BMC Gastroenterology

RESEARCH

Open Access

Prognostic value of ALBI score for all-cause mortality in metabolic associated fatty liver disease patients: a cohort study from NHANES 2003–2018

Guoxing Zhou[1], Weiwei Han[2], Jinhong Luan[1] and Baozhu Ma[1*]

Abstract

Background & aims Metabolic Associated Fatty Liver Disease (MAFLD) is a prevalent chronic liver disorder with severe potential outcomes. While the albumin-bilirubin (ALBI) score demonstrates prognostic utility in other chronic liver diseases, its specific role and predictive performance in MAFLD patients, particularly regarding all-cause mortality, remain incompletely understood. This study aims to investigate the association between ALBI scores and all-cause mortality in individuals with MAFLD and to evaluate its prognostic potential using large-scale NHANES data.

Methods Drawing on data from the population-based National Health and Nutrition Examination Survey (NHANES) conducted between 2003 and 2018, we employed weighted multivariable Cox proportional hazards regression to assess the relationship between ALBI scores and all-cause mortality in a cohort of 5,666 MAFLD patients. ALBI scores were calculated and categorized into tertile (Q1: ALBI < -2.96; -2.96 ≤ ALBI < -2.70; Q3: ≥ -2.70). MAFLD was diagnosed using the U.S. Fatty Liver Index (US-FLI) with a cutoff score of ≥ 30, while excluding other chronic liver diseases. Statistical analyses incorporated NHANES sampling weights and adjusted for potential confounders using multivariable Cox regression models. Additionally, we conducted threshold effect analysis to identify potential inflection points in the ALBI-mortality relationship and used Kaplan-Meier survival analysis to visualize survival differences across ALBI tertiles.

Results In this cohort study of 5,666 MAFLD patients, 1,093 (19.29%) experienced mortality during a median follow-up of 8.5 years. Following adjustment for confounding factors, elevated ALBI scores demonstrated a significant correlation with an increased risk of death from any cause ($p < 0.001$). The hazard ratios (HR) for mortality across ALBI tertile (Q1-Q3) were 1.00 (reference), 1.32 (1.05–1.65), and 1.74 (1.42–2.12), respectively. Each 1-unit increase in ALBI score was associated with a 193% higher risk of death (HR: 2.93, 95% CI: 2.02–4.24). Threshold effect analysis identified an inflection point at ALBI = -2.69, using piecewise Cox regression, mortality risk increased sharply above this threshold (HR = 4.86, 95% CI: 3.32–7.11, $p < 0.0001$). ROC curve analysis showed AUC values of 0.715, 0.646, and 0.652 for 1-, 2-, and 3-year mortality, respectively, with calibration curves indicating strong agreement between predicted and actual probabilities.

*Correspondence:
Baozhu Ma
mabaozhu@hljucm.edu.cn

Full list of author information is available at the end of the article

Conclusion Our study demonstrates that ALBI scores are a moderate predictor of all-cause mortality in MAFLD patients, particularly at ALBI ≥ -2.69, with an AUC of 0.715 for 1-year mortality. These findings highlight the potential of ALBI scores to identify high-risk patients early, supporting their use in clinical prognostic assessments. Future research should validate these results in diverse populations.

Keywords MAFLD, ALBI score, Metabolic syndrome, All-cause mortality, Threshold effect, Survival analysis

Introduction

Emerging as a major global health challenge, Non-alcoholic Fatty Liver Disease (NAFLD) affects approximately 30.2% of adults, characterized pathologically by abnormal lipid deposition within liver parenchyma [1–3]. Its escalating prevalence mirrors the worldwide epidemic of metabolic dysregulation and obesity-related comorbidities. NAFLD exhibits bidirectional pathophysiological relationships with metabolic syndrome constituents—particularly visceral adiposity-induced insulin resistance, atherogenic lipid profiles, and cardiorenal pathologies [4, 5]. These interconnected metabolic aberrations accelerate hepatic extracellular matrix remodeling and independently predict decompensated cirrhosis and hepatocarcinogenesis [6, 7]. Current clinical paradigms confront dual limitations: reliance on imperfect diagnostic modalities (ultrasound, MRI, or biopsy) with inherent sensitivity constraints [8, 9], therapeutic options are currently limited to lifestyle interventions, as no approved disease-modifying pharmacologic agents exist [10, 11]. These gaps highlight an urgent need for non-invasive prognostic biomarkers to optimize therapeutic monitoring and outcome prediction.

It is important to note the recent paradigm shift in the nomenclature of fatty liver disease. An international expert consensus statement in 2020 proposed replacing NAFLD with Metabolic Associated Fatty Liver Disease (MAFLD) [12]. This change was driven by several key considerations. Unlike NAFLD, MAFLD does not require the exclusion of other liver disease causes, such as viral hepatitis or significant alcohol consumption, allowing for a more inclusive and clinically practical diagnosis. The new terminology also better reflects the disease's etiology by explicitly acknowledging its strong association with metabolic dysfunction and metabolic syndrome, moving away from a diagnosis of exclusion to one based on positive criteria [13]. This shift aims to reduce stigma associated with the term "non-alcoholic" and "fatty," improve disease awareness, and facilitate more precise patient identification and management. In this study, we have adopted the term MAFLD to align with the latest academic nomenclature and to reflect the strong metabolic associations of the disease.

The albumin-bilirubin index (ALBI) has gained recognition as an objective hepatic function metric in chronic liver diseases. Calculated from standardized serum albumin and bilirubin measurements, this composite score quantifies synthetic and excretory liver capacities through validated algorithms [14–17]. Recent comparative analyses reveal ALBI's enhanced discriminative power versus traditional staging systems in identifying preclinical hepatic impairment, a critical advantage given MAFLD's protracted subclinical progression [18, 19]. However, demographic heterogeneity (age, sex, ethnic background) and metabolic comorbidities (e.g., diabetes, dyslipidemia) may confound ALBI's prognostic performance. Mechanistically, adipose tissue-derived inflammatory mediators and glucolipotoxic stress may synergistically impair hepatocellular integrity [20–22], thereby modulating ALBI components. Additionally, epigenetic modifications and lifestyle factors (nutritional habits, sedentary behavior) likely contribute to interindividual variability in ALBI trajectories among MAFLD patients.

NHANES is a survey representative of the nation that systematically gathers health and dietary information from the U.S. general population, employing a sophisticated multi-stage probability sampling method, with data made public every two years. NHANES (www.cdc.gov/nchs/nhanes) is designed to assess the health and nutritional status of adults and children in the United States. The survey is distinctive in that it incorporates both physical examinations and interviews. Several cross-sectional, nationally representative health examination surveys are part of the NHANES program. Questions about demographics, health insurance status, dietary habits, acute and chronic medical issues, mental health, and prescription drug use are all included in the health interview. Exam components can change between survey cycles but typically include blood pressure, dental exams, vision, hearing, dermatology, fitness, balance and strength testing, respiratory testing, taste and smell, and body measurements (weight, height, skin folds, body composition scans). Hematology, organ and endocrine function (e.g., thyroid, kidney), environmental exposure, dietary biomarkers, metabolic and cardiovascular health, and infectious disease are a few examples of laboratory components.

This nationwide cohort study, utilizing prospectively collected population-based NHANES data (2003–2018), aimed to rigorously investigate the association between ALBI scores and all-cause mortality in individuals with MAFLD and to evaluate its prognostic performance. We employed weighted multivariable Cox proportional

hazards regression, complemented by threshold effect analysis, Kaplan-Meier survival analysis, and ROC curve analysis, to assess ALBI's independent predictive capacity after adjusting for comprehensive sociodemographic, metabolic, and behavioral confounders. Ultimately, this study sought to establish the independent association of ALBI scores with all-cause mortality in MAFLD patients and to determine the predictive performance of ALBI scores for short-term mortality within this population.

Materials and methods

Study design and participants

This study utilized data from the National Health and Nutrition Examination Survey (NHANES) conducted between 2003 and 2018. Ethical approval was obtained from the Centers for Disease Control and Prevention (CDC) Institutional Review Board. All participants provided written informed consent. The study was conducted in accordance with the Declaration of Helsinki and relevant guidelines and regulations. The methods used in this study were approved by the CDC Institutional Review Board, and the data used are de-identified and publicly accessible, thus exempting the study from further review.

The CDC Institutional Review Board granted ethical clearance, and all participants provided written informed consent. To maintain data integrity, individuals lacking essential ALBI score elements, mortality data, or MAFLD diagnosis standards were not included. Missing data in the remaining variables were addressed using multiple imputation with chained equations (MICE), producing five complete datasets. The imputation models incorporated all analytical variables and auxiliary covariates to preserve underlying data structure and relationships. The specific criteria for inclusion and exclusion are detailed in Fig. 1.

ALBI formula and grouping

The ALBI score was calculated using the following formula: ALBI = 0.66×log[bilirubin(μmol/L)]−0.085×albumin(g/L), ALBI is divided into 3 grades, the score of ≤−2.60 is grade 1; the score of −2.60< score≤−1.39 is grade 2; the score of >−1.39 is grade 3 [23]. For the purposes of analysis in our cohort, we re-defined ALBI grades by tertiles (denoted Q1–Q3) rather than using the original grade 1–3 cutoffs, due to the limited number of patients falling into original grade 3. Specifically, these tertiles were defined as: group Q1 (ALBI scores < −2.96), group Q2 (ALBI scores −2.96 ≤ ALBI < −2.70), and group Q3 (ALBI scores ≥ −2.70). It is important to note that ALBI is a reverse scale where more negative values indicate better liver function. Thus, lower (more negative) ALBI scores correspond to healthier liver status.

Definition of MAFLD

Fatty liver was defined using the US-FLI, which is calculated as follows: US-FLI = $e^y/(1+e^y)$ × 100, where y = −0.8073 × non-Hispanic black + 0.3458×Mexican American + 0.0093×age + 0.6151 ×$\log_e$ (gamma-glutamyl transferase) + 0.0249 × waist circumference + 1.1792 × $\log_e$ (insulin) + 0.8242 × $\log_e$ (glucose) − 14.7812. The variables for 'non-Hispanic black' and 'Mexican American' were coded as 1 if the participant identified with that ethnicity and 0 otherwise [22]. Fatty liver is defined by a US-FLI score of ≥ 30, as recommended [24, 25]. MAFLD is identified by a US-FLI score of ≥ 30, discounting other established reasons for chronic liver disease. These include viral hepatitis, indicated by positive markers such as hepatitis B surface antigen, hepatitis C antibody, or hepatitis C RNA, and significant alcohol consumption (≥ 2 drinks per day for men or ≥ 1 drink per day for women).

Covariates

Study participants were stratified into three age cohorts: young adults (20–39 years), middle-aged (40–59 years), and older adults (≥ 60 years). Racial/ethnic categorization included non-Hispanic White, non-Hispanic Black, Mexican American, and other self-identified groups. Educational status was categorized into three tiers: incomplete secondary education, secondary education completion (high school diploma or equivalent), and postsecondary attainment (associate degree or higher). Socioeconomic status was evaluated using poverty-income ratio (PIR) tertile: low-income (PIR < 1.0), middle-income (PIR 1.0–3.0), and high-income (PIR > 3.0).

Tobacco exposure history was classified as: lifetime nonsmokers (< 100 cigarettes consumed), active smokers (≥ 100 cigarettes with current use), and former smokers (≥ 100 cigarettes with cessation). Occupational physical activity levels were ascertained through validated questionnaires, dichotomized as engagement or non-engagement in moderate-intensity work-related tasks. Anthropometric evaluation utilized WHO-defined BMI categories: normal weight (< 25 kg/m²), overweight (25–29.9 kg/m²), and obese (≥ 30 kg/m²). Nutritional intake was quantified using 24-hour dietary recall-derived total caloric consumption. Comorbidity profiles incorporated self-reported diagnoses of hypertension, dyslipidemia, and diabetes mellitus.

Comprehensive biochemical profiling encompassed hemoglobin concentration, hepatic transaminases (ALT, AST), and lipid panel components—total cholesterol, triglycerides, LDL cholesterol, and HDL cholesterol. All laboratory parameters were measured using standardized automated assays following NHANES protocols.

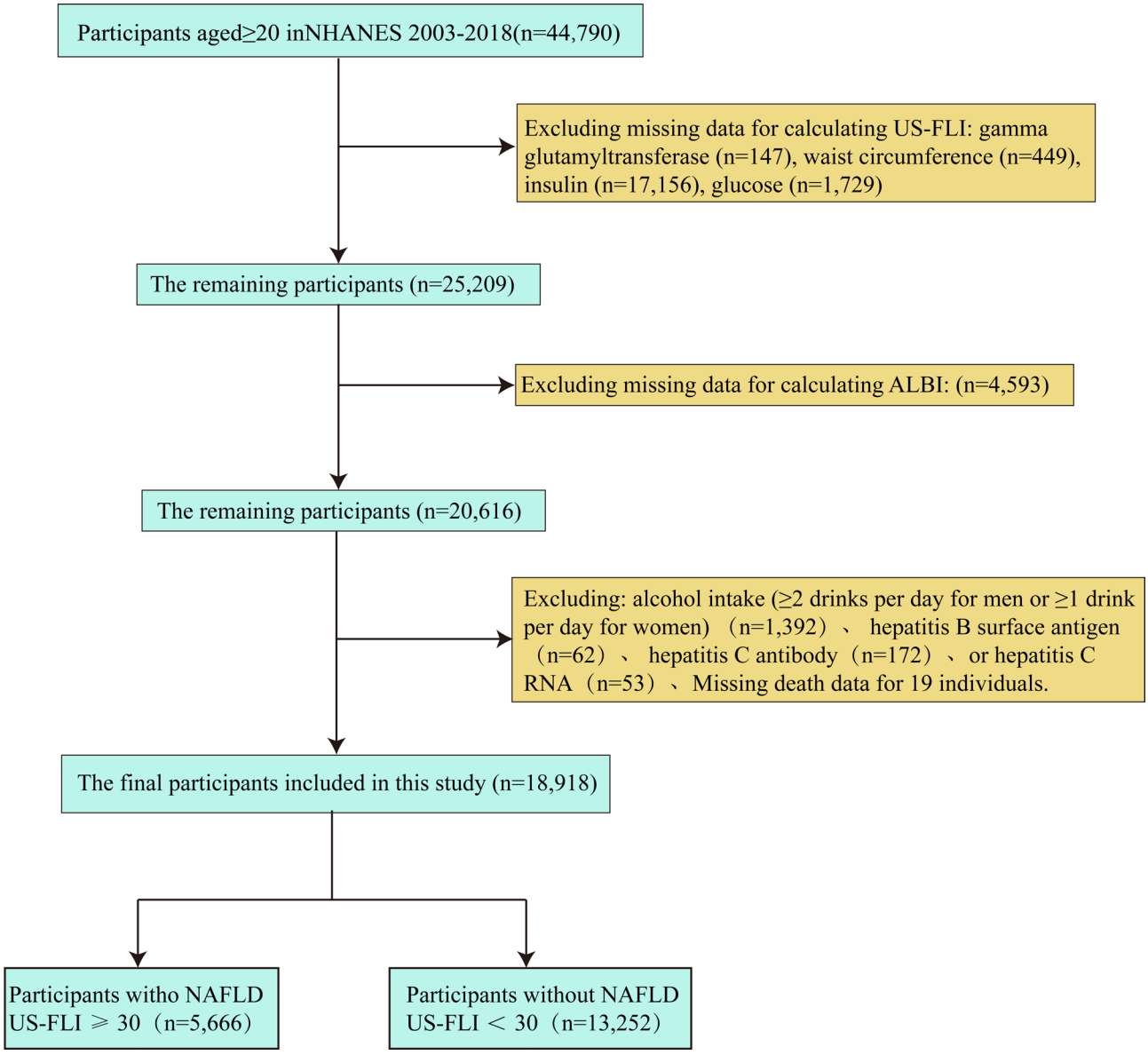

Fig. 1 Flow chart illustrating selection of the study population in NHANES from 2003 to 2018

Statistical analysis

Analytical procedures incorporated sampling weights to address the multistage probability sampling framework of NHANES. Event timing spanned from study entry to mortality occurrence, participant withdrawal, or administrative censoring (December 31, 2019), with temporal intervals quantified in monthly units. Continuous metrics are presented as weight-adjusted means (95% confidence intervals), while categorical variables are summarized as proportion estimates (95% confidence intervals). For comparative analyses, we used the Chi-square test (χ^2) to compare observed and expected frequencies for categorical variables. For continuous variables, we employed the Mann–Whitney U test (U) for non-parametric comparisons and the T-test (T) for parametric comparisons. All statistical tests were two-tailed, with a significance level set at $\alpha = 0.05$. Following NCHS guidelines to combine NHANES 2003–2018 data, each participant's two-year sampling weight was divided by the eight included two-year cycles (spanning 16 years), generating a multi-year weight for the entire study period. For mortality analysis, we utilized NHANES-provided adjusted follow-up weights, linked to the public-use mortality file, which account for the original survey design and loss to follow-up.

Mortality risk stratification utilized the lowest ALBI tertile (Q1) as the reference category. Weighted multivariable proportional hazards regression frameworks assessed associations between ALBI gradients and all-cause mortality, generating hazard ratios (HRs) with

corresponding confidence bounds. The proportional hazards assumption was verified using Schoenfeld residual tests, with global test $p = 0.32$ (ALBI-specific test $p = 0.17$), confirming compliance with the fundamental assumptions of the Cox model. Survival probability disparities across ALBI strata were graphically represented through Kaplan-Meier plots with weighted log-rank testing. Three sequential adjustment tiers were implemented: Minimally adjusted: Univariate analysis; Partially adjusted: Demographic covariates (sex, age, racial/ethnic group, educational attainment, socioeconomic status); Fully adjusted: Behavioral, anthropometric, and metabolic parameters (occupational activity, caloric intake, smoking history, BMI category, cardiometabolic comorbidities, hepatic enzymes, lipid profile) Nonparametric associations were investigated through penalized spline regression within generalized additive models. Threshold identification employed iterative segmented regression techniques when nonlinear patterns emerged, with piecewise Cox models applied to interval-specific risk estimation. Computational workflows were executed in R statistical environment (v4.3.1) and EmpowerStats analytical platform, applying two-tailed significance thresholds ($\alpha = 0.05$) with multiplicity-unadjusted interpretation. Sensitivity analyses confirmed model robustness across alternative adjustment strategies.

Results

Selection of the study population

The NHANES 2003–2018 cohort initially included 80,312 participants. After excluding 35,522 individuals aged ≤ 20 years, 44,790 adults were eligible for analysis. Subsequent exclusion of 24,174 participants with missing US-FLI or ALBI data yielded 20,616 subjects. Following sequential exclusions for: Heavy alcohol use (>14 drinks/week in men; >7 drinks/week in women); Hepatitis B surface antigen (HBsAg) positivity; Hepatitis C virus (HCV) antibody positivity with detectable HCV RNA. The final cohort comprised 5,666 MAFLD patients diagnosed by US-FLI criteria.

Baseline characteristics

Table 1 presents the demographic characteristics of the 5,666 MAFLD participants, categorized by survival status. Of these participants, 1,093 died within a median follow-up time of 102 months. Compared to survivors, participants who died were more often male (56.03% vs. 51.68%, $p = 0.0418$). A larger proportion of non-survivors were aged > 59 years (80.67% vs. 29.94%, $p < 0.0001$). Non-survivors also had a higher prevalence of non-Hispanic white ethnicity (83.42% vs. 72.16%, $p < 0.0001$), diabetes (29.67% vs. 13.69%, $p < 0.0001$), hypertension (60.93% vs. 41.16%, $p < 0.0001$), and hyperlipidemia (57.28% vs. 44.40%, $p < 0.0001$). Notably, the mortality group exhibited significantly higher levels of ALBI (mortality group: −2.74 vs. control: −2.88, $P < 0.001$) than the control group.

Association of ALBI with mortality

As of December 31, 2019, the median follow-up duration was 8.5 years, with 1,093 deaths (19.3%) recorded. A significant positive association emerged between higher ALBI scores and all-cause mortality in MAFLD patients. In the fully adjusted survey-weighted Cox regression model (Model 3), hazard ratios (HRs) for mortality across ascending ALBI tertile (Q1–Q3) were 1.00 (reference), 1.32 (95% CI: 1.05–1.65), and 1.74 (95% CI: 1.42–2.12), demonstrating a dose-response relationship ($P_{trend} < 0.001$; Table 2). When analyzed as a continuous variable, each 1-unit ALBI increase was associated with a 193% elevated mortality risk (HR: 2.93, 95% CI: 2.02–4.24).

Non-linear and threshold analysis

Nonlinear analysis via restricted cubic splines confirmed this positive correlation (generalized additive model $P < 0.001$; Fig. 2). Threshold effect analysis identified a nonlinear relationship ($P = 0.0005$ by log-likelihood ratio test), with an inflection point at ALBI = −2.69. Below this threshold (ALBI < −2.69), each 1-unit ALBI increase corresponded to a 55% mortality risk elevation (adjusted HR: 1.55, 95% CI: 1.05–2.30, $P = 0.027$). Above −2.69 (ALBI ≥ −2.69), mortality risk escalated sharply (adjusted HR: 4.86, 95% CI: 3.32–7.11, $P < 0.0001$; Table 3). This indicates that individuals with ALBI scores ≥ −2.69 had a 386% higher risk of mortality compared to those with scores < −2.69. While the overall linear model indicated strong mortality association (HR: 2.74, $P < 0.0001$), the amplified risk beyond −2.69 suggests critical prognostic implications for MAFLD patients, emphasizing the need for early intervention in individuals exceeding this threshold.

Kaplan-Meier survival analysis reinforced these findings, with significantly divergent survival curves across ALBI strata (log-rank $P < 0.001$; Fig. 3).

Predictive performance of ALBI for all-cause mortality

We developed an ALBI-based prognostic model for 1-, 2-, and 3-year mortality. Receiver operating characteristic (ROC) analysis demonstrated moderate discriminative ability, with area under the curve (AUC) values of 0.715 (95% CI: 0.67–0.76), 0.646 (0.60–0.69), and 0.652 (0.61–0.70) for 1-, 2-, and 3-year predictions, respectively (Figure 4A–C). The 1-year AUC exceeded 0.70, indicating clinically useful discrimination, while 2- and 3-year predictions retained modest prognostic value.

Table 1 Baseline characteristics of MAFLD patients by survival status (*n*=5666)

Characteristic	Total	Surviving participants (*n*>=4573)	Dead participants (*n*>=1093)	*P*-value
Age group, *n* (%)				<0.0001
20-39	23.22 (21.78,24.73)	26.63 (25.12,28.20)	2.70 (1.54,4.71)	
40-59	39.61 (37.66,41.60)	43.43 (41.29,45.59)	16.62 (13.30,20.58)	
>59	37.16 (35.05,39.32)	29.94 (27.88,32.08)	80.67 (76.59,84.20)	
Gender, *n* (%)				0.0418
Male	52.30 (50.83,53.77)	51.68 (50.13,53.23)	56.03 (51.99,59.99)	
Female	47.70 (46.23,49.17)	48.32 (46.77,49.87)	43.97 (40.01,48.01)	
Race/ethnicity, *n* (%)				<0.0001
Non-Hispanic white	73.76 (71.00,76.36)	72.16 (69.31,74.85)	83.42 (79.03,87.04)	
Non-Hispanic black	4.52 (3.81,5.35)	4.56 (3.82,5.44)	4.30 (3.13,5.87)	
Hispanic	10.36 (8.66,12.35)	11.27 (9.47,13.37)	4.86 (3.28,7.14)	
Other	11.36 (10.00,12.87)	12.01 (10.48,13.73)	7.43 (5.35,10.23)	
Education levels, *n* (%)				<0.0001
Less than High school	18.35 (16.67,20.15)	16.27 (14.55,18.14)	30.88 (26.84,35.23)	
High school or equivalent	25.29 (23.25,27.46)	24.48 (22.22,26.89)	30.22 (26.42,34.30)	
College or above	56.36 (53.91,58.78)	59.26 (56.65,61.81)	38.91 (34.68,43.31)	
Family income–poverty ratio, *n* (%)				<0.0001
<1.0	21.04 (19.43,22.74)	20.12 (18.43,21.91)	26.60 (22.61,31.00)	
1.0-3.0	37.25 (35.20,39.34)	35.93 (33.74,38.17)	45.22 (41.26,49.25)	
>3.0	41.71 (39.20,44.27)	43.96 (41.17,46.78)	28.18 (24.26,32.47)	
Marital status, *n* (%)				<0.0001
Married	68.52 (66.53,70.44)	69.82 (67.63,71.92)	60.71 (56.32,64.94)	
Separated	20.09 (18.64,21.62)	17.65 (16.23,19.17)	34.82 (30.25,39.68)	
Never married	11.39 (10.08,12.84)	12.54 (11.08,14.15)	4.47 (2.73,7.24)	
BMI group, *n* (%)				0.0026
< 25	15.21 (13.92,16.59)	14.49 (13.05,16.06)	19.50 (16.81,22.51)	
25-30	30.49 (28.74,32.30)	30.29 (28.31,32.34)	31.71 (28.20,35.44)	
≥ 30	54.30 (52.15,56.44)	55.22 (52.72,57.69)	48.79 (44.97,52.63)	
Diabetes, *n* (%)				<0.0001
Yes	15.97 (14.48,17.58)	13.69 (12.29,15.22)	29.67 (25.52,34.19)	
No	84.03 (82.42,85.52)	86.31 (84.78,87.71)	70.33 (65.81,74.48)	
Hypertension, *n* (%)				<0.0001
Yes	43.97 (41.73,46.24)	41.16 (38.77,43.59)	60.93 (56.20,65.46)	
No	56.03 (53.76,58.27)	58.84 (56.41,61.23)	39.07 (34.54,43.80)	
Hyperlipidemia, *n* (%)				<0.0001
Yes	46.23 (44.16,48.31)	44.40 (42.09,46.73)	57.28 (53.60,60.88)	
No	53.77 (51.69,55.84)	55.60 (53.27,57.91)	42.72 (39.12,46.40)	
Smoking status, *n* (%)				<0.0001
Current smokers	16.47 (15.04,18.01)	16.21 (14.67,17.88)	18.06 (14.65,22.06)	
Former smokers	31.95 (29.89,34.08)	29.98 (27.66,32.41)	43.79 (39.65,48.03)	
Never smokers	51.58 (49.62,53.54)	53.81 (51.56,56.05)	38.14 (33.98,42.49)	
BMI, kg/m2	32.02 (31.70,32.34)	32.24 (31.87,32.61)	30.66 (30.15,31.17)	<0.0001
Daily calorie intake, kcal/d	2078.65 (2050.46,2106.83)	2125.98 (2095.09,2156.87)	1793.43 (1749.19,1837.68)	<0.0001
ALT, U/L	28.79 (28.17,29.41)	29.31 (28.66,29.96)	25.65 (23.91,27.39)	0.0002
AST, U/L	26.90 (26.30,27.50)	26.60 (26.02,27.18)	28.71 (26.22,31.20)	0.1133
HDL, mg/dL	50.02 (49.49,50.54)	50.39 (49.80,50.98)	47.78 (46.87,48.70)	<0.0001
LDL, mg/dL	114.82 (113.40,116.25)	114.84 (113.33,116.35)	114.73 (111.79,117.66)	0.9438
TG, mg/dL	161.24 (157.61,164.86)	160.60 (156.48,164.72)	165.10 (158.11,172.10)	0.2887
TC, mg/dL	196.93 (195.21,198.65)	197.21 (195.40,199.02)	195.27 (191.82,198.73)	0.2882
ALBI score	−2.86 (−2.88,−2.85)	−2.88 (−2.90,−2.87)	−2.74 (−2.77,−2.72)	<0.0001

Abbreviations: *MAFLD* Metabolic Associated Fatty Liver Disease, *NHANES* National Health and Nutrition Examination Survey, *BMI* Body mass index, *ALT* Alanine aminotransferase, *AST* Asparate aminotransferase, *TC* Total cholesterol, *TG* Triglyceride, *LDL* Low-density lipoprotein cholesterol, *HDL* High-density lipoprotein cholesterol, *ALBI* Albumin-bilirubin score

Table 2 Hazard ratios for all-cause mortality by ALBI Tertiles in MAFLD patients

ALBI	Model 1			Model 2			Model 3		
	HR	95% CI	*P*-value	HR	95% CI	*P*-value	HR	95% CI	*P*-value
Continuous[a]	3.98	2.69, 5.88	<0.001	3.26	2.26, 4.71	<0.001	2.93	2.02, 4.24	<0.001
Categorical[b]									
Q1	1.00	-	-	1.00	-	-	1.00	-	-
Q2	1.58	1.24, 2.02	<0.001	1.34	1.07, 1.68	0.010	1.32	1.05, 1.65	0.016
Q3	2.43	1.90, 3.11	<0.001	1.79	1.48, 2.16	<0.001	1.74	1.42, 2.12	0.001
P for trend			<0.001			<0.001			<0.001

HR Hazard ratio, *CI* Confidence interval

Model 1: Non-adjusted

Model 2: Adjusted for Gender, Age, Race, Education, Marital status, PIR

Model 3: Adjusted for Age, Age group, Gender, race, Education, Marital status, PIR, BMI, BMI group, Smoking, Total caloric intake, Hypertension, High cholesterol, Diabetes,, ALT, AST, TC, TG, LDL, HDL

[a]Each 1 unit increase in ALBI

[b]Q1: < −2.96; Q2: −2.96 ≤ ALBI < −2.70; Q3:≥−2.70

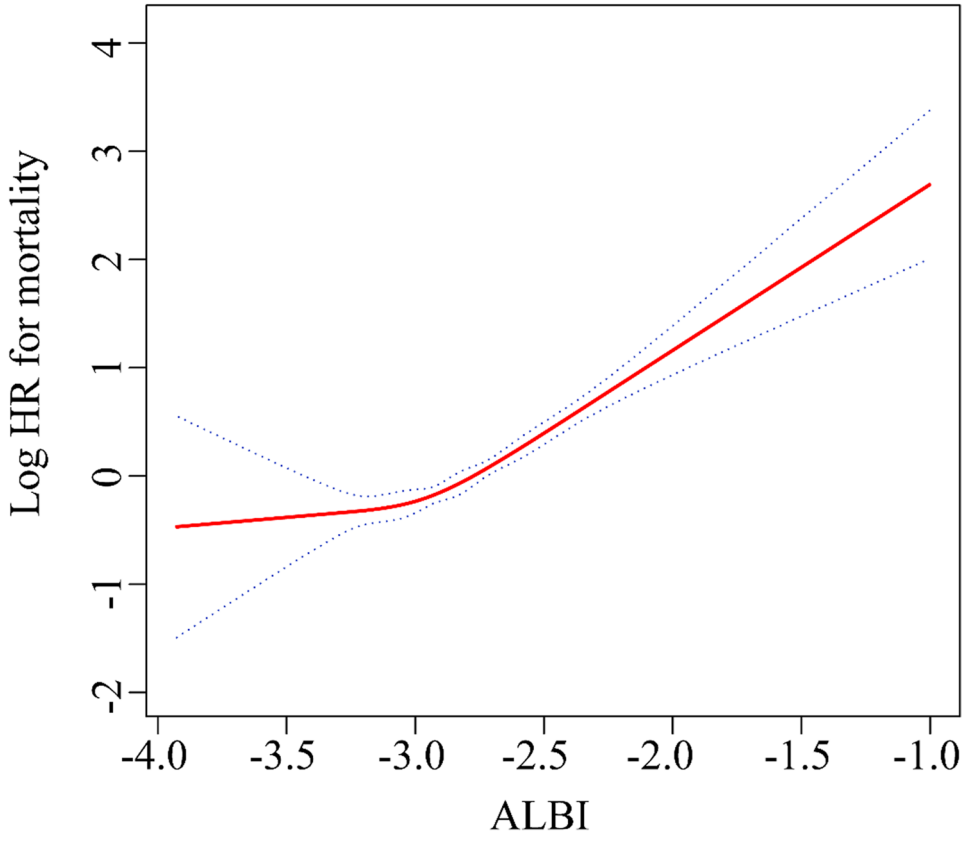

Fig. 2 Smooth curve fitting of the relationship between ALBI and all-cause mortality

Calibration curves revealed excellent agreement between predicted and observed mortality probabilities across all timepoints (Fig. 5A–C). The 1-year calibration showed near-perfect alignment (Hosmer-Lemeshow $P = 0.32$), with maintained concordance at 2 years ($P = 0.25$) and 3 years ($P = 0.28$), supporting model reliability for longitudinal risk stratification.

Discussion

The growing global burden of non-alcoholic fatty liver disease (MAFLD) necessitates reliable prognostic tools, particularly given its strong metabolic comorbidities and progressive nature. Our analysis revealed a clear independent association between albumin-bilirubin (ALBI) grading and mortality risk in MAFLD populations, thereby establishing its clinical utility for outcome prediction. Unlike conventional approaches dependent

Table 3 Threshold effect analysis of ALBI score on all-cause mortality in MAFLD patient

	Adjusted HR (95% CI),*P*-value[a]
Fitting by the standard linear model	2.74 (2.17, 3.46) <0.0001
Fitting by the two-piecewise linear model	
Inflection point	−2.69
ALBI < −2.69	1.55 (1.05, 2.30) 0.0272
ALBI ≥−2.69	4.86 (3.32, 7.11) <0.0001
P for Log-likelihood ratio	3.13 (1.65, 5.94) 0.0005

ALBI Albumin-Bilirubin Score, *HR* Hazard Ratio, *CI* Confidence Interval

[a]Adjusted for Age, Age group, Gender, race, Education, Marital status, PIR, BMI, BMI group, Smoking, Total caloric intake, Hypertension, High cholesterol, Diabetes, ALT, AST, TC, TG, LDL, HDL

on isolated biochemical parameters, this investigation pioneers the application of ALBI stratification within a nationally representative NHANES cohort (2003–2018), demonstrating superior prognostic performance through advanced survival modeling. Adjusted multivariate regression models confirmed a dose-dependent mortality pattern, with patients in upper ALBI tertile showing 1.74-fold increased mortality risk (95% CI 1.42–2.12) compared to baseline. Notably, each ALBI unit increment corresponded to near-tripled mortality hazard (HR = 2.93, 95% CI 2.02–4.24), with accelerated risk progression observed beyond the − 2.69 threshold. These findings advocate for ALBI integration into standard clinical algorithms to facilitate risk-adapted surveillance protocols.

Our results align with emerging evidence on ALBI's prognostic capacity while addressing critical knowledge gaps. Cross-validation with international cohorts confirms ALBI's effectiveness in survival stratification across chronic liver diseases [26–30], particularly its predictive value for hepatic decompensation events ($n = 490$ cohort analysis) [31]. However, observed discrepancies in cardiovascular mortality associations [32] underscore the need for etiology-specific mortality analyses, potentially reflecting population heterogeneity or methodological variations in endpoint ascertainment. The mechanistic plausibility of our findings stems from ALBI's dual reflection of hepatic synthetic (albumin) and excretory (bilirubin) functions–key determinants compromised in progressive MAFLD [33]. This biological rationale supports ALBI's superiority over single-parameter assessments in capturing multidimensional liver dysfunction.

Methodologically, this study employed rigorous analytic approaches to ensure robust conclusions.

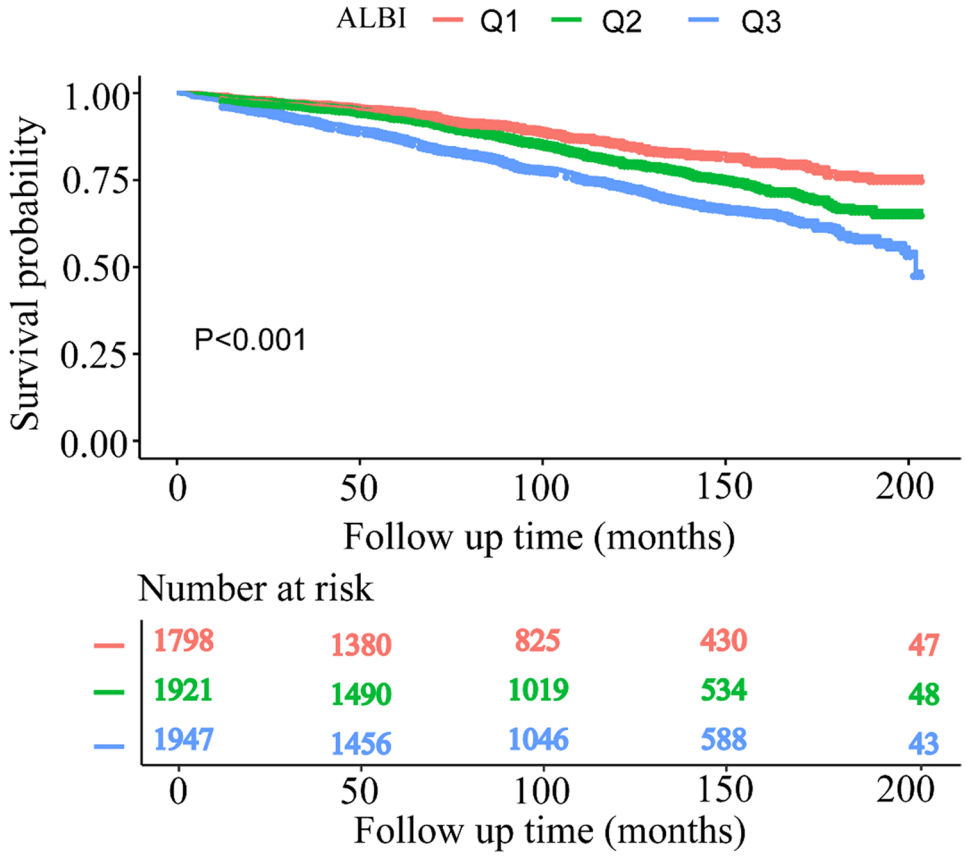

Fig. 3 Kaplan-Meier analysis of all-cause mortality by tertile of ALBI (Q1-Q3) in participants with MAFLD. The survival probabilities are tracked over a median follow-up of 8.5 years, and the number of participants at risk at various time points is presented below the graph

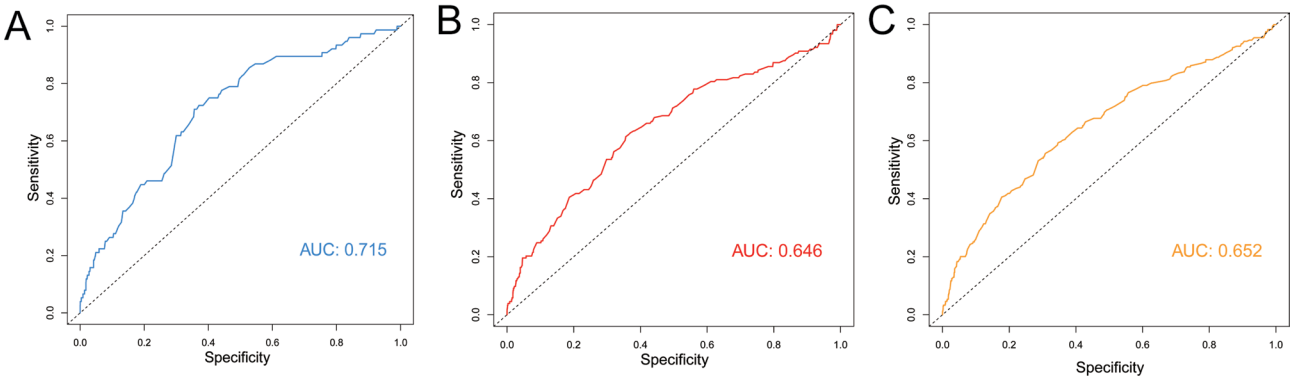

Fig. 4 ALBI-Based Mortality Prediction ROC Analysis in MAFLD, **A** 1-Year (AUC = 0.715, 0.68–0.75), **B** 2-Year (AUC = 0.646, 0.60–0.69), **C** 3-Year (AUC = 0.652, 0.61–0.70)

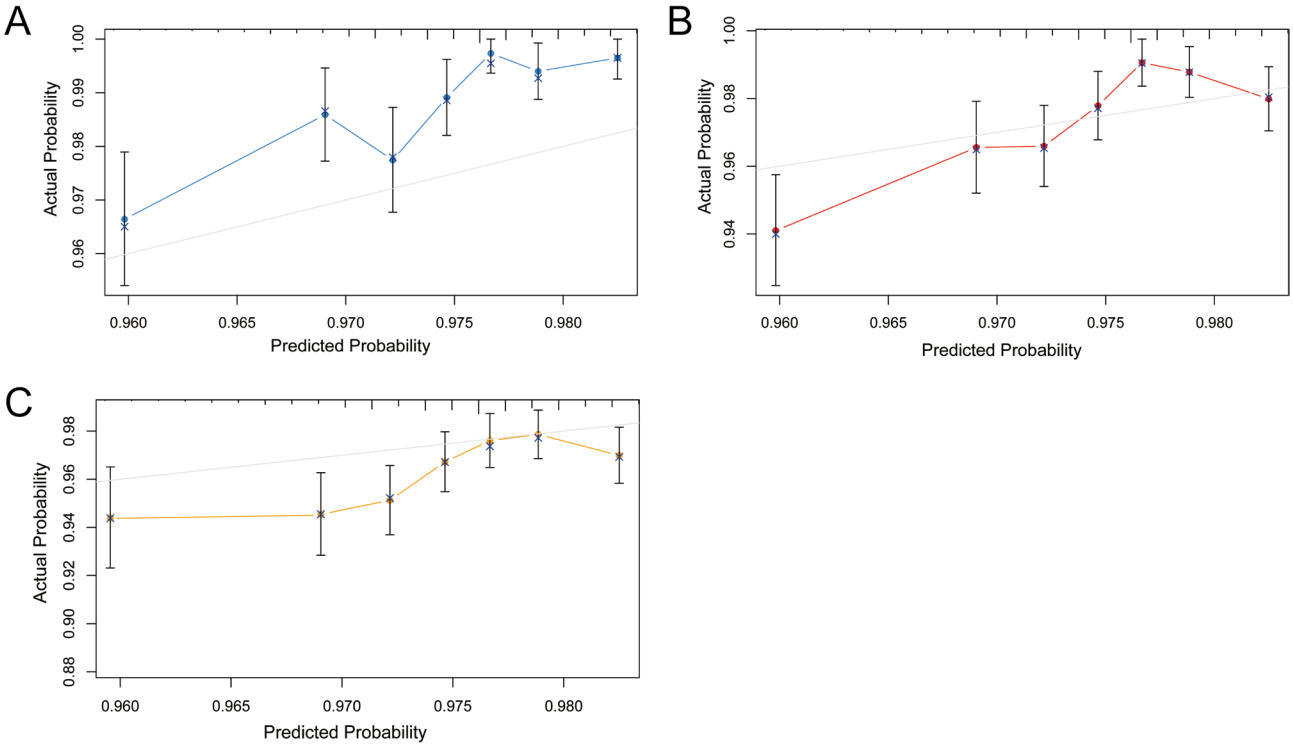

Fig. 5 Validation of the Calibration Curves for the Prediction Model, **A**) 1-Year, **B**) 2-Year, **C**) 3-Year

Multivariable-adjusted Cox proportional hazards models accounted for 27 demographic, metabolic, and lifestyle covariates, maintaining statistical significance across all sensitivity analyses. Survival curve analyses revealed temporal divergence in mortality outcomes, with high-ALBI subgroups showing 38% reduced 10-year survival compared to low-grade counterparts. The linear exposure-response relationship persisted across alternative modeling strategies, including restricted cubic spline and quartile-based analyses. Such methodological consistency strengthens causal inference regarding ALBI's prognostic relevance in MAFLD progression.

In clinical practice, the ALBI score's utility could primarily revolve around the following aspects: `Risk Stratification and Tailored Surveillance: The ALBI score can serve as a robust tool for risk stratification. Patients with higher ALBI scores, especially those surpassing the identified inflection point of −2.69, may necessitate more intensive monitoring for both liver-related complications and overall mortality. This could translate into a need for more frequent clinical visits, laboratory assessments, and advanced imaging surveillance. Such a targeted approach would help optimize resource allocation and efficiently identify high-risk individuals who require closer clinical attention. Guiding Therapeutic Intervention: An elevated

ALBI score could act as a critical trigger for escalating therapeutic interventions. This might include recommending more aggressive lifestyle modifications, initiating specific pharmacological treatments, or prompting timely referral to a hepatologist for advanced liver disease management and potential consideration for clinical trial enrollment. By identifying patients most likely to benefit, the ALBI score can empower clinicians to implement early and decisive therapeutic strategies. Enhancing Patient Communication and Shared Decision-Making: The inherent simplicity and strong prognostic capability of the ALBI score can significantly improve patient-provider communication. It allows for a clearer explanation of an individual's specific risk profile, thereby empowering patients to become more actively involved in understanding and adhering to their personalized management plan.

It should be emphasized that, as an observational study, the association between ALBI score and mortality identified herein cannot be interpreted as causal, and elevated ALBI scores may simply represent markers of advanced liver disease or systemic comorbidities. While our findings suggest that ALBI scores have moderate predictive performance for all-cause mortality in MAFLD patients, particularly at ALBI ≥ −2.69, with an AUC of 0.715 for 1-year mortality, the clinical utility of ALBI scores in routine practice should be approached with caution. The moderate AUC values (0.64-0.71) indicate that ALBI scores, while significant, have limitations in their predictive accuracy. Therefore, clinicians should consider these limitations when using ALBI scores for risk stratification and decision-making. Specifically, ALBI scores should not be used in isolation but rather in conjunction with other clinical assessments and diagnostic tools to provide a more comprehensive evaluation of patient risk. Future research, including prospective intervention studies and validation in diverse populations, is needed to further establish the clinical applicability and robustness of ALBI scores in MAFLD management.

Although our study demonstrates a significant association between ALBI scores and all-cause mortality in MAFLD patients, the generalizability of these findings is limited by the specific characteristics of the NHANES cohort used in this analysis. The NHANES dataset, while nationally representative of the U.S. population, may not fully capture the diversity of MAFLD patients in other regions or healthcare settings. Therefore, our findings should be interpreted with caution when considering their application to other populations. Future research should prioritize external validation studies in diverse cohorts, including those with different ethnic compositions, healthcare systems, and disease severities. Such validation efforts are crucial to confirm the robustness and applicability of ALBI scores as a prognostic tool in various clinical contexts. Additionally, further studies should explore the potential impact of regional variations in lifestyle, environmental factors, and healthcare access on the predictive performance of ALBI scores.

Several study limitations merit consideration. First, the diagnostic reliance on the US-FLI algorithm, a non-invasive MAFLD indicator, rather than histopathological confirmation or imaging modalities, may introduce spectrum bias and potential misclassification. While the US-FLI is practical for large epidemiologic datasets like NHANES, it may not perfectly capture all cases of MAFLD and could lead to both false positive and false negative classifications. Future studies should consider validating these findings using more accurate diagnostic methods, such as liver ultrasound or higher FLI cutoffs. Second, although we adjusted for key confounders, residual confounding from unmeasured variables (e.g., pharmacotherapy, environmental toxins) remains possible. Third, the observational design precludes definitive causal conclusions, necessitating validation through prospective intervention studies. Future investigations should prioritize multi-ethnic validation cohorts and incorporate emerging biomarkers (e.g., cytokeratin-18, FibroScan® parameters) to enhance prognostic modeling precision. Fourth, we did not directly compare the prognostic performance of ALBI with that of established indices (such as FIB-4, NFS, or other markers reflecting liver fibrosis or nutritional status). Consequently, based solely on our findings, we cannot definitively determine the incremental prognostic value of ALBI relative to these conventional scores. Fifthly, it's possible that due to data imputation, our analytical sample differs from the complete MAFLD population within NHANES with respect to health status or other characteristics. Sixthly, the prognostic performance of ALBI score in our community-based NHANES cohort using laboratory-defined MAFLD criteria may differ from clinically diagnosed MAFLD populations, particularly in hepatology-referred patients with established fibrosis progression. Further validation in biopsy-proven MAFLD cohorts is warranted to clarify its clinical utility across different healthcare settings.

Conclusion

In summary, this large-scale epidemiologic investigation establishes ALBI grading as a significant predictor of all-cause mortality in MAFLD, with critical risk stratification value at the−2.69 cutoff. The demonstrated exposure-response relationship and consistent survival differences underscore ALBI's clinical relevance for guiding therapeutic intensification and surveillance intervals. These

findings support the consideration of ALBI in existing MAFLD management frameworks and offer actionable insights for personalized care pathways, pending further validation. Subsequent research directions should focus on mechanistic studies elucidating ALBI's pathophysiological determinants and multicenter trials evaluating ALBI-guided intervention efficacy.

Abbreviations

MAFLD	Metabolic Associated Fatty Liver Disease
ALBI	Albumin-Bilirubin Score
NHANES	National Health and Nutrition Examination Survey
US-FLI	U.S. Fatty Liver Index
HCC	Hepatocellular Carcinoma
CDC	Centers for Disease Control and Prevention
IRB	Institutional Review Board
BMI	Body Mass Index
PIR	Poverty-Income Ratio
ALT	Alanine Aminotransferase
AST	Aspartate Aminotransferase
HDL	High-Density Lipoprotein Cholesterol
LDL	Low-Density Lipoprotein Cholesterol
TG	Triglycerides
TC	Total Cholesterol
MRI	Magnetic Resonance Imaging
HR	Hazard Ratio
CI	Confidence Interval
ROC	Receiver Operating Characteristic
AUC	Area Under the Curve
WHO	World Health Organization

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12876-025-04117-1.

Supplementary Material 1.

Acknowledgements

We would like to thank the staff of the National Health and Nutrition Examination Surveys (NHANES) database and Centers for Disease Control and Prevention (CDC).

Disclaimer

This article does not necessarily represent the views and policies of the National Institutes of Health.

Authors' contributions

GZ had full access to all the data in the study and took responsibility for the integrity of the data and the accuracy of the data analysis. BM contributed to the concept and design of the study. GZ, WH, JL, and BM were involved in the acquisition, analysis, and interpretation of data. GZ drafted the manuscript. BM critically revised the manuscript for important intellectual content. GZ performed the statistical analysis. BM provided administrative, technical, and material support. BM supervised the study. All authors agreed to be accountable for all aspects of the work and approved the final version of the paper.

Funding

This work was supported by the Scientific Research Foundation of Heilongjiang University of Chinese Medicine (Grant No. 2019MS17).

Data availability

This study utilized publicly available datasets, which can be accessed at the following link: https://www.cdc.gov/nchs/nhanes/.

Declarations

Ethics approval and consent to participate

Ethical approval was obtained from the CDC Institutional Review Board, and the study was conducted in accordance with the Declaration of Helsinki and relevant guidelines and regulations.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

[1]First Affiliated Hospital, Heilongjiang University of Chinese Medicine, Harbin 150000, Heilongjiang, China
[2]Second Affiliated Hospital, Heilongjiang University of Chinese Medicine, Harbin 150000, Heilongjiang, China

Received: 4 March 2025 / Accepted: 25 June 2025
Published online: 07 August 2025

References

1. Amini-Salehi E, Letafatkar N, Norouzi N, et al. Global prevalence of nonalcoholic fatty liver disease: an updated review and meta-analysis comprising a population of 78 million from 38 countries. Arch Med Res. 2024;55:103043.
2. Gofton C, Upendran Y, Zheng MH, et al. MAFLD: how is it different from NAFLD? Clin Mol Hepatol. 2022;28(Suppl 1):S17–31.
3. Paik JM, Henry L, Younossi ZM. Nonalcoholic fatty liver disease mortality May not be decreasing: a need for careful interpretation of GBD 2019 estimates of liver deaths. Cell Metab. 2023;35:1087–8.
4. Yoon SJ, Kim SK, Lee NY, et al. Effect of Korean red ginseng on metabolic syndrome. J Ginseng Res. 2021;45:380–9.
5. Weihe P, Weihrauch-Blüher S. Metabolic syndrome in children and adolescents: diagnostic criteria, therapeutic options and perspectives. Curr Obes Rep. 2019;8:472–9.
6. Akhtar DH, Iqbal U, Vazquez-Montesino LM, et al. Pathogenesis of insulin resistance and atherogenic dyslipidemia in nonalcoholic fatty liver disease. J Clin Transl Hepatol. 2019;7:362–70.
7. Li F, Ye J, Sun Y, et al. Distinct dose-dependent association of free fatty acids with diabetes development in nonalcoholic fatty liver disease patients. Diabetes Metab J. 2021;45:417–29.
8. Sanyal AJ, Castera L, Wong VW-S. Noninvasive assessment of liver fibrosis in NAFLD. Clin Gastroenterol Hepatol. 2023;21:2026–39.
9. Xia T, Du M, Li H, et al. Association between liver MRI proton density fat fraction and liver disease risk. Radiology. 2023;309:e231007.
10. Li H, Liang J, Han M, et al. Polyphenols synergistic drugs to ameliorate nonalcoholic fatty liver disease via signal pathway and gut microbiota: a review. J Adv Res. 2025;68:43–62.
11. Wan X, Ma J, Bai H, et al. Drug advances in NAFLD: individual and combination treatment strategies of natural products and small-synthetic-molecule drugs. Biomolecules. 2025;15:140.
12. Eslam M, Newsome PN, Sarin SK, et al. A new definition for metabolic dysfunction-associated fatty liver disease: an international expert consensus statement. J Hepatol. 2020;73:202–9.
13. Rinella ME, Lazarus JV, Ratziu V, et al. A multisociety Delphi consensus statement on new fatty liver disease nomenclature. Hepatology. 2023;78:1966–86.
14. Kariyama K, Nouso K, Hiraoka A, et al. EZ-ALBI score for predicting hepatocellular carcinoma prognosis. Liver Cancer. 2020;9:734–43.
15. Toyoda H, Johnson PJ. The ALBI score: from liver function in patients with HCC to a general measure of liver function. JHEP Rep. 2022;4:100557.
16. Xu SX, Yang F, Ge N, et al. Role of albumin-bilirubin score in non-malignant liver disease. World J Gastroenterol. 2024;30:999–1004.
17. Eryuruk U, Tasdemir MN, Karasu HI, et al. Comparison of the efficacy of the Gadoxetic acid MRI-derived relative enhancement index and functional liver imaging score in predicting liver function: validation with albumin-bilirubin grade. Abdom Radiol (NY). 2024;49:1456–66.
18. Hiraoka A, Kumada T, Kudo M, et al. Albumin-bilirubin (ALBI) grade as part of the evidence-based clinical practice guideline for HCC of the Japan society of

hepatology: a comparison with the liver damage and Child-Pugh classifications. Liver Cancer. 2017;6:204–15.
19. Hiraoka A, Kumada T, Michitaka K, et al. Usefulness of albumin-bilirubin grade for evaluation of prognosis of 2584 Japanese patients with hepatocellular carcinoma. J Gastroenterol Hepatol. 2016;31:1031–6.
20. Li F, Guan Z, Gao Y, et al. ER stress promotes mitochondrial calcium overload and activates the ROS/NLRP3 axis to mediate fatty liver ischemic injury. Hepatol Commun. 2024;8:e0399.
21. Ibrahim SH, Hirsova P, Gores GJ. Non-alcoholic steatohepatitis pathogenesis: sublethal hepatocyte injury as a driver of liver inflammation. Gut. 2018;67:963–72.
22. Shen X, Yang L, Yan S, et al. Fetuin A promotes lipotoxicity in β cells through the TLR4 signaling pathway and the role of Pioglitazone in anti-lipotoxicity. Mol Cell Endocrinol. 2015;412:1–11.
23. Johnson PJ, Berhane S, Kagebayashi C, et al. Assessment of liver function in patients with hepatocellular carcinoma: a new evidence-based approach—the ALBI grade. J Clin Oncol. 2015;33:550–8.
24. Golabi P, Paik JM, Harring M, et al. Prevalence of high and moderate risk nonalcoholic fatty liver disease among adults in the united states, 1999–2016. Clin Gastroenterol Hepatol. 2022;20:2838–47.
25. Younossi ZM, Stepanova M, Younossi Y, et al. Epidemiology of chronic liver diseases in the USA in the past three decades. Gut. 2020;69:564–8.
26. Wang Z, Fan Q, Wang M, et al. Comparison between Child-Pugh score and albumin-bilirubin grade in patients treated with the combination therapy of transarterial chemoembolization and Sorafenib for hepatocellular carcinoma. Ann Transl Med. 2020;8:537.
27. Kudo M, Finn RS, Cheng AL, et al. Albumin-bilirubin grade analyses of Atezolizumab plus bevacizumab versus Sorafenib in patients with unresectable hepatocellular carcinoma: a post hoc analysis of the phase III IMbrave150 study. Liver Cancer. 2023;12:479–93.
28. Toyoda H, Lai PBS, O'Beirne J, et al. Long-term impact of liver function on curative therapy for hepatocellular carcinoma: application of the ALBI grade. Br J Cancer. 2016;114:744–50.
29. Reincke M, Schultheiss M, Doppler M, et al. Hepatic decompensation after transarterial radioembolization: a retrospective analysis of risk factors and outcome in patients with hepatocellular carcinoma. Hepatol Commun. 2022;6:3223–33.
30. Kim KP, Kim KM, Ryoo BY, et al. Prognostic efficacy of the albumin-bilirubin score and treatment outcomes in hepatocellular carcinoma: a large-scale, multicenter real-world database study. Liver Cancer. 2024;13:610–28.
31. Ooi H, Asai Y, Koriyama Y, et al. Effect of ceftriaxone dosage and albumin-bilirubin score on the risk of ceftriaxone-induced liver injury. Biol Pharm Bull. 2023;46:1731–6.
32. Liu Y, Zhong GC, Tan HY, et al. Nonalcoholic fatty liver disease and mortality from all causes, cardiovascular disease, and cancer: a meta-analysis. Sci Rep. 2019;9:11124.
33. Semeya AA, Elgamal R, Othman AAA. Correlation of serum zinc levels with hepatic encephalopathy severity in patients with decompensated liver cirrhosis: a prospective observational study from Egypt. Biol Trace Elem Res. 2025;208.

Publisher's Note