BMC Cardiovascular Disorders

RESEARCH

Open Access

Associations of the C-reactive protein-albumin-lymphocyte index with all-cause and cardiovascular mortality among individuals with cardiovascular disease: evidence from the NHANES 2001–2010

Dunzheng Han[1†], Lanlan Wu[1†], Haobin Zhou[1], Yuting Xue[1], Shangfei He[1], Zhuang Ma[1], Shuwen Su[1], Peixin Li[1], Shenrong Liu[1] and Zheng Huang[1*]

Abstract

Background Evidence regarding the C-reactive protein–albumin–lymphocyte (CALLY) index and mortality risk in individuals with cardiovascular disease (CVD) is scarce. This study investigated the relationships of the CALLY index with all-cause and cardiovascular mortality risk in CVD patients among American adults.

Methods This study enrolled 2183 CVD individuals from five NHANES cycles (2001–2010), and mortality outcomes were determined by linking the data to National Death Index (NDI) records up to December 31, 2019. Weighted multivariate Cox regression models and subgroup analyses were performed to assess the associations of the CALLY index with all-cause and cardiovascular mortality. A restricted cubic spline (RCS) was used to visualize the association of the CALLY index with mortality risk.

Results During a median follow-up of 122 months (interquartile range, 71–157 months), 1208 (weighted percentage, 49.62%) of the 2183 CVD individuals died, including 398 (weighted percentage, 24.85%) with cardiovascular deaths and 810 (weighted percentage, 75.15%) with noncardiovascular deaths. Cox regression revealed an inverse correlation between the CALLY index and the risk of all-cause and cardiovascular mortality after adjusting for covariates. Compared with individuals with a lower CALLY index, those with a higher CALLY index had a significantly lower risk of both all-cause (HR 0.58, 95% CI: 0.48, 0.71, $p < 0.001$) and cardiovascular mortality (HR 0.54, 95% CI: 0.38, 0.76, $p < 0.001$). The RCS regression analysis revealed a nonlinear association between the CALLY index and all-cause and cardiovascular mortality ($p < 0.05$ for nonlinearity) in CVD patients. The associations were consistent in the subgroup analyses regardless of age, sex, income, education level, race, smoking status, diabetes, and hypertension (all p values for interactions > 0.05).

Conclusion An increased CALLY index is independently associated with decreased all-cause and cardiovascular mortality in CVD patients.

Keywords Cardiovascular disease, Mortality, C-reactive protein-albumin-lymphocyte index

†Dunzheng Han and Lanlan Wu contributed equally to this work.

*Correspondence:
Zheng Huang
huangzhengGY@126.com

Introduction

With the rapid aging process, the incidence of cardiovascular disease (CVD) is increasing worldwide. Annually, an estimated 18 million people succumb to cardiovascular diseases, with one in four Americans affected by them [1]. The high incidence of CVD is emerging as a critical public health concern [2]. Therefore, identifying more risk factors in a timely manner is important for preventing, delaying, or reducing the progression of cardiovascular disease and related deaths.

Despite the advancement of knowledge regarding the etiology of CVD, the identification of additional risk factors remains a crucial step in the development of effective prevention and management strategies. In the pathophysiological cascade of CVD, it is believed that inflammation, nutritional status, and immune function aberrations exert pivotal influences. Persistent inflammation has been implicated in the genesis of atherosclerosis and cardiovascular events. CRP is an important biomarker for predicting cardiovascular risk. Another study suggested that elevated CRP levels at baseline are significantly associated with increased risks of major adverse cardiovascular events (MACEs), including myocardial infarction, stroke, cardiovascular death, and hospitalization for unstable angina or heart failure, in patients with stable CAD [3]. In addition to inflammation, the nutritional status of the body is also an important factor that influences the prognosis of individuals with CVD. Adverse dietary habits and nutritional deficits may precipitate metabolic dysregulation, thereby increasing susceptibility to cardiovascular disease. Albumin has been used as a biochemical indicator of nutritional status [4]. Furthermore, the level of albumin is also influenced by inflammation [5]. Many scholars have demonstrated that low albumin level is an independent risk factor for cardiovascular diseases [6, 7]. Multiple studies of cardiovascular diseases have revealed that cardiovascular diseases are strongly connected to the immune response and that lymphocytes are a prognostic marker for cardiovascular disease [8, 9]. Dysregulated activation of immune cells and subsequent release of inflammatory mediators may precipitate myocardial injury and vascular inflammation, thereby exacerbating the severity of cardiovascular pathology. Given the interconnected roles of inflammation, malnutrition, and immune dysfunction in the progression of CVD, relying solely on individual biomarkers may oversimplify the assessment of disease risk. To address this limitation, composite indices integrating multiple parameters have been introduced. The CALLY index [10], developed by Hiroya Iida et al., is a parameter that combines CRP, albumin, and lymphocytes, offering a more comprehensive assessment of systemic inflammation, nutritional status, and immune competence. Unlike conventional single-marker approaches, CALLY index reflects the cumulative impact of these interrelated processes—key drivers of cardiovascular disease progression. Emerging evidence suggests that composite indices like CALLY index may outperform individual biomarkers in predicting mortality. For instance, in cancer patients, a low CALLY index correlates with advanced disease stages and poor survival [11–19]. Additionally, CALLY index has shown a significant negative linear relationship with all-cause mortality and CVD mortality in elderly patients [20] and those with COPD [21]. Recent studies have also identified a significant negative correlation between the CALLY index and the risk of cardiorenal syndrome [22], sarcopenia [23], and metabolic syndrome risk [24], highlighting its potential value in cardiovascular risk stratification.

The relationship between the CALLY index and mortality risk in individuals with CVD has not been clearly demonstrated. To address this research gap, we conducted a study to investigate the relationships between the CALLY index and all-cause and cardiovascular mortality risk in a large, nationally representative sample of CVD individuals.

Methods

Study population and design

The study population and design utilize data from the National Health and Nutrition Examination Survey (NHANES), a cross-sectional survey conducted by the National Center for Health Statistics (NCHS). Each NHANES cycle features a new, nationally representative cohort, with all participants providing written informed consent in compliance with the Institutional Review Board requirements of the Centers for Disease Control and Prevention (CDC). For detailed information on the NHANES study design and data collection methods, please refer to the CDC website (https://www.cdc.gov/nchs/nhanes/) [25].

The data for this research were taken from seven cycles of the NHANES (2001–2010), with a total of 2183 individuals (Fig. 1). We enrolled eligible individuals with CVD aged $\geq$ 20 years. Individuals without complete information or who were pregnant or had cancer were excluded.

Definition of cardiovascular disease

The definition of cardiovascular disease in the NHANES is based on data collected from individual interviews. A positive response to questions regarding congestive heart failure, coronary heart disease, angina, heart attack, or stroke indicates the presence of CVD [25].

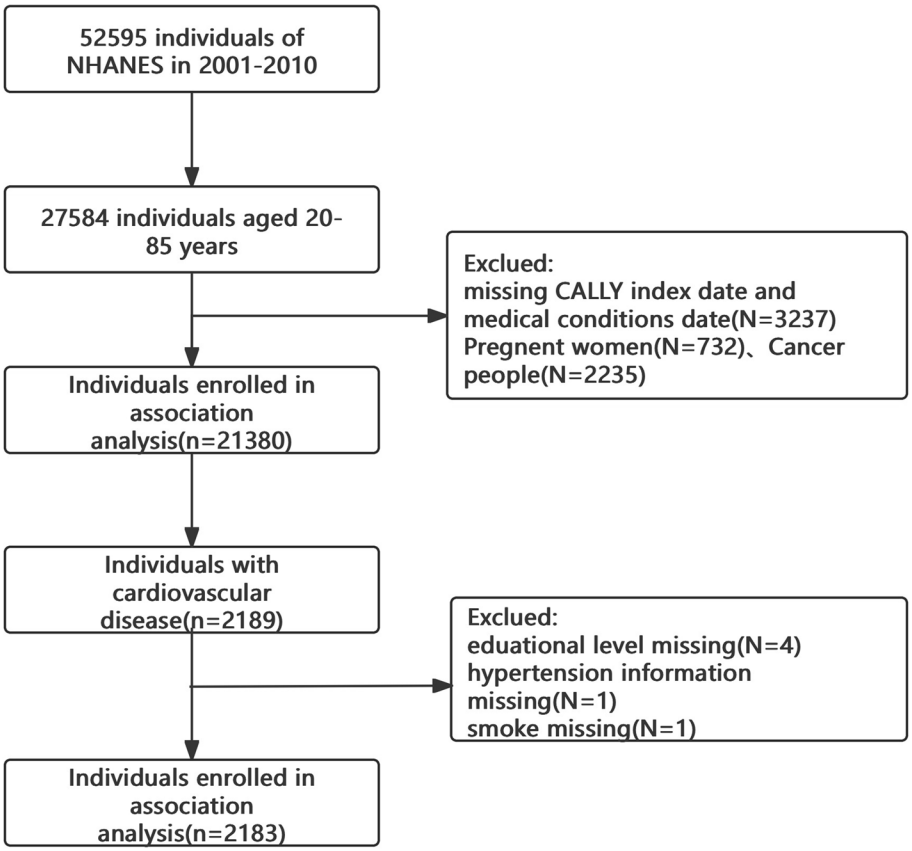

Fig. 1 Flow chart of inclusion and exclusion of individuals in the current study

Assessment of the CALLY index

The CALLY index was calculated using the formula [11]:

$$\text{CALLY index} = \frac{\text{Albumin (g/L)} * \text{Lymphocytes } (10^9/\text{L})}{\text{CRP (mg/L)} \times 10}$$

For additional details on the laboratory procedures, refer to the CDC website [26]. Participants were divided into four quartile groups (Q1, Q2, Q3, Q4) based on their CALLY index values, with Q1 serving as the reference group.

Mortality outcomes of the study population

Mortality outcomes for the study population were sourced from the NDI database maintained by the CDC. Each participant was followed from their NHANES participation date until either the date of death or December 31, 2019. Cardiovascular deaths were identified according to the International Statistical Classification of Diseases [27].

Assessment of covariates

Demographic and health-related information, including age, sex, race, education level, poverty income ratio, smoking status, medication use, and disease status, was obtained from NHANES interviews and laboratory date. Race was classified as non-Hispanic Black, non-Hispanic White, Mexican American, other Hispanic, and other races. Education level was divided into three categories: less than high school, high school or equivalent, and college or higher. The poverty income ratio was categorized into three groups: 0–1.0, 1.0–3.0, and greater than 3.0. Smoking status was categorized as never smoker, former smoker, or current smoker [28]. Body mass index (BMI) was calculated by dividing weight in kilograms by height in meters squared and was classified as ≤ 25 or > 25. Diabetes was identified by self-reported diagnosis, use of diabetes medication or insulin, fasting plasma glucose ≥ 7.0 mmol/L, or HbA1c $\geq 6.5\%$ [25]. Hypertension was defined by self-reported history, use of antihypertensive medication, or by an average systolic blood pressure ≥ 130 mmHg and/or diastolic blood

pressure ≥ 80 mmHg [29]. We additionally calculated the proportion of participants who were taking antiplatelet agents (clopidogrel, aspirin, cilostazol, prasugrel, dipyridamole) and lipid-lowering drugs.

Statistical analysis

Statistical analyses were performed using R version 4.2.1 alongside Free Statistics software version 1.9. Following the NHANES analytic and reporting guidelines [30], we applied sample weights, clustering, and stratification across all analyses to properly account for the survey's complex design, which is essential for accurate interpretation of NHANES data. Study participants were divided into four groups based on the quartiles (Q1–Q4) of the CALLY index. Continuous variables are expressed as means with standard deviations (SDs). Categorical variables are reported as frequencies and percentages. Baseline characteristics across the CALLY index quartiles were compared using one-way ANOVA for continuous variables and the Pearson chi-square test for categorical variables. The relationships between the CALLY index and both all-cause and cardiovascular mortality in individuals with CVD were evaluated using survey-weighted Cox regression analysis. The crude model was unadjusted; Model 1 was adjusted for age, race, and sex; and Model 2 included adjustments for sex, age, race, income, diabetes, uric acid, serum creatinine (SCR), smoking status, and medication use. Survival probabilities were estimated using the Kaplan–Meier method. RCS and smooth curve fitting were employed to visualize potential nonlinear relationships between the log-transformed CALLY index and both all-cause and cardiovascular mortality in CVD patients. Stratified analyses were performed based on sex, age (≤ 60 years or > 60 years), BMI, race, education, income, smoking status, diabetes status, and hypertension. A p-value of less than 0.05 was considered statistically significant.

Results

Characteristics of the population

Table 1 shows the baseline characteristics of the individuals stratified by quartiles of the CALLY index. This study comprised a sample of 2,183 CVD individuals (the weighted population was 16,313,828). The average age of the individuals was 63.38(14.04) years, and 1250 (53.74%) were men. With the increase in the CALLY index, a greater proportion of individuals were male and richer, never smoked, and had a higher BMI. Compared with individuals in the lower quartile, individuals in the highest quartile presented significantly lower levels of cholesterol, SCR and uric acid. Compared with individuals in the Q1 group, those in the other three groups had a lower prevalence of diabetes and hypertension. The supplementary table results show that cardiovascular individuals with adverse outcomes have higher CRP levels and lower lymphocyte counts and albumin and CALLY index.

Associations of the CALLY index with all-cause mortality

During a median follow-up of 122 months (interquartile range, 71–157 months), 1208 (weighted percentage, 49.62%) of the 2183 CVD individuals died, including 398 (24.85%) with cardiovascular deaths and 810 (75.15%) with noncardiovascular deaths. Multiple regression analysis was conducted via a complex sampling design. As shown in Table 2, three Cox proportional hazard regression models revealed that the CALLY index was independently associated with long-term all-cause mortality and cardiovascular mortality. This relationship was significant in the unadjusted crude model ($P < 0.001$). After adjusting for sex, age, race, income, diabetes status, uric acid status, SCR, smoking status, and medication use in Model 2, the CALLY index remained negatively associated with all-cause mortality ($P < 0.001$). In the sensitivity analysis, the multivariate-adjusted HRs and 95% CIs from the lowest quartile to the highest quartile were 1.00 (reference), 0.60 (0.50, 0.74), 0.66 (0.55, 0.80), and 0.58 (0.48, 0.71). In weighted restrictive cubic spline regression, a significant nonlinear relationship between the CALLY index and all-cause mortality was observed after adjustment for covariates from Model 2 ($P < 0.001$) (Fig. 2A). The weighted Kaplan–Meier survival rates for all-cause mortality differed between the high- and low-CALLY index groups ($p < 0.001$), and the survival rate was lower in the low-CALLY group (Fig. 3A). All-cause mortality decreased with increasing CALLY index.

Associations of CALLY with cardiovascular mortality

A total of 1373 individuals were included to calculate the associations of the CALLY index with cardiovascular mortality, with the exception of 810 noncardiovascular deaths. Weighted multivariable Cox regression analyses also confirmed the association of the CALLY index with cardiovascular mortality (Table 2). This relationship was significant in the unadjusted crude model ($P < 0.001$). In Model 2, the CALLY index remained negatively associated with all-cause mortality ($P = 0.002$). The multivariate-adjusted HRs and 95% CIs from the lowest to highest CALLY index quartile were 1.00 (reference), 0.59 (0.40, 0.88), 0.64 (0.44, 0.91), and 0.54 (0.38, 0.76) and we observed that the CALLY index was nonlinearly correlated with cardiovascular mortality (Fig. 2B). The weighted Kaplan–Meier survival plots indicated that cardiovascular mortality was greater in individuals with a lower CALLY index than in those with a higher CALLY index ($p < 0.001$) (Fig. 3B).

Table 1 Weighted baseline characteristics according to the CALLY index quartiles

Variable	Total	Q1	Q2	Q3	Q4	*P* value
Age (years)	63.38 (14.04)	63.48 (13.68)	63.20 (14.18)	64.83 (14.25)	62.10 (13.96)	0.134
Male, No. (%)	1250 (53.74)	283 (47.03)	290 (47.72)	320 (56.32)	357 (63.23)	< 0.001
Race, No. (%)						0.029
Mexican American	296 (4.58)	72 (4.84)	68 (4.11)	72 (4.28)	84 (5.09)	
Other Hispanic	439 (12.02)	134 (16.15)	117 (12.75)	100 (10.05)	88 (8.98)	
Non-Hispanic White	1264 (75.70)	300 (73.60)	319 (75.16)	331 (78.77)	314 (75.26)	
Non-Hispanic Black	105 (2.63)	27 (2.26)	23 (3.00)	26 (2.28)	29 (2.95)	
Other Race	79 (5.07)	13 (3.16)	18(4.98)	16 (4.18)	32 (7.73)	
Poverty income ratio, No. (%)						0.007
≤ 1	479 (16.89)	149 (20.71)	126 (18.58)	103 (15.48)	101 (13.12)	
> 1, ≤ 3	1098 (46.80)	265 (45.48)	269.00 (46.61)	298 (52.20)	266 (43.16)	
> 3	606 (36.31)	132 (33.81)	150.00 (34.82)	144 (32.32)	180 (43.72)	
Education levels, No. (%)						0.215
Less than high school	875 (31.06)	228 (32.54)	213 (29.41)	220 (33.33)	214 (29.18)	
High school diploma	522 (26.58)	135 (27.45)	130 (28.09)	136 (27.99)	121 (23.03)	
More than high school	786 (42.36)	183 (40.02)	202 (42.50)	189 (38.68)	212 (47.79)	
Hypertension, No. (%)	1791 (79.71)	449 (80.16)	472 (84.74)	433 (76.4)	437 (77.56)	0.043
Diabetes,No. (%)	780 (31.22)	230 (38.64)	209 (32.39)	173 (27.56)	168 (26.76)	0.004
Smoking status,No. (%)						0.431
Never smoker	842 (38.16)	185 (34.35)	207 (38.29)	228 (40.17)	222 (39.62)	
Former smoker	902 (39.89)	234 (40.58)	223 (38.12)	221 (40.45)	224 (40.43)	
Current smoker	439 (21.96)	127 (25.08)	115 (23.58)	96 (19.38)	101 (19.95)	
BMI (kg/m2), No. (%)						< 0.001
≤ 25	483 (21.58)	101 (16.87)	81 (13.67)	118 (21.20)	183 (33.81)	
> 25	1700 (78.42)	445 (83.13)	464 (86.33)	427 (78.80)	364 (66.19)	
Medication use						
Antihypertensives	1345 (58.16)	357 (62.72)	350 (59.31)	330 (57.31)	308 (53.47)	0.1114
Lipid-lowering drugs	924 (42.92)	197 (37.60)	237 (43.23)	240 (45.01)	250 (45.52)	0.1911
Antiplatelet drugs	441 (19.45)	100 (19.02)	101 (17.32)	123 (20.04)	117 (21.00)	0.5751
Cholesterol(mmol/L)	191.00 (46.78)	193.79 (47.95)	192.33 (46.32)	194.87 (45.70)	183.60 (46.43)	0.0283
HDL (mmol/L)	50.28 (15.57)	50.48 (16.98)	49.25 (14.91)	49.71 (14.29)	51.63 (15.93)	0.171
Uric acid(umol/L)	355.86 (95.39)	374.29 (108.77)	355.92 (95.84)	354.10 (87.079)	340.68 (86.30)	0.0002
SCR (umol/L)	96.46 (66.56)	108.23 (99.85)	95.87 (62.00)	93.10 (57.43)	89.44 (29.07)	0.0012

Continuous variables were presented as the mean (standard deviation, SD). The *P* value was calculated using a weighted Student's t-test or Mann–Whitney U test. Categorical variables were presented as a percentage (%). The *P* value was calculated using the weighted chi-square test

Abbreviations: *Q* Quartile, *HDL-C* High-density lipoprotein cholesterol, *SCR* Serum creatinine

Subgroup analysis

Subgroup analysis was conducted to evaluate potential heterogeneity in the association between the CALLY index and the risk of all-cause mortality across different subgroups. As shown in Figs. 4 and 5, the analyses revealed that the association between the CALLY index and both all-cause mortality and cardiovascular mortality was consistent across various subgroups, including age, sex, race, BMI, hypertension, diabetes, income, education, and smoking status. No significant interaction was found between the baseline CALLY index and the stratified variables (p interaction > 0.05). The predictive performance of the CALLY index, CRP, albumin, and lymphocytes in predicting all-cause mortality and cardiovascular mortality in CVD patients is presented in Supplementary Table S1, further exhibiting the CALLY index's superior predictive power over individual biomarkers.

Discussion

Our study examines the association between the CALLY index and the risk of death in individuals with CVD via a publicly available database. On the basis of simple calculations of CRP, albumin, and lymphocytes,

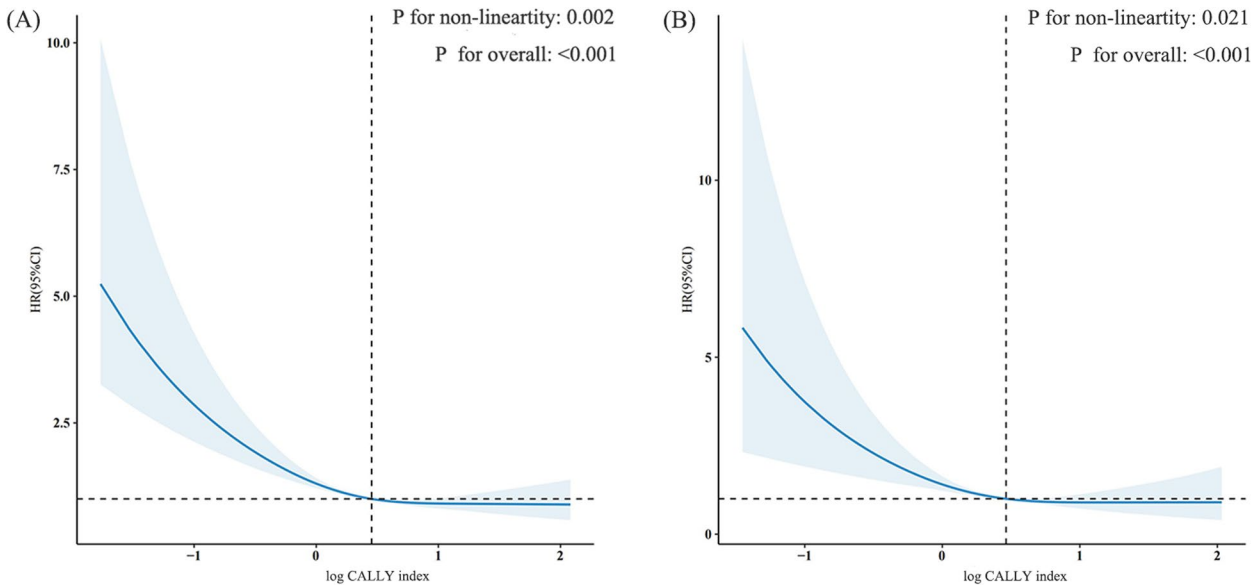

Fig. 2 Effect of log-CALLY index level on survival: hazard ratios from segmented Cox regression analysis. **A** All-cause mortality; **B** Cardiovascular mortality

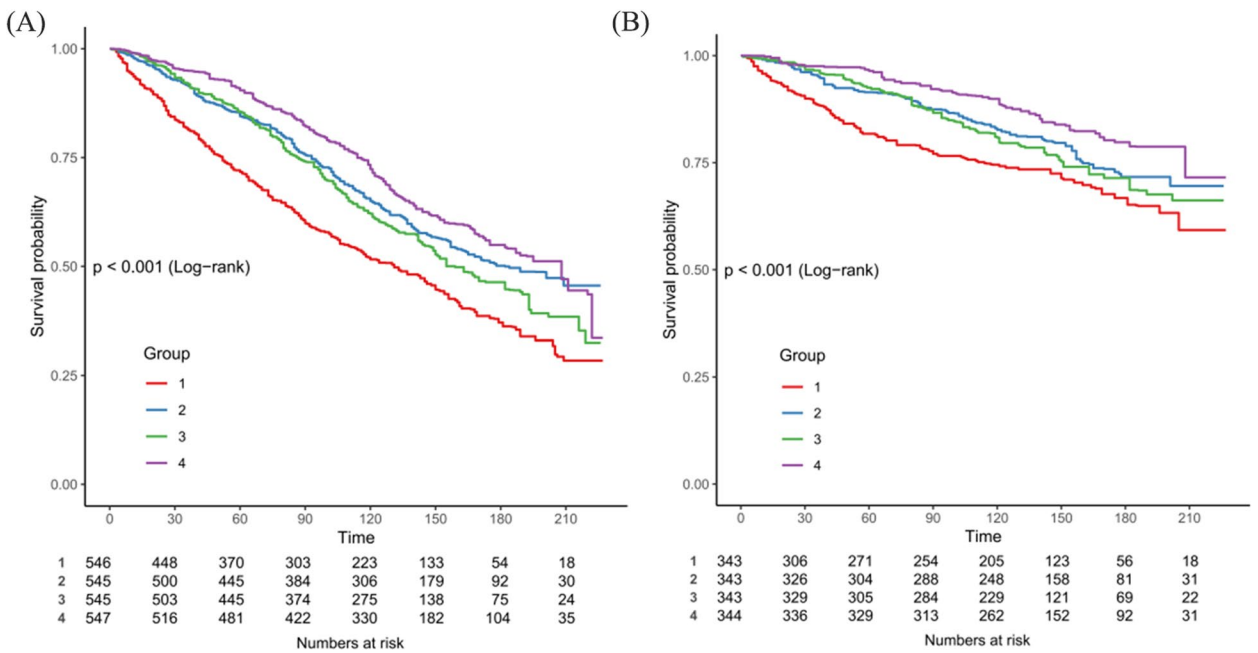

Fig. 3 Kaplan-Meier curves for survival probability, with follow-up in years. **A** All-cause mortality; **B** Cardiovascular mortality

we found an association between the CALLY index and mortality in individuals with CVD. A lower CALLY index was significantly associated with increased rates of both all-cause mortality and cardiovascular mortality. The CALLY index emerged as an independent predictor of survival, even after adjusting for common risk factors.

The majority of cardiovascular diseases start with an inflammatory process. Atherosclerosis serves as a fundamental mechanism in the development of CVD, wherein inflammation plays a pivotal role in both disease initiation and progression [31, 32]. Inflammation exacerbates local and systemic inflammatory states by promoting endothelial cell injury, accelerating the infiltration of

Table 2 Weighted Cox analysis model between CALLY index with all-cause and cardiovascular mortality among individuals with cardiovascular disease

Characteristic	Crude model		Model 1		Model 2	
	HRs(95%CI)	*P*-value	HRs(95%CI)	*P*-value	HRs(95%CI)	*P*-value
All-cause mortality						
CALLY index category						
Quartile 1	Ref		Ref		Ref	
Quartile 2	0.64 (0.51, 0.80)	< 0.001	0.56 (0.45, 0.69)	< 0.001	0.60 (0.50,0.74)	< 0.001
Quartile 3	0.74 (0.61, 0.90)	0.003	0.58 (0.48, 0.70)	< 0.001	0.66 (0.55, 0.80)	< 0.001
Quartile 4	0.55 (0.43, 0.70)	< 0.001	0.49 (0.40, 0.60)	< 0.001	0.58 (0.48, 0.71)	< 0.001
P for trend[a]		< 0.001		< 0.001		< 0.001
Cardiovascular mortality						
CALLY index category						
Quartile 1	Ref		Ref		Ref	
Quartile 2	0.69 (0.48,0.98)	0.040	0.51 (0.35,0.75)	< 0.001	0.59 (0.40, 0.88)	0.009
Quartile 3	0.78 (0.56, 1.08)	0.134	0.55 (0.39,0.78)	< 0.001	0.64 (0.44, 0.91)	0.014
Quartile 4	0.49 (0.37, 0.66)	< 0.001	0.43 (0.31,0.59)	< 0.001	0.54 (0.38, 0.76)	< 0.001
P for trend[a]		< 0.001		< 0.001		0.002

Crude model: Non-adjusted

Model 1: Adjusted for age,race,and,gender

Model 2: Adjusted for gender, age, race, income, diabetes, uric acid, SCR, smoking status, antihypertensives, lipid-lowering drugs, and antiplatelet drugs

HR Hazard ratio, *CL* Confidence interval

[a] Linear trend tests were conducted by treating categorical variables as continuous parameters

leukocytes into the vascular wall, and compromising plaque stability, thereby increasing the risk of rupture. Furthermore, inflammation stimulates the release of cytokines and chemokines, contributing to the inflammatory cascade. Nutritional and immunological decline are among the most prevalent symptoms associated with inflammation [33]. As our understanding of the intricate pathological mechanisms underlying cardiovascular diseases continues to deepen, comprehensive evaluations of inflammation, nutritional status, and immune function have emerged as crucial tools for optimizing individual outcomes and guiding therapeutic decisions.

Given the intricate pathophysiological characteristics of CVD, relying solely on a single biomarker may be insufficient to fully capture the multidimensional health risks of patients. Recent studies have demonstrated that several indices, including the TyG, PLR, and NLR, which are calculated on the basis of blood cell count, can serve as indicators to predict complications and poor prognoses of cardiovascular diseases [34]. The CALLY index innovatively integrates multiple physiological parameters closely associated with cardiovascular health, providing a multidimensional indicator for health risk assessment. It has the potential to be a promising prognostic marker.

CRP, an acute-phase protein, is produced by the liver in response to inflammation or cardiovascular disease [35, 36]. There is a well-established positive correlation between CRP and cardiovascular disease and all-cause mortality. Peripheral lymphocytes play a pivotal role in initiating and propagating the atherosclerotic process through the activation of B and T lymphocytes and participate in regulating immune responses at all stages of atherosclerosis. A low lymphocyte count often indicates compromised immune function. which are linked to both the incidence and mortality of cardiovascular disease. Lymphocytes are capable of regulating the inflammatory response by reducing the release of inflammatory cytokines and inhibiting the activation of neutrophils and monocytes, thereby protecting the heart from damage [37]. Moreover, low serum albuminlevels are strongly negatively correlated with the risk of death from cardiovascular diseases [38–40]. Low albumin levels may reflect a systemic inflammatory response and a malnutritional state [41]. Several studies have indicated that serum albumin possesses both anti-inflammatory and immunomodulatory attributes [42]. Reduced albumin synthesis due to inflammation may compromise the immune system and suppress cellular immunity [43, 44]. Some studies have suggested that low albumin levels may lead to hyperviscosity and abnormal blood coagulation, which are involved in the regulation of glucose homeostasis, lipid metabolism [45] and energy balance and are closely related to metabolic diseases such as diabetes [46]

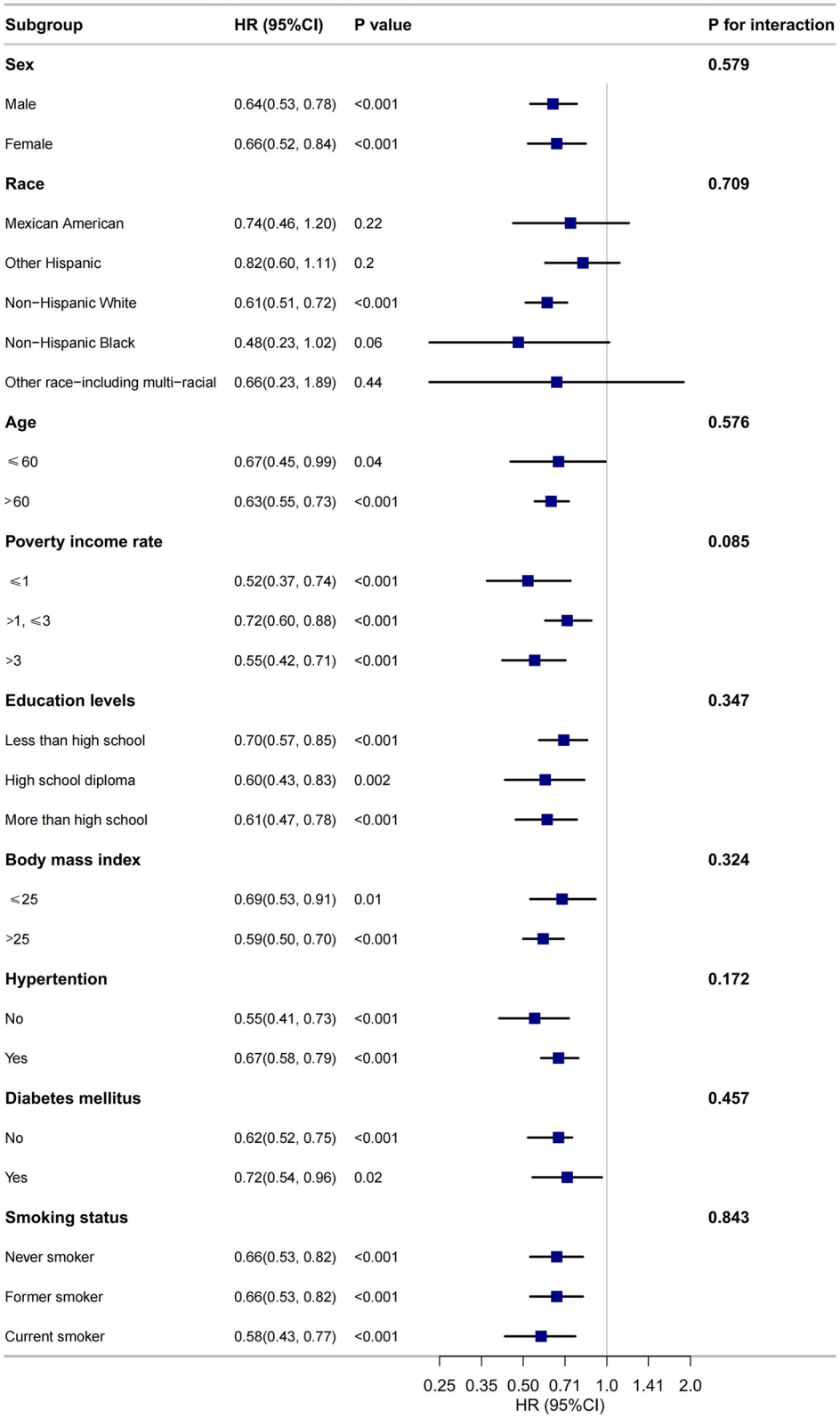

Fig. 4 Subgroup analysis of the associations between the CALLY index and all-mortality

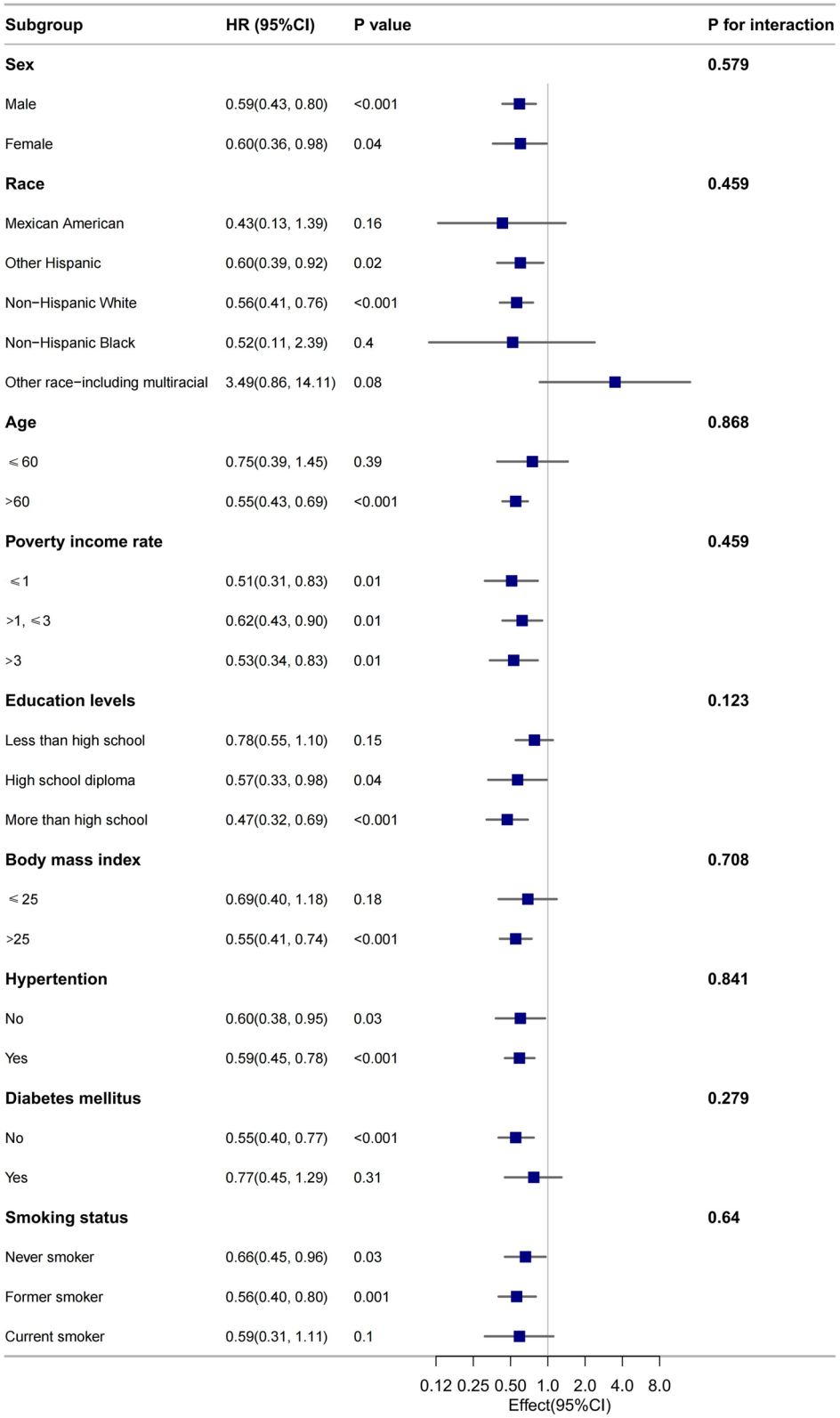

Fig. 5 Subgroup analysis of the associations between the CALLY index and cardiovascular mortality

and hypertension [47], which in turn affect the incidence and prognosis of cardiovascular disease. Moreover, the serum albumin level, CRP level and lymphocyte count are susceptible to a variety of physiological and pathological factors. The interaction between inflammation, nutrition and immunity creates a complex vicious cycle that can further promote the progression of cardiovascular disease. By combining the CALLY index with representative indicators such as inflammation (CRP), nutrition (serum albumin) and immunity (lymphocyte), the prognostic value of these three indicators can be fully utilized, and the prognosis can be comprehensively predicted by utilizing their interaction. The CALLY index observed in CVD patients in this study can be explained by low lymphocyte values, low albumin values, and high CRP values, which are generally consistent with the results observed in our study. This may be related primarily to the inflammatory response. Further research could investigate the potential of the CALLY index in the early screening and diagnosis of CVD, as well as its use in treatment and follow-up.

The strengths of our study include the inclusion of a large sample size of individuals and a substantial follow-up duration. Additionally, all individuals were sourced from the NHANES survey, which mitigates the risk of selection bias. However, there are noteworthy potential issues or limitations that should be mentioned. First, CRP levels, albumin levels, and lymphocyte counts were only assessed at baseline. Further assessments at more frequent intervals would allow for a more accurate evaluation of the association between the CALLY index and mortality risk. The CALLY index may also be influenced by other unknown factors. Future research should combine the CALLY index with other emerging biomarkers and clinical parameters to increase its sensitivity and specificity in predicting cardiovascular events. Moreover, as the findings are based on a sample size determined by the NHANES study conducted from 2001–2010, the results require validation in a larger and different population.

Conclusion

We revealed that an increased CALLY index is associated with a lower hazard of all-cause heart disease mortality among U.S. adults. Our findings indicate the importance of incorporating the CALLY index into routine clinical practice as a biomarker for predicting all-cause and cardiovascular mortality.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12872-025-04596-w.

Supplementary Material 1.

Acknowledgements
The authors thank the NHANES 2001--2010 participants for their invaluable contributions.

Authors' contributions
Study concept and design: HB Zhou, SR Liu and DZ Han; acquisition of data: LL Wu, SW Su, and Z Ma; analysis and interpretation of data: YT Xue and SF He; drafting of the manuscript: LL Wu, PX Li and SW Su; critical revision of the manuscript: Zheng Huang.

Funding
This project was supported by the National Outstanding Youth Science Fund Project of the National Natural Science Foundation of China. (No. 82100263).

Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
The National Center for Health Statistics and the Ethics Review Board approved the protocol for NHANES, and all participants provided written informed consent. The authors have disclosed no conflicts of interest.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Author details
[1]Department of Cardiology, The First Affiliated Hospital, Guangzhou Medical University, 151 Yanjiang West Road, Guangzhou, Guangdong 510120, China.

Received: 11 August 2024 Accepted: 19 February 2025
Published online: 03 March 2025

References

1. Garbers S, et al. Healthy weight and cardiovascular health promotion interventions for adolescent and young adult males of color: a systematic review. Am J Mens Health. 2018;12(5):1328–51.
2. Virani SS, et al. Heart disease and stroke statistics-2020 update: a report from the American Heart Association. Circulation. 2020;141(9):e139–596.
3. Luo S, et al. Predictive value of baseline C-reactive protein level in patients with stable coronary artery disease: a meta-analysis. Medicine (Baltimore). 2022;101(35):e30285.
4. Yu H, et al. Effect of omega-3 fatty acids on chronic obstructive pulmonary disease: a systematic review and meta-analysis of randomized controlled trials. Int J Chron Obstruct Pulmon Dis. 2021;16:2677–86.
5. de Ulíbarri Pérez JI, et al. Nutritional screening; control of clinical undernutrition with analytical parameters. Nutr Hosp. 2014;29(4):797–811.
6. Shaper AG, Wannamethee SG, Whincup PH. Serum albumin and risk of stroke, coronary heart disease, and mortality: the role of cigarette smoking. J Clin Epidemiol. 2004;57(2):195–202.
7. Nelson JJ, et al. Serum albumin level as a predictor of incident coronary heart disease: the Atherosclerosis Risk in Communities (ARIC) study. Am J Epidemiol. 2000;151(5):468–77.
8. Ilatovskaya DV, Halade GV, DeLeon-Pennell KY. Adaptive immunity-driven inflammation and cardiovascular disease. Am J Physiol Heart Circ Physiol. 2019;317(6):H1254-h1257.
9. Wu S, et al. The association between systemic immune-inflammation index and all-cause mortality in acute ischemic stroke patients: analysis from the MIMIC-IV database. Emerg Med Int. 2022;2022:4156489.
10. Iida H, et al. Superiority of CRP-albumin-lymphocyte index (CALLY index) as a non-invasive prognostic biomarker after hepatectomy for hepatocellular carcinoma. HPB (Oxford). 2022;24(1):101–15.
11. Yang M, et al. Association between C-reactive protein-albumin-lymphocyte (CALLY) index and overall survival in patients with colorectal cancer:

From the investigation on nutrition status and clinical outcome of common cancers study. Front Immunol. 2023;14:1131496.
12. Tsunematsu M, et al. The impact of C-reactive protein-albumin-lymphocyte (CALLY) index on the prognosis of patients with distal cholangiocarcinoma following pancreaticoduodenectomy. Ann Gastroenterol Surg. 2023;7(3):503–11.
13. Furukawa K, et al. Impact of C-reactive protein-albumin-lymphocyte (CALLY) index on prognosis after hepatectomy for colorectal liver metastasis. Surg Oncol. 2023;47:101911.
14. Takeda Y, et al. Prognostic usefulness of the C-reactive protein-albumin-lymphocyte (CALLY) index as a novel biomarker in patients undergoing colorectal cancer surgery. Asian J Surg. 2024;47(8):3492–8.
15. Ma R, et al. Clinical implications of C-reactive protein-albumin-lymphocyte (CALLY) index in patients with esophageal cancer. Surg Oncol. 2024;53:102044.
16. Hashimoto I, et al. Clinical Impact of the C-reactive Protein-albumin-lymphocyte Index in post-gastrectomy patients with gastric cancer. In Vivo. 2024;38(2):911–6.
17. Fukushima N, et al. Prognostic significance of the preoperative C-reactive protein-albumin-lymphocyte (CALLY) index on outcomes after gastrectomy for gastric cancer. Surg Today. 2024;54(8):943–52.
18. Liu XY, et al. The value of CRP-albumin-lymphocyte index (CALLY index) as a prognostic biomarker in patients with non-small cell lung cancer. Support Care Cancer. 2023;31(9):533.
19. Feng J, et al. Clinical significance of preoperative CALLY index for prognostication in patients with esophageal squamous cell carcinoma undergoing surgery. Sci Rep. 2024;14(1):713.
20. Luo L, et al. C-reactive protein-albumin-lymphocyte index as a feasible nutrition-immunity-inflammation marker of the outcome of all-cause and cardiovascular mortality in elderly. Clin Nutr ESPEN. 2024;63:346–53.
21. Ding Y, et al. The Association Between the CALLY Index and All-Cause Mortality in Patients with COPD: Results from the Cohort Study of NHANES 2007–2010. Int J Chron Obstruct Pulmon Dis. 2025;20:159–69.
22. Xu Z, et al. Associations of C-reactive protein-albumin-lymphocyte (CALLY) index with cardiorenal syndrome: insights from a population-based study. Heliyon. 2024;10(17):e37197.
23. Li Y, et al. Higher CALLY index levels indicate lower sarcopenia risk among middle-aged and elderly community residents as well as hospitalized patients. Sci Rep. 2024;14(1):24591.
24. Wu L, et al. Association between the C-reactive protein-albumin-lymphocyte index and metabolic syndrome: evidence from the 2003–2010 national health and nutrition examination survey. Diabetol Metab Syndr. 2025;17(1):39.
25. Zhang Q, et al. The triglyceride-glucose index is a predictor for cardiovascular and all-cause mortality in CVD patients with diabetes or pre-diabetes: evidence from NHANES 2001–2018. Cardiovasc Diabetol. 2023;22(1):279.
26. McQuillan GM, McLean JE, Chiappa M, Corporation H, Lukacs SL. National Health and Nutrition Examination Survey Biospecimen Program: NHANES III (1988–1994) and NHANES 1999–2014. Vital Health Stat. 2015;2(170):1–14.
27. Di D, et al. Exposure to phenols, chlorophenol pesticides, phthalate and PAHs and mortality risk: a prospective study based on 6 rounds of NHANES. Chemosphere. 2023;329:138650.
28. Chen Y, et al. Magnesium depletion score predicts diabetic retinopathy risk among diabetes: findings from NHANES 2005–2018. Biol Trace Elem Res. 2023;201(6):2750–6.
29. Yuan M, et al. Hypertension and NAFLD risk: Insights from the NHANES 2017–2018 and Mendelian randomization analyses. Chin Med J (Engl). 2024;137(4):457–64.
30. Johnson CL, Paulose-Ram R, Ogden CL, Carroll MD, Kruszon-Moran D, Dohrmann SM, Curtin LR. National health and nutrition examination survey: analytic guidelines, 1999–2010. Vital Health Stat. 2013;2(161):1–24.
31. Kim KW, Ivanov S, Williams JW. Monocyte recruitment, specification, and function in atherosclerosis. Cells. 2020;10(1):15.
32. Fearon WF, Fearon DT. Inflammation and cardiovascular disease: role of the interleukin-1 receptor antagonist. Circulation. 2008;117(20):2577–9.
33. Macciò A, et al. Editorial: biological mechanism-based and patient-centered management of cancer-related symptoms and syndromes. Front Physiol. 2018;9:1819.
34. Dick SA, Epelman S. Chronic heart failure and inflammation: what do we really know? Circ Res. 2016;119(1):159–76.
35. Miller VM, Redfield MM, McConnell JP. Use of BNP and CRP as biomarkers in assessing cardiovascular disease: diagnosis versus risk. Curr Vasc Pharmacol. 2007;5(1):15–25.
36. Vilian ATE, et al. Efficient electron-mediated electrochemical biosensor of gold wire for the rapid detection of C-reactive protein: a predictive strategy for heart failure. Biosens Bioelectron. 2019;142:111549.
37. Charach G, et al. Usefulness of total lymphocyte count as predictor of outcome in patients with chronic heart failure. Am J Cardiol. 2011;107(9):1353–6.
38. Grimm G, et al. Sex differences in the association between albumin and all-cause and vascular mortality. Eur J Clin Invest. 2009;39(10):860–5.
39. Cheng YL, et al. Prognostic Nutritional Index and the Risk of Mortality in Patients With Acute Heart Failure. J Am Heart Assoc. 2017;6(6):e004876.
40. Patel A, et al. Frailty and outcomes after myocardial infarction: insights from the CONCORDANCE registry. J Am Heart Assoc. 2018;7(18):e009859.
41. Fanali G, et al. Human serum albumin: from bench to bedside. Mol Aspects Med. 2012;33(3):209–90.
42. Chen Z, et al. Preoperative albumin to globulin ratio predicts survival in clear cell renal cell carcinoma patients. Oncotarget. 2017;8(29):48291–302.
43. He X, et al. Preoperative Albumin to Globulin Ratio (AGR) as prognostic factor in renal cell carcinoma. J Cancer. 2017;8(2):258–65.
44. Liu X, Guo X, Zhang Z. Preoperative Serum Hypersensitive-c-Reactive-Protein (Hs-CRP) to Albumin Ratio Predicts Survival in Patients with Luminal B Subtype Breast Cancer. Onco Targets Ther. 2021;14:4137–48.
45. Abdollahi A, et al. Albumin knockout mice exhibit reduced plasma free fatty acid concentration and enhanced insulin sensitivity. Physiol Rep. 2022;10(5):e15161.
46. Matsuura S, et al. Sarcopenia is associated with the Geriatric Nutritional Risk Index in elderly patients with poorly controlled type 2 diabetes mellitus. J Diabetes Investig. 2022;13(8):1366–73.
47. Choi JW, Park JS, Lee CH. Genetically determined hypoalbuminemia as a risk factor for hypertension: instrumental variable analysis. Sci Rep. 2021;11(1):11290.

Publisher's Note