Submitted: 13 May, 2025 Accepted: 16 September, 2025 Published: 30 January, 2026 DOI:10.22514/jomh.2026.007

ORIGINAL RESEARCH

JOMH Journal of Men's Health

Stability of the CMI-ALS axis in prostate cancer patients: a new target for prognostic assessment and treatment optimization

Guan-an Zhao[1], Peng Li[1,*]

[1]Department of Urology, Lishui Hospital of Wenzhou Medical University, The First Affiliated Hospital of Lishui University, Lishui People's Hospital, 323000 Lishui, Zhejiang, China

***Correspondence**
lp18957091072@163.com
(Peng Li)

Abstract

Background: The Cardiometabolic index (CMI) is used to assess individual cardiovascular metabolic health status and risk of metabolic disorders. Allostatic load score (ALS) quantifies the body's physiological response to stress. This study aimed to investigate the relationship between the CMI and ALS in patients with prostate cancer using data from the National Health and Nutrition Examination Survey (NHANES). **Methods**: A total of 139 patients with prostate cancer were included in the analysis. Receiver operating characteristic (ROC) curve and decision curve analysis (DCA) were employed to assess the predictive accuracy and clinical net benefit. Multivariate linear regression was conducted to evaluate the relationship between CMI and ALS. Additionally, various analytical techniques, including quantile regression and logistic regression, were utilized to verify the stability and independence of their relationship. Collinearity, partial correlation, stepwise linear regression, multivariate regression, and mediation effect analyses were performed to examine whether the shared factor high-density lipoprotein cholesterol (HDL-C) influenced the CMI-ALS relationship. **Results**: The area under the curve (AUC) for CMI in predicting ALS was 0.650, indicating CMI can distinguish positive and negative samples more accurately than a random guess (AUC: 0.500), and has predictive ability. DCA indicated a clinical net benefit within the threshold probability range of 0.25 to 0.61. A positive relationship between CMI and ALS was observed (β [95% Confidence interval (CI)]: 0.598 [0.319, 0.877]). The relationship was found to be both stable and independent (all $p < 0.05$), unaffected by confounding factors. Furthermore, this relationship was not attributable to shared variables, confirming that CMI independently contributed to ALS (all $p < 0.05$). **Conclusions**: The study demonstrated a positive relationship between CMI and ALS in patients with prostate cancer. The find highlights the importance of monitoring CMI in those patients for early clinical intervention to mitigate allostatic load.

Keywords

Prostate cancer; Cardiometabolic index; Allostatic load; Inflammation

1. Introduction

Prostate cancer is one of the most prevalent malignancies in men, ranking second only to lung cancer. In 2022, over 1.46 million cases and 396,000 deaths were reported globally [1]. Projections indicate an increase in incidence, with diagnoses expected to reach 2.4 million and attributable deaths to climb to 712,000 by 2040, driven primarily by demographic changes [2]. Cancer individuals often experience metabolic dysregulation [3], and therapies such as chemotherapy, radiotherapy, and hormone treatment further exacerbate these disturbances, significantly compromising their quality of life [4]. For instance, androgen deprivation therapy (ADT), a key treatment for advanced prostate cancer, while effective in inhibiting tumor growth, triggers severe metabolic alterations. Research demonstrates that after 12 months of ADT, patients exhibit an average 10% increase in visceral fat and a 13% reduction in insulin sensitivity within just 12 weeks [5]. These metabolic shifts contribute to a markedly higher incidence of cardiovascular diseases (CVDs) compared to non-ADT patients [6]. In addition, compared to other tumors, the occurrence and development of prostate cancer are more closely related to metabolic disorders, mainly because it involves an abnormal androgen receptor. Abnormal androgen receptors will lead to abnormal androgen levels in the body, which in turn affect normal metabolism [7]. Most studies have shown that most metabolic-related diseases are associated with the development of prostate cancer, such as metabolic syndrome and prostate cancer survival [8], diabetes [9], and abnormal lipid metabolism [10].

The cardiometabolic index (CMI) is a composite measure of metabolism derived from blood lipid parameters, specifically triglycerides (TG) and high-density lipoprotein cholesterol (HDL-C), as well as the waist-to-height ratio. It is highly sensitive to visceral fat accumulation and insulin resistance [11]. Initially developed as a predictor for diabetes risk [12], CMI has gained broader clinical relevance. A growing body of research has established its positive correlation with CVD risk and metabolic syndrome [13], making it a valuable tool for quantifying metabolic disturbances in cancer individuals. However, current studies predominantly focus on the cross-sectional relationship between CMI and traditional cardiovascular events, with limited exploration into the mechanisms driving systemic physiological disruptions. These potential mechanisms may include endothelial dysfunction and blood-brain barrier damage, systemic inflammatory response, metabolic disorders, insulin resistance, and others.

Chronic metabolic disturbances may contribute to the accumulation of allostatic load through multiple pathways [13]. The allostatic load score (ALS) serves as a comprehensive indicator of dysregulation across various physiological systems. It reflects the cumulative strain on the body due to fluctuating responses from the neuroendocrine, cardiovascular, immune, and other systems under prolonged stress. ALS is also utilized to assess chronic stress: the higher the score, the greater the chronic stress burden. The ALS is calculated by integrating biomarkers such as cortisol, C-reactive protein (CRP), and systolic blood pressure (SBP) [14]. Additionally, this index is linked to cancer development and prognosis, reflecting tumor progression [15, 16], and can be employed to quantify tumor severity.

Although the interplay between CMI and advanced ALS has been implicated in systemic metabolic dysregulation across various cancers, a crucial knowledge gap remains, particularly among prostate cancer patients. This is especially important given the high prevalence of metabolic comorbidities in this population and their documented association with cancer progression [17, 18]. To our knowledge, no previous study has quantitatively investigated the CMI-ALS relationship in prostate cancer, despite its potential to clarify mechanistic links between metabolic disorders and physiological imbalances that directly affect clinical outcomes. In this study, we address this unmet need by utilizing the National Health and Nutrition Examination Survey (NHANES) database to calculate CMI and ALS indices in prostate cancer patients. Our analysis not only establishes their association but also provides the first evidence-based framework for targeting metabolic interventions to enhance the quality of life in this understudied cohort.

2. Materials and methods

2.1 Data accession and study population

This study utilized data from the NHANES 2007–2020 dataset, managed by the National Center for Health Statistics (NCHS) at the Centers for Disease Control and Prevention (CDC). The NHANES survey collects data through interviews and physical examinations conducted by trained professionals. A complex, multi-stage, stratified, and clustered probability sampling design is employed to generate a representative sample of the U.S. population. The survey has received approval from the CDC's ethics board, with all participants providing voluntary informed consent. This study includes the most recent data from NHANES; however, due to the small target population, the scope was expanded to encompass data from 2007 to 2020. During this period, 3902 patients with tumors were identified, of which 156 were excluded due to unspecified tumor types. An additional 3178 patients were excluded for not having a prostate cancer diagnosis. After screening, 568 patients with prostate cancer remained. Further exclusions were made for 233 patients without ALS data and 196 without CMI data. Ultimately, 139 patients with prostate cancer were included in the analysis. Additionally, to test whether the sample size is sufficient for analysis, we used G*Power software (version 3.1.9.7, Heinrich Heine University Dusseldorf, Dusseldorf, NRW, Germany) to estimate the sample size. The results showed that the minimum required sample size was 114 for an effect size of $d = 0.7$, α error probability = 0.05, power ($1 - \beta$ error probability) = 0.95, and an allocation ratio of N2/N1 = 1. Therefore, 139 samples are sufficient for data analysis. Fig. 1 shows the patient selection process. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) for this study is included in the **Supplementary material**.

2.2 CMI and ALS calculation

The calculation formula of CMI includes waist circumference (WC), triglyceride (TG), height (cm), and high-density lipoprotein cholesterol (HDL-C, mg/dL). The calculation formula for CMI is as follows: CMI = (TG/HDL-C) × (WC/height).

In this study, ALS is defined by the following eight indicators: systolic and diastolic blood pressure, serum total cholesterol, HDL-C, glycated hemoglobin (HbA1c), albumin (Alb), body mass index (BMI), and CRP levels. For the selection of variables used to calculate ALS, each researcher is required to follow previously published ALS equations. The number of parameters falling into the highest risk quartile (with the lower quartile being in HDL-C and albumin, and the others being in the upper quartile) is summed to calculate each subject's allostatic load. The ALS ranges from 0 to 8, with higher scores indicating increased health risks [19–21]. Notably, due to the absence of CRP data in the 2015–2016 dataset, the highest quartile of high-sensitivity CRP was assigned a value of 1 to calculate the score of CRP components in ALS.

2.3 Covariates

Based on previous studies and hypotheses, this study included the following covariates: age (years), poverty income ratio (PIR), cotinine (ng/mL), waist circumference (WC, cm), albumin (g/dL), total calcium (mmol/L), phosphate (mmol/L), sodium (mmol/L), potassium (mmol/L), creatinine (mg/dL), uric acid (mg/dL), white blood cells (WBC, 1000 cells/μL), lymphocytes (1000 cells/μL), monocytes (1000 cells/μL), segmented neutrophils (1000 cells/μL), eosinophils (1000 cells/μL), basophils (1000 cells/μL), red blood cells (RBC, million cells/μL), hemoglobin (g/dL), mean cell hemoglobin

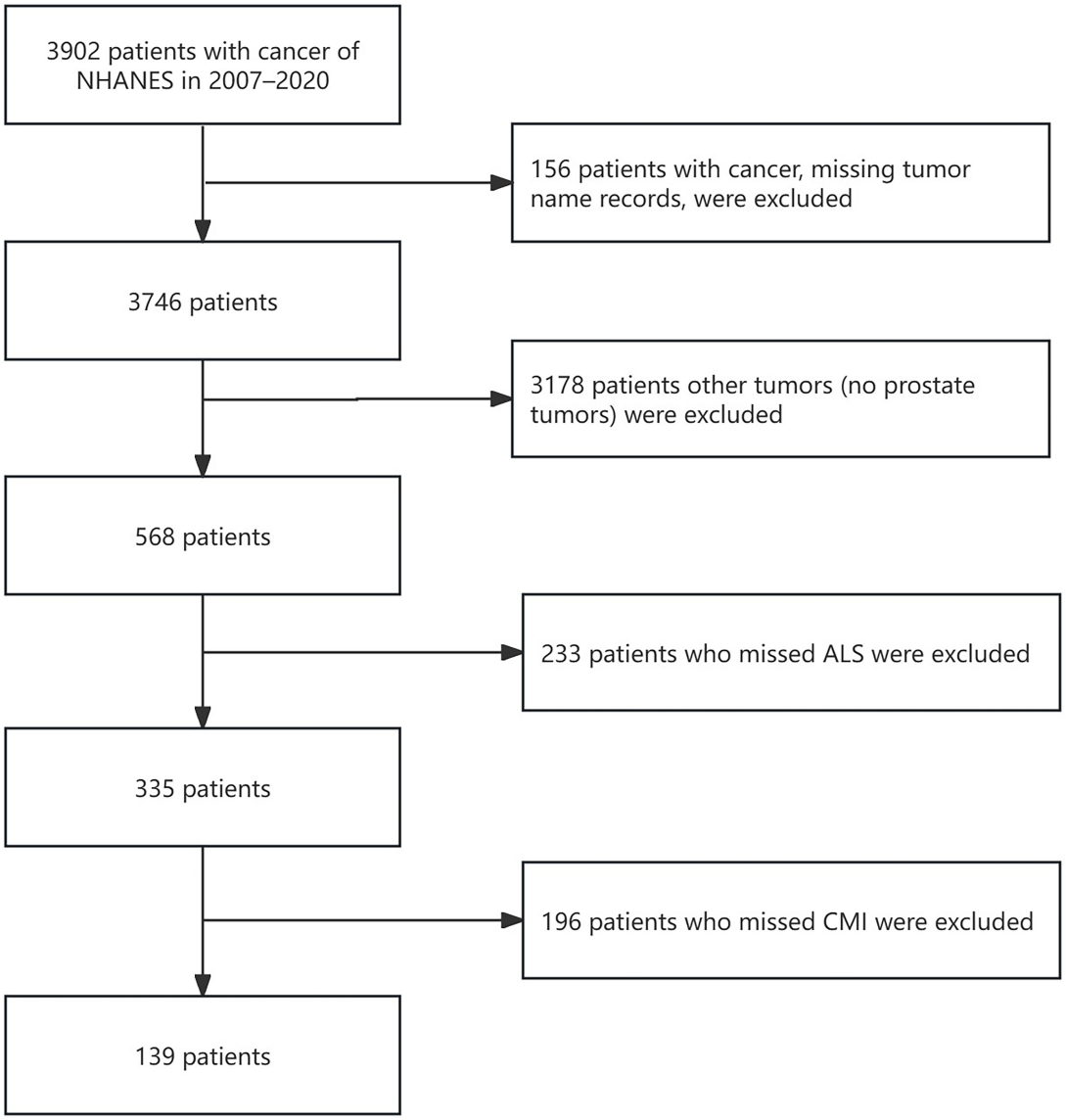

FIGURE 1. Flow chart of patients with prostate cancer. ALS: allostatic load score; CMI: cardiometabolic index; NHANES: the National Health and Nutrition Examination Survey.

concentration (MCHC, g/dL), red cell distribution width (RDW, %), platelets (1000 cells/μL), a body shape index (ABSI), race (Mexican American *vs.* other), education level (below high school *vs.* high school *vs.* above high school), marital status (married *vs.* other), smoking status (yes *vs.* no), alcohol consumption (never *vs.* former vs. current), obesity (yes *vs.* no), hypertension (yes *vs.* no), diabetes mellitus (DM, yes *vs.* no), arthritis (yes *vs.* no), thyroid disease (yes *vs.* no), and hepatic disease (yes *vs.* no).

A BMI $\geq$29.9 kg/m^2 was considered obese. Thyroid disease was defined based on the affirmative answer to the question: "Has a doctor or other health professional ever told you that you had another thyroid disease?". Hepatic disease was diagnosed based on the "yes" answer to the question: "Has a doctor or other health professional ever told you that you had any kind of liver condition?". DM was defined by the presence of at least one of the following four criteria: (1) a 2-hour blood glucose level $\geq$11.1 mmol/L during an oral glucose tolerance test (OGTT); (2) fasting blood glucose $\geq$7.0 mmol/L; (3) a diagnosis of diabetes made by a physician; or (4) current use of insulin or other antihyperglycemic medications. Hypertension is diagnosed if any of the following conditions are met: (1) systolic and diastolic blood pressure readings that meet the diagnostic criteria for hypertension; (2) a physician's diagnosis of hypertension; or (3) current use of antihypertensive medications. Smoking status was categorized into smokers (cotinine $>$15 ng/mL) and non-smokers (cotinine $\leq$15 ng/mL) based on blood cotinine levels [22]. Alcohol consumption was classified as never, former, or current use, as per previous studies [23].

2.4 Statistical analysis

Data were analyzed by SPSS software (Version 23.0, IBM Corporation, Armonk, NY, USA). Baseline characteristics of the study population were described according to ALS subgroups. Normality of continuous variables was assessed using the Shapiro-Wilk test or visual inspection of histogram distributions. Normally distributed continuous variables are presented as mean $\pm$ standard deviation (SD), with between-group comparisons performed using the independent Student's

t-test. Non-normally distributed continuous variables are expressed as median (25%, 75%) (interquartile range, IQR), with between-group comparisons analyzed via the Mann-Whitney U test. Categorical variables are summarized as frequencies and percentages (n, %), and intergroup differences were evaluated using the chi-square test (χ^2 test) or Fisher's exact test (if any cell in the contingency table had an expected count <5).

Receiver operating characteristic (ROC) curve and decision curve analysis (DCA) were employed to assess the predictive performance and clinical net benefit of CMI for ALS >3, respectively. After adjusting for potential confounders in different models, multiple linear regression was used to examine the relationship between ALS and CMI (or CMI quartiles), calculating the beta values and 95% confidence intervals. Additionally, trend regression analysis explored the trend in the relationship between these variables. Logistic regression, using the same adjusted models, analyzed the association between CMI and ALS median groups, calculating the odds ratio (OR) and 95% confidence intervals (CI). To analyze the influence of CMI on the values of ALS at different positions, quantile regression was used to examine the impact of CMI on the 9th (3rd) quantile of ALS, evaluating the details and stability of CMI's effect on ALS.

Given that HDL-C is a shared factor between CMI and ALS, multiple methods were employed to assess whether the relationship between CMI and ALS is influenced by HDL-C. These methods included: (1) collinearity analysis to explore the relationship between CMI and ALS, with a variance inflation factor (VIF) >5 indicating collinearity; (2) partial correlation analysis to determine if HDL-C affects the relationship between CMI and ALS; (3) stepwise linear regression analysis to explore the independence and robustness of the relationship between CMI and ALS; (4) multivariate regression analysis to evaluate the stability of the relationship between CMI and ALS; (5) mediation analysis to explore the mediating role of HDL-C between CMI and ALS. A *p*-value of less than 0.05 was considered statistically significant.

3. Results

3.1 Baseline characteristics of the study population

Table 1 shows that the median age of patients with prostate cancer we included was 71 years, and their median CMI was 0.618. Table 1 also demonstrates significant differences in PIR, WBC, segmented neutrophils, hemoglobin, RDW, platelets, and CMI between the ALS ≤3 group and the ALS >3 group. The ALS >3 group exhibited significantly lower PIR (2.470 (1.090, 3.710) *vs.* 3.140 (1.690, 5.000)), hemoglobin (14.000 (13.300, 15.100) *vs.* 14.800 (13.800, 15.400)), and hematocrit (42.100 (38.300, 44.600) *vs.* 43.800 (40.600, 45.700)) compared to the ALS ≤3 group (all $p < 0.05$). Conversely, WBC (6.700 (5.700, 8.400) *vs.* 6.100 (5.000, 7.500)), segmented neutrophils (4.200 (3.400, 5.400) *vs.* 3.800 (2.900, 4.400)), platelets (229.000 (193.000, 268.000) *vs.* 205.000 (181.000, 251.000)), RDW (13.600 (13.200, 14.500) *vs.* 13.300 (12.800, 13.900)), and CMI (0.866 (0.474, 1.287) *vs.* 0.497 (0.307, 0.905)) were significantly higher in the ALS >3 group (all $p < 0.05$). Table 2 highlights significant differences between the two groups regarding smoking status.

3.2 Association between CMI and ALS and their stability assessment

ROC and DCA were initially employed to evaluate the clinical value of CMI in predicting ALS in patients with prostate cancer. The ROC analysis revealed an AUC of 0.650, with sensitivity, specificity, and accuracy values of 0.681, 0.587, and 0.612, respectively. Although AUC 0.650 shows that the predictive ability of CMI for ALS is at a lower-middle level (generally considered 0.7–0.8 as a medium predictive value), its sensitivity is better than its specificity, indicating that this indicator is more suitable for "exclusion" rather than "diagnosis" scenarios. In clinical practice, this feature may help reduce the risk of missed diagnosis (Fig. 2A). DCA demonstrated that within the threshold probability range of 0.25 to 0.61, CMI provided a substantial clinical net benefit in predicting ALS (Net benefit up to 0.14) (Fig. 2B).

Then, a significant independent linear relationship between CMI and ALS was revealed via linear regression analysis (Crude model: β [95% CI]: 0.598 [0.319, 0.877]; model 1: β [95% CI]: 0.574 [0.293, 0.855]; model 2: β [95% CI]: 0.561 [0.278, 0.845]; model 3: β [95% CI]: 0.537 [0.258, 0.816]; all $p < 0.05$, Table 3). Trend regression analysis further confirmed a positive trend, with ALS increasing as CMI elevated (p for trend < 0.05, Table 3).

To validate the stability of this association, ALS was treated as a categorical variable based on its median, and logistic regression was applied. The analysis confirmed a significant relationship between CMI and ALS in the crude model (OR [95% CI]: 2.298 [1.235, 4.279], $p = 0.009$, Table 4), indicating for every 1-unit increase in CMI, the chance of having an ALS greater than 3 increases by 2.298 times. Moreover, this significant relationship remained robust even after adjusting for confounding factors (model 1: OR [95% CI]: 1.992 [1.073, 3.698]; model 2: OR [95% CI]: 2.731 [1.286, 5.800]; model 3: OR [95% CI]: 2.184 [1.077, 4.429]; all $p < 0.05$, Table 4). Quantile regression analysis was then employed to investigate local heterogeneity in the relationship between ALS and CMI. Results revealed that the correlation coefficients remained stable within the range of 0.5–0.6, regardless of whether ALS was divided by the 9th or 3rd quantile (Fig. 3A,B), indicating consistent sensitivity of ALS to CMI across different quantiles. The linear regression coefficient was approximately 0.55, and these findings collectively suggest that the overall effect observed in linear regression is stable, with quantile regression further supporting the robustness of the results.

To test the robustness of the relationship between CMI and ALS, we performed a statistical subgroup analysis using linear regression analysis. The results demonstrated a statistically significant linear association in most subgroups, including age ≥71 (β [95% CI]: 0.568 [0.257, 0.879]), age <71 (β [95% CI]: 0.698 [0.141, 1.256]), PIR ≥2.66 (β [95% CI]: 0.614 [0.268, 0.960]), PIR <2.66 (β [95% CI]: 0.512 [0.030, 0.993]), above high school (β [95% CI]: 0.550 [0.215, 0.884]), and married (β [95% CI]: 0.616 [0.296, 0.937]) groups (Table 5).

TABLE 1. Continuous characteristics of patients with prostate cancer according to the two groups of the baseline ALS.

Variables	Total (n = 139)	ALS ≤3 (n = 92)	ALS >3 (n = 47)	*t/z*	*p*
Age, yr	71.000 (3.000, 78.000)	71.000 (65.000, 79.000)	71.000 (62.000, 77.000)	0.672	0.500
PIR	2.660 (1.580, 5.000)	3.140 (1.690, 5.000)	2.470 (1.090, 3.710)	2.029	0.040
Total calcium, mmol/L	2.350 (2.300, 2.400)	2.350 (2.300, 2.400)	2.350 (2.300, 2.400)	0.401	0.689
Phosphate, mmol/L	1.130 (1.030, 1.230)	1.130 (1.033, 1.227)	1.130 (1.030, 1.290)	−0.370	0.713
Sodium, mmol/L	140.000 (138.000, 142.000)	141.000 (138.000, 142.000)	140.000 (138.000, 141.000)	1.086	0.275
Potassium, mmol/L	4.200 (4.000, 4.400)	4.100 (3.980, 4.400)	4.200 (4.000, 4.400)	−0.367	0.714
Creatinine, mg/dL	1.030 (0.920, 1.220)	1.020 (0.920, 1.210)	1.080 (0.970, 1.220)	−0.750	0.454
Uric acid, mg/dL	6.227 ± 1.468	6.146 ± 1.452	6.385 ± 1.486	−0.906	0.366
WBC, 1000 cells/μL	6.400 (5.200, 8.000)	6.100 (5.000, 7.500)	6.700 (5.700, 8.400)	−2.262	0.024
Lymphocyte, 1000 cells/μL	1.600 (1.300, 2.100)	1.600 (1.300, 2.000)	1.700 (1.300, 2.200)	−0.545	0.586
Monocyte, 1000 cells/μL	0.600 (0.500, 0.700)	0.500 (0.400, 0.700)	0.700 (0.500, 0.700)	−1.770	0.073
Segmented neutrophils, 1000 cell/μL	3.900 (3.000, 4.700)	3.800 (2.900, 4.400)	4.200 (3.400, 5.400)	−2.186	0.029
Eosinophils, 1000 cells/μL	0.200 (0.100, 0.300)	0.200 (0.100, 0.300)	0.200 (0.100, 0.300)	−0.588	0.546
Basophils, 1000 cells/μL	0.000 (0.000, 0.100)	0.000 (0.000, 0.100)	0.000 (0.000, 0.100)	−0.639	0.454
RBC, million cells/μL	4.750 (4.520, 5.060)	4.760 (4.530, 5.000)	4.670 (4.220, 5.060)	0.928	0.354
Hemoglobin, g/dL	14.500 (13.500, 15.400)	14.800 (13.800, 15.400)	14.000 (13.300, 15.100)	2.186	0.029
Hematocrit, %	42.900 (40.200, 45.600)	43.800 (40.600, 45.700)	42.100 (38.300, 44.600)	2.329	0.020
MCHC, g/dL	33.714 ± 1.037	33.684 ± 0.947	33.772 ± 1.192	−0.474	0.637
RDW, %	13.400 (12.900, 14.300)	13.300 (12.800, 13.900)	13.600 (13.200, 14.500)	−2.524	0.012
Platelets, 1000 cells/μL	216.000 (185.000, 262.000)	205.000 (181.000, 251.000)	229.000 (193.000, 268.000)	−2.433	0.015
ABSI	86.029 ± 3.360	85.775 ± 3.466	86.525 ± 3.084	−1.242	0.216
CMI	0.618 (0.359, 1.006)	0.497 (0.307, 0.905)	0.866 (0.474, 1.287)	−2.894	0.004

Note: Normally distributed continuous variables are presented as mean ± standard deviation (SD), and abnormally distributed continuous variables are presented as median (25%, 75%). ALS: allostatic load score; CMI: cardiometabolic index; PIR: poverty income ratio; WBC: white blood cell; RBC: red blood cell; RDW: red cell distribution width; MCHC: mean cell hemoglobin concentration; ABSI: a body shape index.

TABLE 2. Categorical characteristics of patients with prostate cancer according to the two groups of the baseline ALS.

Variables	Total (n = 139)	ALS ≤3 (n = 92)	ALS >3 (n = 47)	χ^2	*p*
Race, n (%)					
Mexican America	15 (10.791)	10 (10.870)	5 (10.638)	0.002	0.967
Other	124 (89.209)	82 (89.130)	42 (89.362)		
Education level, n (%)					
Below high school	29 (20.863)	16 (17.391)	13 (27.660)		
High school	36 (25.899)	25 (27.174)	11 (23.404)	1.990	0.370
Above high school	74 (53.237)	51 (55.435)	23 (48.936)		
Marital status, n (%)					
Married	94 (67.626)	66 (71.739)	28 (59.574)	2.103	0.147
Other	45 (32.374)	26 (28.261)	19 (40.426)		

TABLE 2. Continued.

Variables	Total (n = 139)	ALS ≤3 (n = 92)	ALS >3 (n = 47)	χ^2	*p*
Smoking, n (%)					
No	98 (86.726)	68 (94.444)	30 (73.171)	10.270	0.001
Yes	15 (13.274)	4 (5.556)	11 (26.829)		
Drinking, n (%)					
Never	12 (8.759)	9 (9.890)	3 (6.522)		
Former	42 (30.657)	26 (28.571)	16 (34.783)	0.821	0.663
Current	83 (60.584)	56 (61.538)	27 (58.696)		
Hypertension, n (%)					
No	38 (27.338)	27 (29.348)	11 (23.404)	0.553	0.457
Yes	101 (72.662)	65 (70.652)	36 (76.596)		
DM, n (%)					
No	72 (51.799)	52 (56.522)	20 (42.553)	2.431	0.119
Yes	67 (48.201)	40 (43.478)	27 (57.447)		
Arthritis, n (%)					
Yes	75 (54.348)	48 (52.747)	27 (57.447)	0.276	0.599
No	63 (45.652)	43 (47.253)	20 (42.553)		
Thyroid disease, n (%)					
Yes	11 (7.971)	8 (8.696)	3 (6.522)	0.198	0.657
No	127 (92.029)	84 (91.304)	43 (93.478)		
Hepatic disease, n (%)					
Yes	8 (5.755)	5 (5.435)	3 (6.383)	0.052	0.820
No	131 (94.245)	87 (94.565)	44 (93.617)		

Note: The missing values for smoking and drinking were 26 and 2, respectively. ALS: allostatic load score; DM: diabetes mellitus.

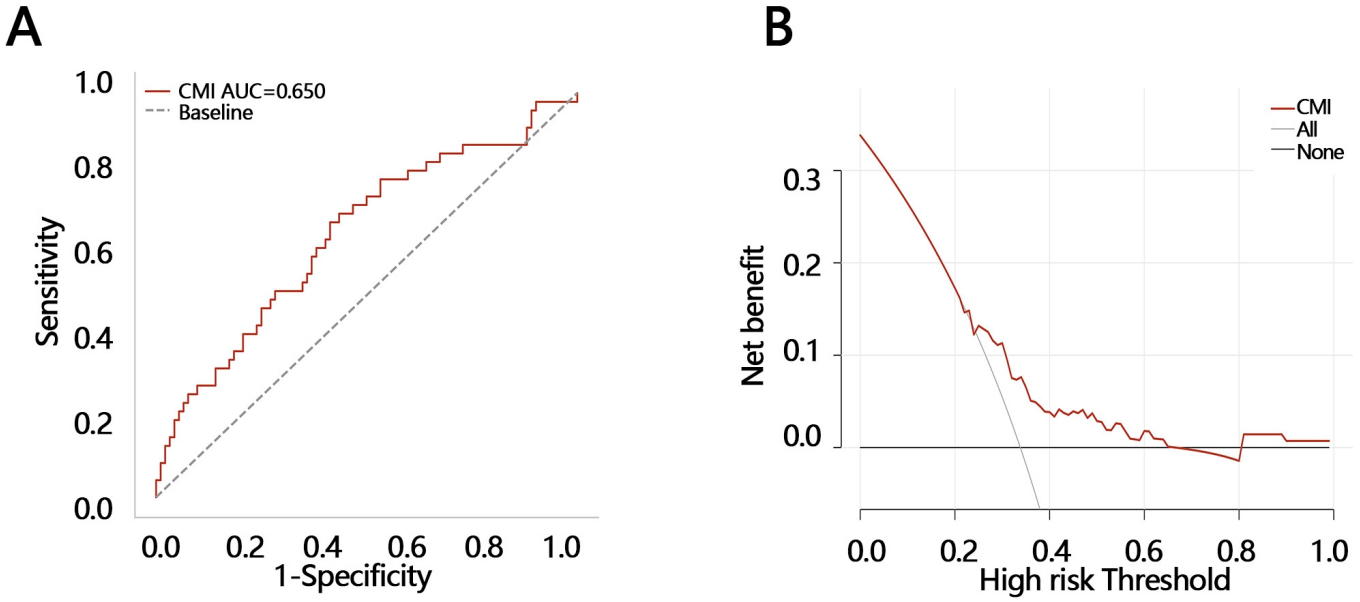

FIGURE 2. The clinical value analysis of CMI in predicting ALS (allostatic load score). (A) ROC: receiver operating characteristic; (B) DCA: decision curve analysis. CMI: cardiometabolic index; AUC: area under the curve.

TABLE 3. Linear regression analysis between CMI /quartiles of CMI and ALS.

Variable	Crude model		Model 1		Model 2		Model 3	
	β [95% CI]	*p*	*β* [95% CI]	*p*	*β* [95% CI]	*p*	*β* [95% CI]	*p*
CMI	0.598 [0.319, 0.877]	<0.001	0.574 [0.293, 0.855]	<0.001	0.561 [0.278, 0.845]	<0.001	0.537 [0.258, 0.816]	<0.001
Q1	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Q2	0.308 [−0.350, 0.966]	0.360	0.326 [−0.344, 0.996]	0.341	0.169 [−0.533, 0.871]	0.638	0.090 [−0.557, 0.738]	0.784
Q3	0.936 [0.278, 1.594]	0.005	0.900 [0.244, 1.555]	0.007	1.155 [0.421, 1.888]	0.002	0.917 [0.270, 1.564]	0.005
Q4	1.222 [0.564, 1.880]	<0.001	1.234 [0.546, 1.922]	<0.001	1.212 [0.504, 1.920]	0.001	1.004 [0.343, 1.666]	0.003
p for trend	0.430 [0.223, 0.636]	<0.001	0.429 [0.214, 0.644]	<0.001	0.463 [0.240, 0.686]	<0.001	0.388 [0.180, 0.596]	0.001

Crude model: without adjustment.
Model 1: adjusting for PIR.
Model 2: adjusting for smoking.
Model 3: adjusting for hemoglobin, RDW, platelets, WBC, and segmented neutrophils.
CMI: cardiometabolic index; ALS: allostatic load score; CI: confidence interval; Ref: reference; PIR: poverty income ratio; RDW: red cell distribution width; WBC: white blood cell.

TABLE 4. Logistic regression analysis between CMI and ALS.

Variable	Crude model		Model 1		Model 2		Model 3	
	OR [95% CI]	*p*	OR [95% CI]	*p*	OR [95% CI]	*p*	OR [95% CI]	*p*
CMI	2.298 [1.235, 4.279]	0.009	1.992 [1.073, 3.698]	0.029	2.731 [1.286, 5.800]	0.009	2.184 [1.077, 4.429]	0.030

Note: ALS was divided into two groups according to the median.
Crude model: without adjustment.
Model 1: adjusting for PIR.
Model 2: adjusting for smoking.
Model 3: adjusting for hemoglobin, RDW, platelets, WBC, and segmented neutrophils.
CMI: cardiometabolic index; ALS: allostatic load score; OR: odds ratio; CI: confidence interval; PIR: poverty income ratio; RDW: red cell distribution width; WBC: white blood cell.

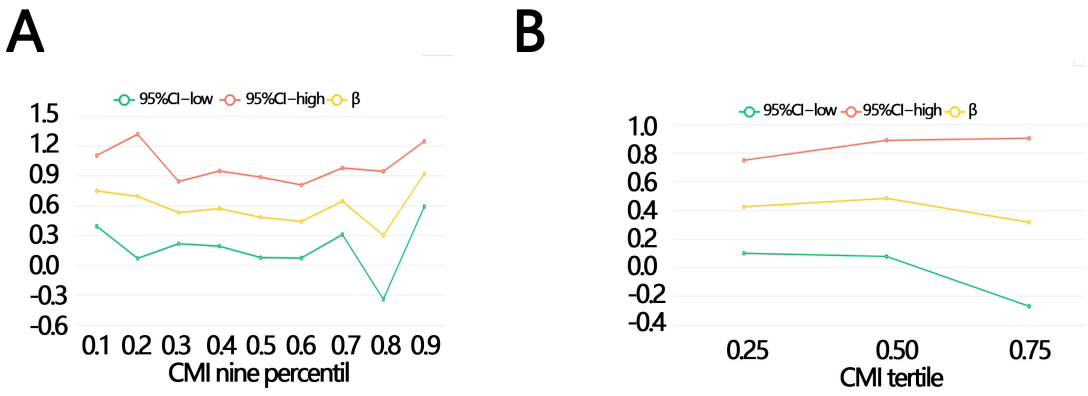

FIGURE 3. Quantile regression analysis of the association between the ALS and CMI. (A) Analysis employing continuous CMI demonstrates the changing relationship across its distribution (10th, 20th, 30th, 40th, 50th, 60th, 70th, 80th, 90th percentiles) with ALS. The slope illustrates how the predicted ALS value alters for a one-unit increase in CMI at different quantiles. (B) Analysis comparing ALS levels across population subgroups defined by CMI tertiles reveals disparities in predicted ALS values between the groups at specified quantiles. Abbreviations: CMI: cardiometabolic index; CI: confidence interval; ALS: allostatic load score.

TABLE 5. The linear regression analysis between ALS and CMI in subgroups.

Variables	β [95% CI]	p
Age (yr)		
≥71	0.568 [0.257, 0.879]	0.001
<71	0.698 [0.141, 1.256]	0.017
PIR		
≥2.66	0.614 [0.268, 0.960]	0.001
<2.66	0.512 [0.030, 0.993]	0.041
Education level		
Below high school	0.619 [−0.062, 1.301]	0.086
High school	0.723 [−0.139, 1.585]	0.109
Above high school	0.550 [0.215, 0.884]	0.002
Marital status		
Married	0.616 [0.296, 0.937]	<0.001
Other	0.544 [−0.001, 1.089]	0.057

Note: Age and PIR were divided into two groups according to the median. ALS: allostatic load score; CMI: cardiometabolic index; PIR: poverty income ratio; CI: confidence interval.

3.3 The effect of shared variable on the relationship between CMI and ALS

Given that HDL-C is a shared variable in the computation of both CMI and ALS, the real association between CMI and ALS may be covered due to the existence of the shared variable HDL-C. Therefore, several methods were employed to reveal the role of shared variables in their association, including collinearity analysis, partial correlation analysis, stepwise regression, and multiple regression analysis. Finally, mediation analysis was also conducted to investigate whether HDL-C mediates the relationship between CMI and ALS.

Collinearity analysis revealed that the VIFs for CMI and ALS were 1.129 and 1.128, respectively, indicating no collinearity caused by HDL-C between the two variables. Partial correlation analysis demonstrated that the correlation between CMI and ALS remained significant both before and after controlling for HDL-C (before: Partial Coefficient of Correlation (pcor) = 0.338, $p < 0.001$; after: pcor = 0.286, $p = 0.001$). In the stepwise regression, HDL-C was included first, resulting in an R^2 of 0.035. Upon adding CMI, the R^2 increased to 0.114, with an increment of 0.079. This change in R^2 was statistically significant ($p = 0.001$). This finding indicates that CMI independently contributes significantly to ALS. Further multivariate regression analysis, incorporating both HDL-C and CMI, confirmed that after adjusting for the shared variable, the correlation coefficient between CMI and ALS remained at 0.594 ($p < 0.001$), signifying the stability of their relationship. The result of mediation analysis showed no mediating effect of HDL-C ($p = 0.928$, Table 6). These findings collectively suggest that CMI has a statistically significant independent contribution to ALS, maintains a stable association with ALS, and that this relationship is not a spurious correlation arising from shared variables.

4. Discussion

This study presents the first analysis evaluating the relationship between CMI and ALS using NHANES data in patients with prostate cancer. Our findings established a positive correlation between ALS and CMI after adjusting for potential confounders. Various analytical approaches confirmed the robustness of this relationship, and different methodologies were employed to ensure that shared factors between the two variables did not affect the association, thereby strengthening the reliability of our conclusions.

The analysis revealed that higher CMI values in patients with prostate cancer were associated with elevated ALS levels. These findings may be linked to the pathogenesis of prostate cancer itself.

In prostate cancer, androgen receptor (AR) pathway activation drives tumor progression by promoting cancer cell survival and proliferation [24]. Standard therapy includes AR antagonists, which competitively block the AR, preventing endogenous androgen binding and halting androgen-dependent signaling and tumor growth [25]. However, this treatment induces adverse metabolic effects: altered body composition (increased fat mass, decreased lean mass), dyslipidemia, and reduced insulin sensitivity [26], along with elevated fasting insulin levels. These pathological alterations, evident through an increased waist-to-height ratio, directly correlate with higher CMI values.

In patients with prostate cancer, the increase in CMI indicated fat accumulation. Adipose tissue secret pro-inflammatory cytokines and trigger systemic low-grade inflammation [5]. These inflammatory signals cross the blood-brain barrier and impact the hypothalamus, leading to persistent activation of the hypothalamic-pituitary-adrenal (HPA) axis and an increase in glucocorticoid secretion. Meanwhile, it induces the activation of pro-inflammatory microglia in the hypothalamic arcuate nucleus, further amplifies the central inflammatory signal, and inhibits the negative feedback sensitivity of the glucocorticoid receptor. Chronic elevation of cortisol levels results in glucocorticoid receptor desensitization, disrupting negative feedback regulation and creating a vicious cycle of inflammation-HPA axis dysregulation [27]. This process is shown in ALS by an increase in inflammatory markers such as CRP and cortisol circadian rhythm disorders [28]. Fat accumulation also promotes heightened leptin secretion, which removes inhibitory regulation of the brainstem solitary nucleus and enhances sympathetic nervous system output. This overactivation of the sympathetic nervous system results in elevated blood pressure [24]. Moreover, leptin also releases a large amount of free fatty acids through β3-adrenergic receptor-mediated lipolysis, thereby activating the Toll-like receptor 4/Nuclear Factor kappa-light-chain-enhancer of activated B cells (NF-κB) pathway and forming a "sympathetic-fat inflammation" positive feedback loop. These changes are manifested in ALS through abnormal dynamic blood pressure monitoring. Furthermore, insulin resistance, as indicated by an increase in CMI, can impair skeletal muscle glucose uptake via the Phosphoinositide 3-kinase/Protein kinase B (PI3K/Akt) signaling pathway, continuously activate

TABLE 6. The mediation analysis of HDL-C in the relationship between CMI and ALS.

Path	Coefficient [95% CI]	SE	*p*	Significance
HDL-C∼CMI	−0.254 [−0.323, −0.185]	0.035	<0.001	Yes
ALS∼HDLC	−0.693 [−1.305, −0.081]	0.309	0.027	Yes
Total	0.598 [0.317, 0.879]	0.142	<0.001	Yes
Direct	0.587 [0.254, 0.919]	0.168	0.001	Yes
Indirect	0.012 [−0.247, 0.231]	0.116	0.928	No

CMI: cardiometabolic index; ALS: allostatic load score; HDL-C: high-density lipoprotein cholesterol; CI: confidence interval; SE: standard error.

the liver Forkhead Box O1 signaling pathway, and promote the expression of key enzymes in gluconeogenesis, while enhancing the expression of gluconeogenesis enzymes, resulting in chronic hyperglycemia [25]. Hyperglycemia activates the receptor for advanced glycation endproducts (RAGE) receptor via advanced glycation end products (AGEs), inducing endothelial inflammation and fibrosis [26]. Increases in fasting blood glucose and HbA1c in ALS reflect this process.

Although this study found that the predictive efficacy of CMI for ALS was at a moderate level (AUC = 0.65), this indicator has unique application value in clinical practice: First, CMI, as a composite parameter derived from conventional blood lipid detection and body measurement indicators, can be obtained immediately without additional detection costs, and a comprehensive assessment of allostatic load requires the detection of 8 biomarkers. If CMI is used to screen prostate cancer patients with higher ALS, it can avoid over-detection of low-risk patients and significantly optimize the allocation of medical resources. Secondly, CMI is more sensitive than traditional obesity indicators to reflect the dynamic changes of visceral fat. In this study, the risk of ALS progression in patients with an annual increase of one score in CMI was increased by about 2.298 times ($p = 0.009$), suggesting that it can be used as a real-time monitoring indicator of intervention efficacy.

5. Strength and limitations

This study robustly validates its findings through various analytical methods, demonstrating a positive correlation between CMI and ALS in patients with prostate cancer. The results provide a comprehensive research framework for similar studies. Moreover, this study identifies CMI as a reliable predictive factor for clinical interventions aimed at managing chronic stress in patients with prostate cancer. Focusing on CMI facilitates early intervention for patients with elevated CMI, potentially reducing their ALS, improving survival rates, and extending lifespan. However, this study has several limitations. (1) The study population is drawn from the NHANES database, which may introduce racial and geographical biases. (2) As this study is cross-sectional, causal relationships cannot be established. (3) The incomplete availability of some data (such as other ALS components, thyroid hormone test data, or liver pathological data) could result in both measurement bias and disease misclassification. (4) The sample data was not collected in the last five years. Due to the COVID-19 pandemic starting in 2019, the data were only updated until 2020. Although we examined newer datasets, critical metrics were largely unrecorded, making recent data too fragmentary for reliable use. In addition, the outbreak may increase the chronic pressure of patients, thereby increasing ALS, which make the results biased. Therefore, future studies should verify CMI's predictive ability for ALS in a prospective multi-center large sample and simultaneously conduct an interventional randomized trial for CMI (such as the Mediterranean diet combined with sodium-glucose transporter 2 (SGLT2) inhibitors) to assess its effect on allostatic load biomarkers (such as cortisol and Interleukin-6 (IL-6)) and progression-free survival. Additionally, the molecular mechanism of CMI driving should be analyzed through animal models and organoid experiments to provide a theoretical basis for early intervention of CMI, thus reducing the allostatic load of patients and improving survival for patients with prostate cancer.

6. Conclusions

In this study, we found that CMI was positively correlated with ALS in prostate cancer patients. Our findings demonstrate that elevated CMI levels may increase allostatic load, consequently heightening the risk of poor clinical outcomes. Furthermore, they suggest that clinical monitoring of CMI could enable early interventions to reduce allostatic load levels, thereby potentially improving the prognosis for patients with prostate cancer.

ABBREVIATIONS

CMI, cardiometabolic index; ROC, Receiver operating characteristic; DCA, decision curve analysis; HDL-C, high-density lipoprotein cholesterol; ADT, androgen deprivation therapy; TG, Triglycerides; ALS, allostatic load score; CRP, C-reactive protein; SBP, systolic blood pressure; NHANES, National Health and Nutrition Examination Survey; NCHS, National Center for Health Statistics; CDC, Centers for Disease Control and Prevention; WC, waist circumference; HbA1c, glycated hemoglobin; Alb, Albumin; BMI, body mass index; PIR, poverty income ratio; WBC, white blood cell; RBC, red blood cell; MCHC, mean cell hemoglobin concentration; RDW, red cell distribution width; ABSI, a body shape index; DM,

diabetes mellitus; OGTT, oral glucose tolerance test; SD, standard deviation; OR, odds ratio; CI, confidence intervals; AR, androgen receptor; AGEs, advanced glycation end products; AUC, area under the curve; CVDs, cardiovascular diseases; IQR, interquartile range; VIF, variance inflation factor; HPA, hypothalamic-pituitary-adrenal; NF-κB, Nuclear Factor kappa-light-chain-enhancer of activated B cells; PI3K, Phosphoinositide 3-kinase; Akt, Protein kinase B; RAGE, receptor for advanced glycation endproducts; SGLT2, sodium-glucose transporter 2; IL-6, Interleukin-6.

AVAILABILITY OF DATA AND MATERIALS

The study data was from the NHANES 2007–2020 dataset. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

AUTHOR CONTRIBUTIONS

GAZ—designed the research study; performed the research. PL—analyzed the data. GAZ and PL—wrote the manuscript. Both authors contributed to editorial changes in the manuscript. Both authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The Ethics Committee of Lishui Hospital of Wenzhou Medical University deemed that this research is based on open-source data, so the need for ethics approval was waived. All participants providing informed consent.

ACKNOWLEDGMENT

Not applicable.

FUNDING

This research was funded by The Public Welfare Technology Application Research Project of Lishui, grant number 2023SJZC102.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

SUPPLEMENTARY MATERIAL

Supplementary material associated with this article can be found, in the online version, at https://oss.jomh.org/files/article/201711802510100704/attachment/Supplementary%20material.docx.

REFERENCES

[1] Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, *et al*. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: A Cancer Journal for Clinicians. 2024; 74: 229–263.

[2] Schafer EJ, Laversanne M, Sung H, Soerjomataram I, Briganti A, Dahut W, *et al*. Recent patterns and trends in global prostate cancer incidence and mortality: an update. European Urology. 2025; 87: 302–313.

[3] Chiefari M, Eziandio C. Metabolic disorders in cancer patients. Tumori Journal. 2001; 87: 82–84.

[4] Peng Q, Shen Y, Xu Y, Feng Z, Xu Y, Wang Y, *et al*. Association of metabolic dysregulation with treatment response in rectal cancer patients undergoing chemoradiotherapy. BMC Medical Genomics. 2025; 18: 48.

[5] Saylor PJ, Smith MR. Metabolic complications of androgen deprivation therapy for prostate cancer. Journal of Urology. 2013; 189: S34–S42; discussion S43–S44.

[6] Keating NL, O'Malley A, Freedland SJ, Smith MR. Diabetes and cardiovascular disease during androgen deprivation therapy: observational study of veterans with prostate cancer. JNCI: Journal of the National Cancer Institute. 2012; 104: 1518–1523.

[7] Yin LJ, Wang XH. Research advance in the effects of androgen and its receptor on the development of obesity, obesity-related diseases and disorders of glucose and lipid metabolism. Acta Physiologica Sinica. 2018; 70: 319–328. (In Chinese)

[8] Guerrios-Rivera L, Howard LE, Wiggins EK, Hoyo C, Grant DJ, Erickson TR, *et al*. Metabolic syndrome is associated with aggressive prostate cancer regardless of race. Cancer Causes & Control. 2023; 34: 213–221.

[9] Drab A, Wdowiak K, Kanadys W, Zajączkowski K, Koczkodaj P, Religioni U, *et al*. Diabetes mellitus and prostate cancer risk—a systematic review and meta-analysis. Cancers. 2024; 16: 4010.

[10] Alberto M, Yim A, Lawrentschuk N, Bolton D. Dysfunctional lipid metabolism—the basis for how genetic abnormalities express the phenotype of aggressive prostate cancer. Cancers. 2023; 15: 341.

[11] Yu C, Hu W, Lei X. Association between cardiometabolic index (CMI) and suicidal ideation: the mediating role of depression and cardiovascular disease. Journal of Affective Disorders. 2025; 380: 487–495.

[12] Wakabayashi I, Daimon T. The "cardiometabolic index" as a new marker determined by adiposity and blood lipids for discrimination of diabetes mellitus. Clinica Chimica Acta. 2015; 438: 274–278.

[13] Lazzer S, D'Alleva M, Isola M, De Martino M, Caroli D, Bondesan A, *et al*. Cardiometabolic Index (CMI) and Visceral Adiposity Index (VAI) highlight a higher risk of metabolic syndrome in women with severe obesity. Journal of Clinical Medicine. 2023; 12: 3055.

[14] McCrory C, Fiorito G, Ni Cheallaigh C, Polidoro S, Karisola P, Alenius H, *et al*. How does socio-economic position (SEP) get biologically embedded? A comparison of allostatic load and the epigenetic clock(s). Psychoneuroendocrinology. 2019; 104: 64–73.

[15] Obeng-Gyasi S, Li Y, Carson WE, Reisenger S, Presley CJ, Shields PG, *et al*. Association of allostatic load with overall mortality among patients with metastatic non-small cell lung cancer. JAMA. 2022; 5: e2221626.

[16] Mira RS. The relationship between allostatic load and progress of multimorbidity among older americans. Innovation in Aging. 2023; 7: 1138–1139.

[17] Hu S, Chang CP, Dodson MW, Deshmukh V, Newman M, Date A, *et al*. Endocrine and metabolic diseases among survivors of prostate cancer in a population-based cohort. Journal of Clinical Oncology. 2024; 42: 306.

[18] Lifshitz K, Ber Y, Margel D. Role of metabolic syndrome in prostate cancer development. European Urology Focus. 2021; 7: 508–512.

[19] Dai Z, Zhou X. Associations between allostatic load and hepatic steatosis and liver fibrosis: evidence from NHANES 2017–2020. BMC Public Health. 2024; 24: 1602.

[20] Du EY, Jiang K, Carlson MC, Reed NS, Deal JA. Hearing impairment and allostatic load in older adults. JAMA Otolaryngology—Head & Neck Surgery. 2023; 149: 597–606.

[21] Petrova D, Ubago-Guisado E, Garcia-Retamero R, Redondo-Sánchez D, Pérez-Gómez B, Catena A, *et al*. Allostatic load and depression symptoms in cancer survivors: a national health and nutrition examination survey study. Cancer Nursing. 2024; 47: 290–298.

[22] Kim S. Overview of cotinine cutoff values for smoking status classification. International Journal of Environmental Research and Public Health. 2016; 13: 1236.

[23] Wang M, Lu X, Zheng X, Xu C, Liu J. The relationship between sleep duration and thyroid function in the adult US population: NHANES 2007–2012. PLOS ONE. 2023; 18: e0291799.
[24] Voora R, Hinderliter AL. Modulation of sympathetic overactivity to treat resistant hypertension. Current Hypertension Reports. 2018; 20: 92.
[25] Szablewski L. Insulin resistance: the increased risk of cancers. Current Oncology. 2024; 31: 998–1027.
[26] Seeman T, Gruenewald T, Karlamangla A, Sidney S, Liu K, McEwen B, *et al*. Modeling multisystem biological risk in young adults: the coronary artery risk development in young adults study. American Journal of Human Biology. 2010; 22: 463–472.
[27] Li Y, Zhang J, Zheng X, Lu W, Guo J, Chen F, *et al*. Depression, anxiety and self-esteem in adolescent girls with polycystic ovary syndrome: a systematic review and meta-analysis. Frontiers in Endocrinology. 2024; 15: 1399580.
[28] McEwen BS. Neurobiological and systemic effects of chronic stress. Chronic Stress. 2017; 1: 2470547017692328.

How to cite this article: Guan-an Zhao, Peng Li. Stability of the CMI-ALS axis in prostate cancer patients: a new target for prognostic assessment and treatment optimization. Journal of Men's Health. 2026; 22(1): 79-89. doi: 10.22514/jomh.2026.007.