-half group as a validation cohort. The characteristics of the patients in the second-half group are shown in Table IV. Our criterion provided a significantly higher ratio of avoiding EGD (48/169: 28.4%  $vs.\ 26/169:\ 15.4\%,\ p<0.01$ ) than the original ALBI-PLT score. The missing ratios of patients with HRV were not significantly different between our criterion (1/38: 2.6%) and the original ALB-PLT score (0/38: 0%) (p>0.05) (Table V).

When we analyzed the whole cohort with the 338 patients, the EGD avoidance ratio with our criterion was significantly higher than that with the original ALBI-PLT score (138/338:  $40.8\% \ vs. \ 69/338: \ 20.4\%, p<0.01$ ). However, no significant difference was observed with regard to the ratio of patients with HRV missing (2/55:  $3.6\% \ vs. \ 1/55: \ 1.8\%; \ p>0.05$ ) (Table VI).

Predictive performance of the presence of HRV using our cut-off values. Finally, we excluded non-cirrhotic patients and those with decompensated cirrhosis and sub-analyzed the remaining 87 patients who had compensated cirrhosis (Child-Pugh grade A). Characteristics of the patients with compensated cirrhosis are shown in Table VII. Our criterion provided a higher ratio of patients who were able to avoid EGD than that with the original ALBI-PLT score (28/87: 32.2% vs. 10/87: 11.5%, p<0.01) without increasing the number of overlooked patients with HRV (Table VIII).

### **Discussion**

Variceal hemorrhaging is a life-threatening complication in patients with CLDs. However, EGD, the gold-standard diagnostic examination, is quite invasive, therefore, the prediction of HRV with blood tests is considered clinically

Table I. Characteristics of the enrolled patients with chronic liver diseases (N=338).

Age (years)	61.5 (52-69)
Sex (Male / Female)	154/184
Etiology (HBV/HCV/HBV+HCV/ALD/NASH/AIH/PBC/Others)	42/197/1/15/14/44/12/13
History of hepatocellular carcinoma (+/-)	60/278
AST (IU/l)	43 (29.75-65.25)
ALT (IU/l)	37 (23-64.25)
γ-GTP (IU/l)	44 (24-95.5)
ALP (IU/I)	254.5 (194-352)
Albumin (g/dl)	3.8 (3.4-4.0)
Total bilirubin (mg/dl)	0.9 (0.6-1.3)
Platelet count ( $\times 10^9/1$ )	130.5 (87.75-183)
Prothrombin time (%)	83.8 (74.2-93.9)
ALBI score	-2.433 (-2.677 to -2.093)
ALBI grade (1/2/3)	110/216/12
mALBI grade (1/2a/2b/3)	110/111/105/12
ALBI-PLT score (2/3/4/5)	69/103/159/7
High risk varices (+/–)	55/283

Quantitative variables are expressed as the median (Interquartile range). HBV: Hepatitis B virus; HCV: hepatitis C virus; ALD: alcoholic-related liver disease; NASH: nonalcoholic steatohepatitis; AIH: autoimmune hepatitis; PBC, primary biliary cholangitis; ALBI: albumin-bilirubin; mALBI: modified ALBI; ALBI-pLT: ALBI-platelet.

Table II. Characteristics of the first-half group (N=169).

Age (years)	65 (51-68)
Sex (Men/Women)	73/96
Etiology (HBV/HCV/HBV+HCV/ALD/NASH/AIH/PBC/Others)	19/113/0/2/5/21/5/4
History of hepatocellular carcinoma (+/-)	20/149
AST (IU/I)	41 (30-56)
ALT (IU/l)	37 (25-67)
γ-GTP (IU/l)	41 (22-84.5)
ALP (IU/l)	241 (183.5-331)
Total bilirubin (mg/dl)	0.8 (0.6-1.1)
Albumin (g/dl)	3.9 (3.6-4.1)
Platelet count $(\times 10^9/l)$	143 (98-188)
Prothrombin time (%)	89.8 (81.4-97)
ALBI score	-2.534 (-2.702 to -2.340)
Prothrombin time (%)	89.8 (81.4-97)
ALBI grade (1/2/3)	69/98/2
mALBI grade (1/2a/2b/3)	69/68/30/2
ALBI-PLT score (2/3/4/5)	43/62/62/2
High risk varices (+/–)	17/152

Quantitative variables are expressed as the median (Interquartile range). HBV: Hepatitis B virus; HCV: hepatitis C virus; ALD: alcoholic-related liver disease; NASH: nonalcoholic steatohepatitis; AIH: autoimmune hepatitis; PBC: primary biliary cholangitis; ALBI: albumin-bilirubin; mALBI: modified ALBI; ALBI-PLT: ALBI-platelet.

relevant. The ALBI-PLT score can identify patients who are expected to be able to avoid EGD, according to the designated values of two variables: the ALBI score ( $\leq$ -2.60) and the platelet count ( $>150\times10^9/l$ ) (13). The cut-off value of the ALBI score (-2.60) was previously determined, resulting in classifications of ALBI grade 1 or 2. However, ALBI grade 2 includes heterogeneous patients with various degrees of liver function, thus Hiraoka *et al.* proposed the

'modified ALBI grade' (mALBI grade), which divides ALBI grade 2 into two categories (grades 2a and 2b). We recently found that the endoscopic findings differ between patients with ALBI grades 2a and 2b (19).

Based on our previous study, we suspected that we could determine better cut-off values of the ALBI score and platelet count. Regarding the prediction of HRV with noninvasive techniques, the most desirable ratio of missing HRV is less than

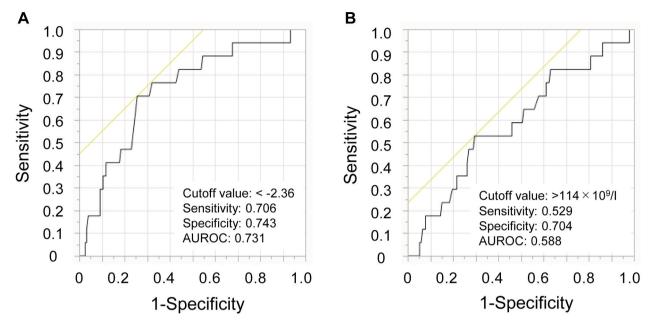


Figure 1. Receiver operating characteristic (ROC) curve of the ALBI score and platelet count for predicting the presence of high-risk varices. The cut-off values were determined with ROC curves. (A) The ROC curve of the ALBI score. (B) The ROC curve of the platelet count. AUROC: Area under the receiver operating characteristic curve; ALBI: albumin-bilirubin.

Table III. The ratio of endoscopy avoidance and the missing ratio of the high-risk varices in the first-half group.

	ALBI-PLT score	Our criterion (ALBI score <-2.36 and Platelet count >11.4/ $\times$ 10 $^9$ /I)	<i>p</i> -Value
Ratio of EGD avoidance (%)	43/169 (25.4%)	90/169 (53.3%)	<0.01
False negative ratio (%)	1/17 (5.9%)	1/17 (5.9%)	

ALBI: Albumin-bilirubin; ALBI-PLT: ALBI-platelet; EGD: esophagogastroduodenoscopy.

Table IV. Characteristics of the second-half group (N=169).

63 (53-70)
81/88
23/84/1/13/9/23/7/9
40/129
46 (29-72)
38 (20.5-62)
47 (28-108)
272 (207.5-374.5)
1.0 (0.7-1.4)
3.6 (3.2-3.9)
113 (76.5-177.5)
77.9 (67.6-86.95)
-2.256 (-2.589 to -1.856)
41/118/10
41/43/75/10
26/41/97/5
38/131

Quantitative variables are expressed as the median (Interquartile range). HBV: Hepatitis B virus; HCV: hepatitis C virus; ALD: alcoholic-related liver disease; NASH: nonalcoholic steatohepatitis; AIH: autoimmune hepatitis; PBC: primary biliary cholangitis; ALBI: albumin-bilirubin; mALBI: modified ALBI; ALBI-pLT: ALBI-platelet.

Table V. Ratio of endoscopy avoidance and the ratio of missing high-risk varices in the second-half group (N=169).

	ALBI-PLT score	Our criterion (ALBI score <-2.36 and Platelet count >11.4/ $\times$ 10 $^9$ /l)	<i>p</i> -Value
Ratio of EGD avoidance (%) False negative ratio (%)	26/169 (15.4%)	48/169 (28.4%)	<0.01
	0/38 (0%)	1/38 (2.6%)	NS

ALBI: Albumin-bilirubin; ALBI-PLT: ALBI-platelet; EGD: esophagogastroduodenoscopy; NS: not significant (p>0.05).

Table VI. Ratio of endoscopy avoidance and the ratio of missing high-risk varices in all enrolled patients (N=338).

	ALBI-PLT score	Our criterion (ALBI score <-2.36 and Platelet count >11.4/ $\times$ 10 $^9$ /I)	<i>p</i> -Value
Ratio of EGD avoidance (%)	69/338 (20.4%)	138/338 (40.8%)	<0.01
False negative ratio (%)	1/55 (1.8%)	2/55 (3.6%)	NS

ALBI: Albumin-bilirubin; ALBI-PLT: ALBI-platelet; EGD: esophagogastroduodenoscopy; NS: not significant (p>0.05).

Table VII. Characteristics of the enrolled patients with compensated cirrhosis (Child-Pugh grade A) (N=87).

Age (years)	63 (53-69)
Sex (Male/Female)	46/41
Etiology (HBV/HCV/HBV+HCV/ALD/NASH/AIH/PBC/Others)	6/67/0/3/4/5/0/2
History of hepatocellular carcinoma (+/-)	21/66
AST (IU/l)	49 (34-75)
ALT (IU/l)	46 (31-75)
γ-GTP (IU/l)	44 (30-84)
ALP (IU/l)	252 (193-332)
Albumin (g/dl)	3.8 (3.6-3.9)
Total bilirubin (mg/dl)	0.8 (0.7-1.2)
Platelet count ( $\times 10^9/l$ )	114 (79-147)
Prothrombin time (%)	81 (75.7-89.5)
ALBI score	-2.478 (-2.622 to -2.218)
ALBI grade (1/2/3)	25/62/0
mALBI grade (1/2a/2b/3)	25/36/26/0
ALBI-PLT score (2/3/4/5)	10/26/51/0
High risk varices (+/-)	15/72

Quantitative variables are expressed as the median (Interquartile range). HBV: Hepatitis B virus; HCV: hepatitis C virus; ALD: alcoholic-related liver disease; NASH: nonalcoholic steatohepatitis; AIH: autoimmune hepatitis; PBC: primary biliary cholangitis; ALBI: albumin-bilirubin; mALBI: modified ALBI; ALBI-pLT: ALBI-platelet.

5% (20-22). In some subgroup-analyses, the missing ratios with the original ALBI-PLT score and our criterion reached around 6% (Table III and Table VIII). However, these results were obtained with just one patient missing, thus our criterion appears to meet the standard for a total cohort with a larger number of cases (Table VI). Thus, we consider our modification of the cutoff values to more effectively spare patients from unnecessary EGD than the original ALBI-PLT score.

In this study, we enrolled 169 patients in each group according to the date of the liver biopsy, but the number of patients with HRV in the second-half group was higher than that in the first-half group, suggesting that the second-half

group included more cases of advanced disease than the first-half group. Despite this unexpected difference between the groups, our criterion showed a better performance for avoiding EGD in the second-half group and the total cohort than the original ALBI-PLT score. In addition, a subgroup analysis with patients with compensated cirrhosis also provided similar results. Our results suggest that the cut-off values can be applied to patients with various liver functions.

Several limitations associated with the present study warrant mention. First, our study was a retrospective single-center one. Second, noninvasive prediction of HRV is more important for those with compensated cirrhosis (Child-Pugh grade A) than

Table VIII. The ratio of endoscopy avoidance and the missing ratio of the high-risk varices in the patients with compensated cirrhosis (Child-Pugh grade A) (N=87).

	ALBI-PLT score	Our criterion (ALBI score <-2.36 and Platelet count >11.4/ $\times$ 10 $^9$ /I)	<i>p</i> -Value
Ratio of EGD avoidance (%)	10/87 (11.5%)	28/87 (32.2%)	<0.01
False negative ratio (%)	1/15 (6.7%)	1/15 (6.7%)	1

ALBI: Albumin-bilirubin; ALBI-PLT: ALBI-platelet; EGD: esophagogastroduodenoscopy.

those without cirrhosis or those with decompensated cirrhosis (Child-Pugh grade B or C). Although we studied a total of 338 patients, the number of patients with compensated cirrhosis was relatively small. Third, given the findings of our previous study, we modified the cut-off values of the two variables used in the ALBI-PLT score; however, we did not compare the utility with that of other noninvasive methods, including those that involved TE-based techniques (22-25).

In summary, according to the findings of a ROC analysis, we therefore propose new cut-off values for the ALBI-PLT score (ALBI score, -2.36; platelet count, 114×10<sup>9</sup>/l), which can more accurately identify HRV than the original cut-off values.

## **Conflicts of Interest**

The Authors declare that there are no conflicts of interest in association with this study.

## **Authors' Contributions**

MI-Y collected and analyzed the data; HE designed the study, analyzed the data, and wrote the manuscript. IW designed the study and interpreted the data; YY, NA, NI, TT, AF, RY, SK, KY, SO, RN, HS, and TN collected and interpreted the data; SN and HI collected the data and supervised the study. All of the Authors reviewed and edited the manuscript and approved the final version of the manuscript.

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