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Association between NAFLD and liver fibrosis with nutritional risk index based on the NHANES 2017–2018

Jieming Jian[1†], Rui Zhang[1†], Yuan Dong[1], Hongting Zheng[1*] and Xiaoyu Liao[1*]

Abstract

Background Nutrition and its associated inflammation have been acknowledged as vital factors in the etiopathogenesis of non-alcoholic fatty liver disease (NAFLD) and liver fibrosis. The nutritional risk index (NRI) has been widely recognized as a valid indicator of nutritional status in several diseases, including osteoporosis and cardiovascular disease. However, the role of NRI in NAFLD and liver fibrosis remains unclear.

Methods Participants were selected from the National Health and Nutrition Examination Survey data for the 2017–2018 cycle. Association between NRI and both NAFLD and liver fibrosis was evaluated using multiple logistic regression and restricted cubic spline (RCS) analysis. Mediation analysis was employed to assess the influence of inflammation on the association between NRI and both NAFLD and liver fibrosis.

Results Compared to their respective control groups, individuals with NAFLD and liver fibrosis exhibited higher NRI levels. Multiple logistic regression analyses indicated that NRI was positively associated with the odds of NAFLD and liver fibrosis across both continuous scales and quantile groups, with adjustments for relevant covariables. The RCS model demonstrated a dose-response effect between NRI and the odds of NAFLD, but not with liver fibrosis. Receiver operating characteristic (ROC) analysis revealed the area under the ROC curves of 0.798 and 0.775 for NAFLD and liver fibrosis, respectively. Mediation analysis showed that inflammation accounted for 3.139% of the effect of NRI on the odds of NAFLD, suggesting inflammation might partially mediate the impact of NRI on NAFLD.

Conclusions Our findings indicate that NRI may serve as a potential associated marker for these liver diseases, underscoring the importance of nutritional status in their etiopathogenesis.

Keywords Nutritional risk index, NAFLD, Liver fibrosis, Inflammation

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Introduction

Non-alcoholic fatty liver disease (NAFLD) is the most prevalent chronic hepatic disorder, affecting approximately 30% of the global population and serving as a primary cause of severe hepatopathies [1–3]. Liver fibrosis, a progressive manifestation of NAFLD, has been identified as the key histological determinant of patient survival in individuals with NAFLD, emphasizing the importance of targeting liver fibrosis for therapeutic intervention [4, 5]. However, our understanding of the etiologies, diagnostic approaches, and treatments for NAFLD and liver fibrosis remains limited due to the complex pathological processes [6–8]. Recent studies of NAFLD and liver fibrosis have focused on metabolic disorders [9], highlighting the significant impact of nutritional factors on the progression and outcomes of these liver conditions [10].

Nutrition exerts an important influence on the etiopathogenesis of NAFLD. Extensive research has evaluated the association between unhealthy nutritional habits, such as a Western diet rich in refined carbohydrates and fats but low in fiber, and the development of NAFLD [10, 11]. Diets rich in sugars and fats have been shown to cause excessive postprandial glucose and lipid spikes, which induce oxidative stress and activate pro-inflammatory signaling pathways, such as nuclear factor kappa-B (NF-κB) [12]. This process triggers the release of pro-inflammatory cytokines in liver Kupffer cells, which can lead to the onset and progression of NAFLD [12, 13]. The significant role of inflammation in the etiopathogenesis of liver diseases is well established; however, its variability is considerable. Studies have demonstrated that healthy dietary choices can effectively reduce inflammation levels and slow or even reverse the progression of NAFLD [14]. For example, oleic acid, derived from vegetable oils, has shown a beneficial anti-inflammatory effect by activating AMP-activated protein kinase and peroxisome proliferator-activated receptor γ, while inhibiting TLRs and NF-κB pathways [15]. Therefore, nutritional intervention represents a viable strategy for the prevention and management of NAFLD [12–14].

The nutritional risk index (NRI), which is calculated by assessing serum albumin levels, height, and weight, is recognized as a straightforward and precise tool for evaluating nutritional status [16, 17]. It has been reported that the effectiveness of NRI is on par with the gold standard, the Global Leadership Initiative on Malnutrition (GLIM) criteria, for assessing nutritional status in various conditions, including hemodialysis, head and neck cancer, and diabetic retinopathy [18–21]. The relevance of nutritional status, as assessed by NRI, to diseases such as osteoporosis, cardiovascular disease, and rheumatoid arthritis has been well-documented [22–25]. Further, NRI has been linked to inflammatory markers like C-reactive protein, lymphocytes, and Chitinase-3-like protein 1 (YKL-40), suggesting its association with inflammation [26–28]. Despite these findings, the impact of nutritional status, as measured by NRI, on the progression of NAFLD and liver fibrosis remains not fully understood. To address this gap, this study utilized a representative sample of U.S. adults from the National Health and Nutrition Examination Survey (NHANES) to conduct multiple logistic regression and restricted cubic spline (RCS) analyses. We assessed the association between NRI and both NAFLD and liver fibrosis across various subgroups through stratified analysis and evaluated the diagnostic capacity of NRI for these conditions using receiver operating characteristic (ROC) analysis. Additionally, the potential mediating effect of inflammation on the association between NRI and these liver diseases was explored.

Methods

Study design and participants

NHANES is a comprehensive national population survey conducted in the United States, approved by the Ethics Review Board of the National Center for Health Statistics (Protocol number: 2018-01). Written informed consent was obtained from all participants. This survey employs a rigorous sampling methodology utilizing complex, multistage, probabilistic techniques. Data collection includes household interviews, mobile physical examinations, and laboratory tests [29]. The present study leveraged data from the 2017–2018 U.S. NHANES database, which is known for its comprehensive vibration-controlled transient elastography (VCTE) examination data, thereby enabling a thorough cross-sectional analysis [30]. The process of participant screening is depicted in Supplementary Figure S1. From an initial cohort of 9,254 individuals, we excluded those under 20 years of age ($n=3683$), heavy drinkers ($n=1388$), individuals with hepatitis B or C ($n=101$), those taking lipid-lowering medications ($n=1177$), and participants missing liver ultrasound transient elastography data ($n=484$) or data required for indicator computations ($n=188$). Ultimately, 2,233 participants were enrolled for further analysis.

Definition of NAFLD and liver fibrosis

The diagnosis of hepatic steatosis (HS) was established when the median controlled attenuated parameter (CAP) value was ≥274 dB/m [31]. NAFLD was diagnosed based on the presence of HS, after excluding individuals with heavy alcohol consumption and other potential causes of HS, such as hepatitis B or C [32, 33]. Additionally, a median liver stiffness measurement (LSM) value of ≥7.0 kPa was indicative of liver fibrosis in the NAFLD population [31].

NRI, C-reactive protein-albumin-lymphocyte (CALLY), clinical data, and laboratory tests

All variables were obtained from the original database, with comprehensive details available in the Supplementary Materials. Definitions of ethnicity, education level, household income poverty ratio (PIR) [34, 35], smoking status, diabetes [36, 37], hypertension [38], and overweight/obesity are outlined in the Supplementary Materials. The indicators were calculated as follows: NRI is determined by the equation: 1.519 × serum albumin (g/L) + 41.7 × (present weight / ideal body weight); ideal body weight is calculated using the formula: height (cm) − 100 − (height (cm) − 150) / 4 for males and height (cm) − 100 − (height (cm) − 150) / 2.5 for females. A higher NRI indicates a more favorable nutritional status [16, 25, 39]. CALLY is defined as (serum albumin × lymphocyte counts) / (high-sensitivity C-reactive protein (hs-CRP) × 10). It reflects the severity of the systemic inflammatory response, with lower values indicating more pronounced inflammation [40].

Statistical analysis

Continuously distributed variables that followed a normal distribution were presented as mean ± standard deviations (SD) and analyzed using the Student's t-test. In contrast, variables not following a normal distribution were depicted as median (interquartile range (IQR)) and assessed using the Mann-Whitney U-test. Categorical variables were expressed as percentages [n (%)] and analyzed using the chi-square test. Three logistic regression models were constructed to explore the odds ratio (OR) with a 95% confidence interval (CI) for NAFLD or liver fibrosis using NRI and NRI per IQR as continuous variables or quartiles of NRI as categorical variables. Model 1 represented the unadjusted model; Model 2 incorporated adjustments for age, sex, ethnicity, education level, and PIR; and Model 3 additionally considered smoking status, diabetes, and hypertension. Results were shown with an OR and a 95% CI. To investigate the nonlinear association and dose-response effect between NRI and both NAFLD and liver fibrosis, RCS was employed. The number of knots for the RCS analysis was set at 3, positioned at the 10th, 50th, and 90th percentiles of the NRI, respectively. Stratified analysis based on age, sex, ethnicity, education level, PIR, presence of diabetes and hypertension, as well as smoking status was conducted to assess the association between NRI and both NAFLD and liver fibrosis in diverse populations. Additionally, interaction analysis was used to evaluate the latent interactions between NRI and the aforementioned covariables. ROC was performed to assess the diagnostic capacity of NRI for NAFLD and liver fibrosis, with optimal cutoff points determined by the "addfor" algorithm. A mediation analysis was performed to explore the role of CALLY in mediating the association between NRI and NAFLD, as well as liver fibrosis [41].

All statistical analyses were conducted using R software version 4.4.0. RCS was performed with the "rms" package, and optimal cutoff points were determined using the "CatPredi" package. Statistical significance was established at a two-tailed $P < 0.05$.

Results

Baseline characteristics

A total of 2,233 participants were enrolled based on predefined inclusion and exclusion criteria. The median age was 51.0 years (IQR: 36.0 to 64.0 years), with males comprising 49.2% and females 50.8% of the cohort. Baseline characteristics for groups categorized as non-NAFLD, NAFLD, non-liver fibrosis, and liver fibrosis are detailed in Supplementary Table S1. Group sizes were 1,295 (57.9%) for non-NAFLD, 938 (42.1%) for NAFLD, 696 (74.2% of the NAFLD group) for non-liver fibrosis, and 242 (25.8% of the NAFLD group) for liver fibrosis. NAFLD and liver fibrosis patients had a higher mean age and showed a greater prevalence of diabetes and hypertension. A male predominance was noted only in the NAFLD group. NAFLD patients were predominantly on behalf of Mexican Americans and non-Hispanic whites, while liver fibrosis patients were predominantly on behalf of non-Hispanic blacks. Compared to their respective control groups, individuals with NAFLD and liver fibrosis had higher levels of waist circumference, body mass index (BMI), fasting plasma glucose (FPG), insulin, alanine transaminase (ALT), aspartate aminotransferase (AST), γ-glutamyl transferase (GGT), hs-CRP, the homeostatic model assessment for insulin resistance (HOMA-IR), and NRI but lower levels of serum albumin, high-density lipoprotein cholesterol (HDL-C), and CALLY. The NAFLD group also exhibited elevated levels of low-density lipoprotein cholesterol (LDL-C), total cholesterol (TC), triglycerides (TG), and lymphocyte counts compared with the control group. No significant differences were found in LDL-C, TC, TG, and lymphocyte counts between the liver fibrosis group and the non-liver fibrosis group.

Dose-response effect between NRI and NAFLD as well as liver fibrosis

The association between the NRI and the odds of NAFLD and liver fibrosis is presented in Table 1. A significant positive trend was observed in the odds of NAFLD (P for trend < 0.001) and liver fibrosis (P for trend = 0.027) across increasing quartiles of the NRI. Compared to the first NRI quartile group (Q1), the fourth NRI quartile group (Q4) exhibited markedly increased odds of NAFLD (OR = 25.911; 95% CI: 25.451–26.372) and liver fibrosis (OR = 11.325; 95% CI: 10.100–12.549), after

Table 1 Association of NRI with the odds of NAFLD and liver fibrosis in the NHANES

	Model 1		Model 2		Model 3	
	OR (95% CI)	**P value**	**OR (95% CI)**	**P value**	**OR (95% CI)**	**P value**
NAFLD						
NRI	1.095 (1.083, 1.108)	< 0.001	1.107 (1.092, 1.122)	< 0.001	1.099 (1.080, 1.118)	< 0.001
NRI per IQR	4.176 (3.489, 4.998)	< 0.001	4.913 (3.961, 6.094)	< 0.001	4.383 (3.357, 5.723)	< 0.001
Quartiles of NRI						
Q1	Ref		Ref		Ref	
Q2	3.647 (2.241, 5.934)	< 0.001	3.960 (1.935, 8.106)	0.006	3.978 (3.500, 4.398)	0.111
Q3	9.279 (5.816, 14.805)	< 0.001	10.484 (5.280, 20.817)	< 0.001	9.941 (9.503, 10.379)	0.062
Q4	23.084 (14.919,35.717)	< 0.001	31.869 (16.112, 63.034)	< 0.001	25.911 (25.451, 26.372)	0.046
P for trend	< 0.001		< 0.001		< 0.001	
Liver fibrosis						
NRI	1.068 (1.042, 1.095)	< 0.001	1.087 (1.057, 1.118)	< 0.001	1.081 (1.037, 1.126)	0.009
NRI per IQR	2.829 (1.922, 4.165)	< 0.001	3.705 (2.388, 5.747)	< 0.001	3.375 (1.768, 6.443)	0.009
Quartiles of NRI						
Q1	Ref		Ref		Ref	
Q2	1.994 (0.625, 6.361)	0.219	2.587 (0.561, 11.929)	0.159	3.180 (1.999, 4.361)	0.306
Q3	1.428 (0.383, 5.334)	0.566	2.174 (0.382, 12.390)	0.283	2.183 (0.842, 3.524)	0.458
Q4	7.014 (2.251, 21.851)	0.003	12.924 (3.212, 52.008)	0.007	11.325 (10.100, 12.549)	0.160
P for trend	0.002		0.003		0.027	

Model 1 was an unadjusted model. Model 2 included adjustment for age, sex, ethnicity, education level, and PIR. Model 3 further accounted for smoking status, diabetes, and hypertension. NRI, nutritional risk index; NAFLD, non-alcoholic fatty liver disease; NHANES, National Health and Nutrition Examination Survey; OR, odds ratio; CI, confidence interval; IQR, interquartile range; PIR, family income poverty ratio

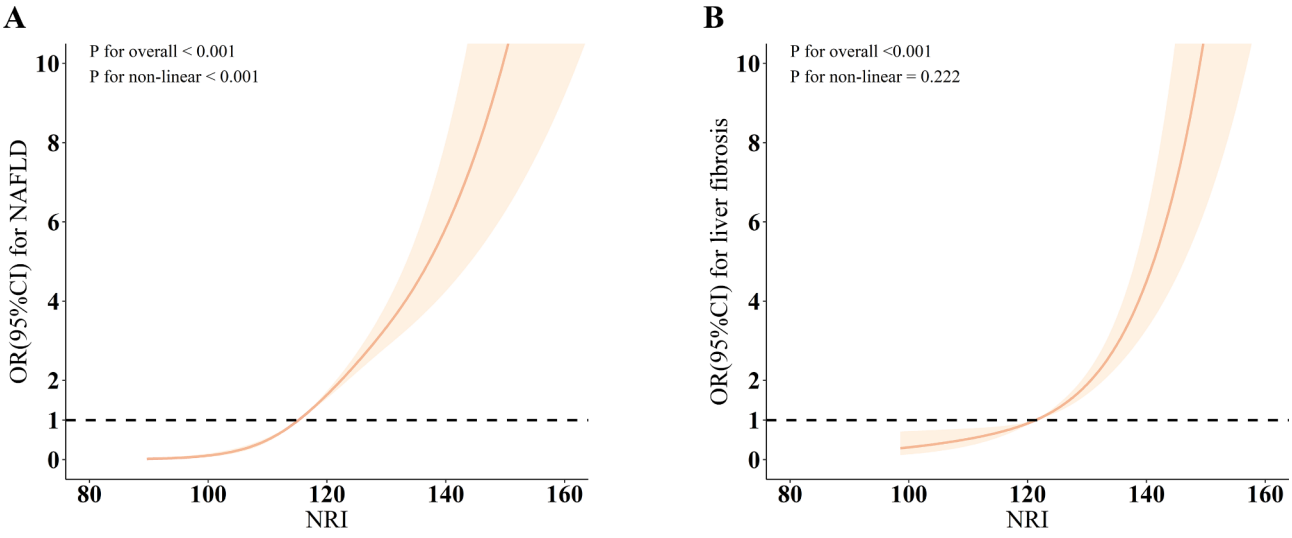

Fig. 1 Restricted cubic spline of the association between NRI and NAFLD and liver fibrosis. **A** NAFLD. **B** Liver fibrosis. The model accounted for age, sex, ethnicity, education level, PIR, smoking status, diabetes, and hypertension. NRI, nutritional risk index; NAFLD, non-alcoholic fatty liver disease; OR, odds ratio; CI, confidence interval; PIR, family income poverty ratio

adjustments for age, sex, ethnicity, education level, PIR, diabetes, hypertension, and smoking status. The positive association between NRI and both NAFLD (OR = 1.099; 95% CI: 1.080–1.118) and liver fibrosis (OR = 1.081; 95% CI: 1.037–1.126) remained robust after accounting for the aforementioned covariables. When further assessed using the NRI per IQR, which is computed through NRI divided by its IQR, a consistent association between NRI per IQR and NAFLD (OR = 4.383; 95% CI: 3.357–5.723), as well as liver fibrosis (OR = 3.375; 95% CI: 1.768–6.443) was found even after adjustments for covariables.

The dose-response effect between NRI and the odds of NAFLD and liver fibrosis is depicted in Fig. 1. RCS regression revealed a nonlinear (J-shaped) association between NRI levels and the odds of NAFLD (P for non-linear < 0.001); however, this pattern was not observed with liver fibrosis (P for non-linear = 0.222). Additionally, a progressive increase in the odds of NAFLD was noted when NRI exceeded 98.623. Subsequently, piecewise

logistic regression analysis was conducted, demonstrating a more pronounced positive association between NRI per IQR and NAFLD (OR=4.517; 95% CI: 3.422–5.962) when NRI is above 98.623 (Table 2).

Association of NRI with NAFLD and liver fibrosis in stratified analysis

To investigate the differential impact of NRI on the susceptibility to developing NAFLD and liver fibrosis among various subpopulations, participants were stratified based on age, sex, ethnicity, education level, PIR, presence of diabetes and hypertension, as well as smoking status. The positive association between NRI and both NAFLD and liver fibrosis was consistent across all subgroups, as depicted in Figs. 2 and 3. Meanwhile, the interaction between NRI and each stratified covariable was not statistically significant for either NAFLD or liver fibrosis.

Diagnostic values of NRI for NAFLD and liver fibrosis

The ROC curve presented in Fig. 4 depicts the efficacy of NRI in screening for NAFLD and liver fibrosis. For NAFLD, NRI achieved an area under the ROC curve (AUC) of 0.798 (95% CI: 0.780–0.816), with the optimal cutoff point determined to be 114.390. Regarding liver fibrosis, the AUC for NRI was 0.775 (95% CI: 0.740–0.809), with the optimal cutoff point identified at 133.810.

The mediating influence of CALLY in the NRI-NAFLD association

To further assess the latent mediating effects of inflammation on the association between NRI and NAFLD as well as liver fibrosis, a mediation analysis was conducted. In this mediation model, NRI was posited as the independent variable, and NAFLD or liver fibrosis served as the dependent variable. Additionally, CALLY was utilized as the mediator variable to reflect systemic inflammatory status. As illustrated in Fig. 5, NRI demonstrated a significant indirect effect on the odds of NAFLD through the levels of CALLY, with a mediation effect quantified at 0.009 (95% CI: 0.002–0.030). These findings suggested that CALLY partially mediates the association between NRI and NAFLD. Despite this mediation, NRI still had a significant direct impact on the development of NAFLD, as evidenced by a direct effect value of 0.286 (95% CI: 0.207–0.310). Consequently, it is inferred that approximately 3.139% of the impact of NRI on the onset of NAFLD is mediated through CALLY. However, CALLY showed no significant mediating effect between NRI and liver fibrosis.

Discussion

Nutrition is closely linked to both the onset and progression of NAFLD and liver fibrosis [12, 13]. The NRI, frequently utilized to assess nutritional status, is associated with the risk of various diseases, including osteoporosis and cardiovascular diseases [22, 24]. However, the association between NRI and both NAFLD and liver fibrosis remains unclear. In this study, we employed a large sample from the NHANES database, which was designed using rigorous random sampling, to examine the association between NRI and the odds of NAFLD and liver fibrosis. Following adjustments for confounding variables, a significant positive association was found between NRI and the odds of NAFLD and liver fibrosis. Additionally, a dose-response effect was observed between NRI and the odds of NAFLD; however, no such effect was observed for liver fibrosis, possibly due to the limited number of liver fibrosis patients in our sample. The ROC analysis further confirmed the diagnostic utility of NRI for these liver conditions. Moreover, we identified that CALLY, a marker of systemic inflammation, serves as a mediator in the effect of NRI on NAFLD.

Nutritional status is closely associated with the onset of NAFLD and liver fibrosis. Extensive research has shown that diets rich in calories, sugars, saturated fatty acids, and trans fatty acids contribute to the etiopathogenesis of NAFLD [11, 42, 43]. Specifically, such diets may promote the development of NAFLD in both non-obese and obese individuals by altering body composition, notably through increased body fat [44]. In contrast, low-calorie, plant-based diets, such as the Mediterranean diet, along with healthy eating behaviors, are advocated as effective dietary strategies for managing NAFLD [10, 45, 46]. The link between unhealthy dietary patterns and NAFLD was further established in a recent study examining the association between the dietary inflammation index (DII) and NAFLD. The DII assesses both nutritional and inflammatory statuses, with higher DII values indicating a stronger association with calorie-dense, processed foods that

Table 2 Association of NRI with the odds of NAFLD by piecewise logistic regression

	Model 1		Model 2		Model 3	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
NAFLD						
NRI per IQR						
> 98.623	4.306 (3.563, 5.203)	< 0.001	5.105 (4.148, 6.282)	< 0.001	4.517 (3.422, 5.962)	< 0.001

Model 1 was an unadjusted model. Model 2 included adjustment for age, sex, ethnicity, education level, and PIR. Model 3 further accounted for smoking status, diabetes, and hypertension. NRI, nutritional risk index; NAFLD, non-alcoholic fatty liver disease; OR, odds ratio; CI, confidence interval; IQR, interquartile range; PIR, family income poverty ratio

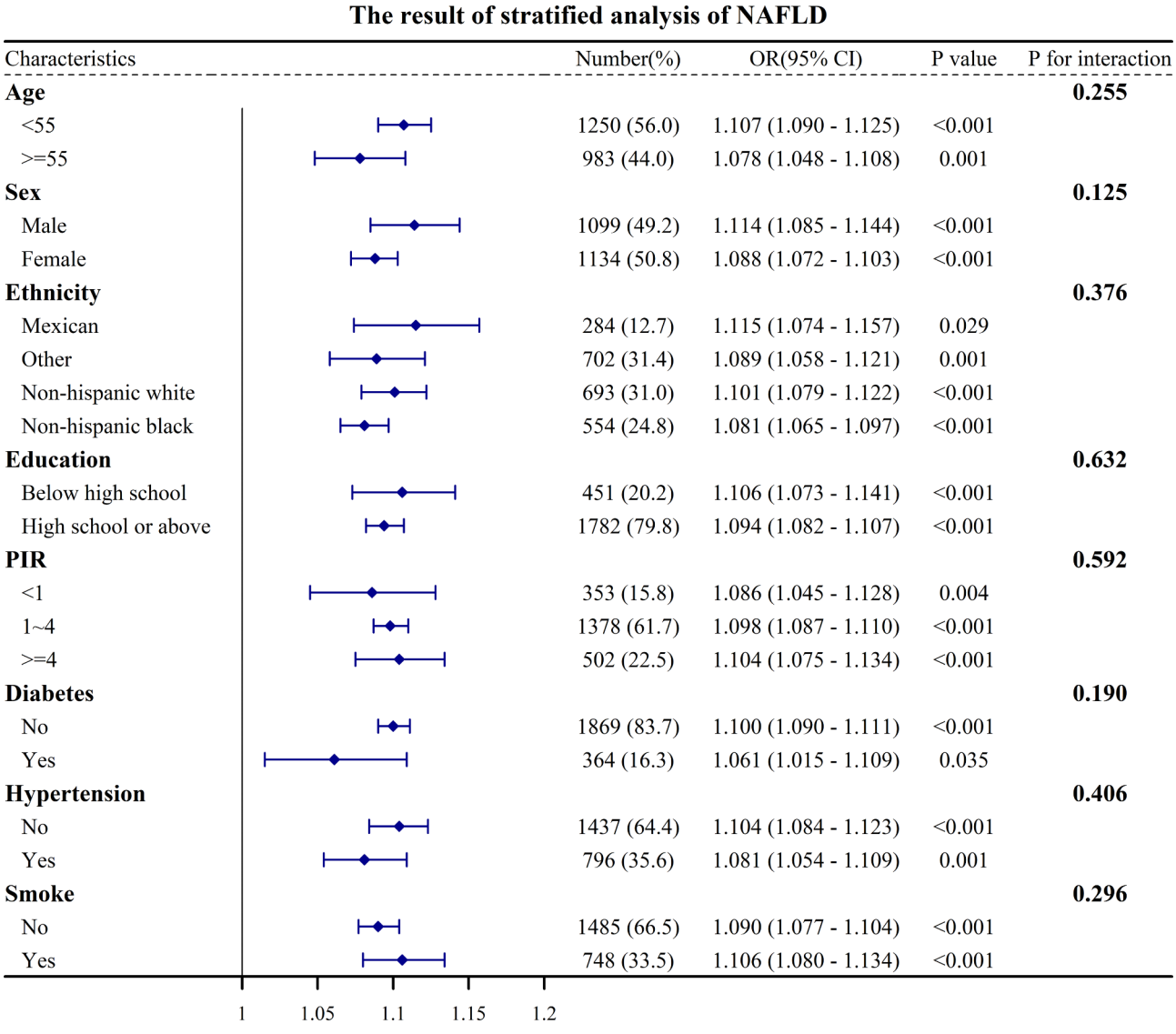

Fig. 2 Forest plot of stratified analysis of the association between NRI and NAFLD. NAFLD, non-alcoholic fatty liver disease; OR, odds ratio; CI, confidence interval; PIR, family income poverty ratio; NRI, nutritional risk index

are rich in fats, cholesterol, and carbohydrates. This work uncovered a significant positive association between DII and susceptibility to NAFLD [47]. Similarly, the prognostic nutrition index (PNI) is also employed to assess nutritional status, with higher PNI values indicating better nutrition. A positive and rapid increase was found in the association between the PNI and NAFLD in this work [48].

Our findings corroborate existing research on the association between NAFLD and both the DII and PNI. However, the parameters utilized in calculating DII, PNI, and NRI differ markedly. The DII incorporates 28 diverse dietary parameters [47], and PNI is based on albumin levels and absolute lymphocyte counts [48]. In contrast, the NRI is derived from routine clinical measurements of serum albumin, weight, and height using a straightforward, objective, and time-efficient formula [16]. Moreover, extensive validation has established NRI as a reliable prognostic indicator for patients with a range of diseases, including acute coronary syndrome, heart failure, osteoporosis, and malignancies [22–24, 39]. Owing to its simplicity and broad applicability, NRI may offer a significant advantage in evaluating the odds of NAFLD and liver fibrosis.

Mediation analysis revealed that CALLY modestly mediates the association between NRI and NAFLD. CALLY is measured by the level of CRP, albumin, and lymphocyte counts, which respectively indicate inflammation, nutritional status, and immune function. This composite index provides a comprehensive assessment of systemic inflammation, surpassing traditional or other composite indicators such as CRP and the

The result of stratified analysis of liver fibrosis

Characteristics	Number(%)	OR(95% CI)	P value	P for interaction
Age				**0.568**
<55	496 (52.9)	1.081 (1.041 - 1.121)	0.005	
>=55	442 (47.1)	1.065 (1.033 - 1.099)	0.005	
Sex				**0.464**
Male	518 (55.2)	1.084 (1.044 - 1.126)	0.004	
Female	420 (44.8)	1.066 (1.036 - 1.096)	0.003	
Ethnicity				**0.803**
Mexican	162 (17.3)	1.094 (1.036 - 1.155)	0.190	
Other	276 (29.4)	1.099 (1.074 - 1.124)	<0.001	
Non-hispanic white	310 (33.0)	1.066 (1.025 - 1.108)	0.015	
Non-hispanic black	190 (20.3)	1.074 (1.046 - 1.103)	0.013	
Education				**0.166**
Below high school	194 (20.7)	1.061 (1.028 - 1.095)	0.010	
High school or above	744 (79.3)	1.076 (1.045 - 1.107)	0.002	
PIR				**0.306**
<1	137 (14.6)	1.108 (1.051 - 1.169)	0.009	
1~4	606 (64.6)	1.080 (1.052 - 1.108)	0.001	
>=4	195 (20.8)	1.038 (0.954 - 1.129)	0.420	
Diabetes				**0.445**
No	693 (73.9)	1.079 (1.038 - 1.123)	0.007	
Yes	245 (26.1)	1.059 (1.013 - 1.106)	0.038	
Hypertension				**0.893**
No	522 (55.7)	1.075 (1.040 - 1.111)	0.004	
Yes	416 (44.3)	1.071 (1.037 - 1.105)	0.004	
Smoke				**0.930**
No	606 (64.6)	1.070 (1.035 - 1.106)	0.005	
Yes	332 (35.4)	1.074 (1.041 - 1.107)	0.003	

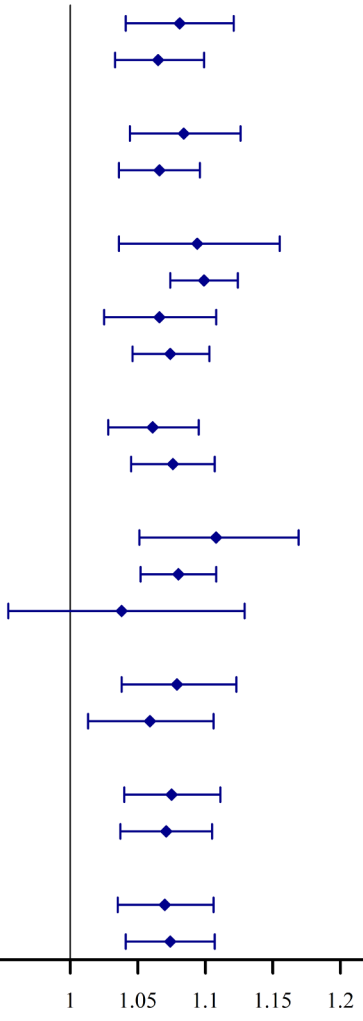

Fig. 3 Forest plot of stratified analysis of the association between NRI and liver fibrosis. OR, odds ratio; CI, confidence interval; PIR, family income poverty ratio; NRI, nutritional risk index

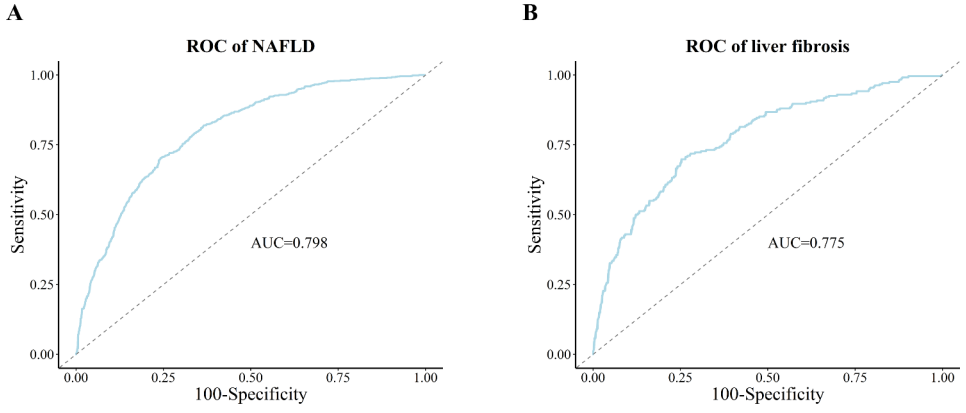

Fig. 4 Receiver operating characteristic curves of NRI in diagnosing NAFLD and liver fibrosis. **A** NAFLD. **B** Liver fibrosis. The model accounted for age, sex, ethnicity, education level, PIR, smoking status, diabetes, and hypertension. NRI, nutritional risk index; NAFLD, non-alcoholic fatty liver disease; ROC, receiver operating characteristic; AUC, area under the ROC curve; PIR, family income poverty ratio

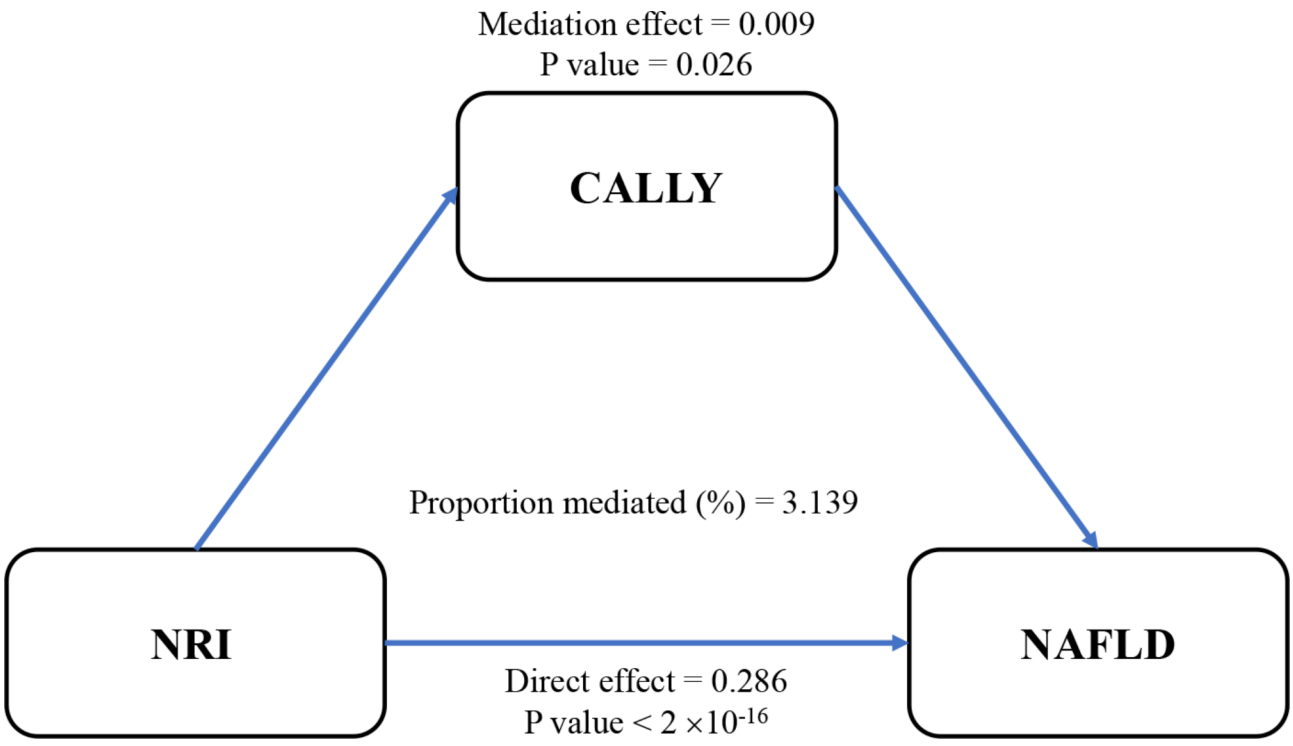

Fig. 5 Mediation analysis of CALLY on NRI-NAFLD association. NRI, nutritional risk index; NAFLD, non-alcoholic fatty liver disease; CALLY, C-reactive protein-albumin-lymphocyte

neutrophil-lymphocyte ratio (NLR) [49]. Furthermore, the prognostic significance of CALLY has been established in conditions including hepatocellular carcinoma, colorectal cancer, and other diseases [49, 50]. The findings that CALLY modestly mediated the association between NRI and NAFLD are also consistent with the current comprehension of the influence of inflammation on the connection between nutrition and NAFLD. It is posited that consumption of high-calorie, high-carbohydrate, and high-fat diets can trigger oxidative stress in adipose tissue, dysbiosis of gut microbiota, and impairments in the intestinal barrier, leading to chronic low-grade systemic inflammation [12, 51]. Subsequently, this chronic systemic inflammation can give rise to insulin resistance [52]. In the state of insulin resistance, inappropriate lipolysis causes aberrant transport of fatty acids to the liver, compromising hepatic capacity for processing fatty acids. Such disturbances in hepatic lipid metabolism may lead to hepatic lipid accumulation and lipid toxicity. Consequently, cellular stress, cell death, and liver inflammation are initiated and exacerbated, leading to the onset and progression of NAFLD [53]. Therefore, our findings further emphasize the important impact of inflammation in explaining the complex relationship between nutrition and NAFLD. However, no mediating effect of CALLY was observed in liver fibrosis, possibly due to the varying lymphocyte counts, a key indicator for calculating CALLY, between the NAFLD and liver fibrosis groups. Clinical studies have consistently demonstrated an increase in peripheral blood lymphocytes in patients with NAFLD compared to controls [48, 54]. Peripheral lymphocytes are identified to be intimately related to intrahepatic inflammation and exert an important impact on the pathogenesis of NAFLD [55]. While in our study, lymphocyte counts in patients with liver fibrosis did not differ significantly from those in controls. This finding may provide an explanation for the non-mediation of CALLY on the association between NRI and liver fibrosis. The absence of lymphocyte elevation in patients with liver fibrosis may be attributed to various pathophysiological processes, including hypersplenism and bone marrow hematopoietic suppression, which occur during the etiopathogenesis of liver fibrosis [56].

It is necessary to acknowledge the limitations inherent in this study. Firstly, due to its cross-sectional design, the causal association between NRI and NAFLD as well as liver fibrosis cannot be inferred. Additionally, the diagnosis of hepatic steatosis in this study was based on imaging rather than on the histological gold standard. Finally, as certain data are derived from subjective interviews and participant-driven questionnaires, there is an inherent risk of imprecise data capture or recall bias. In light of recent international guidelines introducing the concept of MASLD, future research will also aim to explore the association between NRI and MASLD.

Conclusions

In conclusion, our findings suggest a positive association between NRI and the odds of NAFLD and liver fibrosis, thereby underscoring the utility of NRI as an associated marker for these liver conditions. Furthermore, the role of CALLY as a mediator in the association between NRI and NAFLD suggests that NRI not only exerts direct effects on NAFLD but also contributes indirectly by increasing systemic inflammation levels.

Abbreviations

NRI	Nutritional risk index
NAFLD	Non-alcoholic fatty liver disease
NHANES	National Health and Nutrition Examination Survey
GLIM	Global Leadership Initiative on Malnutrition
YKL-40	Chitinase-3-like protein 1
NF-κB	Nuclear factor kappa-B
TLRs	Toll-like receptors
VCTE	Vibration-Controlled Transient Elastography
PIR	Family income poverty ratio
BMI	Body mass index
FPG	Fasting plasma glucose
ALT	Alanine transaminase
AST	Aspartate aminotransferase
GGT	γ-glutamyl transferase
HDL-C	High-density lipoprotein cholesterol
LDL-C	Low-density lipoprotein cholesterol
TC	Total cholesterol
TG	Triglyceride
hs-CRP	High-sensitivity C-Reactive Protein
HOMA-IR	Homeostatic model assessment for insulin resistance
CALLY	C-reactive protein-albumin-lymphocyte
HS	Hepatic steatosis
CAP	Controlled attenuation parameter
LSM	Liver stiffness measurement
SD	Standard deviations
IQR	Interquartile range
OR	Odds ratio
CI	Confidence interval
RCS	Restricted cubic spline
ROC	Receiver operating characteristic
AUC	Area under the ROC curve
PNI	Prognostic nutrition index
DII	Dietary inflammation index
NLR	Neutrophil-lymphocyte ratio
IL-6	Interleukin-6
IL-1β	Interleukin-1β
TNF-α	Tumor necrosis factor-α

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12944-024-02427-z.

Supplementary Material 1

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Author contributions

JM.J. collected, analyzed, and interpreted the data. R.Z. analyzed the data. Y.D. collected the data. JM.J. and XY.L. drafted the manuscript. XY.L. and HT.Z. revised the manuscript and conceived and designed the study. All the listed authors have approved the submitted version.

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Data availability

Publicly available datasets were analyzed in this study. This data can be found here: https://www.cdc.gov/nchs/nhanes/.

Declarations

Ethics approval and consent to participate

The NHANES protocol (Protocol number: 2018-01) was examined and approved by the Research Ethics Review Board of the National Center for Health Statistics and adhered to the provisions of the Declaration of Helsinki. Since the NHANES data released by the NCHS undergo de-identification and anonymization during analysis, conducting secondary analyses on this dataset does not necessitate additional ethical approval or informed consent. The NHANES website provides access to the approval granted by the NCHS Research Ethics Review Board (https://www.cdc.gov/nchs/nhanes/irba98.htm).

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Informed consent

Each patient/participant had completed a written statement of informed consent before taking part.

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