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The association between nutritional-inflammatory status and chronic kidney disease prognosis: a population-based study

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ABSTRACT

Background: Chronic kidney disease (CKD) prognosis is closely tied to the interplay between nutrition and inflammation. However, comprehensive nutritional-inflammatory indices for prognostic evaluation are rare in CKD. This study explored the association of the advanced lung cancer inflammation index (ALI) with estimated glomerular filtration rate (eGFR) and all-cause mortality in CKD patients.

Methods: A total of 1,982 CKD patients from the National Health and Nutrition Examination Survey (NHANES) database (2011–2018) were included in the analysis. Analytical methods included linear regression, cox regression, and restricted cubic spline (RCS) analysis. Subgroup and sensitivity analyses were performed, and further evaluation was conducted using the receiver operating characteristic (ROC) curve and C-index for all-cause mortality across different CKD stages.

Results: Among CKD patients, 1,103 patients (55.7%) were classified as stage I–II, and 879 patients (44.3%) as stage III–V. After adjusting covariates, ALI was found to be positively correlated with eGFR (Beta = 0.11; 95% CI: 0.07–0.15), and negatively related with all-cause mortality (HR = 0.72; 95% CI: 0.63–0.83). Subgroup analysis showed that the positive correlation between ALI and eGFR was stronger in CKD stage III–V compared to stage I–II. However, ALI's protective effect on mortality was weaker in stage III–V. The C-index for ALI was 0.648 in stage I–II and 0.660 in stage III–V.

Conclusion: ALI was significantly associated with eGFR and all-cause mortality in CKD patients. Nutritional and anti-inflammatory interventions in early-stage CKD may improve prognosis, and ALI may have great potential as a multifaceted biomarker to influence the prognosis of CKD, particularly in stages III–V.

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The advanced cancer inflammation index (ALI); estimated glomerular filtration rate (eGFR); nutrition-inflammation interplay; chronic kidney disease (CKD)

1. Introduction

Chronic kidney disease (CKD) is characterized by persistent renal functional or structural abnormalities lasting at least 3 months and impacts approximately 13.4% of the global population [1,2]. The prognosis of CKD is a major public health concern in the United States, with the general population experiencing an average annual decrease in the glomerular filtration rate (GFR) of about 1 mL/min/1.73 m^2 [3,4]. This decline in renal function, with more than half of individuals at risk of GFR dropping below 60 mL/min/1.73 m^2, underscores the significance of the early detection, management, and prevention of severe health outcomes such as progression to end-stage kidney disease (ESKD), and cardiovascular diseases, which are associated with increased mortality [5].

Inflammation plays a pivotal role in the progression and poor prognosis of CKD. Studies have demonstrated that elevated levels of pro-inflammatory cytokines, such as interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and C-reactive protein (CRP), are strongly associated with declining kidney function and an increased risk of cardiovascular disease [6]. Additionally, systemic inflammatory markers, including the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and systemic immune-inflammation index (SII), have been identified as independent predictors of all-cause mortality in CKD populations [7,8].

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Beyond inflammation, malnutrition is also a key determinant of CKD progression and adverse outcomes. The geriatric nutritional risk index (GNRI), a nutritional assessment tool based on serum albumin, height, and weight, has gained increasing attention for its prognostic value in CKD patients [9]. Moreover, emerging evidence suggests that inflammation and malnutrition are intricately linked in CKD, forming a bidirectional relationship that significantly impacts patient outcomes. Pro-inflammatory cytokines contribute to anorexia, chronic fatigue, and muscle protein catabolism, leading to progressive muscle atrophy and frailty in CKD patients [10]. Furthermore, the 2011 American Society for Parenteral and Enteral Nutrition (ASPEN) Clinical Guidelines recommend against using albumin and prealbumin as sole indicators of nutritional status, as these biomarkers are significantly influenced by inflammatory processes rather than reflecting true nutritional depletion [11].

Given the strong interconnection between inflammation and malnutrition, recent studies have highlighted their combined impact on mortality, particularly in ESKD and hemodialysis patients [12]. This underscores the need for an integrated assessment approach that considers both inflammatory and nutritional markers to improve risk stratification and optimize patient management. Developing targeted interventions that address both inflammation and malnutrition may enhance clinical outcomes and reduce mortality in CKD populations.

The advanced lung cancer inflammation index (ALI) differs from previously published indicators or markers because it includes not only NLR and albumin, but also body mass index (BMI), which is used to determine nutritional status. It represents the overall inflammation level and nutritional status of the patient [13]. The expanding role of ALI in the prognosis of chronic diseases, including lung cancer [14], type 2 diabetes mellitus [15], stroke [16], Crohn's disease [17], hypertension [18] and heart failure [19], reveals its robust predictive value in assessing adverse outcomes associated with these chronic diseases, which are also affected by nutrition and inflammation. Thus, ALI is a potentially invaluable tool for CKD management, where conventional single-factor models often fall short.

2. Material and methods

2.1. Study population

This study referred to the National Health and Nutrition Examination Surveys (NHANES) database, accessible at https://www.cdc.gov/nchs/nhanes/, and extracted data from 2011 to 2018, focusing on non-pregnant individuals aged ≥18 years, initially comprising 39,156 participants. Exclusions were based on: (1) pregnant participants (n = 2,48), (2) participants not suffering from CKD (n = 33,620), (3) participants suffering from blood cancer, liver cancer, or lymphomas or have outlier values of ALI (n = 98), and (4) participants' insufficient data to BMI, serum albumin, neutrophil count, lymphocyte count, estimated GFR (eGFR), survival status (n = 3,208). These exclusions were implemented to ensure study consistency and data integrity. After the data of ineligible individuals were excluded, the study included the data of 1,982 CKD patients. These participants were categorized into tertiles based on ALI: Q1 (ALI ≤ 11.03), Q2 11.03 < ALI ≤ 16.96), and Q3 (16.96 < ALI). Figure 1 depicts the participant selection process.

2.2. Assessment of CKD and prognosis

CKD is defined by the presence of a reduced eGFR or proteinuria [20]. Specifically, CKD is identified when eGFR is < 60 mL/min/1.73 m^2, or when the albumin–creatinine ratio (ACR) is> 30 mg/g [21]. CKD prognosis was assessed based on eGFR and all-cause mortality rates. eGFR was calculated using calibrated serum creatinine values by applying the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation, according to Levey et al. [22].

2.3. Variables of interest

The selection of covariates was based on previous literature and clinical experience. Key variables such as age, sex, race, education, smoking status (≥100 lifetime cigarettes in life), intake of caffeine, BMI, and sleep duration were self-reported by the patients. To evaluate parameters such as hemoglobin and uric acid levels, patient blood samples were collected by phlebotomists at mobile examination centers using a standardized protocol. The ALI was calculated as follows: BMI (kg/m^2) × serum albumin (g/dL)/neutrophil-to-lymphocyte ratio [13].

Diabetes mellitus (DM) diagnosis criteria included self-reported physician diagnosis, fasting blood glucose ≥ 7.0 mmol/L (126 mg/dL), insulin or oral hypoglycemic medication usage, glycosylated hemoglobin A1c ≥ 6.5% (48 mmol/mol), or postprandial 2-h plasma glucose ≥ 11.1 mmol/L (200 mg/dL) [23]. Hypertension was determined as average systolic blood pressure ≥130 mm Hg, diastolic blood pressure) ≥80 mm Hg, or self-reported use of hypertension medication [24]. Hyperlipidemia was defined as total cholesterol ≥ 200 mg/dL, triglycerides ≥ 150 mg/dL, high-density lipoprotein (HDL) < 40 mg/dL in males and < 50 mg/dL in females, or low-density lipoprotein (LDL) ≥ 130 mg/dL [25]. Excessive drinking criteria were daily alcohol consumption > 2 drinks for men and > 1 drink for women [26].

SII was defined as the platelet count multiplied by the neutrophil count/lymphocyte count [27].

NLR was defined as the neutrophil count divided by the lymphocyte count [28].

GNRI was defined as 1.489 × albumin (g/L) + 41.7 × [body weight/ideal body weight], ideal body mass = 22 × Height (m) × Height (m) [29].

PLR was defined as dividing the platelet counts by the lymphocyte counts [30].

Prognostic nutritional index (PNI) was defined as [10 × albumin (g/dl)] + (0.005 × lymphocyte count) [31].

2.4. Statistical analysis

Data were analyzed using R statistical software (version 4.1.3) and MSTATA (https://www.mstata.com/). The Shapiro-Wilk test

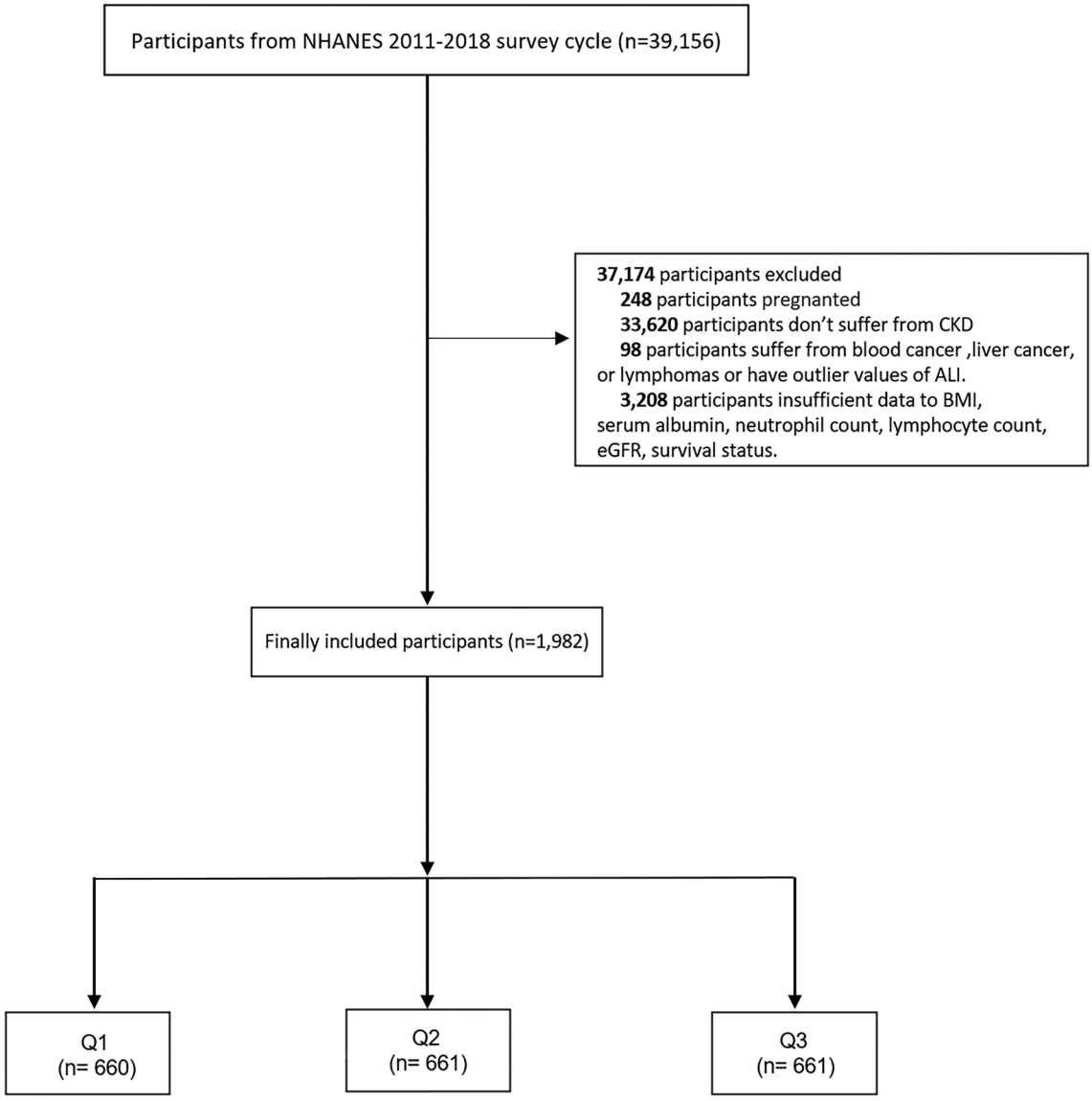

Figure 1. Flowchart of participant selection, NHANES, 2011–2018.

was used to assess normal distribution. Normally distributed variables were presented as mean ± standard deviation (mean ± SD), and group differences were examined through one-way ANOVA test. The Kruskal–Wallis test was conducted for non-normally distributed data. Categorical variables across ALI tertiles were analyzed using the chi-square test. KNN imputation addressed missing covariate data. Before performing linear and cox regression analyses, variables were Z-score normalized. The restricted cubic spline (RCS) analysis with 4 knots, placed according to data distribution, modeled nonlinear relationships. Piecewise regression analysis was made to further analyze the association between ALI and all-cause mortality. To address the potential heterogeneity in CKD stages and its impact on the association between the ALI and CKD prognosis, we conducted a subgroup analysis based on CKD stages. This study then re-excluded the CKD population with eGFR prepared with serum cystatin C, and performed sensitivity analyses for the association of ALI with eGFR and the association of ALI with all-cause mortality in the population. In this study, the total sample was further divided into CKD stages 1-2 and CKD stages 3-5 to exclude selection bias. On this basis, a cox regression model was constructed and ALI was compared with a number of widely used and easily accessible clinical indicators (including CRP, GNRI, NLR,PLR, SII) to further evaluate the diagnostic performance of ALI in predicting all-cause mortality in patients with CKD. Predictive performance was evaluated on the basis of C-index and area under the time-dependent receiver operating characteristic curve (ROC), sensitivity and specificity.

3. Results

3.1. Patient characteristics

In our study, the 1,982 participants including 1,103 (55.7%) stage I-II and 879 (44.3%) stage III-V were stratified into three

Table 1. Patient demographics and baseline characteristics.

Characteristics	ALI				*P*-value
	Total, *N* = 1,982	Q1, *N* = 660	Q2, *N* = 661	Q3, *N* = 661	
Age (years)					<0.001
Median (IQR)	64.00 (50.00, 75.00)	69.00 (52.00,79.00)	65.00 (50.00,75.00)	60.00 (49.00,71.00)	
Sex (%)					<0.001
Male	966 (46.94)	368 (53.64)	299 (43.59)	299 (43.59)	
Female	1,092 (53.06)	318 (46.36)	387 (56.41)	387 (56.41)	
Race (%)					<0.001
Mexican American	257 (12.49)	78 (11.37)	108 (15.74)	71 (10.35)	
Non-Hispanic White	796 (38.68)	341 (49.71)	248 (36.15)	207 (30.17)	
Non-Hispanic Black	501 (24.34)	105 (15.31)	150 (21.87)	246 (35.86)	
Other Hispanic	208 (10.11)	62 (9.04)	72 (10.50)	74 (10.79)	
Other Race - Including Multi-Racial	296 (14.38)	100 (14.58)	108 (15.74)	88 (12.83)	
Education (%)					0.191
< High school	594 (28.86)	182 (26.53)	218 (31.78)	194 (28.28)	
High school	437 (21.23)	142 (20.70)	140 (20.41)	155 (22.59)	
>High school	1,027 (49.90)	362 (52.77)	328 (47.81)	337 (49.13)	
Smoking status (≥100 cigarettes in the life)					0.029
No	1,102 (53.55)	342 (49.85)	391 (57.00)	369 (53.79)	
Yes	956 (46.45)	344 (50.15)	295 (43.00)	317 (46.21)	
Excessive drinking (%)					0.948
No	2,039 (99.08)	680 (99.13)	680 (99.13)	679 (98.98)	
Yes	19 (0.92)	6 (0.87)	6 (0.87)	7 (1.02)	
Intake of caffeine (gram)					0.223
Median (IQR)	237.18 (0.00, 422.18)	244.00 (0.00,456.38)	236.80 (0.00,390.00)	208.85 (0.00,405.00)	
BMI (kg/m^2)					<0.001
Median (IQR)	29.00 (25.00, 33.80)	26.10 (23.02,30.50)	29.10 (25.33,33.40)	32.00 (27.80,37.80)	
Sleep duration (hours)					<0.001
Median (IQR)	7.00 (6.34, 7.63)	7.00 (6.49,8.00)	7.00 (6.43,7.62)	6.96 (6.14,7.45)	
Hemoglobin (g/dL)					0.714
Median (IQR)	13.60 (12.50, 14.70)	13.55 (12.50,14.70)	13.60 (12.60,14.60)	13.60 (12.50,14.70)	
Uric acid (mg/dL)					0.035
Median (IQR)	5.90 (4.80, 7.10)	5.80 (4.70,7.00)	5.80 (4.70,6.90)	6.00 (5.00,7.20)	
DM (%)					0.162
No	1,216 (59.09)	425 (61.95)	392 (57.14)	399 (58.16)	
Yes	842 (40.91)	261 (38.05)	294 (42.86)	287 (41.84)	
Hypertension (%)					0.612
No	641 (31.15)	222 (32.36)	214 (31.20)	205 (29.88)	
Yes	1,417 (68.85)	464 (67.64)	472 (68.80)	481 (70.12)	
Hyperlipidemia (%)					0.070
No	396 (19.24)	151 (22.01)	119 (17.35)	126 (18.37)	
Yes	1,662 (80.76)	535 (77.99)	567 (82.65)	560 (81.63)	
eGFR (mL/min/1.73 m^2)					<0.001
Median (IQR)	69.31 (51.56, 99.28)	63.23 (48.65,94.72)	67.91 (52.60,99.37)	75.47 (54.53,103.29)	
CKD stage					0.024
Stage I-II	1,103 (55.7%)	364 (53.1%)	372 (54.2%)	243 (39.8%)	
Stage III-V	879 (44.3%)	322 (46.9%)	314 (45.8%)	243 (39.8%)	
Survival status (%)					<0.001
Alive	1,750 (85.03)	534 (77.84)	595 (86.73)	621 (90.52)	
Dead	308 (14.97)	152 (22.16)	91 (13.27)	65 (9.48)	

BMI, means body mass index; DM, means diabetes mellitus; eGFR, means estimated glomerular filtration rate; CKD, means chronic kidney disease.

Table 2. Univariable and multivariable linear regression model for analyzing eGFR associated with ALI tertiles and ALI levels.

Factors	Model 1		Model 2		Model 3	
	Beta (95% CI)	*P*-value	Beta (95% CI)	*P*-value	Beta (95% CI)	*P*-value
ALI						
Q1	Reference	Reference	Reference	Reference	Reference	Reference
Q2	0.13 (0.03,0.24)	0.013	0.03 (−0.05,0.11)	0.420	0.02 (−0.05, 0.09)	0.583
Q3	0.24 (0.13,0.35)	<0.001	0.06 (0.02,0.14)	0.031	0.08 (0.01,0.15)	0.041
Continuous ALI for per SD	0.11 (0.07, 0.15)	<0.001	0.04 (0.01,0.07)	0.035	0.05 (0.02,0.08)	0.002

Model 1 was a univariate regression model; model 2 was adjusted for age, sex, and race; and model 3 was adjusted for age, sex, race, education, smoking status, sleep duration, excessive drinks, DM, hyperlipidemia, hypertension, intake of caffeine, hemoglobin, and uric acid.

groups according to ALI tertiles (Table 1). A progressive decrease in median age was noted with higher ALI tertiles (median age: 69, 65, and 60 for low, medium, and high tertiles, respectively; $p < 0.001$). Male participants were more prevalent in the low ALI tertiles (53.64% vs. 43.59%, 43.59% in higher tertiles; $p < 0.001$).

Table 3. Univariable and multivariable cox regression model for analyzing all-cause mortality associated with ALI tertiles and ALI levels.

	Model 1		Model 2		Model 3	
Factors	HR (95% CI)	*P*-value	HR (95% CI)	*P*-value	HR (95% CI)	*P*-value
ALI						
Q1	Reference	Reference	Reference	Reference	Reference	Reference
Q2	0.59 (0.45,0.76)	<0.001	0.67 (0.52,0.88)	0.003	0.68 (0.52,0.89)	0.003
Q3	0.40 (0.29,0.54)	<0.001	0.53 (0.38,0.73)	<0.001	0.53 (0.39,0.74)	<0.001
Continuous ALI for per SD	0.64 (0.56,0.73)	<0.001	0.73 (0.64,0.84)	<0.001	0.72 (0.63,0.83)	<0.001

Model 1 was a univariate regression model; model 2 was adjusted for age, sex, and race; and model 3 was adjusted for age, sex, race, education, smoking status, sleep duration, excessive drinks, DM, hyperlipidemia, hypertension, intake of caffeine, hemoglobin, and uric acid.

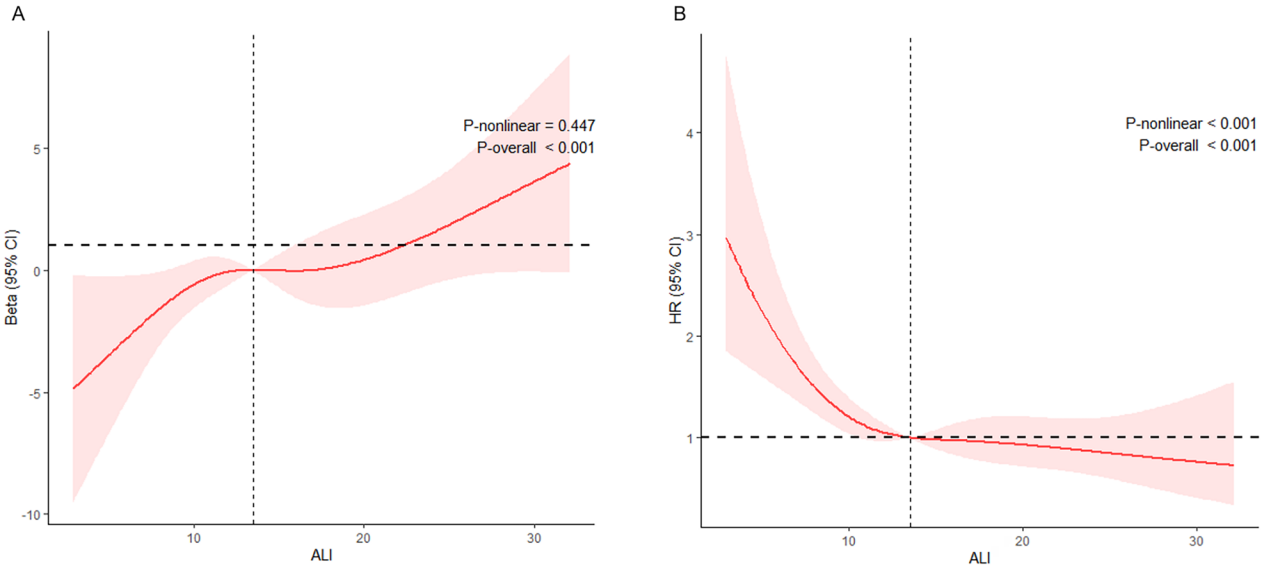

Figure 2. Beta and HR were adjusted for age, sex, race, education, smoke, sleep duration, excessive drinking, DM, hypertension, hyperlipidemia, intake of coffee, hemoglobin, and uric acid. (A) Association between ALI with eGFR among CKD patients. (B)Association between ALI with all-cause mortality among CKD patients. The reference value for ALI was 14.

Table 4. Multivariable segmented cox regression for analyzing all-cause mortality associated with ALI levels.

Characteristic	HR (95% CI)	*P*-value
ALI (<14)	0.50 (0.36, 0.71)	<0.001
ALI (≥14)	0.88 (0.66, 1.18)	0.399

The model was adjusted for age, sex, race, education, smoking status, sleep duration, excessive drinks, DM, hyperlipidemia, hypertension, intake of caffeine, hemoglobin, uric acid.

Uric acid levels were significantly higher in the highest ALI tertiles (6.00 mg/dL) than in the lowest (5.80 mg/dL) and the medium tertiles (5.80 mg/dL; $p = 0.026$). No significant differences were noted in the prevalence of DM, hyperlipidemia, and hypertension across tertiles ($p > 0.050$). Higher ALI was associated with higher eGFR (63.23, 67.91, and 75.47 mL/min/1.73 m^2 for low, medium, and high tertiles, respectively; $p < 0.001$) and decreased mortality (22.16%, 13.27%, and 9.48% for low, medium, and high tertiles; $p < 0.001$). This indicated ALI's potential impact on survival. Statistically significant associations were also observed across tertiles in race, smoking status, BMI, and sleep duration ($p < 0.050$ for each), education ($p = 0.191$), excessive drinking ($p = 0.948$), hemoglobin ($p = 0.714$), and intake of caffeine ($p = 0.223$) showed no significant differences.

3.2. Association between ALI and CKD prognosis

Our study used a multifaceted analytical approach. Three linear regression models (Table 2) and cox regression models (Table 3) evaluated the relationships of ALI with eGFR and all-cause mortality. The crude model (model 1) applied the univariate regression analysis. In model 2, adjustments were made for age, sex, and race. The model 3 expanded upon these adjustments by also considering education, smoking status, sleep duration, excessive drinking, DM, hypertension, hyperlipidemia, intake of caffeine, hemoglobin, and uric acid. In the linear regression analysis, Model 1 exhibited that ALI was significantly positively correlated with eGFR. This association remained significant in adjusted models 2 and 3. In model 3, each standardized unit increase in ALI was associated with an increase of 0.05 mL/min/1.73 m^2 in eGFR (Beta: 0.05, 95% CI: 0.02–0.08; $p < 0.001$). Compared with the lowest ALI tertile, the highest ALI tertile was associated with an increased eGFR of 0.08 mL/min/1.73 m^2 (Beta: 0.08, 95% CI: 0.01–0.15; $p = 0.041$) in model 3.

In the cox regression models (Table 3), model 1 revealed that continuous ALI significantly negatively correlated with all-cause mortality. This association was also statistically significant in adjusted models 2 and 3 (model 2 HR: 0.73, 95%

CI: 0.64–0.84, $p < 0.001$; model 3 HR: 0.72, 95% CI: 0.63–0.83, $p < 0.001$). When ALI was analyzed as tertiles, the highest ALI tertile demonstrated a statistically significant negative association with all-cause mortality across all models (all $p < 0.001$). In Model 3, the highest ALI tertile exhibited a 47% reduction in mortality risk compared to the lowest (HR: 0.53, 95% CI: 0.39–0.74, $p < 0.001$).

3.3. Sensitivity analysis

To assess the sensitivity of the main analysis results to the selection of key variables, we conducted a sensitivity analysis. In this analysis, the eGFR formula calculated using calibrated serum creatinine values and the CKD-EPI equation was replaced with calibrated serum cystatin C values and the CKD-EPI SCysC 2012 equation [32]. This substitution allowed us to evaluate the robustness of the results. The findings of the sensitivity analysis were consistent with those of the main analysis and did not alter the overall conclusions (Table S1-S2).

3.4. Dose-response relationship and piecewise regression analysis

Our RCS analysis explored the dose-response relationship between ALI and both eGFR and all-cause mortality, as depicted in Figure 2. A significantly linear association was noted between ALI and eGFR (p-overall < 0.001, p-nonlinear = 0.447; Figure 2A). This finding implied that ALI and eGFR exhibited a relatively uniform association without any inflection points or threshold effects throughout its spectrum. By contrast, a nonlinear relationship was observed between ALI and all-cause mortality (p-overall < 0.001, p-nonlinear < 0.001; Figure 2B). The inflection point for this relationship was identified at ALI = 14. When ALI was < 14, each standardized unit increase led to a 50% decrease in mortality risk (HR: 0.50, 95% CI: 0.36–0.71; $p < 0.001$; Table 4). Above this threshold, each additional ALI unit was linked to a 12% decrease in mortality risk (HR: 0.88, 95% CI: 0.66–1.18; $p = 0.399$). It indicated that when ALI >14, the negative association between ALI and all-cause mortality in the CKD population weakens.These findings indicated that patients with ALI > 14 have better CKD prognosis.

3.5. Subgroup analysis and model performance comparison

In the subgroup analysis (Figure 3), we found that the positive correlation between ALI and eGFR was stronger in CKD stage III–V patients (Beta: 0.05, 95% CI: 0.03–0.08, $p < 0.001$) compared to CKD stage I–II patients (Beta: 0.01, 95% CI: −0.02–0.04, $p = 0.368$). However, when examining the association between ALI and all-cause mortality, the protective effect of ALI on all-cause mortality was weaker in CKD stage

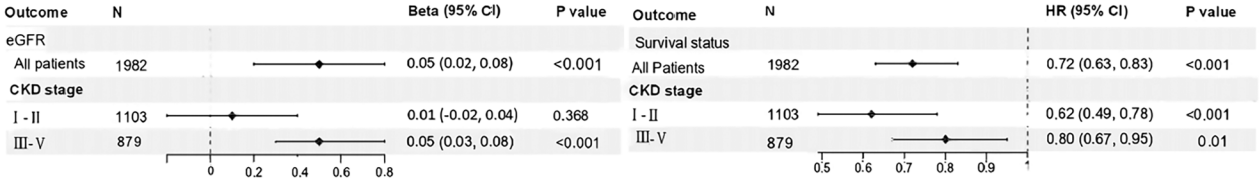

Figure 3. Subgroup analysis of the association between ALI and eGFR/all-cause mortality in CKD patients.

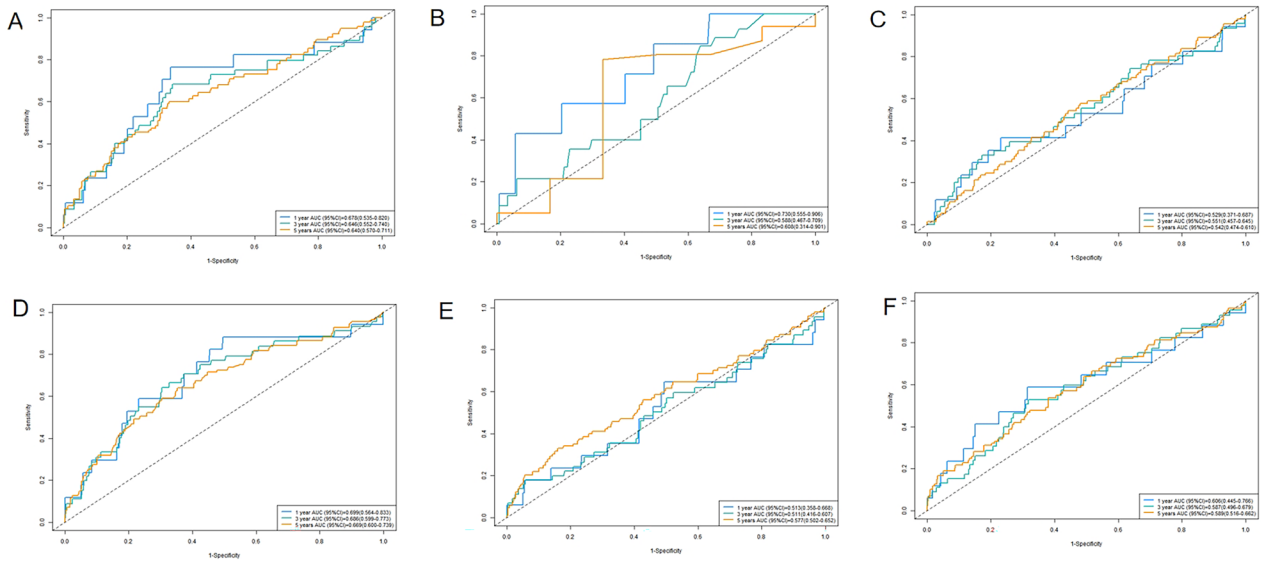

Figure 4. The ROC of nutritional/inflammatory indicators in predicting 1-, 3-, and 5- years all-cause mortality in patients with CKD stage I-II.

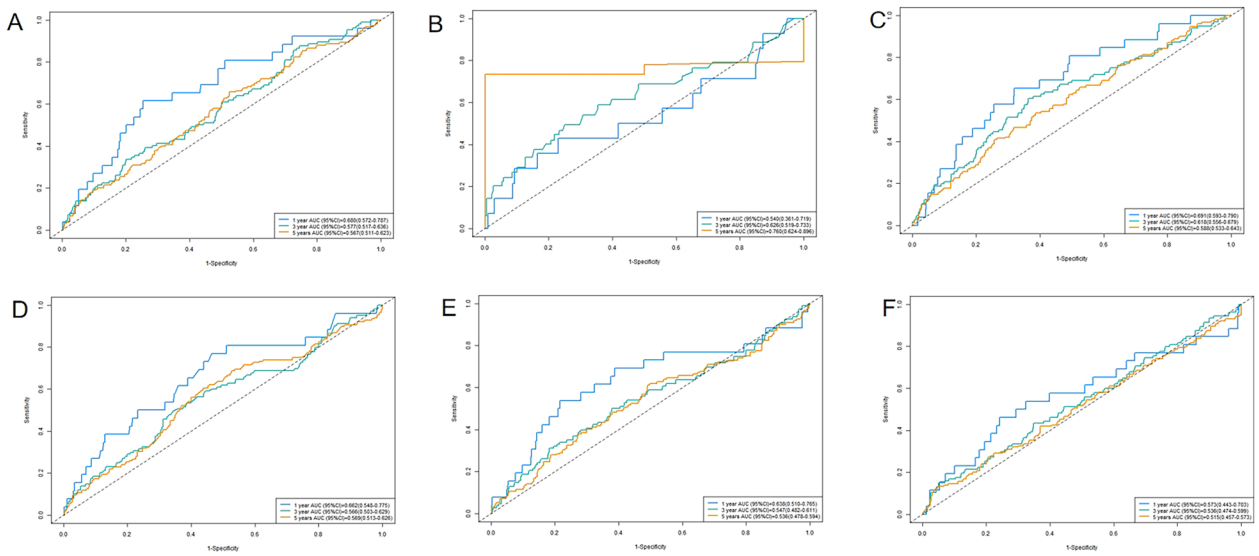

Figure 5. The ROC of nutritional/inflammatory indicators in predicting 1-, 3-, and 5- years all-cause mortality in patients with CKD stage IV-V.

III–V patients (HR: 0.80, 95% CI: 0.67–0.95, $p = 0.01$) compared to CKD stage I–II patients (HR: 0.62, 95% CI: 0.49–0.78, $p < 0.001$).

Further evaluation of subgroup model performance revealed that the AUC for predicting 1-, 3-, and 5-year all-cause mortality using ALI in patients with CKD Stage I-II was 0.678, 0.646, and 0.640, respectively. Notably, the 1-year AUC for ALI outperformed other markers expect CRP and NLR (Figure 4). As shown in Figure 5, in the CKD Stage III-V population, the AUC values for ALI were 0.680, 0.577, and 0.567 for 1-, 3-, and 5-year all-cause mortality, respectively, with the 1-AUC values outperforming other markers expect GNRI.

Moreover, comparisons of the C-index supported these findings. In the CKD stage I-II population, the C-index for ALI was 0.648, ranking second only to NLR (0.673). In contrast, in the CKD Stage III-V population, ALI demonstrated the highest performance with a C-index of 0.660 (Table S3).

4. Discussion

In this study, we demonstrated that ALI is strongly associated with prognosis in individuals with CKD. Further subgroup analysis revealed significant differences in the impact of nutritional and inflammatory status on disease prognosis across different stages of CKD. ROC curve and C-index indicated that ALI had good predictive performance, especially in CKD III-V population. The specific prediction performance was different in different subgroups.

Specifically, ALI was linearly positively correlated with eGFR and nonlinearly negatively correlated with all-cause mortality, with an inflection point of 14. Because of its inherent complexity, ALI being a composite index, can capture essential CKD prognosis-related health aspects. The established nutritional status indicators, BMI, and serum albumin are closely associated with all-cause mortality in CKD patients [33,34]. Concurrently, the neutrophil-to-lymphocyte ratio is considered a novel marker of systemic inflammation, which is also intimately related to CKD progression [35]. All these parameters should be analyzed together as inflammatory processes influence albumin levels. Albumin was inversely related to CRP levels, with CRP being associated with increased mortality in CKD patients [36]. Several epidemiological studies have reported that inflammation and malnutrition are associated with renal impairment [37,38]. In a randomized controlled trial, albumin levels and BMI decreased in ESRD patients over time, whereas CRP and IL-6 levels increased over time [36]. This was accompanied by a progressive deterioration of their condition during the disease. To the best of our knowledge, this is the first study to explore the association between the ALI and eGFR, as well as the varying prognostic implications of the ALI across different stages of chronic kidney disease. Lower ALI was significantly associated with a poorer CKD prognosis, which is somewhat consistent with previous studies [39,40], our study provides further supporting evidence.

Subgroup analysis showed that the positive correlation between ALI and eGFR was more pronounced in patients with CKD stages III-V. Conversely, the protective effect of ALI against all-cause mortality was more pronounced in individuals with CKD stages I-II. Moreover, the 1-year AUC prediction performance of ALI was slightly superior in the CKD III-V group compared to the CKD I-II group. First of all, an existing study have found that inflammation markers are more significantly associated with all-cause mortality in people with CKD Stage I than in other CKD stage populations [41]. However, there is no direct evidence that inflammation and nutritional status have a greater impact on all-cause mortality in patients with early CKD than in patients with advanced CKD. This phenomenon may be related to complex complications (such as cardiovascular disease, acute kidney failure, and dialysis-related complications) in people with advanced CKD that may mask the true impact of nutrition and inflammation on all-cause mortality. Secondly, a large number of studies

have demonstrated that nutrition and inflammatory status are important factors affecting eGFR in patients with advanced CKD [42,43]. The subgroup analysis of this study further highlights the importance of timely nutritional support and anti-inflammatory interventions in the early stages of CKD to optimize outcomes in early-stage patients.

Previous studies have also explored the influence of nutritional inflammatory status on the prognosis of CKD population. For example, a study investigating the prognosis of a Korean CKD population found that elevated CRP levels were associated with increased mortality [44]. In addition, a cross-sectional study demonstrated that the combined use of the GNRI and the NLR effectively assessed all-cause mortality in hemodialysis patients [45]. Similarly, another cross-sectional study revealed that the SII, NLR, and PLR were significantly associated with all-cause mortality in anemic CKD patients [35]. In this study, we evaluated the predictive power of ALI for all-cause mortality in the CKD population in different subgroups and compared it with the nutritional inflammatory measures mentioned above. We found that ALI has the best predictive performance overall in the CKD Stage III-V population. This is consistent with the findings of a study that explored the predictive performance of ALI on all-cause mortality in peritoneal dialysis patients [39]. Our study provides further supporting evidence and adds that the overall prediction performance of ALI is weaker than that of NLR in CKD stage I-II population. The prediction of one-year survival rate is weaker than that of GNRI. This may be due to the difference in calculation formulas and evaluation focus of ALI, GNRI and NLR in patients at CKD stage I-II, which results in their different predictive performance in patients at this stage. ALI combines BMI, albumin concentration, and NLR, primarily reflecting nutritional and inflammatory status. However, weight and albumin levels may not have decreased significantly in patients in the early stage of CKD, and in addition, the value of ALI is affected by NLR, which limits its ability to capture slight changes in patients in the early stage of CKD, thus affecting its predictive effect. In contrast, GNRI measures nutritional risk by a combined assessment of albumin concentration and weight status. Although nutritional problems may not have worsened significantly at CKD stage I-II, GNRI is more sensitive to identify potential nutritional risks, especially subtle changes in body weight and albumin, and thus exhibits strong predictive performance. NLR can detect inflammatory changes early by reflecting the ratio of neutrophils to lymphocytes, which makes it of high prognostic value in patients with early CKD. Therefore, the relatively weak predictive power of ALI in this population may be related to the fact that it is less sensitive than NLR and GNRI in identifying minor nutritional and inflammatory changes.

Recognizing the limitations of our observational study and the specificity of our cohort, future prospective studies need to further validate the utility of ALI across various stages CKD patients.

5. Conclusion

ALI was linearly positively correlated with eGFR and nonlinearly negatively correlated with all-cause mortality in CKD patients. Anti-inflammatory and nutritional support interventions for early CKD patients are very valuable for their prognosis and ALI is a multifaceted biomarker with great potential to influence the prognosis of CKD, especially in patients with stage III-V.

Author contributions

Conceptualization, X.Y., and X.H.; methodology, X.Y., and X.H. and D.H.; software Z.Q. and X.T.; validation, X.T.; formal analysis, X.Y.; investigation, X.Y.; resources, X.Y., Q.L.; data curation, X.Y., writing original draft preparation, X.H.; writing—review and editing, X.Y.; supervision, H.B.; project administration, H.B., and D.H.; funding acquisition, H.B. All authors have read and agreed to the published version of the manuscript.

Ethical approval and participant consent

Written consent was acquired from all individuals involved in the study. This research received ethical clearance from the National Center for Health Statistics (NCHS) Research Ethics Review Board, as detailed on their website (https://wwwn.cdc.gov/nchs/nhanes/default.aspx). The study strictly adhered to relevant regulations, ensuring that all participants or their legal representatives provided informed consent.

Disclosure Statement

No potential conflict of interest was reported by the authors.

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Data availability statement

This study analyzed publicly available datasets, which can be found at the following location: www.cdc.gov/nchs/nhanes/.

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