

# Rethinking variceal screening in hepatocellular carcinoma complicated cirrhosis: The ALBI-PLT score advantage

## Abstract

**Background:** Clinically significant portal hypertension (CSPH) is a major prognostic factor in patients with hepatocellular carcinoma (HCC) complicated by cirrhosis, influencing both survival and treatment outcomes. Esophageal variceal hemorrhage, a severe complication of CSPH, is associated with a poor prognosis. The gold standard for diagnosing CSPH involves invasive procedures like hepatic venous pressure gradient (HVPG) measurement; however, these methods are not always feasible in clinical practice. The Baveno VII consensus recommends non-invasive strategies for variceal screening, but their applicability in HCC patients remains uncertain due to the potential confounding effects of HCC on liver stiffness measurements (LSM). This study explores the use of the ALBI-PLT score, which combines the albumin-bilirubin (ALBI) grade and platelet count, as a non-invasive alternative for predicting varices in HCC patients with compensated cirrhosis.

**Objectives:** The primary objectives were to determine the prevalence and risk factors of varices in HCC patients, validate the predictive ability of the ALBI-PLT score for variceal screening in compensated cirrhosis, and identify a subgroup of patients who could safely forgo endoscopic variceal screening.

**Methods:** This single-center, retrospective, observational study was conducted at the Department of Gastroenterology and Hepatology, Habib Bougatfa University Hospital, Tunisia, over six months (July 2024 - January 2025). A total of 50 patients with cirrhosis complicated by HCC were included. The ALBI score, ALBI grade, and ALBI-PLT score were calculated, and esophageal varices were assessed by esophagogastroduodenoscopy (EGD). The exclusion criteria were as follows: (1) patients with incomplete information regarding HCC etiology, CTP score, cancer stage, treatment, or mortality, (2) patients who did not undergo endoscopic screening of esophageal varices within three months of HCC diagnosis, (3) patients who had undergone splenectomy or partial splenic arterial embolization, as these interventions could affect the ALBI-PLT score, and (4) decompensated patients, defined as those with ascites, varices, hepatic encephalopathy, jaundice, or a CTP score >6. Statistical analysis was performed using SPSS v26, with p-values ≤ 0.05 considered statistically significant.

**Results:** The cohort had a mean age of  $67.5 \pm 12.20$  years, with a male predominance (62%). Hepatitis C was the leading etiology (44%). Esophageal varices were present in 82% of patients, with 18% having no varices, 4% with grade I, 44% with grade II, and 34% with grade III varices. Patients with higher ALBI-PLT scores were significantly more likely to present with high-risk varices, highlighting a strong link between worsening score and variceal severity. Diagnostic performance was strong, with the score achieving an area under the ROC curve of 0.908. A cutoff value of  $\geq 1.5$  best discriminated risk groups, offering both perfect sensitivity and high specificity. At this threshold, patients scoring below 1.5 were very unlikely to harbor high-risk varices and could potentially avoid unnecessary endoscopic screening. Multivariate analysis confirmed the ALBI-PLT score as an independent predictor of high-risk varices.

**Conclusion:** The ALBI-PLT score demonstrated promising diagnostic accuracy for stratifying variceal risk in compensated HCC. A score <1.5 reliably excluded HRV, suggesting that routine EGD may be avoided in this subgroup. However, given the single-center, retrospective design and modest sample size, these findings require validation in larger, multicenter cohorts before clinical application.”

**Keywords:** ALBI score, ALBI grade, ALBI-PLT score, Hepatocellular carcinoma, gastroesophageal varices, endoscopy

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## Introduction

Clinically significant portal hypertension (CSPH) is a critical prognostic factor in patients with hepatocellular carcinoma (HCC), strongly influencing outcomes such as survival and treatment feasibility.<sup>1</sup> Esophageal variceal hemorrhage, a severe manifestation

of CSPH, is associated with a particularly poor prognosis in this population.<sup>2</sup> Consequently, assessing CSPH status is recommended during HCC diagnosis, as outlined in the Barcelona Clinic Liver Cancer (BCLC) staging system.<sup>3</sup> The gold standard for diagnosing CSPH and esophageal varices remains hepatic venous pressure

gradient (HVPG) measurement via hepatic vein catheterization and esophagogastroduodenoscopy (EGD), respectively.<sup>4</sup> However, HVPG is invasive, costly, and typically reserved for candidates for curative HCC treatments,<sup>5</sup> while routine EGD, though effective for identifying high-risk varices (HRV), poses logistical and patient burden challenges.

The Baveno VII consensus introduced non-invasive criteria to reduce unnecessary endoscopies in cirrhosis, largely relying on liver stiffness measurement (LSM) and platelet count. However, their reliability in HCC patients is uncertain, since HCC itself may alter LSM values and confound interpretation.<sup>6,7</sup> This highlights the need for alternative non-invasive tools tailored to the HCC population, particularly those with compensated liver function, where universal endoscopic screening may not be justified. The ALBI grade, introduced as a simple prognostic model, effectively assesses liver functional reserve and predicts outcomes in HCC across diverse regions and treatment modalities.<sup>8</sup> We hypothesized that combining ALBI grade with platelet count (ALBI-PLT score) could identify low-risk compensated HCC patients in whom routine EGD may be safely omitted.

The aims of this study were three fold:

- (1) To determine the prevalence and risk factors of HRV in HCC patients;
- (2) To validate the ALBI-PLT score's ability to predict HRV in those with compensated liver function; and
- (3) To identify a subgroup of patients who can safely forgo endoscopic variceal screening.

## Patients and methods

### Study design:

A single-center, retrospective, observational study was conducted at the Department of Gastroenterology and Hepatology of Habib Bougatfa University hospital of Bizerte, Tunisia over a six-month period (July 2024 to January 2025). The hospital's ethical review board approved this study.

### Data collection:

We conducted a retrospective study of 50 patients with cirrhosis complicated by hepatocellular carcinoma (HCC) at our institution over a six-month period (July 2024 to January 2025). Cirrhosis was confirmed using ultrasound or transient elastography, corroborated by clinical and biochemical parameters. Patients with cirrhosis of any etiology were included. HCC diagnosis was established through imaging (ultrasound, CT, or MRI) and serum alpha-fetoprotein (AFP) levels.

The baseline characteristics including sex, age, biochemistry data, etiology of HCC, Child-Turcotte-Pugh (CTP) score, BCLC stage, status of portal vein thrombosis, HCC treatment and mortality were recorded.

The ALBI score, ALBI grade, and ALBI-PLT score were calculated as follows:

- a) ALBI score:  $[\log_{10} \text{bilirubin } (\mu\text{mol/L}) \times 0.66] - [\text{albumin } (\text{g/L}) \times 0.085]$ .

- b) ALBI grade: Grade 1 ( $\leq -2.60$ ), Grade 2 ( $> -2.60$  to  $-1.39$ ), Grade 3 ( $> -1.39$ ).
- c) ALBI-PLT score: Sum of ALBI grade points (1–3) and platelet count points (1 for  $>150 \times 10^3/\text{mm}^3$ ; 2 for  $\leq 150 \times 10^3/\text{mm}^3$ ), ranging from 2 to 5.

Gastroesophageal varices (GEVs) were evaluated by esophagogastroduodenoscopy (EGD). Varices were classified as grade 1, 2 or 3 with red signs noted. All EGDs were performed by a single experienced hepatologist using a standardized protocol. Therefore, inter-observer variability in variceal grading did not apply in this study.

### Patient selection:

Inclusion criteria:

- a) Age  $\geq 18$  years
- b) Diagnosis of hepatocellular carcinoma on underlying cirrhosis
- c) Compensated cirrhosis (Child–Turcotte–Pugh score  $\leq 6$ )
- d) Underwent EGD within 3 months of HCC diagnosis

Exclusion criteria:

- a) Patients who did not receive endoscopic screening of esophageal varices within three months of HCC diagnosis
- b) Patients with splenectomy, or partial splenic arterial embolization were excluded, as these interventions could affect the ALBI-PLT score.
- c) Decompensated patients. The compensated HCC patients were defined as an absence of ascites, variceal, hepatic encephalopathy or jaundice and a CTP score of 5 or 6.
- d) Patients with missing key were excluded from the analysis.

The study complied with the ethical guidelines of the Declaration of Helsinki and was approved by the Ethics Committee of our Institutional Review Board.

### Statistical analysis:

The statistical analysis software (SPSS) was used to perform statistical analysis on the data (SPSS Inc. Released 2019. IBM SPSS statistics for windows, version 26.0, Armonk, NY: IBM Corp.). Quantitative data were provided as mean  $\pm$  standard deviation (SD), median, and qualitative data as number and percent. To find a correlation between two or more qualitative variables, the Chi-squared ( $\chi^2$ ) or Fischer exact tests were used. For comparison between two groups of quantitative variables and independent parametric results, the Student t-test was used. For comparison between two groups of quantitative variables and independent non-parametric results, the Mann-Whitney test was used. For different potential diagnostic test or marker cut-offs, the Receiver Operating Characteristics (ROC) curve was used. P-value  $\leq 0.05$  to be statistically significant.

### Sample size considerations

This was an exploratory pilot study of all consecutive eligible patients over the study period. No formal sample size calculation was performed. We acknowledge that the modest sample size ( $n=50$ ) limits statistical power, particularly for subgroup analyses, and this is addressed in the Discussion.

## Results

### Patient characteristics

The study cohort consisted of 50 patients diagnosed with hepatocellular carcinoma (HCC) on a background of compensated cirrhosis. The mean age was  $67.5 \pm 12.2$  years, reflecting an older adult population typically affected by chronic liver disease and HCC. A male predominance was noted, with 62% of the patients being male, aligning with the known higher incidence of HCC in men due to hormonal and etiologic risk differences. In terms of underlying liver disease, Hepatitis C virus (HCV) infection was the most common etiology, accounting for 44% of cases, followed by Hepatitis B (26%) and alcohol-related liver disease (20%). Other less common etiologies comprised 10% of the cohort.

On endoscopic evaluation, esophageal varices were found in 82% of patients, underscoring the high burden of portal hypertension in this population. Specifically, 18% of patients had no varices, 4% presented with grade I varices, 44% with grade II, and 34% with grade III varices. Thus, a significant proportion (78%) of patients had medium to large varices (grades II–III), which are more likely to be classified as high-risk varices (HRVs) due to their potential for bleeding. For available AFP measurements, 28% had levels above the commonly used diagnostic threshold of 200 ng/mL, consistent with active HCC. Biological characteristics are detailed in Table 1.

**Table 1** Biological characteristics of the study population

Variable	N	Minimum	Maximum	Mean	Standard Deviation
Platelets ( $\times 10^3/\mu\text{L}$ )	50	29	314	126.6	68.52
Alpha-fetoprotein (ng/mL)	50	1.05	185.5	9.938	34.544
Albumin (g/L)	45	7.74	45	31.3	7.94
Total Bilirubin ( $\mu\text{mol/L}$ )	50	2.21	171.9	35.9	31.90
Alkaline Phosphatase (U/L)	47	95	1,222	375.7	264.25
Gamma-Glutamyl Transferase (U/L)	49	22	767	170.7	146.74
Aspartate Aminotransferase (U/L)	50	17	830	102.9	127.77
Alanine Aminotransferase (U/L)	50	4.10	460	53.2	63.27
International Normalized Ratio (INR)	50	0.89	6.94	1.44	0.83
Hemoglobin (g/dL)	50	7.30	15	11.83	1.85
Prothrombin Time (s)	50	15.30	100	68.8	17.6

Among the 50 patients treated for hepatocellular carcinoma (CHC), 54% received symptomatic treatment, 12% were treated with Sorafenib, 10% underwent radiofrequency therapy, 10% had surgery, 6% received chemoembolization, 4% received palliative care, and 2% underwent liver transplantation. Out of the 50 patients, 30% died from hepatocellular carcinoma (CHC), while 70% were still alive or their status was not related to CHC. Mortality was higher among patients with advanced-stage HCC and those receiving only symptomatic or palliative care, while patients undergoing surgical or loco-regional therapies had lower mortality rates.

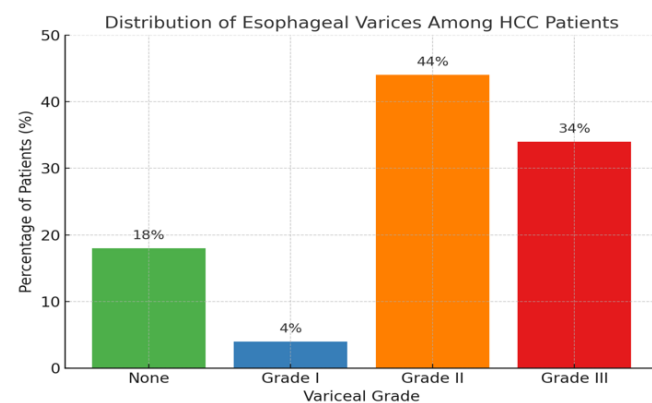
### Diagnostic performance of the ALBI-PLT Score

To evaluate the utility of the ALBI-PLT score in predicting HRV, a Pearson Chi-square test was conducted, revealing a statistically significant association between higher ALBI-PLT scores and the presence of HRV ( $\chi^2 = 43.677$ , degrees of freedom = 4,  $p < 0.001$ ). This strong association suggests that patients with higher ALBI-PLT scores are more likely to have clinically significant varices requiring endoscopic surveillance or prophylactic treatment.

Further evaluation of the score’s diagnostic accuracy was conducted using receiver operating characteristic (ROC) curve analysis. The ALBI-PLT score demonstrated excellent discriminative ability in identifying patients with HRV, with an area under the curve (AUC) of 0.908 (95% confidence interval: 0.736–1.000,  $p < 0.001$ ). An AUC above 0.9 indicates outstanding diagnostic performance, comparable to or exceeding other non-invasive tools currently in use. The optimal cutoff value for the ALBI-PLT score was determined to be  $\geq 1.5$ , based on the Youden Index, which maximizes the sum of sensitivity and specificity. At this threshold, the ALBI-PLT score achieved a sensitivity of 100%, indicating that it correctly identified all patients with HRV. Its specificity was 88.9%, correctly ruling out HRV in the majority of patients without significant varices. The resulting Youden Index was 0.889, further emphasizing the strong discriminative power of the model.

These findings imply that an ALBI-PLT score below 1.5 has a high negative predictive value for HRV. Thus, patients scoring below this threshold are highly unlikely to have significant varices and may safely forgo routine esophagogastroduodenoscopy (EGD), reducing the burden of unnecessary invasive procedures in this vulnerable population.

Multivariate logistic regression analysis confirmed the ALBI-PLT score as an independent predictor of high-risk varices, with an odds ratio (OR) of 6.35 ( $p = 0.002$ ). This means that for each unit increase in the ALBI-PLT score, the odds of having HRV increased more than sixfold, even after adjusting for potential confounders. These results support the clinical utility of the ALBI-PLT score as a simple, reliable, and non-invasive screening tool in HCC patients with compensated cirrhosis (Figure 1&2).

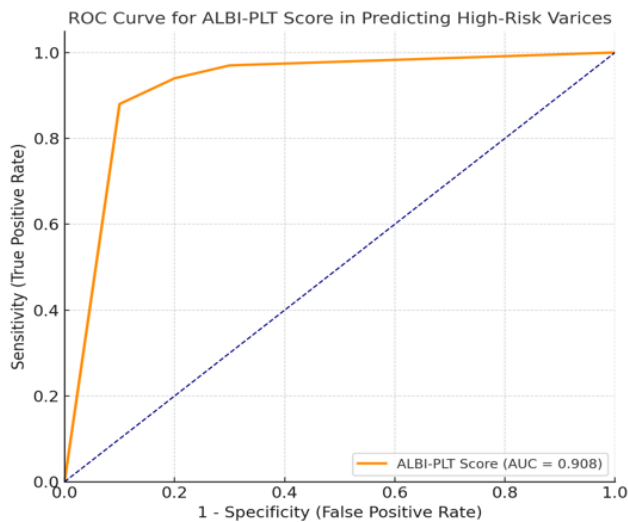


**Figure 1** Distribution of Esophageal Varices among HCC Patients.

## Discussion

In this study, we investigated the utility of the ALBI-PLT score—a composite of the albumin-bilirubin (ALBI) grade and platelet count—as a non-invasive tool for predicting esophageal varices (EV), particularly high-risk varices (HRV), in patients with

hepatocellular carcinoma (HCC) and compensated cirrhosis. Our findings demonstrate a high prevalence of esophageal varices (82%) in this cohort, with a substantial proportion (78%) having grade II or III varices, underscoring the significant burden of clinically relevant portal hypertension (CSPH) in this population.



**Figure 2** ROC Curve for ALBI-PLT Score in Predicting High-Risk Varices showing an AUC of 0.908.

Importantly, the ALBI-PLT score showed excellent diagnostic accuracy for predicting HRV, with an AUC of 0.908, sensitivity of 100%, and specificity of 88.9% at a cutoff value of  $\geq 1.5$ . Logistic regression confirmed its role as an independent predictor (OR = 6.35,  $p = 0.002$ ), highlighting its potential as a reliable and accessible screening tool. Clinically, this cutoff suggests that patients below the threshold of 1.5 are very unlikely to harbor high-risk varices, meaning that a meaningful subset of compensated HCC patients could potentially avoid routine EGD. Although our dataset was modest, applying this threshold would have spared approximately one in five patients from unnecessary endoscopy. However, the wide confidence interval around the ROC curve (0.736–1.000) reflects the limited sample size and indicates that the diagnostic precision should be interpreted cautiously. Similarly, although the odds ratio of 6.35 suggests a strong association, its broad confidence interval weakens robustness and further emphasizes the need for larger validation studies.

Our results align with the evolving landscape of non-invasive variceal screening, particularly in the context of the Baveno VII consensus, which recommends avoiding endoscopy in patients with liver stiffness measurement (LSM)  $< 15$  kPa and platelet count  $> 150 \times 10^9/L$ , provided they are compensated and without risk features [5]. However, the presence of HCC may confound LSM due to tumor-related stiffness, potentially leading to false positives.<sup>6-8</sup> In this setting, the ALBI-PLT score may offer a more robust alternative, especially since it incorporates both hepatic synthetic function and portal hypertension markers.

Previous studies have demonstrated the prognostic and diagnostic value of the ALBI score in cirrhosis and HCC. Hiraoka et al. reported that the ALBI grade correlates well with Child-Pugh classification and overall survival in HCC.<sup>9</sup> The addition of platelet count, a surrogate marker for splenic sequestration and portal hypertension, enhances the predictive accuracy for varices. Elshaarawy et al. also highlighted the diagnostic performance of ALBI-based models in variceal prediction, though their cohorts largely excluded patients with HCC.<sup>10</sup>

Our study extends this evidence by validating the ALBI-PLT score specifically in a real-world HCC population. In parallel, several emerging non-invasive approaches have shown promising results for variceal risk stratification in HCC, complementing traditional ALBI-based assessments. Dil op et al. developed a non-invasive algorithm combining clinical and imaging variables in unresectable HCC patients, achieving a high NPV ( $\sim 97.4\%$ ) and safely avoiding endoscopy in more than half of low-risk patients with minimal misclassification.<sup>11</sup> The BFE-HCC score predicts first variceal hemorrhage in HCC using variables including ALBI, tumor features, and portal vein thrombosis, with an AUC of  $\sim 0.82$ .<sup>12</sup> Zhao et al. derived a CT-based imaging score in HCC patients post-bleeding to predict re-bleeding and mortality.<sup>13</sup> Finally, Wazzan et al. used serum autotaxin and Doppler ultrasound in cirrhosis to predict varices.<sup>14</sup> These studies differ from ours in that many include unresectable HCC, focus on bleeding rather than pre-endoscopic screening, or combine imaging modalities, highlighting the novelty of applying ALBI-PLT in compensated HCC patients for variceal screening.

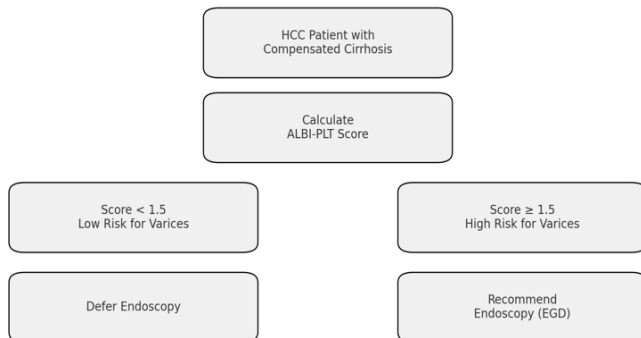
A potential concern, however, is the issue of collinearity between ALBI grade and platelet count. Both parameters are influenced by portal hypertension—ALBI through liver function decline and platelet count through hypersplenism. While their combination improves predictive accuracy, some degree of redundancy cannot be excluded. This underscores the need for further validation in larger datasets, ideally with multivariable models that account for possible collinearity, to confirm that the ALBI-PLT score provides incremental value beyond its individual components.

The clinical relevance of our findings is twofold. First, the ALBI-PLT score could serve as a practical screening strategy in resource-limited settings where access to transient elastography or endoscopy is restricted. Second, by identifying a subgroup of patients with negligible risk of varices, clinicians may reduce the frequency of invasive screening, aligning with patient-centered and cost-effective care models.

Nonetheless, our study has limitations. The retrospective and single-center design introduces potential selection bias and limits generalizability. The cohort was drawn from a North African population, and ethnic or geographic differences in cirrhosis etiology and HCC biology may limit external validity. The modest sample size ( $n = 50$ ) may limit statistical power, and external validation in larger multicenter cohorts is needed. Additionally, we excluded decompensated cirrhotics, in whom variceal bleeding risk is highest; thus, our findings may not apply to this subset. We also did not assess survival outcomes, nor did we perform direct comparisons with transient elastography or other validated non-invasive scores, which would have further contextualized the relative value of ALBI-PLT. Moreover, the AUC and OR estimates, though encouraging, are constrained by wide confidence intervals that reduce statistical precision. Future prospective studies should evaluate longitudinal outcomes such as bleeding risk, mortality, and treatment impact across ALBI-PLT strata, while explicitly considering collinearity between ALBI grade and platelet count as a potential source of bias. Additionally, head-to-head comparisons with emerging non-invasive tools, including the studies cited above, would further clarify the clinical utility of ALBI-PLT.

In conclusion, the ALBI-PLT score appears to be a simple, non-invasive, and accurate predictor of high-risk varices in HCC patients with compensated cirrhosis. It demonstrated strong, though exploratory, diagnostic performance in our cohort. A cutoff value  $< 1.5$  may identify a low-risk population who could safely avoid routine

endoscopy. Direct comparisons with other non-invasive tools were beyond the scope of this study, and future head-to-head evaluations are needed before relative performance can be established. Validation in larger, diverse cohorts is warranted to support its incorporation into clinical guidelines (Figure 3).



**Figure 3** Proposed algorithm using ALBI-PLT Score in predicting varices.

## Conclusion

The ALBI-PLT score is a valuable non-invasive tool for screening esophageal varices in HCC patients with compensated cirrhosis. A score <1.5 effectively identifies low-risk patients who may be spared from routine endoscopy. Incorporation of this score into clinical algorithms may optimize resource use and improve patient care.

## Declarations

### Ethical approval

The study was approved by the Institutional Ethics Committee of Habib Bougatfa University Hospital.

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### Conflicts of interest

The authors declare no conflicts of interest.

### Competing interests disclosure:

The authors have no competing interests or relevant affiliations with any organization or entity with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

### Author contributions

E. Slama: Conception, writing the first draft of the paper, S. Ben Hamida: First revision, H. Elloumi: supervising and critical review, I. Cheikh: supervising and critical review.

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