Journal of Health, Population and Nutrition

RESEARCH

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A cross-sectional study examining the relationship between the advanced lung cancer inflammation index and prostate cancer

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Abstract

Background Prostate cancer (PCa), a significant health concern among middle-aged and elderly men globally, has increasingly been associated with metabolic and inflammatory processes. The advanced lung cancer inflammation index (ALI), a novel marker reflecting nutritional and inflammatory status, has not yet been thoroughly investigated in the context of PCa. This study investigated the potential link between ALI and PCa.

Methods We first conducted a cross-sectional study utilizing data from the National Health and Nutrition Examination Survey (NHANES). The relationship between ALI and PCa was examined by NHANES-provided survey weights. Smoothed curve fitting and threshold effect analyses were conducted to evaluate possible nonlinear associations. Then we analyzed the correlation between the prognosis of PCa patients and ALI.

Results Out of 15,042 adult participants, 683 (4.54%) were diagnosed with PCa. The risk of PCa decreased across increasing quartiles of ALI. Multivariate logistic regression analysis revealed that compared to participants in the lowest ALI quartile (Q1: 2.89–41.94), those in higher quartiles (Q2: 41.94–59.08, Q3: 59.08–80.88, and Q4: ≥80.88) had progressively lower odds of developing PCa in both unadjusted and adjusted models. Smoothed curve fitting indicated a U-shaped relationship between ALI and PCa. Longitudinal follow-up data indicated that lower ALI values were positively correlated with a poor survival in cancer patients.

Conclusion Our study revealed a non-linear relationship between ALI and the risk of PCa development. Specifically, there was a negative correlation between ALI and PCa risk when the ALI value was < 100. Furthermore, we found that lower ALI levels are strongly associated with a poor survival in cancer patients. Additional large-scale prospective studies are needed to confirm these findings and investigate the underlying mechanisms.

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Keywords Advanced lung cancer inflammation index, Prostate cancer, NHANES, Cross-sectional study, Inflammatory markers, Follow-up study

Background

Prostate cancer (PCa) is one of the most common malignant tumors threatening the health and quality of life of elderly men [1]. Globally, PCa ranks fourth in overall prevalence and eighth in mortality [2, 3]. Among men, it is the second most common malignancy and the fifth leading cause of cancer-related deaths [2, 3]. The pathogenesis of PCa is multifactorial, involving a complex interplay of various molecular and cellular pathways [4]. Notably, inflammation and malnutrition are critical factors that significantly influence disease progression and prognosis [5, 6]. Inflammation, in particular, exacerbates malnutrition by promoting protein catabolism, increasing energy expenditure, and suppressing appetite, all of which collectively contribute to higher prevalence and mortality rates in PCa patients [6]. Furthermore, localized inflammation within the body, such as pelvic inflammatory disease, has been reported to exacerbate the progression of PCa and promote the development of an aggressive tumor phenotype [7].

Recent studies have increasingly highlighted the role of nutrition- and inflammation-related indices as effective predictors of PCa [8, 9]. Inflammatory markers such as the neutrophil-to-lymphocyte ratio (NLR), systemic immune-inflammation index (SII) [10, 11], and systemic inflammatory response index (SIRI) have been associated with PCa development and prognosis [12–14]. Similarly, nutritional indices, including the geriatric nutritional risk index (GNRI) and prognostic nutritional index (PNI), have been demonstrated to serve as significant prognostic indicators for PCa progression [15–18]. While these studies have individually explored the relationships between inflammatory or nutritional factors and PCa risk, there remains a gap in the development of a comprehensive indicator that integrates both inflammation and nutritional aspects to characterize PCa risk.

The advanced lung cancer inflammation index (ALI) is a recently developed composite measure designed to comprehensively evaluate both nutritional and inflammatory status. ALI is calculated using the formula (BMI * ALB / NLR), incorporating body mass index (BMI), serum albumin (ALB), and the neutrophil-to-lymphocyte ratio (NLR). Serum albumin and BMI are widely utilized in clinical assessments of nutritional status in PCa patients [19–21]. In the context of cancer, elevated NLR has been consistently associated with poorer survival outcomes and reduced responsiveness to therapy across various malignancies [22, 23]. Initially developed to predict prognosis in lung cancer, where lower ALI levels have been strongly correlated with increased mortality risk [24], its application has since been extended to other inflammatory conditions, including hypertension [25], diabetes [26], coronary heart disease [27], chronic kidney disease [28], and Crohn's disease [29]. Furthermore, recent studies have investigated the relationship between ALI and various cancers, such as gastric cancer [30], colorectal cancer [31], and liver cancer [32, 33]. However, the association between ALI and PCa, particularly its role as a combined nutritional and inflammatory index, remains to be fully elucidated.

Mounting evidence indicates that cancer-related inflammation and malnutrition are prevalent among the majority of patients with malignancies, significantly impacting their prognosis. Consequently, biomarkers based on inflammation and nutritional status are expected to emerge as valuable predictors of long-term outcomes. This study examined the relationship between the ALI and PCa in U.S. adults. Initially, we assessed the association between ALI levels and the risk of PCa development. Subsequently, we investigated the correlation between ALI and cancer prognosis. Our results revealed a non-linear relationship between ALI and PCa risk. Specifically, when ALI values were below 100, a negative correlation was observed between ALI and PCa risk. Thus, we hypothesized that higher ALI levels would be associated with a reduced risk of PCa. Notably, our analysis identified ALI as an independent factor influencing the overall survival and cancer-specific survival of participants. Longitudinal follow-up data indicated that lower ALI values were positively correlated with a poor survival from cancer, highlighting the potential utility of ALI as a prognostic indicator in cancer.

Method

Data population sources and study

This cross-sectional study analyzed data from multiple cycles of the National Health and Nutrition Examination Survey (NHANES) [34, 35], spanning the years 1999–2018 and 2021–2023, with an initial enrollment of 113,249 participants. Data from the 2019–2020 cycle were excluded due to incomplete data collection. A series of exclusion criteria were applied to refine the study population: 71,272 participants younger than 40 years, 21,724 females, and 4,801 participants with missing data on the ALI or PCa were excluded. Additionally, 142 participants were excluded due to incomplete data on marital status, race, alcohol consumption, education level, physical activity, smoking status, or comorbidities. A further 266 participants were excluded due to unavailable comorbidity data. After applying these exclusion criteria, the final

analytic sample comprised 15,042 male participants aged 40 years or older. Of these, 683 participants had PCa and 14,359 did not (Fig. 1).

Data collection

Definition of ALI and PCa

The Advanced Lung Cancer Inflammation Index (ALI) was calculated using the formula:

$$\text{ALI} = \text{BMI}\,(\text{kg/m}^2) \times \text{Serum Albumin Level}\,(\text{g/dL})/\text{NLR}$$

BMI was determined as body weight (kg) divided by height squared (m^2), based on data obtained from physical examinations. The NLR was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count, both measured from blood samples [36].

Participants were categorized into four quartiles based on their ALI levels [28]: Q1 (2.89–41.94), Q2 (41.94–59.08), Q3 (59.08–80.88), and Q4 (≥ 80.88).

The primary outcome of this study was the presence of PCa, which was determined based on self-reported physician-diagnosed cases. Participants were classified as having PCa if they reported a previous diagnosis made by a physician or other medical professional. Detailed information on all covariates is available at www.cdc.gov/nchs/nhanes/index.htm.

Definition of covariates

Covariates were selected based on prior literature and their potential to confound the association between ALI and prostate cancer. These included sociodemographic factors (age, race, education level, marital status) [37, 38], lifestyle behaviors (smoking, alcohol consumption, physical activity) [39, 40], and comorbidities, which may influence both inflammation and cancer risk [41].

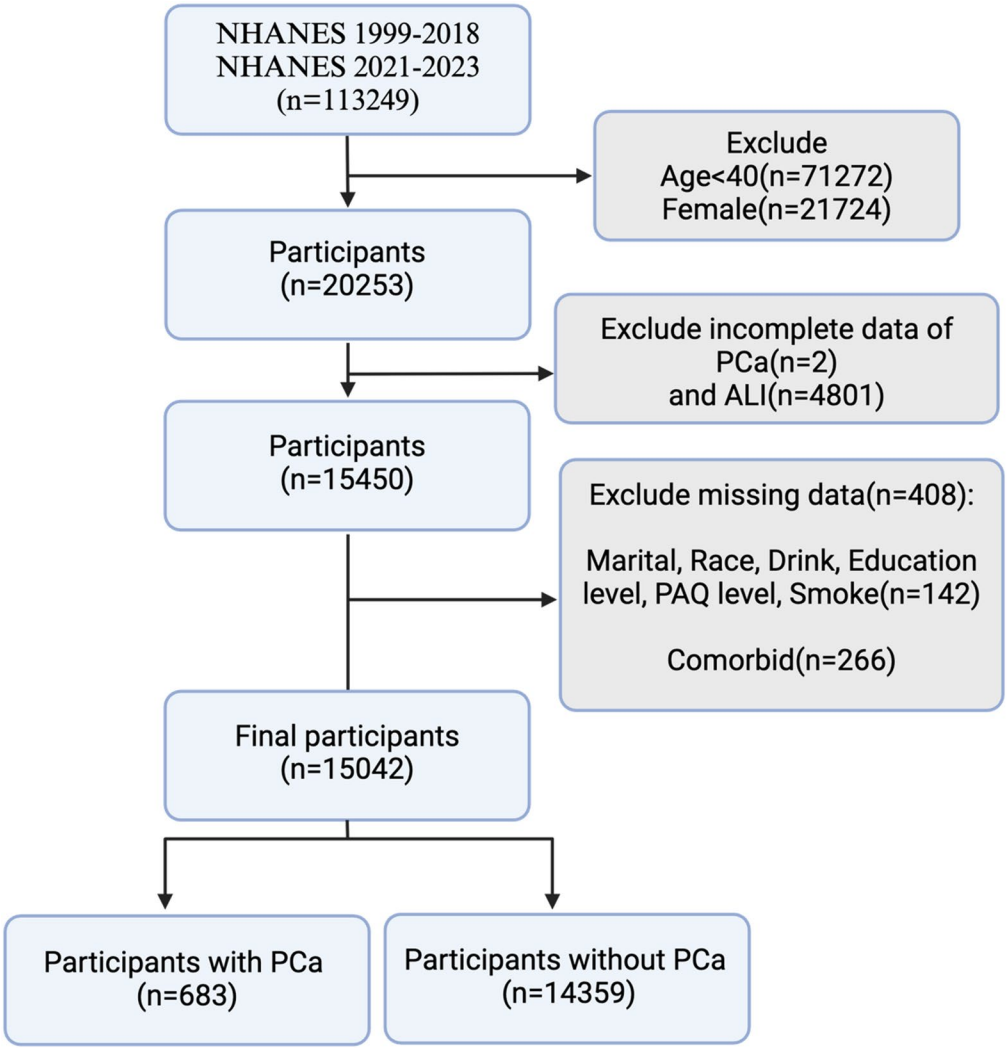

Fig. 1 Flowchart of the sample selection from NHANES 1999–2018 and 2021–2023

To account for potential confounders in the analysis of PCa, several covariates were included based on their established relevance in previous research. These covariates comprised: Age: (Included as a continuous variable), Race/Ethnicity(Categorized as Mexican American, Other Hispanic, Non-Hispanic White, Non-Hispanic Black, and Other Race), Education Level(Classified as less than high school, high school graduate, or above high school), Marital Status(Grouped into married/living with a partner and widowed/divorced/separated/never married), Smoking Status(Categorized as never smoked, former smoker, or current smoker), Alcohol Consumption(Classified as non-drinkers or drinkers), Physical Activity(Grouped into inactive, moderate, vigorous, or both moderate and vigorous activity levels), BMI(Considered both as a continuous variable and categorized into normal (< 25 kg/m²), overweight (25–30 kg/m²), and obese (≥ 30 kg/m²)), Comorbidities(Evaluated as binary variables (yes/no), including anemia, thyroid disease, diabetes, kidney failure, liver disease, rheumatoid arthritis, coronary heart disease, stroke, and hypertension). These covariates were adjusted in the statistical models to better isolate the relationship between ALI and PCa. Detailed descriptive statistics for these variables, stratified by ALI quartiles, are presented in Table 1.

Statistical analyses

In this study, continuous variables were summarized as means with standard deviations (SD) and compared across groups using independent sample t-tests or ANOVA. Categorical variables were presented as frequencies (n) and percentages (%) and analyzed using chi-square tests [42]. Specifically, For the 1999–2002 cycles, we used the 4-year MEC weights (WTMEC4YR) due to it special estimate method in the NHANES analytical guidelines. For all other 2-year cycles, we applied the corresponding 2-year MEC weights (WTMEC2YR). These weights will be used in regression later.

The association between ALI and PCa was investigated using multiple logistic regression models. In Model 1, no adjustments were made, whereas Model 2 was adjusted for potential confounders, including age, education level, marital status, race, drinking and smoking status, physical activity, and comorbid conditions. Odds ratios (OR) and their corresponding 95% confidence intervals (CI) were computed to evaluate the relationship between ALI (analyzed both as a continuous variable and across quartiles) and PCa. To assess potential nonlinear associations, restricted cubic spline (RCS) analysis was performed, and threshold effect analysis was conducted to identify inflection points in the relationship [43, 44]. All statistical analyses were performed using R Studio (version 4.2.3) and EmpowerStats software, with statistical significance defined as a p-value < 0.05.For the nonlinear analysis, a restricted cubic spline model with 3 degrees of freedom was employed, corresponding to 2 internal knots automatically placed by R at approximately the 33rd and 66th percentiles of the ALI distribution. This spline model was fitted using logistic regression to estimate the adjusted association between ALI (as a continuous variable) and the prevalence of prostate cancer. Predicted values were then transformed into probabilities for visualization purposes [45]. To account for multiple comparisons, the false discovery rate (FDR) correction method was applied. All statistical tests were two-tailed, and an FDR-adjusted p-value of less than 0.05 was considered statistically significant [46].

Result

Baseline characteristics of study participants

This study included a total of 15,042 male participants aged 40 years or older, categorized into quartiles based on their ALI levels: Q1 (2.89–41.94), Q2 (41.94–59.08), Q3 (59.08–80.88), and Q4 (≥ 80.88). The baseline characteristics of participants across these quartiles are summarized in Table 2. Participants in higher ALI quartiles (Q3 and Q4) tended to be younger, with mean ages of 58.1 years and 56.5 years, respectively, compared to 64.9 years in Q1. Educational attainment was also higher in these groups, with 71.5% and 70.9% of participants in Q3 and Q4, respectively, having education levels beyond high school, compared to 68.8% in Q1, although this was not statistically different. Racial composition differed significantly across quartiles. Non-Hispanic White participants

Table 1 Multivariate logistic regression analyses of ALI, ALI quartile and PCa

	Model 1				Model 2				
	OR	Lower 95%CI	Upper 95%CI	*P* value	OR	Lower 95%CI	Upper 95%CI	*P* value	
ALI	0.9682	0.9461	0.9908	0.0061	0.9933	0.9868	0.9999	0.0405	
ALI quartile									
Q1 (2.89–41.94)	**Reference**				**Reference**				**FDR**
Q2 (41.94–59.08)	0.6752	0.5541	0.8227	< 0.0001	0.8406	0.6632	1.0403	0.1078	0.1078
Q3 (59.08–80.88)	0.5002	0.4034	0.6204	< 0.0001	0.7419	0.5671	0.9705	0.0302	0.0453
Q4 (≥ 80.88)	0.4531	0.3630	0.5657	< 0.0001	0.6912	0.5441	0.8781	0.0026	0.0078

Model 1, no covariates were adjusted

Model 2, adjust Age, Education level, Marital, Race, Drink, Smoke, Physical activity, Presence of Comorbid Conditions

Table 2 Baseline characteristics of study participants

	[ALL]	Q1	Q2	Q3	Q4	*p*.overall
	N = 15,042	*N* = 3761	*N* = 3760	*N* = 3760	*N* = 3761	
Age	60.0 (12.5)	64.9 (12.6)	60.5 (12.4)	58.1 (11.9)	56.5 (11.3)	< 0.001
Education level:						0.059
< High school	2280 (15.2%)	591 (15.7%)	597 (15.9%)	559 (14.9%)	533 (14.2%)	
Completed high school	2176 (14.5%)	579 (15.4%)	528 (14.1%)	510 (13.6%)	559 (14.9%)	
> High school	10,572 (70.3%)	2586 (68.8%)	2632 (70.1%)	2687 (71.5%)	2667 (70.9%)	
Race:						< 0.001
Mexican American	2404 (16.0%)	501 (13.3%)	616 (16.4%)	688 (18.3%)	599 (15.9%)	
Other Hispanic	1121 (7.45%)	217 (5.77%)	295 (7.85%)	309 (8.22%)	300 (7.98%)	
Non-Hispanic White	7243 (48.2%)	2227 (59.2%)	1975 (52.5%)	1755 (46.7%)	1286 (34.2%)	
Non-Hispanic Black	3013 (20.0%)	502 (13.3%)	563 (15.0%)	666 (17.7%)	1282 (34.1%)	
Other Race	1261 (8.38%)	314 (8.35%)	311 (8.27%)	342 (9.10%)	294 (7.82%)	
Marital status:						< 0.001
Married/Living with partner	10,923 (72.6%)	2557 (68.0%)	2765 (73.5%)	2861 (76.1%)	2740 (72.9%)	
Widowed/Divorced/Separated/Never married	4119 (27.4%)	1204 (32.0%)	995 (26.5%)	899 (23.9%)	1021 (27.1%)	
Drink:						0.010
No	11,242 (86.3%)	2799 (86.1%)	2773 (85.1%)	2828 (86.2%)	2842 (87.9%)	
Yes	1778 (13.7%)	450 (13.9%)	485 (14.9%)	453 (13.8%)	390 (12.1%)	
Smoke:						< 0.001
Never	5970 (39.7%)	1278 (34.0%)	1455 (38.7%)	1622 (43.1%)	1615 (42.9%)	
Former	5833 (38.8%)	1555 (41.3%)	1472 (39.1%)	1396 (37.1%)	1410 (37.5%)	
Current	3239 (21.5%)	928 (24.7%)	833 (22.2%)	742 (19.7%)	736 (19.6%)	
Physical activity level:						< 0.001
Inactive	5493 (43.2%)	1413 (45.8%)	1365 (42.6%)	1355 (42.0%)	1360 (42.5%)	
Moderate	3549 (27.9%)	901 (29.2%)	908 (28.3%)	909 (28.2%)	831 (26.0%)	
Vigorous	1019 (8.01%)	224 (7.25%)	237 (7.40%)	266 (8.24%)	292 (9.12%)	
Both moderate and vigorous	2658 (20.9%)	550 (17.8%)	693 (21.6%)	697 (21.6%)	718 (22.4%)	
Presence of Comorbid Conditions:						< 0.001
No	3821 (25.4%)	799 (21.2%)	1028 (27.4%)	1018 (27.1%)	976 (26.0%)	
Yes	11,217 (74.6%)	2962 (78.8%)	2730 (72.6%)	2741 (72.9%)	2784 (74.0%)	
Prostate_Cancer:						< 0.001
No	14,359 (95.5%)	3506 (93.2%)	3584 (95.3%)	3628 (96.5%)	3641 (96.8%)	
Yes	683 (4.54%)	255 (6.78%)	176 (4.68%)	132 (3.51%)	120 (3.19%)	

were predominant in Q1 (59.2%) but less represented in Q4 (34.2%). In contrast, the proportion of Non-Hispanic Black participants increased markedly from Q1 (13.3%) to Q4 (34.1%). Marital status and physical activity levels also varied. Q3 had the highest percentage of participants married or living with a partner (76.1%), while vigorous physical activity was most common in Q4 (9.12%).

Presence of comorbid conditions were more prevalent in the lower quartiles, with 78.8% of Q1 participants reporting comorbid conditions compared to 74.0% in Q4. Similarly, PCa prevalence was highest in Q1 (6.78%) and lowest in Q4 (3.19%).

Overall, participants in the lower ALI quartiles were older, less physically active, and had higher comorbidity burdens, whereas those in the higher quartiles were younger, more active, and healthier overall. All differences in baseline characteristics across ALI quartiles were statistically significant ($p < 0.05$).

Association between ALI and PCa

The results of the multivariate logistic regression analyses examining the association between ALI and PCa are presented in Table 1. In the unadjusted model (Model 1), a 10-unit increase in ALI was associated with a 3% reduction in the likelihood of developing PCa (OR = 0.9682, 95% CI: 0.9461–0.9908, $p = 0.0061$). After adjusting for potential confounders in Model 2, including age, education level, marital status, race, drinking and smoking status, physical activity, and comorbidities, the association slightly weakened, with each unit increase in ALI associated with a 0.7% reduction in PCa likelihood (OR = 0.9933, 95% CI: 0.9868–0.9999, $p = 0.0405$).

To explore potential subgroup-specific effects, we conducted subgroup analyses. When ALI was categorized into quartiles, a clear dose-response trend was observed. Compared to participants in the lowest quartile (Q1: 2.89–41.94), those in higher quartiles (Q2: 41.94–59.08, Q3: 59.08–80.88, and Q4: ≥80.88) exhibited

progressively lower odds of developing PCa in both unadjusted and adjusted models. In the fully adjusted model, participants in Q4 demonstrated a 31% reduction in the likelihood of developing PCa (OR = 0.6912, 95% CI: 0.5541–0.8781, $p = 0.0026$) compared to Q1. Similarly, participants in Q3 had a 26% reduction (OR = 0.7419, 95% CI: 0.5671–0.9705, $p = 0.0302$), while the reduction in Q2 (OR = 0.8406, 95% CI: 0.6632–1.0403) showed no statistical significance ($p = 0.1078$). This suggests that the initially observed association in Q2 may have been confounded by other factors—like age, comorbidity, which likely varies across ALI quartiles and determinant of prostate cancer risk. In contrast, the continued significance of Q3 and Q4 even after adjustment indicates that the protective association of higher ALI values with prostate cancer is more robust in those higher quartiles.

Restricted cubic splines analysis

The relationship between ALI and PCa was examined using smoothed curve fitting. Data points with ALI values greater than 200 were excluded from the analysis as they were classified as outliers. The results revealed a "U-shaped" association after adjusting for age, education level, marital status, race, drinking and smoking status, physical activity, and comorbidities. The p-value for non-linearity was 0.0271, indicating statistical significance. When ALI values were less than 100, the prevalence decreased as ALI increased. However, for ALI values greater than 100, the prevalence showed an upward trend as ALI increased, although this trend was no longer statistically significant ($p > 0.05$) (Fig. 2).

Threshold effect of ALI on PCa

The relationship between ALI and PCa was further assessed using threshold effect analysis (Table 3). Participants were stratified into two subgroups based on an

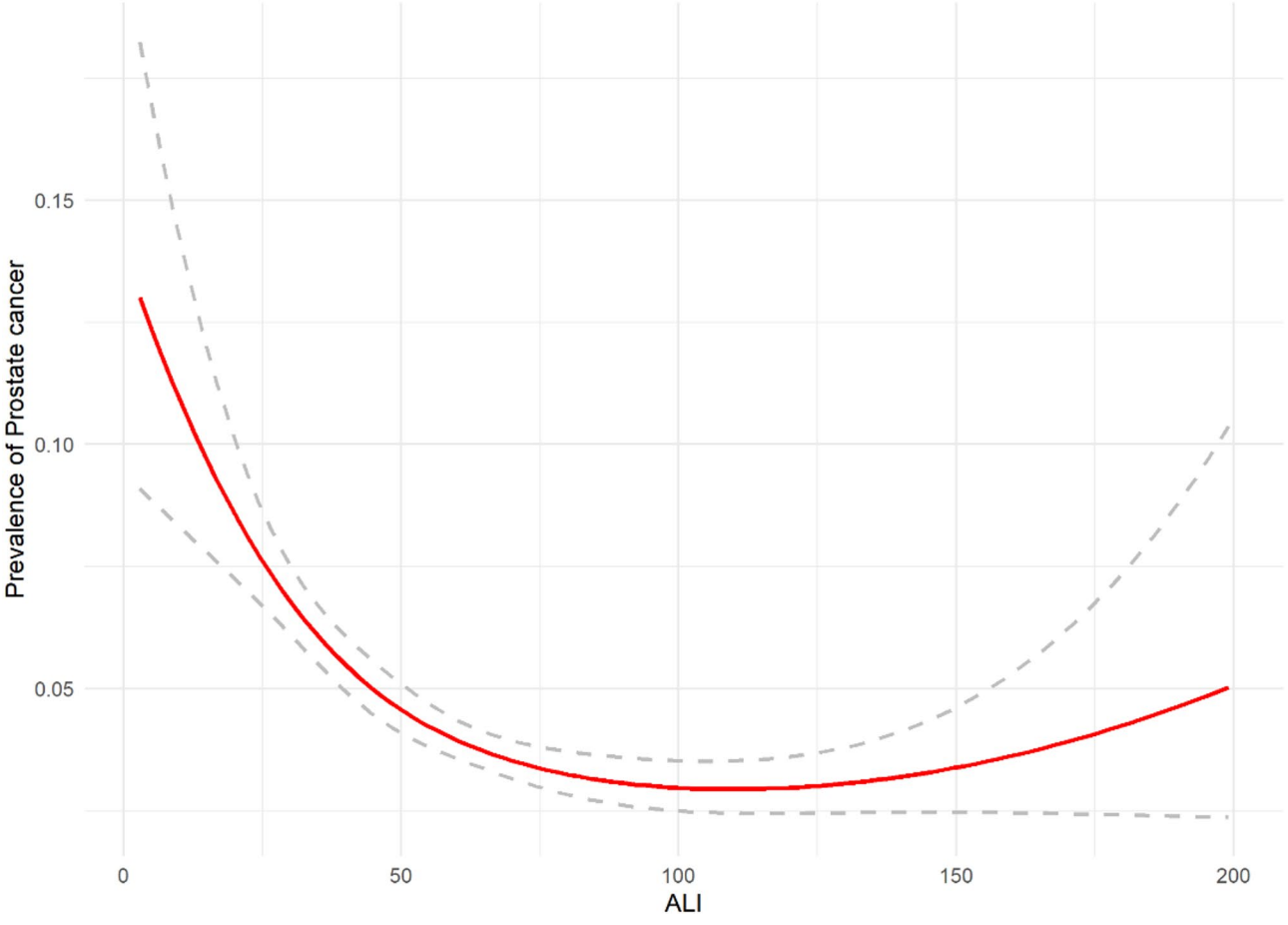

Fig. 2 Association between ALI and PCa. The red solid line represents the smoothed curve fit between ALI and PCa. The grey dashed lines represent the 95% confidence interval of the fit. These confidence intervals represent the range of values within which we can be 95% confident the true prevalence lies at each ALI value. Narrower confidence intervals suggest greater precision and less uncertainty around the prevalence estimates, while wider intervals indicate greater uncertainty. Specifically, the intervals are wider at the extreme ends of ALI values (particularly at lower and higher ALI), reflecting greater uncertainty due to fewer data points in these ranges. Conversely, intervals are narrower near the middle values of ALI, around the point of ALI = 100, indicating higher confidence in these prevalence estimates

Table 3 Threshold effects of ALI on PCa

	ALI subgroup	OR	Lower 95%CI	Upper 95%CI	*P* value
Model 1	< 100	0.8494	0.8157	0.8844	< 0.0001
	≥ 100	1.0009	0.9979	1.0040	0.5471
Model2	< 100	0.9041	0.8479	0.9640	0.0021
	≥ 100	0.9979	0.9643	1.0326	0.9042

Model 1, no covariates were adjusted

Model 2, adjust Age, Education level, Marital, Race, Drink, Smoke, Physical activity, Presence of Comorbid Conditions

ALI threshold of 100. In Model 1 (unadjusted), participants with ALI < 100 exhibited a significantly lower risk of PCa (OR = 0.8494, 95% CI: 0.8157–0.8844, $p < 0.0001$) compared to those with ALI ≥ 100, where no significant association was observed (OR = 1.0009, 95% CI: 0.9979–1.0040, $p = 0.5471$). In Model 2, after adjusting for covariates including age, education level, marital status, race, drinking and smoking status, physical activity, and comorbid conditions, the protective effect of ALI < 100 remained statistically significant (OR = 0.9041, 95% CI: 0.8479–0.9640, $p = 0.0021$). However, the association for ALI ≥ 100 remained non-significant (OR = 0.9979, 95% CI: 0.9643–1.0326, $p = 0.9042$).

Survival analysis

In this study, we reviewed the NHANES-linked mortality follow-up data and found that cause-specific mortality for prostate cancer was not available. The dataset includes only all-cause mortality and all-cancer-related mortality. Therefore, we were unable to directly assess prostate cancer–specific mortality. In order to explore the value of ALI in the prognosis of clinical cancer patients, we examined the association between ALI and both cancer-related and all-cause mortality (Follow-up data were obtained from: https://www.cdc.gov/nchs/data-linkage/mortality-public.htm).

We then divided the ALI values into four intervals according to quartiles and analyzed the relationship between ALI and overall survival based on the follow-up data of the respondents. We found that ALI values in the Q1 interval were associated with a worse prognosis compared with values in the Q2-Q4 intervals (Fig. 3).

The association between ALI and PCa across different BMI subgroups

BMI is an important component of ALI. Next, we explored the relationship between ALI and Pca in people with different BMI. For individuals with a BMI of 20–25, ALI demonstrated a statistically significant protective effect against PCa, with an OR of 0.9812 (95% CI: 0.9711–0.9932, $p = 0.0017$). This suggests that higher ALI values are associated with reduced odds of PCa within this BMI category. In contrast, for the BMI > 25 subgroup, the OR was 0.9753 (95% CI: 0.9466–1.0049, $p = 0.1010$), and for the BMI < 20 subgroup, the OR was 0.9905 (95% CI: 0.9763–1.0049, $p = 0.1962$). Neither of these associations reached statistical significance (Table 4).

Due to ALI formula include BMI, we re-analysis model after remove the BMI. And we calculated generalized variance inflation factors (GVIFs). Each row value

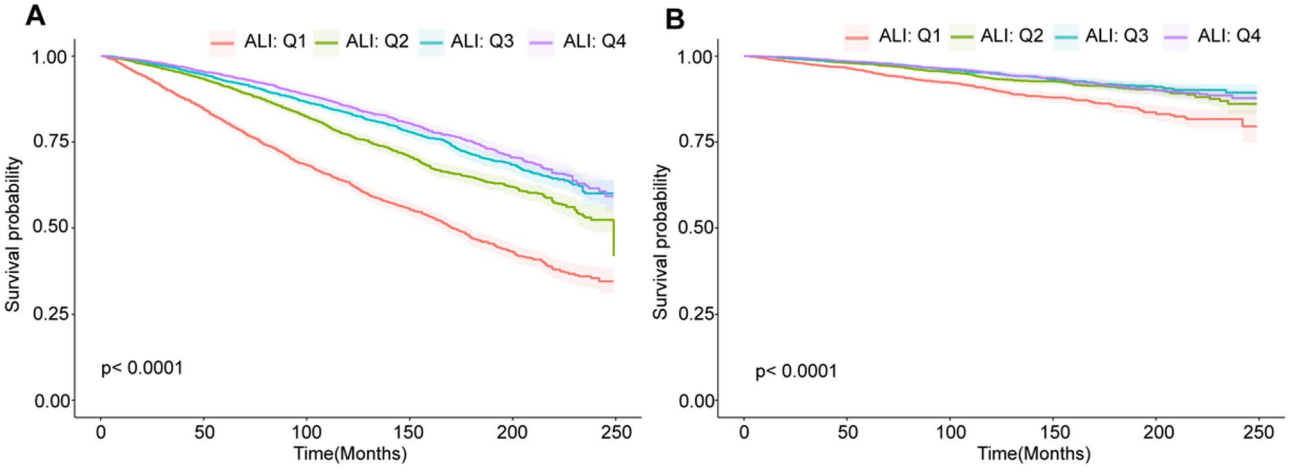

Fig. 3 Kaplan-Meier analysis of ALI quartiles survival in participants and cancer patients. (**A**) Kaplan-Meier curves in all participants with ALI quartiles. (**B**) Kaplan-Meier curves in cancer patients with ALI quartiles. For cancer patients, Q4 has a higher survival rate

Table 4 The association of ALI and PCa in BMI subgroup analysis

	Subgroup	OR	Lower 95%CI	Upper 95%CI	p_value	FDR
ALI	> 25	0.9905	0.9763	1.0049	0.1962	0.2944
	20–25	0.9812	0.9711	0.9932	0.0017	0.0051
	< 20	0.9753	0.9466	1.0049	0.1010	0.1010

of vairable mean this variable to other variables. All adjusted GVIF values [GVIF^(1/(2*Df))] were below 2, indicating no concerning multicollinearity in the model. This suggests the regression estimates are stable and not significantly distorted by correlations among predictors (Supplementary Table 1).

Sample size calculation

Although this study utilized secondary data from NHANES and did not perform a priori sample size estimation, we conducted a post-hoc power analysis to evaluate whether our sample was sufficient to detect the observed effect. In our primary binary logistic regression model (Model 2), comparing ALI ≥ 100 vs. < 100, the prostate cancer prevalence was 6.78% in the ALI < 100 group (n = 13,081) and 3.19% in the ALI ≥ 100 group (n = 1,961), totaling 15,042 participants. The exposure group accounted for 13.0% of the sample. Using the powerLogisticBin() function in R (powerMediation package) with the observed parameters (p1 = 0.0678, p2 = 0.0319, B = 0.1304, n = 15,042, α = 0.05), the estimated statistical power was 82.8%.

Discussion

Our goal was to explore the relationship between the ALI and PCa in U.S. adults. Initially, we assessed the association between ALI levels and the risk of PCa development. Our results revealed a non-linear relationship between ALI and PCa risk. Specifically, when ALI values were below 100, a negative correlation was observed between ALI and PCa risk. Thus, we hypothesized that higher ALI levels would be associated with a reduced risk of PCa. Subsequently, we investigated the correlation between ALI and cancer prognosis. Longitudinal follow-up data indicated that lower ALI values were positively correlated with an increased likelihood of mortality from cancer, highlighting the potential utility of ALI as a prognostic indicator in cancer. This study is the first to investigate the link between ALI and PCa.

The current study initially examined the relationship between the ALI and the risk of PCa. Our findings demonstrate that elevated ALI levels are associated with a reduced risk of PCa, as confirmed by both unadjusted and adjusted models. After adjusting for variables including age, education level, marital status, race, alcohol consumption, smoking status, physical activity, and comorbidities, our analysis revealed a U-shaped association. Specifically, for ALI values below 100, the reference point was set at an ALI of 0, illustrating a clear protective effect as ALI increases toward 100. However, for ALI values above 100, the reference shifted to ALI = 100, with no statistically significant additional protective benefit observed for higher ALI values beyond this point. To further validate these results, we performed subgroup analyses comparing ALI values below and above 100. Furthermore, ALI values at or above 100 demonstrated greater overall protective effects compared to those below 100 (Fig. 2). The cutoff value of ALI = 100 was determined based on visual inspection of the restricted cubic spline plot, as this value corresponded to the lowest prevalence of PCa. Moreover, as illustrated in the spline plot, the prevalence of PCa did not continue to decrease beyond an ALI value of approximately 100, providing a rationale for selecting this cutoff point for subgroup analyses.

The mechanisms behind this U-shaped pattern are unclear but may relate to ALI components, including BMI, albumin, and NLR. First, BMI, a simple and widely used nutritional measure, can indicate malnutrition or protein-energy wasting [47]. Although obesity increases PCa risk, the "obesity paradox" suggests that higher BMI may improve survival outcomes [48–50]. Thus, maintaining an optimal BMI might reflect better nutritional health, enhancing immune function and reducing inflammation. Second, serum albumin, synthesized by hepatocytes and secreted into the bloodstream, is a key indicator of a patient's nutritional status and disease severity [28]. Low albumin correlates with higher PCa risk [51, 52]. Additionally, albumin molecules can inhibit pro-inflammatory cytokines like TNF-α, IL-1, and IL-6, reducing tissue damage [53, 54]. Finally, NLR, a ratio of neutrophils to lymphocytes, reflects systemic inflammation and immune responses [13, 55]. High NLR predicts poorer outcomes, including shorter survival and treatment resistance in advanced PCa [22, 23, 56]. Specifically, a high NLR predicts shorter overall survival in patients with metastatic castration-resistant PCa [22, 56–58]. Moreover, NLR correlates with tumor myeloid infiltration, indicating a worse tumor microenvironment [59, 60]. Therefore, within a moderate range, ALI effectively captures the interplay of nutrition and inflammation in PCa patients.

We then examined the relationship between the ALI and the prognosis of cancer. Previous studies have revealed that ALI was a prognostic predictor of overall survival in cancers such as colon, gastric, and liver cancer [30, 61–64]. Our current analysis reveals that lower ALI values were positively associated with higher mortality rates from cancer. Meanwhile, the correlation between ALI levels and mortality rates suggests that ALI not only serves as a reliable indicator of cancer prognosis but also as an important reference for all-cause mortality. ALI predicts the prognosis of cancer patients by reflecting both the body's nutritional status and its response to inflammatory conditions. It has been reported that inflammation plays a critical role in the occurrence and development of PCa [65]. This finding suggests that, in addition to the albumin-to-globulin ratio [66], NLR [14],

and SII [67], which are recognized as independent prognostic factors for PCa, ALI may also serve as a valuable prognostic tool for PCa patients, which requires more accurate PCa patient survival data to verify in the future.

Numerous investigations have examined the relationship between various factors and the risk of developing PCa. However, no prior studies have comprehensively integrated both systemic inflammatory status and nutritional metabolic status in cancer patients [68]. For instance, one study delved into the relationship between the SII and prostate-specific antigen levels among American men aged 40 and older without a PCa diagnosis, identifying a non-linear correlation [69]. Furthermore, systemic immune and inflammatory conditions, as quantified by SII, were found to be independently and positively associated with the risk of PCa in middle-aged and elderly men in the U.S [11]. Another study revealed that elevated SII levels in patients with metastatic castration-resistant prostate cancer were linked to poor overall survival, while in non-metastatic PCa patients, high SII levels were associated with unfavorable outcomes in terms of biochemical recurrence-free survival and certain adverse pathological features [70]. The ALI is considered a more robust indicator of systemic inflammation compared to other biomarkers, as it integrates both nutritional and inflammatory markers. Several studies have demonstrated the superiority of ALI over other parameters. For example, one study revealed that ALI provided better predictive accuracy for 5-year overall survival (OS) and 5-year disease-free survival (DFS) in colon cancer patients compared to the PNI and SII [71]. Additionally, other research indicated that ALI surpassed albumin, NLR, and BMI in predicting complications, 5-year progression-free survival, and 5-year OS in patients with colon and oral cavity cancers [63, 72]. Notably, one study demonstrated that ALI outperformed NLR, platelet-to-lymphocyte ratio (PLR), monocyte-to-lymphocyte ratio (MLR), SII, and PNI in predicting OS and DFS in cholangiocarcinoma patients through time-dependent receiver operating characteristic analysis [73]. These findings collectively suggest that ALI may offer a higher discriminatory value compared to other biomarkers.

In the early stages of PCa, the disease typically progresses slowly and remains localized within the prostate gland, often without presenting noticeable physical signs or symptoms. However, in more advanced stages, symptoms such as urinary dysfunction, hematuria, and bone pain can significantly impair a patient's health and quality of life. Systemic inflammatory response, acknowledged as the seventh hallmark of cancer, is closely linked to the initiation and progression of malignancies [74, 75]. Research has demonstrated that malnutrition can weaken anti-tumor immune responses and impair wound healing, thereby diminishing treatment efficacy and increasing the likelihood of severe postoperative complications [76]. Additionally, lymphopenia has been identified as a factor associated with unfavorable outcomes in cancer patients [77]. A growing body of evidence emphasizes the role of inflammation, driven by diverse factors, in the progression of PCa [69, 78–82]. For instance, inflammatory markers such as C-reactive protein (CRP) and interleukin-6 have been observed to increase in tandem with PCa progression [83, 84]. Furthermore, recent studies have identified significant correlations between systemic inflammatory markers, such as the SII and Systemic Immune Inflammation Response Index (SIRI), and the development of PCa [11, 14, 78].

Baseline measurements of BMI and serum albumin, which serve as objective indicators of nutritional status, have been associated with both short-term and long-term outcomes in cancer patients [85]. These metrics are commonly utilized in clinical practice to assess patient triage and management. In advanced cancer cases, malnutrition and cachexia are often characterized by reduced serum albumin levels and lower BMI values. Moreover, patients with PCa frequently experience a combination of inflammation and metabolic disturbances, highlighting the importance of assessing both nutritional and inflammatory states comprehensively. The ALI, calculated by multiplying BMI with albumin and dividing by the NLR, provides a holistic evaluation of systemic health by integrating nutritional and inflammatory components. This index may enhance our understanding of a patient's functional status and serve as a valuable predictor of therapeutic outcomes in PCa patients.

In addition, although the p-value for education level ($p = 0.059$) marginally exceeded the commonly accepted threshold for statistical significance, we elected to include this variable in our final model. This was based on the recognition that education level functions as a key indicator of socioeconomic status, potentially influencing both ALI and PCa risk through various pathways. These pathways include, but are not limited to, healthcare access, health literacy, and behavioral factors. Given its role as a confounding variable, retaining education level in the model helps mitigate the risk of residual confounding, thereby strengthening the validity of our analysis.

Clinically, our findings have notable implications. Specifically, lower ALI values, which are indicative of malnutrition and chronic inflammation, were found to correlate with a higher risk of PCa [86]. These findings suggest that clinicians could utilize ALI as a tool to identify individuals at elevated risk of PCa and implement early interventions. Such interventions might include optimizing nutritional status, managing inflammation, and developing personalized treatment plans. As a composite index, ALI offers a more comprehensive assessment of

nutritional and inflammatory status compared to single biomarkers, making it a valuable addition to existing risk assessment tools. Our results also provide insights into the "obesity paradox," implying that maintaining a balanced BMI could be beneficial for PCa patients. Furthermore, targeted nutritional interventions, particularly for patients with lower BMI, may enhance survival outcomes and improve quality of life. To explore this further, the study population was stratified into three BMI categories: under 20, 20–25, and greater than 25. Within each BMI category, logistic regression models were constructed, with ALI (treated as a continuous variable) as the exposure and PCa as the outcome. Consistent covariate adjustments were applied across all subgroups to ensure comparability. This stratified analysis aimed to investigate potential effect modification—specifically, whether BMI influences the relationship between ALI and PCa risk. Given the well-established biological connections between nutritional status, systemic inflammation, and adiposity, stratifying by BMI was deemed clinically relevant. Moreover, as a readily accessible indicator in clinical practice, pre-treatment assessment of ALI can enhance physicians' ability to predict clinical outcomes more effectively and facilitate timely adjustments to treatment regimens, ultimately contributing to reduced mortality.

Conclusion

Our study demonstrated a non-linear association between ALI and the risk of developing PCa. Specifically, a negative correlation was observed between ALI values and PCa risk when ALI was below 100. Furthermore, lower ALI values were significantly associated with poorer cancer survival outcomes, which underscores the potential utility of ALI as a prognostic indicator in cancer. However, it is important to note that causality cannot be established due to the cross-sectional design of the study. Therefore, high-quality, large-scale prospective studies are warranted to further confirm and validate the clinical significance of ALI in PCa.

Abbreviations

PCa	Prostate cancer
ALI	Advanced lung cancer inflammation index
NHANES	The National Health and Nutrition Examination Survey
NLR	Neutrophil-to-lymphocyte ratio
SII	Systemic immune-inflammation index
SIRI	Systemic inflammatory response index
GNRI	Geriatric nutritional risk index
PNI	Prognostic nutritional index
BMI	Body mass index
OR	Odds ratios
CI	Confidence intervals
RCS	Restricted cubic spline
OS	Overall survival
DFS	Disease-free survival
MLR	Monocyte-to-lymphocyte ratio
PLR	Platelet-to-lymphocyte ratio

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s41043-025-00933-z.

Supplementary Material 1

Acknowledgements

Follow-up data were obtained from: https://www.cdc.gov/nchs/data-linkage/mortality-public.htm.

Author contributions

MJH and JP: Conceptualization, Methodology, Software, Writing – original draft. MJH, QLT and DN: Formal analysis, Writing – review & editing. MJH and QLT: Substantively revision. TYT: Writing – review & editing. FC and YTW: Supervision, Writing – review & editing. JP and HQL: Funding acquisition, Investigation, Supervision, Writing – review & editing.

Funding

The present study was funded by the National Natural Science Foundation of China (82272689), the Sanming Project of Medicine in Shenzhen(SZSM202011011).

Data availability

No datasets were generated or analysed during the current study.

Declarations

Human ethics and consent to participate declarations

The studies involving humans were approved by NHANES data collection procedures and the NCHS Research Ethics Review Board (ERB). The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study. The specific NCHS ERB protocol numbers for the NHANES cycles included in our study are as follows:

Survey Name	NCHS ERB Protocol Number / Description
NHANES 2021–2022	Protocol #2021-05
NHANES 2019–2020	Continuation of Protocol #2018-01
NHANES 2017–2018	Protocol #2018-01 (Effective from October 26, 2017)
	Continuation of Protocol #2011-17 (Effective until October 26, 2017)
NHANES 2015–2016	Continuation of Protocol #2011-17
NHANES 2013–2014	Continuation of Protocol #2011-17
NHANES 2011–2012	Protocol #2011-17
NHANES 2009–2010	Continuation of Protocol #2005-06
NHANES 2007–2008	Continuation of Protocol #2005-06
NHANES 2005–2006	Protocol #2005-06
NHANES 1999–2004	Protocol #98 – 12

The information also can be found in https://www.cdc.gov/nchs/nhanes/about/erb.html#print.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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Received: 27 February 2025 / Accepted: 19 May 2025
Published online: 29 May 2025

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