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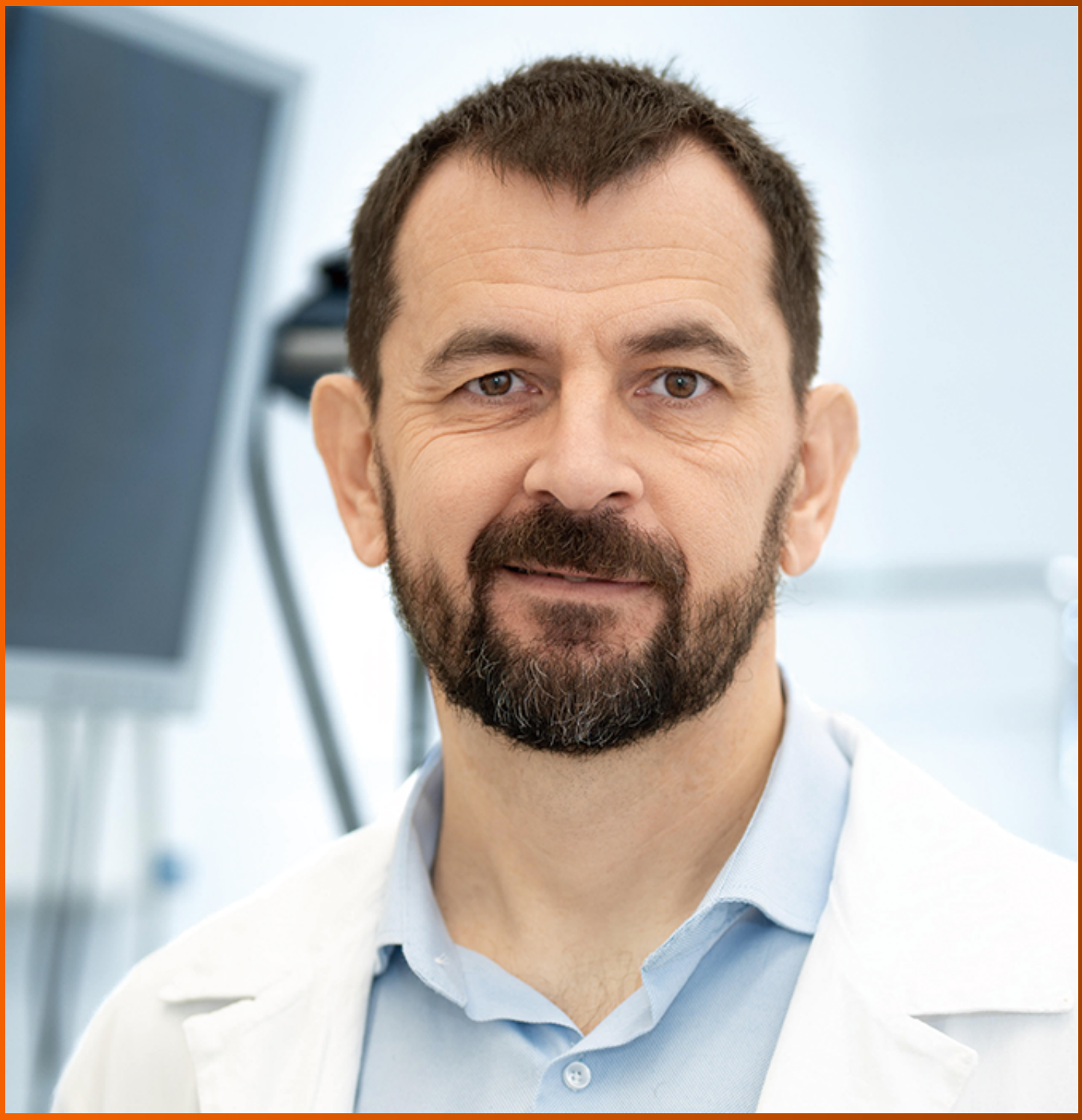

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EDITORIAL

Role of albumin-bilirubin score in non-malignant liver disease

Shi-Xue Xu, Fan Yang, Nan Ge, Jin-Tao Guo, Si-Yu Sun

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Abstract

The albumin-bilirubin (ALBI) score, which was proposed to assess the prognosis of patients with hepatocellular carcinoma, has gradually been extended to other liver diseases in recent years, including primary biliary cholangitis, liver cirrhosis, hepatitis, liver transplantation, and liver injury. The ALBI score is often compared with classical scores such as the Child-Pugh and model for end-stage liver disease scores or other noninvasive prediction models. It is widely employed because of its immunity to subjective evaluation indicators and ease of obtaining detection indicators. An increasing number of studies have confirmed that it is highly accurate for assessing the prognosis of patients with chronic liver disease; additionally, it has demonstrated good predictive performance for outcomes beyond survival in patients with liver diseases, such as decompensation events. This article presents a review of the application of ALBI scores in various non-malignant liver diseases.

Key Words: Albumin-bilirubin score; Liver cirrhosis; Primary biliary cholangitis; Hepatitis; Liver transplantation; Liver injury

Core Tip: The application of albumin-bilirubin score in liver diseases is not limited to hepatocellular carcinoma. In addition to predicting disease progression, it can also be used to predict survival in other non-malignant liver diseases.

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INTRODUCTION

The albumin-bilirubin (ALBI) score, obtained by combining serum albumin and bilirubin measurements, was initially proposed by Johnson *et al*[1] for evaluating liver function in patients with hepatocellular carcinoma (HCC). This evidence-based model is calculated based on objective laboratory values with the following formula: ALBI score = 0.66 × log10 [total bilirubin (μmol)] - 0.085 × [albumin (g/L)]. Based on this calculation, patients can be stratified into three classes: grade I (≤ -2.60), grade II (> -2.60 but ≤ -1.39), and grade III (> -1.39)[1].

The Child-Pugh score was the earliest scoring system proposed and applied to assess the prognosis of patients with cirrhosis. It consists of five components: Albumin, bilirubin, prothrombin/international normalized ratio (INR), ascites magnitude, and hepatic encephalopathy stage. An increasing number of researchers have pointed out that the assessment of ascites and hepatic encephalopathy in clinical practice is subjective and lacks objective evaluation standards[2]. In contrast, the ALBI score not only eliminates subjective scoring components (ascites and hepatic encephalopathy) but also evaluates bilirubin and albumin as continuous variables rather than assigning scores based on cutoff values. Compared with the widely used model for end-stage liver disease (MELD) score, which incorporates bilirubin, creatinine, and INR to predict the survival of patients with chronic liver disease, the ALBI score has lower testing costs. The ALBI score has been widely applied in patients with HCC[2] and has gradually been applied in the assessment of nonmalignant liver diseases. This article presents an overview of the application of ALBI scoring in nonmalignant liver diseases.

ALBI SCORE IN PRIMARY BILIARY CHOLANGITIS

Primary biliary cholangitis (PBC) is an autoimmune liver disease that causes progressive destruction of the intrahepatic bile ducts and is marked by the presence of highly specific anti-mitochondrial autoantibodies in the serum. In the preclinical stage, patients with PBC may remain asymptomatic with normal liver function[3], but due to the risk of progression to cirrhosis and liver failure, it is necessary to identify high-risk subgroups. Progressive elevation of serum bilirubin levels and a decline in liver synthetic function are poor prognostic factors for PBC[4]. The ALBI score not only combines these two factors but is also significantly correlated with histological changes, another poor prognostic factor for PBC[5,6]. In a retrospective study that included 61 patients with primary biliary cirrhosis, Chan *et al*[7] compared the prognostic performance of the Child-Pugh, MELD, Mayo risk, Yale, European, Newcastle, and ALBI scores. The ALBI score outperformed or showed similar prognostic performance to the other models in terms of discriminatory ability, homogeneity, and monotonicity of gradients. It has also been identified as the only independent predictor of these prognostic scores as well as histological stage[7]. Considering the small sample size in this study, a cohort study was performed that included 8768 patients; the authors found that a higher ALBI grade was associated with significantly higher all-cause mortality or the need for liver transplantation (LT), as well as liver-related mortality or the need for LT; the 5-year cumulative LT-free survival rates for patients in the ALBI grades I, II, and III groups were 97.2%, 82.4%, and 38.8%, respectively[6]. Time-dependent receiver operating characteristic curve (ROC) analysis showed that the ALBI score had higher areas under the ROC (AUROCs) than other markers for predicting overall survival and the incidence of LT[8].

The ALBI score also plays a predictive role when the disease progresses to liver cirrhosis. In patients with compensated PBC cirrhosis, a higher ALBI score was independently associated with liver-related mortality or LT and showed comparable or even better diagnostic accuracy for predicting 5-year liver-related mortality than the conventional Mayo risk and MELD scores[9]. Another study that included patients with PBC, 79.9% of whom were in the cirrhotic stage, similarly validated the application of the ALBI score to PBC cirrhosis[10]. Currently, there is a lack of research on the application of the ALBI score in the decompensated PBC cirrhosis population, and future large-scale prospective studies are required to validate its use in this specific population. Additionally, whether the ALBI score can be used to monitor the response of patients with PBC to ursodeoxycholic acid therapy remains unknown.

ALBI SCORE IN HEPATITIS B VIRAL INFECTION

Hepatitis B imposes a significant medical burden and requires substantial financial resources for its annual management and treatment. The ALBI score has been widely studied and validated as a prognostic indicator in patients with hepatitis B-related liver diseases including chronic hepatitis B, cirrhosis, and acute-on-chronic liver failure. In patients with chronic hepatitis B, the ALBI score is significantly correlated with the fibrosis stage, suggesting that it can be used for both fibrosis staging and distinguishing advanced liver fibrosis from cirrhosis. ALBI scores < -2.190 also correlated with better HCC-free survival[11]. In patients with acute-on-chronic liver failure, a high ALBI score upon admission may serve as a predictor of 3-month mortality[12].

The application of the ALBI score is more extensive in patients with hepatitis B-related cirrhosis. Chen *et al*[13] demonstrated superior predictive ability for long-term prognosis in patients with hepatitis B virus (HBV)-related cirrhosis compared with the Child-Pugh and MELD scores. In contrast, Wang *et al*[14] and Qi[15] found that the ALBI score was not superior to the Child-Pugh or MELD scores in predicting long-term prognosis in patients with HBV-related cirrhosis. In cirrhotic patients with acute-on-chronic liver failure, Peng *et al*[16] suggested that the ALBI score was not applicable for predicting in-hospital mortality, as it demonstrated poor discriminatory power with an AUROC of 0.57 [95% confidence interval (CI): 0.38-0.75; $P = 0.52$].

ALBI SCORE IN HEPATITIS C VIRAL INFECTION

Similar to its application in chronic hepatitis B, the ALBI score can also be used to diagnose the fibrosis stages in patients with chronic hepatitis C; a lower ALBI score is also associated with better HCC-free survival and overall survival[17]. Another common clinical scenario for hepatitis C infection is when patients receive direct-acting antiviral (DAAs) therapy to achieve viral clearance. In a population of patients with cirrhosis receiving DAA therapy, the ALBI score was significantly associated with the risk of HCC development. ALBI grade is also an independent risk factor for HCC occurrence[18]; even after hepatitis C virus eradication and achievement of sustained virologic response, the ALBI score remains significantly associated with a higher risk of HCC development in patients with hepatitis C virus-related cirrhosis[19,20].

ALBI SCORE IN ETIOLOGY-UNSPECIFIED CIRRHOSIS

Mortality

Liver cirrhosis is the end stage of chronic liver disease and is often accompanied by complications such as ascites, variceal bleeding, and hepatic encephalopathy. Individuals with compensated cirrhosis have a five-fold higher mortality risk compared to the general population, while those with decompensated cirrhosis have a ten-fold higher risk[21]. Hsieh *et al*[22] analyzed 242 patients with liver cirrhosis who underwent hemodynamic testing, exploring the value of various non-invasive and hemodynamic indicators in predicting prognosis in patients with liver cirrhosis. Among the various non-invasive scoring systems, the ALBI score demonstrated the strongest correlation with the hepatic venous pressure gradient and showed good predictive performance for 3-month (AUROC = 0.691) and 6-month mortality (AUROC = 0.740). Fragaki *et al*[23] also demonstrated the advantage of using ALBI in predicting the 1-, 2-, and 24-month survival rates in patients with liver cirrhosis (AUROCs = 0.912, 0.781, and 0.780, respectively). In the subgroup of individuals with decompensated cirrhosis, ALBI score was independently associated with death [hazard ratio (HR) = 3.03; 95%CI: 1.92-4.78; $P < 0.001$][23], and higher ALBI grade indicated a significantly higher risk of death/LT (HR = 2.13; 95%CI: 1.59-2.85; $P < 0.001$)[24]. The AUROC of the ALBI score for predicting in-hospital mortality was 0.873[25]. In patients with cirrhosis who experience post-banding ulcer bleeding following endoscopic variceal ligation treatment, ALBI grade III was significantly associated with a higher 6-week mortality [odds ratio (OR) = 4.8; 95%CI: 1.18-19.6; $P = 0.029$][26]. In cirrhotic patients who underwent transjugular intrahepatic portosystemic shunt placement, the ALBI score and grade have been identified as significant predictors of 30-d mortality from hepatic failure as well as of overall survival; however, their predictive performance was inferior to that of the MELD score[27].

Decompensation event

Gastroesophageal varices represent a life-threatening complication of liver cirrhosis, manifesting in 40% of the patients with compensated cirrhosis and in up to 85% of those with decompensated cirrhosis. Left unmanaged, acute variceal bleeding occurs in approximately 12% of cases annually, posing a life-threatening risk to individuals with cirrhosis[28]. Timely identification of patients with liver cirrhosis who are at risk of variceal bleeding is crucial for improving prognosis through primary and secondary prevention measures[29,30]. Miyamoto *et al*[31] further divided ALBI grade II into stages IIa and IIb according to platelet level and found that patients with ALBI grade III had higher risks and rates of gastroesophageal varices compared to those with ALBI grades I-IIa. In addition, in patients who underwent endoscopic treatment for esophageal variceal bleeding, there were significant correlations between ALBI grade III and rebleeding (OR = 2.67; 95%CI: 1.34-5.3; $P = 0.005$)[26]. The study conducted by Navadurong *et al*[32] not only explored esophageal variceal bleeding as a decompensated event but also included ascites and hepatic encephalopathy as endpoints of observation. At 3 years of follow-up, time-dependent ROC analysis showed that the ALBI score-predicted decompensation risk was an AUROC of 0.86 (95%CI: 0.78-0.92) in cirrhotic patients. The cumulative incidences of decompensation over 3 years were 3.1%, 22.6%, and 50% in patients with ALBI grades I, II, and III, respectively. The OR for decompensation in patients with ALBI grade III was 23.33[32]. Despite these findings, this study did not analyze different decompensated events as separate endpoints or perform subgroup analysis targeting specific decompensated events.

Others

The ALBI score can serve not only as a predictive factor but also as an assessment tool to evaluate the current liver function of patients. Zhu *et al*[33] investigated the value of using the ALBI score in patients with cirrhosis undergoing splenectomy for hypersplenism. In this study, the ALBI score was utilized as an indicator to assess the liver function of patients, whereas ALBI grading was used as a predictive factor for postoperative benefits. Their findings indicated that

improvement in liver function after splenectomy may manifest as a decrease in the ALBI score, and this change is more commonly observed in patients classified as ALBI grade II or III.

ALBI SCORE IN LT

LT has always been considered the best option and only effective treatment for end-stage liver disease; however, owing to the high cost of medical care, scarcity of donor organs, and increasing number of patients awaiting LT, surgical procedures are limited. To improve the outcomes of LT recipients, it is necessary to conduct preoperative evaluations of liver function to screen and identify the most suitable candidates for LT. To this end, several studies have explored the application of the ALBI score in the prognosis of LT. Zhang *et al*[34] divided 272 patients who underwent right lobe LT based on their ALBI grade. Patients with ALBI grade III demonstrated higher susceptibility to bacterial pneumonia and early allograft dysfunction than those with grades I and II. The ALBI score demonstrated a higher predictive accuracy for 30-d mortality (AUROC = 0.702) than the Child-Pugh and MELD scores (AUROCs = 0.669 and 0.540, respectively). Another study demonstrated that ALBI grade III was an independent risk factor for overall survival after LT (HR = 1.836; 95%CI: 1.151-2.921; P = 0.010). It also revealed that ALBI grade III was associated with poorer overall survival in patients without HCC who underwent LT; this difference was not observed in patients with HCC[35]. Ma *et al*[36] calculated that the cutoff value of the ALBI score for predicting post-LT survival was -1.48. Patients with ALBI scores > -1.48 had lower overall survival rates and higher incidences of post-LT complications such as biliary complications, intra-abdominal bleeding, sepsis, and acute kidney injury.

LIVER INJURY

Recently, Chou *et al*[37] explored the application of ALBI score for traumatic liver injury. Research has found that the ALBI score is independently associated with the risk of mortality, and patients with ALBI grade III have significantly higher mortality rates and longer hospital stays compared to those with lower ALBI grades. Their findings suggest that ALBI grade could serve as a valuable tool for categorizing the risk of mortality in adult trauma patients with liver injury.

CONCLUSION

Recognized for its simplicity and objectivity, the ALBI score is widely employed by clinical physicians for evaluating various liver diseases, not just liver cancer. Compared to the classic Child-Pugh and MELD scores, it exhibits wider applicability because it is more sensitive to subtle liver function changes. Despite these advantages, the ALBI score also has limitations. In certain liver diseases and extrahepatic conditions that can affect bilirubin levels, such as cholangiocarcinoma, intrahepatic bile duct stones, and hemolysis, this scoring system may not be applicable. The ALBI score also does not allow prediction of patient responses to specific treatments, as each patient has unique physiological characteristics, disease conditions, and treatment history. Doctors need to consider relevant indicators and clinical information to comprehensively assess disease status. It is recognized that no single scoring system can fully capture the complexity of a patient's condition, and several aspects of ALBI scoring require further research. The potential applicability of the ALBI score in assessing benign non-liver disease, particularly metabolic disorders, is worth exploring. The correlation between the ALBI score and other liver function indicators such as coagulation function and liver enzyme levels should also be investigated to provide a more comprehensive evaluation of liver function status, which may contribute to better prognosis prediction. Additionally, the application of the ALBI score in predicting treatment response requires further research, such as for its use in guiding clinical medication. In summary, while the ALBI score is an important liver function assessment tool, further research is needed to enhance its application value in clinical practice.

FOOTNOTES

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