Research paper

C-reactive Protein-Albumin-Lymphocyte (CALLY) Index in Chronic Kidney Disease and Mortality: Insights into Inflammation, Nutrition, and Immune Status

Keywords

Chronic kidney disease, Immune function, Nutritional status, Inflammatory markers, Population-based study

Abstract

Introduction

The C-reactive protein-albumin-lymphocyte (CALLY) index represents a novel composite biomarker integrating inflammatory, nutritional, and immune parameters. We aim to examine the relationship between CALLY index and chronic kidney disease (CKD) prevalence.

Material and methods

This cross-sectional analysis utilized data from the National Health and Nutrition Examination Survey. CKD was defined as an estimated glomerular filtration rate (eGFR) <60 mL/min/1.73m² and/or urinary albumin-to-creatinine ratio (UACR) ≥30 mg/g. Multivariable logistic regression and restricted cubic spline (RCS) analyses assessed the relationship between CALLY index and the CKD prevalence. Among CKD patients, Cox proportional hazards models evaluated CALLY index's associations with all-cause and cardiovascular mortality.

Results

Among the 26996 participants, 4997 individuals were diagnosed with CKD. Participants with CKD demonstrated lower CALLY index values compared to those without CKD. Multivariable logistic regression indicated compared to the lowest quartile, the highest quartile showed 29.5% reduced CKD risk (OR: 0.705, 95% CI: 0.589-0.845, p<0.001). RCS model demonstrated a significant L-shaped association between CALLY index and the CKD prevalence. Among CKD patients, higher CALLY index significantly predicted better survival outcomes for both all-cause and cardiovascular mortality.

Conclusions

The CALLY index demonstrates inverse associations with CKD risk and mortality, suggesting its potential utility as a comprehensive biomarker for CKD risk stratification and prognosis assessment.

C-reactive Protein-Albumin-Lymphocyte (CALLY) Index in Chronic Kidney Disease and Mortality: Insights into Inflammation, Nutrition, and Immune Status

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ABSTRACT

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Methods: This cross-sectional analysis utilized data from the National Health and Nutrition Examination Survey. CKD was defined as an estimated glomerular filtration rate (eGFR) <60 mL/min/1.73m² and/or urinary albumin-to-creatinine ratio (UACR)

≥30 mg/g. Multivariable logistic regression and restricted cubic spline (RCS) analyses assessed the relationship between CALLY index and CKD risk. Among CKD patients, Cox proportional hazards models evaluated CALLY index's associations with all-cause and cardiovascular mortality.

Results: Among the 26996 participants, 4997 individuals were diagnosed with CKD. Participants with CKD demonstrated lower CALLY index values compared to those without CKD. Multivariable logistic regression indicated compared to the lowest quartile, the highest quartile showed 29.5% reduced CKD risk (OR: 0.705, 95% CI: 0.589-0.845, $p<0.001$). RCS model demonstrated a significant L-shaped association between CALLY index and the CKD prevalence. Among CKD patients, higher CALLY index significantly predicted better survival outcomes for both all-cause and cardiovascular mortality.

Conclusions: The CALLY index demonstrates inverse associations with CKD risk and mortality, suggesting its potential utility as a comprehensive biomarker for CKD risk stratification and prognosis assessment.

Keywords: Chronic kidney disease; Inflammatory markers; Nutritional status; Immune function; Population-based study

1. Introduction

Chronic kidney disease (CKD) affects approximately 10-15% of the global population, significantly increasing patients' cardiovascular event risk and all-cause mortality while imposing a substantial economic burden on healthcare systems [1,2]. Given this formidable disease burden, early identification of high-risk populations for CKD and accurate prognostic risk assessment in diagnosed patients hold paramount clinical significance for disease prevention, early intervention, and the development of individualized therapeutic strategies [3,4].

The development and progression of CKD represents a complex process involving multiple pathophysiological mechanisms, primarily encompassing chronic inflammatory responses, oxidative stress, endothelial dysfunction, immune system dysregulation, and nutritional-metabolic abnormalities [5-10]. Based on the complexity and diversity of CKD pathogenesis, composite biomarkers that integrate multiple pathophysiological pathways have demonstrated significant advantages in disease risk prediction and prognostic assessment in recent years [11,12]. The CALLY index, as an emerging composite biomarker, is calculated using albumin, lymphocyte, and c-reactive protein (CRP), quantifying the complex interactions among inflammatory cascades, nutritional status, and immune function, potentially providing a more comprehensive and precise information integration platform for disease risk prediction and prognostic assessment [13,14]. However, despite the demonstrated prognostic predictive value of the CALLY index in oncology and cardiovascular disease fields, its application research in renal disease remains relatively sparse, representing a significant research gap [14-19].

To address this critical knowledge gap, we utilized the National Health and Nutrition Examination Surveys (NHANES) data to conduct systematic analysis of relationships between the CALLY index and CKD prevalence, including its prognostic value among CKD patients in a nationally representative study population. We hypothesized that the CALLY index would demonstrate significant associations with CKD risk and mortality outcomes, with higher values indicating better prognosis.

2. Materials and methods

2.1 Study population

Data for this investigation originated from NHANES, a comprehensive national survey administered by the National Center for Health Statistics within the Centers for Disease Control and Prevention (CDC) structure. The survey utilizes a stratified, multistage randomized sampling framework to achieve national U.S. population representation. The study received ethical approval from the National Center for Health Statistics (NCHS) Ethics Review Board (https://www.cdc.gov/nchs/nhanes/about/erb.html) (Protocol #98-12 for 1999-2004; Protocol #2005-06 for 2005-2010). The analysis incorporated six consecutive NHANES examination cycles conducted from 1999-2000 to 2009-2010 (https://wwwn.cdc.gov/nchs/nhanes). Participants across these cycles completed comprehensive questionnaires and underwent extensive physical examinations and laboratory assessments [20]. Exclusion criteria included individuals below 20 years of age, pregnant participants, and those with missing CALLY index, estimated glomerular filtration rate (eGFR), and urinary albumin-to-creatinine ratio (UACR) data, yielding a final study sample of 26996 subjects.

2.2 Calculation of CALLY index and definition of CKD

The CALLY index was computed using the formula: albumin (g/L) × lymphocyte count (10^9/L) / [CRP (mg/L) × 10] [13]. CKD identification was established through an eGFR under 60 mL/min/1.73 m^2 and/or UACR ≥30 mg/g, indicating albuminuria [21]. The eGFR calculation employed the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation, which integrates patient age, sex, race, and serum creatinine (Scr) concentrations [22].

2.3 Mortality

The research utilized the NHANES Public-Use Linked Mortality File encompassing data through December 31, 2019, employing probabilistic algorithms to match National Death Index (NDI) records for mortality status verification. Follow-up time for CKD study participants was determined by the interval spanning from baseline evaluation to the most recent documented survival date or censoring in the mortality file. The investigation's main endpoints comprised all-cause mortality and cardiovascular deaths within the CKD study population. Cardiovascular-related mortality was specified according to International Statistical Classification of Diseases, 10th Revision (ICD-10) standards and NCHS categorization of heart disease (054-068) and cerebrovascular conditions (070).

2.4 Covariates

Several confounding factors were included in our analysis. Demographics encompassed age, sex, race (Mexican American, Non-Hispanic White, Non-Hispanic Black, Other Hispanic, other races), marital status (married/unmarried), poverty-income ratio (PIR), and educational achievement (above high school or not). Behavioral factors included smoking history (former/current users). Clinical parameters comprised hypertension, diabetes, cardiovascular diseases (CVDs), and biomarkers: body mass index (BMI), triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-c), and low-density lipoprotein cholesterol (LDL-c), and uric acid (UA). Hypertension was identified by self-reported diagnosis, average systolic/diastolic blood pressure ≥140/90 mmHg, or antihypertensive medication. Diabetes was defined through self-report, fasting plasma glucose (FPG) ≥7.0 mmol/L, hemoglobin A1c (HbA1c) ≥6.5%, or current use of antidiabetic medications. CVDs included coronary heart disease, myocardial infarction, stroke, heart failure, and angina.

2.5 Statistical analysis

A population-weighted, multi-stage survey design was implemented following the Centers for Disease Control and Prevention (CDC) weighting standards. Descriptive analyses presented continuous variables as weighted means with 95% confidence intervals (CI) and categorical variables as unweighted frequencies with weighted percentages. Statistical comparisons employed weighted t-tests for continuous measures and chi-square tests for categorical outcomes. The CALLY index-CKD relationship was analyzed using three logistic regression models: unadjusted baseline, demographic-controlled (age, sex, race, marital status, PIR, education level, and smoking history), and fully adjusted incorporating hypertension, diabetes mellitus, CVDs, BMI, TG, HDL-c, LDL-c, and UA levels. SHapley Additive exPlanations (SHAP) values were further implemented to elucidate feature contributions. Rooted in game theory's Shapley framework, SHAP values enable equitable allocation of influence for each predictor across specific instances during model inference. Feature importance and swarm plot visualizations were generated for the top 10 predictors. Dose-response associations were examined via restricted cubic spline (RCS) methodology using four knots with median Ln CALLY index as referent category. Covariate-specific subgroup analyses were also performed. Survival analysis utilized Cox proportional hazards modeling to evaluate CALLY index associations with all-cause and cardiovascular mortality among CKD patients. Kaplan-Meier estimation calculated cumulative mortality risk across CALLY index quartiles, with log-rank testing comparing survival distributions. Statistical analysis was performed using R software, with statistical significance set at two-sided $p<0.05$.

3. Results

3.1 Baseline characteristics

Table 1 data reveal pronounced differences between CKD and non-CKD subjects. Participants with CKD showed advanced age, increased female proportion, and distinctive racial composition featuring higher Non-Hispanic Black and lower Mexican American percentages ($p<0.001$). Socioeconomic indicators demonstrated reduced PIR and educational attainment ($p<0.001$). Enhanced comorbidity prevalence encompassed hypertension, diabetes, and CVDs ($p<0.001$). Physical parameters showed elevated BMI, while lipid evaluations indicated increased TG and reduced LDL-c, with unaltered TC and HDL-c ($p<0.001$). Laboratory findings included higher UA, CRP, and UACR concentrations, coupled with decreased albumin, lymphocyte levels, and eGFR, yielding lower CALLY measurements (p<0.001). **Table 2** presents ordered variations across CALLY index categories. Lower categories contained older participants with female predominance and elevated Non-Hispanic Black representation (p<0.001). Socioeconomic factors improved systematically across categories, reflected in increasing PIR and educational standards (p<0.001). Disease prevalence diminished substantially from lower to higher categories, affecting hypertension, diabetes, and CVDs (p<0.001). BMI showed progressive decrease across categories (p<0.001). TG and TC achieved maximum levels in category two, HDL-c rose continuously, while LDL-c peaked in category two (p<0.001). Biomarker trajectories were distinct: UA, CRP, and UACR decreased systematically, whereas albumin, lymphocytes, and eGFR increased correspondingly (p<0.001). CKD incidence correlated negatively with CALLY categories (p<0.001).

Table 1 Demographic and Clinical Characteristics of Participants by CKD Status.

Table 2 Demographic and Clinical Characteristics of Participants by CALLY Index Quartiles.

3.2 Associations between CALLY index and CKD

The multivariable logistic regression findings presented in **Table 3** illustrate the relationship between Ln CALLY index and CKD susceptibility using three sequential adjustment models. When stratified by quartiles, the analysis revealed a consistent inverse dose-dependent pattern, utilizing the first quartile (Q1) as the baseline comparator. Statistical significance for trend was observed across all models, with ascending CALLY quartiles associated with decreased CKD susceptibility (p<0.001). The comprehensive adjustment model indicated that Q2 participants experienced a 22.3% significant reduction in risk (OR: 0.777, 95% CI: 0.672-0.898, p<0.001), while Q3 showed significant risk attenuation of 24.1% (OR: 0.759, 95% CI: 0.650-0.885, p<0.001). The uppermost quartile (Q4) provided maximum protection, reducing risk by 29.5% relative to the reference group (OR: 0.705, 95% CI: 0.589-0.845, p<0.001). SHAP analysis identified age as the strongest predictor for CKD, followed closely by UA, hypertension, and diabetes (**Figure 1a**). Ln CALLY was ranked sixth in terms of contribution, indicating a moderate meaningful role in CKD risk (**Figure 1a**). Swarm plot results showed that higher Ln CALLY values (highlighted in yellow) corresponded to lower SHAP scores, implying a reduced risk of CKD (**Figure 1b**). Further RCS modeling validated a L-shaped relationship between Ln CALLY index and CKD risk (**Figure 2**). Subsequent piecewise regression analysis identified the optimal inflection point at Ln CALLY index = 0.543 (**Table 4**). Below this threshold, each unit increase in Ln CALLY index corresponded to a 24.7% risk reduction (OR: 0.753, 95% CI: 0.674-0.842, p<0.001), while above the inflection point, the protective effect plateaued (OR: 0.955, 95% CI: 0.889-1.027, p=0.218).

Table 3 Multivariable Logistic Regression Analysis of CALLY Index and CKD Risk.

Figure 1 SHAP Value Analysis of Predictive Features. (a) Mean Absolute SHAP Value Ranking of Top 10 Features (b) SHAP Value Distribution Swarm Plot Showing Top 10 Features Impact and Value Relationships.

Figure 2 Restricted Cubic Spline Curve Demonstrating the Relationship Between Ln CALLY Index and CKD Risk.

Table 4 Piecewise Regression Analysis of CALLY Index Threshold Effects on CKD Risk.

3.3 Subgroup analyses

Subgroup analysis confirmed the protective association between the Ln CALLY index and CKD was robust across age divisions (<60 years: OR 0.859, ≥60 years: OR 0.892), BMI categories (<25 kg/m²: OR 0.900, 25-30 kg/m²: OR 0.850, ≥30 kg/m²: OR 0.881), and disease status (non-diabetic: OR 0.879, diabetic: OR 0.877; non-hypertensive: OR 0.907, hypertensive: OR 0.863; non-CVDs: OR 0.877, CVDs: OR 0.884), with all interaction p>0.05, validating the homogeneous effects across these patient characteristics. However, a statistically significant interaction by sex was detected (p for interaction = 0.014), suggesting the protective effect was more pronounced in males (OR 0.831) compared to females (OR 0.931) (**Figure 3**).

Figure 3 Subgroup-Specific Associations Between Ln CALLY Index and CKD Risk.

3.4 Associations between CALLY index and mortality among CKD patients

We examined 4993 CKD patients for CALLY index-mortality correlations after excluding 4 cases with missing mortality information. Throughout 125 months median tracking, 2653 all-cause fatalities were recorded, with 980 deaths from cardiovascular origins. Kaplan-Meier survival function analysis revealed significantly reduced cumulative death risks for both total and cardiovascular mortality when contrasting highest with lowest CALLY index quartiles (p<0.001) (**Figure 4**). Fully adjusted Cox proportional hazards analysis showed that higher log (CALLY index) baseline concentrations significantly decreased all-cause death risk (HR=0.862, 95%CI: 0.816-0.910, p<0.001) and cardiovascular mortality risk (HR=0.885, 95%CI: 0.808-0.970, p=0.009) (**Table 5**). Complete model adjustment demonstrated that fourth-quartile subjects had 0.622-fold reduced all-cause mortality risk and 0.697-fold decreased cardiovascular death risk compared to first-quartile subjects.

Figure 4 Kaplan-Meier Survival Curves for All-Cause and Cardiovascular Mortality According to CALLY Index Quartiles.

Table 5 Multivariable Cox Regression Analysis of CALLY Index and Mortality Outcomes among CKD Patients.

4. Discussion

Our analysis of the NHANES database establishes a remarkable non-linear, L-shaped inverse correlation between the CALLY index and CKD risk, while simultaneously demonstrating its prognostic significance for both all-cause and cardiovascular mortality in CKD individuals.

Compared to single biomarkers, composite indices can simultaneously capture multidimensional pathophysiological information involved in disease development and progression, providing more accurate and comprehensive risk assessment capabilities [23]. The prognostic role of the CALLY index was first systematically investigated in oncology. A low CALLY index is an independent predictor of all-cause and cardiovascular mortality among patients with cancer [16]. We also observed a similar pattern in our CKD cohort, where a lower CALLY score corresponds to a poorer mortality outcome. Additionally, the application of the CALLY index has been further translated to the cardiometabolic area. Research in this field indicates that a low index value is associated with an increased risk of adverse cardiovascular events, including a higher incidence of stroke in the hypertensive population [18]. Moreover, an association between the CALLY index and cardiorenal syndrome has been documented by Zhehao Xu et al. in the U.S. population [15]. The CALLY index integrates three fundamental pathophysiological components that collectively reflect the complex interplay between nutritional homeostasis, immune competence, and inflammatory burden in renal disease progression. Serum albumin, as a classic biomarker reflecting nutritional status and hepatic synthetic function, exhibits decreased levels that represent a significant manifestation of protein-energy wasting syndrome in CKD patients [24-26]. Hypoalbuminemia is also associated with poor prognosis in CKD patients [26,27]. CKD accompany the alterations of immune system [28]. Lymphocyte count, serving as an important indicator of immune function, might reflect damage to the hematopoietic and immune systems caused by the uremic environment when reduced, as well as Th1/Th2 immune response imbalance and regulatory T cell dysfunction [29-32]. Lymphocyte depletion may be associated with CKD progression to some extent [28]. CRP, as an acute phase reactant and sensitive marker of systemic inflammation, may participate in the renal injury process through mechanisms such as complement system activation and promotion of endothelial dysfunction when persistently elevated, and may be related to upregulated expression of fibrosis-related genes [33,34]. Elevated CRP levels show a positive correlation trend with CKD incidence risk [35,36]. Previously, He et al. also reported the association between the C-reactive protein to lymphocyte ratio (CLR) and the prevalence of CKD in US adults [34]. Additionally, this non-linear L-shaped pattern reveals a threshold phenomenon wherein CKD risk demonstrates substantial reduction with moderate increases in CALLY values, followed by a plateau phase where additional index elevation yields diminishing protective returns. Such biphasic behavior suggests that therapeutic strategies targeting nutritional optimization, immune preservation, and inflammatory control may exhibit maximal effectiveness in populations with lower baseline CALLY scores, while individuals with elevated indices might require alternative risk mitigation approaches focused on conventional cardiovascular risk factors. Given that our analysis was based on NHANES, the elevated mean BMI likely reflects the high prevalence of overweight/obesity in the U.S. adult population rather than selection bias [37,38]. Because BMI is closely linked to metabolic dysregulation and low-grade inflammation, we adjusted for BMI in the fully adjusted models, and the associations were generally consistent across BMI categories.

This study has several limitations that warrant consideration. The cross-sectional study design prevents determination of causal associations between the CALLY index and CKD risk. Although NHANES offers population-representative data, the limited follow-up duration may not adequately capture the long-term predictive capacity of the CALLY index, while the use of single laboratory values for CKD diagnosis could compromise diagnostic precision. Additionally, we adjusted for multiple covariates. However, some factors (e.g., medications, diet, and other inflammatory/immune biomarkers) were unavailable across NHANES cycles, and residual confounding may remain. Finally, although the CALLY index integrates information on inflammation, nutritional status, and immune status, it may still not fully capture all dimensions of the complex pathophysiology of CKD. Future studies incorporating additional clinical parameters and emerging biomarkers may improve the precision of CKD risk stratification and prognostic assessment.

5. Conclusion

Based on large-scale NHANES data, this study found a nonlinear L-shaped negative association between the CALLY index and CKD risk and demonstrated that the CALLY index can predict all-cause and cardiovascular mortality in CKD patients. As a composite biomarker integrating inflammation, nutrition, and immunity, the CALLY index may serve as a novel tool for risk stratification and prognosis assessment in CKD.

Author Contribution

Y. S. and Y.B. wrote the manuscript. Q. S. and C. Z. prepared tables and figures. T. W. reviewed the manuscript.

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Data availability

This study utilized data from the NHANES, which is freely available to the public at https://wwwn.cdc.gov/nchs/nhanes.

Clinical Trail Number: Not applicable

Compliance with ethical standards

Conflict of Interest: No competing interests are declared by the authors.

Ethics Approval: This study used NHANES data (1999-2010) approved by the National Center for Health Statistics (NCHS) Ethics Review Board (https://www.cdc.gov/nchs/nhanes/about/erb.html) (Protocol #98-12 for 1999-2004; Protocol #2005-06 for 2005-2010). All procedures adhered to the Declaration of Helsinki.

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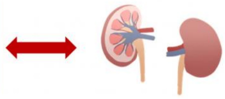
Is the novel inflammatory-nutritional-immune CALLY index associated with the prevalence of chronic kidney disease?

CALLY index

Inflammatory (CRP)
Nutrition (Albumin)
Immune (Lymphocyte)

Chronic Kidney Disease



- **Data source:** NHANES cohort (1999-2010)
- **Inclusion:** Age>20 with complete CALLY, eGFR, UACR
- **Study population:** 26,996 U.S. adults.
- **Methods:**
  Multivariable logistic regression & RCS for CKD prevalence
  Cox models for mortality in CKD subset
  Subgroup analysis

Integrates definition

Integrates nutrition, immunity, and inflammation

Sex difference

Stronger protection in men than women

CALLY Index

Albumin×lymphocyte/CRP

Prognostic value

Higher CALLY predicts lower all-cause and cardiovascular mortality

Risk association

Nonlinear effect: L-shaped inverse association with CKD risk

Multivariable logistic regression & RCS for CKD prevalence

Table 3 Multivariable Logistic Regression Analysis of CALLY Index and CKD Risk

CKD risk	Model 1	Model 2	Model 3
	OR (95%CI) P value		
Continuous			
Ln CALLY index	0.735 (0.718, 0.753) <0.001	0.833 (0.809, 0.857) <0.001	0.878 (0.837, 0.922) <0.001
Quartiles			
Q1	reference	reference	reference
Q2	0.702 (0.648, 0.761) <0.001	0.760 (0.692, 0.834) <0.001	0.777 (0.672, 0.898) <0.001
Q3	0.543 (0.499, 0.591) <0.001	0.666 (0.604, 0.735) <0.001	0.759 (0.650, 0.885) <0.001
Q4	0.357 (0.325, 0.392) <0.001	0.581 (0.521, 0.647) <0.001	0.705 (0.589, 0.845) <0.001
P for trend	<0.001	<0.001	<0.001

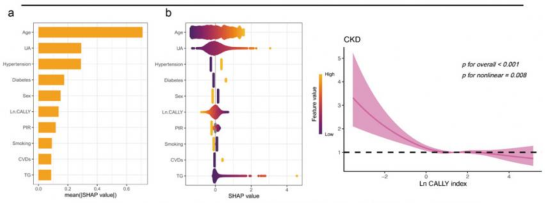


Table 4 Piecewise Regression Analysis of CALLY Index Threshold Effects on CKD Risk

Ln CALLY index	OR (95% CI) P value
Total	0.878 (0.837, 0.922) <0.001
Breakpoint	0.543
OR1 (Ln CALLY index < 0.543)	0.753 (0.674, 0.842) <0.001
OR2 (Ln CALLY index > 0.543)	0.955 (0.889, 1.027) 0.218
OR2/OR1	1.268 (1.086, 1.481) 0.003
P for logarithmic likelihood ratio	0.003

Cox models for mortality in CKD subset

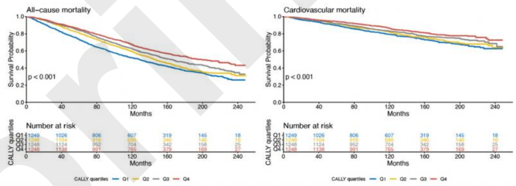


Table 1 Demographic and Clinical Characteristics of Participants by CKD Status

Characteristics	Overall (n=26996)	Non-CKD (21999)	CKD (4997)	P value
Age (years)	46.91 (46.41, 47.42)	44.55 (44.12, 44.98)	61.49 (60.63, 62.35)	<0.001
Sex, n%				<0.001
Female	13444 (51.00%)	10846 (49.96%)	2598 (57.37%)	
Male	13552 (49.00%)	11153 (50.04%)	2399 (42.63%)	
Race, n%				0.008
Mexican American	5502 (8.03%)	4637 (8.23%)	865 (6.77%)	
Other Hispanic	1822 (4.41%)	1545 (4.49%)	277 (3.93%)	
Non-Hispanic White	13476 (71.28%)	10768 (71.11%)	2708 (72.34%)	
Non-Hispanic Black	5112 (10.52%)	4143 (10.37%)	969 (11.49%)	
Other Race	1084 (5.76%)	906 (5.81%)	178 (5.46%)	
Smokers, n%	13072 (48.18%)	10513 (47.91%)	2559 (49.82%)	0.080
Married, n%	14562 (57.76%)	12028 (58.27%)	2534 (54.63%)	<0.001
PIR	3.04 (2.97, 3.11)	3.10 (3.03, 3.17)	2.69 (2.60, 2.78)	<0.001
Above high school, n%	12328 (56.43%)	10460 (58.08%)	1868 (46.19%)	<0.001
Hypertension, n%	11505 (37.21%)	7788 (31.93%)	3717 (69.73%)	<0.001
Diabetes, n%	4074 (11.29%)	2342 (8.27%)	1732 (29.95%)	<0.001
CVDs, n%	3047 (8.55%)	1679 (5.97%)	1368 (24.53%)	<0.001
BMI (kg/m2)	28.48 (28.31, 28.64)	28.31 (28.14, 28.49)	29.50 (29.21, 29.79)	<0.001
TG (mg/dL)	150.88 (148.26, 153.49)	147.84 (145.01, 150.68)	169.61 (163.64, 175.57)	<0.001
TC (mg/dL)	198.40 (197.60, 199.20)	198.52 (197.68, 199.36)	197.67 (195.79, 199.54)	0.391
HDL-c (mg/dL)	53.12 (52.71, 53.52)	53.15 (52.71, 53.58)	52.92 (52.11, 53.73)	0.598
LDL-c (mg/dL)	116.36 (115.41, 117.30)	117.18 (116.23, 118.14)	111.15 (108.89, 113.41)	<0.001
UA (mg/dL)	5.44 (5.41, 5.47)	5.35 (5.32, 5.38)	5.96 (5.89, 6.03)	<0.001
eGFR (mL/min/1.73m2)	93.94 (93.15, 94.73)	97.56 (96.92, 98.20)	71.64 (70.19, 73.09)	<0.001
UACR (mg/g)	30.86 (27.30, 34.42)	7.40 (7.25, 7.54)	175.64 (152.13, 199.15)	<0.001
Albumin (g/L)	42.75 (42.64, 42.85)	42.94 (42.83, 43.05)	41.57 (41.42, 41.73)	<0.001
Lymphocytes (10^9)	2.15 (2.13, 2.17)	2.16 (2.14, 2.17)	2.09 (2.03, 2.16)	0.041
CRP (mg/dL)	0.40 (0.39, 0.41)	0.37 (0.36, 0.39)	0.56 (0.52, 0.61)	<0.001
CALLY index	11.23 (10.76, 11.70)	11.84 (11.34, 12.35)	7.43 (6.73, 8.13)	<0.001

Data reported as weighted means and confidence intervals for continuous variables, unweighted counts and weighted percentages for categorical variables.

Abbreviation: PIR - Poverty-Income Ratio; CVDs - Cardiovascular Diseases; BMI - Body Mass Index; TG - Triglycerides; TC - Total Cholesterol; HDL-C - High-Density Lipoprotein Cholesterol; LDL-C - Low-Density Lipoprotein Cholesterol; UA - Uric Acid; eGFR - Estimated Glomerular Filtration Rate; UACR - Urinary Albumin-to-Creatinine Ratio; CRP - C-Reactive Protein; CALLY Index - C-Reactive Protein-Albumin-Lymphocyte Index; CKD - Chronic Kidney Disease.

Table 2 Demographic and Clinical Characteristics of Participants by CALLY Index Quartiles

Characteristics	Quartile 1	Quartile 2	Quartile 3	Quartile 4	P value
Age (years)	50.27 (49.66, 50.88)	49.21 (48.54, 49.89)	47.15 (46.42, 47.88)	42.29 (41.74, 42.83)	<0.001
Sex, n%					<0.001
Female	4040 (62.33%)	3521 (54.22%)	3002 (45.09%)	2881 (45.06%)	
Male	2709 (37.67%)	3228 (45.78%)	3745 (54.91%)	3870 (54.94%)	
Race, n%					<0.001
Mexican American	1345 (8.24%)	1445 (8.22%)	1450 (8.33%)	1262 (7.46%)	
Other Hispanic	414 (4.05%)	457 (4.75%)	472 (4.29%)	479 (4.51%)	
Non-Hispanic White	3269 (70.00%)	3370 (71.30%)	3413 (72.30%)	3424 (71.32%)	
Non-Hispanic Black	1548 (14.06%)	1258 (10.89%)	1112 (8.99%)	1194 (8.92%)	
Other Race	173 (3.65%)	219 (4.84%)	300 (6.09%)	392 (7.80%)	
Smokers, n%	3373 (50.01%)	3318 (49.03%)	3295 (48.55%)	3086 (45.76%)	0.001
Married, n%	3466 (55.19%)	3744 (58.72%)	3863 (60.98%)	3489 (56.06%)	<0.001
PIR	2.83 (2.74, 2.92)	3.00 (2.93, 3.08)	3.09 (3.01, 3.17)	3.19 (3.11, 3.28)	<0.001
Above high school, n%	2839 (52.05%)	2955 (54.28%)	3065 (56.01%)	3469 (61.86%)	<0.001
Hypertension, n%	3703 (49.45%)	3164 (41.68%)	2722 (36.15%)	1916 (25.23%)	<0.001
Diabetes, n%	1502 (18.90%)	1130 (12.79%)	848 (8.97%)	594 (6.37%)	<0.001
CVDs, n%	1108 (13.16%)	825 (10.11%)	661 (6.82%)	453 (5.35%)	<0.001
BMI (kg/m2)	32.46 (32.16, 32.77)	29.83 (29.58, 30.08)	27.70 (27.50, 27.91)	25.09 (24.93, 25.24)	<0.001
TG (mg/dL)	155.77 (151.22, 160.31)	164.92 (159.14, 170.70)	156.04 (150.21, 161.87)	131.16 (127.79, 134.53)	<0.001
TC (mg/dL)	198.56 (196.98, 200.14)	203.76 (202.28, 205.24)	200.71 (198.90, 202.52)	191.87 (190.65, 193.09)	<0.001
HDL-c (mg/dL)	50.69 (50.12, 51.27)	51.41 (50.79, 52.04)	52.75 (52.13, 53.37)	56.66 (56.01, 57.32)	<0.001
LDL-c (mg/dL)	116.78 (114.83, 118.73)	120.97 (119.28, 122.66)	117.15 (115.55, 118.75)	110.99 (109.23, 112.75)	<0.001
UA (mg/dL)	5.66 (5.60, 5.72)	5.57 (5.52, 5.62)	5.46 (5.41, 5.52)	5.14 (5.10, 5.19)	<0.001
eGFR (mL/min/1.73m2)	91.33 (90.30, 92.35)	91.83 (90.80, 92.86)	93.67 (92.61, 94.73)	97.89 (97.10, 98.68)	<0.001
UACR (mg/g)	52.33 (41.23, 63.43)	35.83 (28.59, 43.06)	20.49 (17.81, 23.17)	19.83 (14.94, 24.71)	<0.001
Albumin (g/L)	40.51 (40.37, 40.65)	42.28 (42.15, 42.41)	43.28 (43.17, 43.40)	44.35 (44.22, 44.48)	<0.001
Lymphocytes (10^9)	1.99 (1.96, 2.02)	2.12 (2.09, 2.15)	2.17 (2.14, 2.20)	2.27 (2.23, 2.31)	<0.001
CRP (mg/dL)	1.23 (1.19, 1.27)	0.33 (0.33, 0.34)	0.15 (0.15, 0.15)	0.05 (0.05, 0.05)	<0.001
CALLY index	0.96 (0.94 ,0.97)	2.87 (2.84 ,2.89)	6.74 (6.68 ,6.80)	29.83 (28.83 ,30.83)	<0.001
CKD, n%	1779 (20.90%)	1355 (15.48%)	1098 (12.39%)	765 (8.81%)	<0.001

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Q1	reference	reference	reference
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P for trend	<0.001	<0.001	<0.001

OR: odds ratio.

95% CI: 95% confidence interval.

Model 1: non-adjusted.

Model 2: adjusted for age, sex, race, marital status, PIR, education level, and smoking history.

Model 3: adjusted for age, sex, race, marital status, PIR, education level, smoking history, hypertension, diabetes, CVDs, BMI, TG, HDL-c, LDL-c, and UA levels.

Table 4 Piecewise Regression Analysis of CALLY Index Threshold Effects on CKD Risk

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Breakpoint	0.543
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OR2/OR1	1.268 (1.086, 1.481) 0.003
P for logarithmic likelihood ratio	0.003

OR: odds ratio.

95% CI: 95% confidence interval.

Adjusted for age, sex, race, marital status, PIR, education level, smoking history, hypertension, diabetes, CVDs, BMI, TG, HDL-c, LDL-c, and UA levels.

Table 5 Multivariable Cox Regression Analysis of CALLY Index and Mortality Outcomes among CKD Patients

	HR (95%CI), P value		
	Model 1	**Model 2**	**Model 3**
All-cause mortality			
Ln CALLY index	0.853 (0.828, 0.879) <0.001	0.860 (0.832, 0.889) <0.001	0.862 (0.816, 0.910) <0.001
Quartiles			
Q1	reference	reference	reference
Q2	0.846 (0.764, 0.937) 0.001	0.797 (0.715, 0.888) <0.001	0.807 (0.684, 0.954) 0.012
Q3	0.736 (0.662, 0.818) <0.001	0.723 (0.646, 0.809) <0.001	0.773 (0.651, 0.917) 0.003
Q4	0.610 (0.547, 0.681) <0.001	0.626 (0.557, 0.703) <0.001	0.622 (0.514, 0.751) <0.001
P for trend	<0.001	<0.001	<0.001
Cardiovascular mortality			
Ln CALLY index	0.864 (0.823, 0.907) <0.001	0.869 (0.823, 0.917) <0.001	0.885 (0.808, 0.970) 0.009
Quartiles			
Q1	reference	reference	reference
Q2	0.883 (0.746, 1.046) 0.151	0.809 (0.676, 0.970) 0.022	0.711 (0.535, 0.944) 0.018
Q3	0.785 (0.660, 0.933) 0.006	0.762 (0.634, 0.917) 0.004	0.779 (0.587, 1.033) 0.083
Q4	0.638 (0.532, 0.765) <0.001	0.641 (0.528, 0.777) <0.001	0.697 (0.512, 0.948) 0.021
P for trend	<0.001	<0.001	0.038

HR, hazards ratio.

95% CI: 95% confidence interval.

Model 1: non-adjusted.

Model 2: adjusted for age, sex, race, marital status, PIR, education level, and smoking history.

Model 3: adjusted for age, sex, race, marital status, PIR, education level, smoking history, hypertension, diabetes, CVDs, BMI, TG, HDL-c, LDL-c, and UA levels.

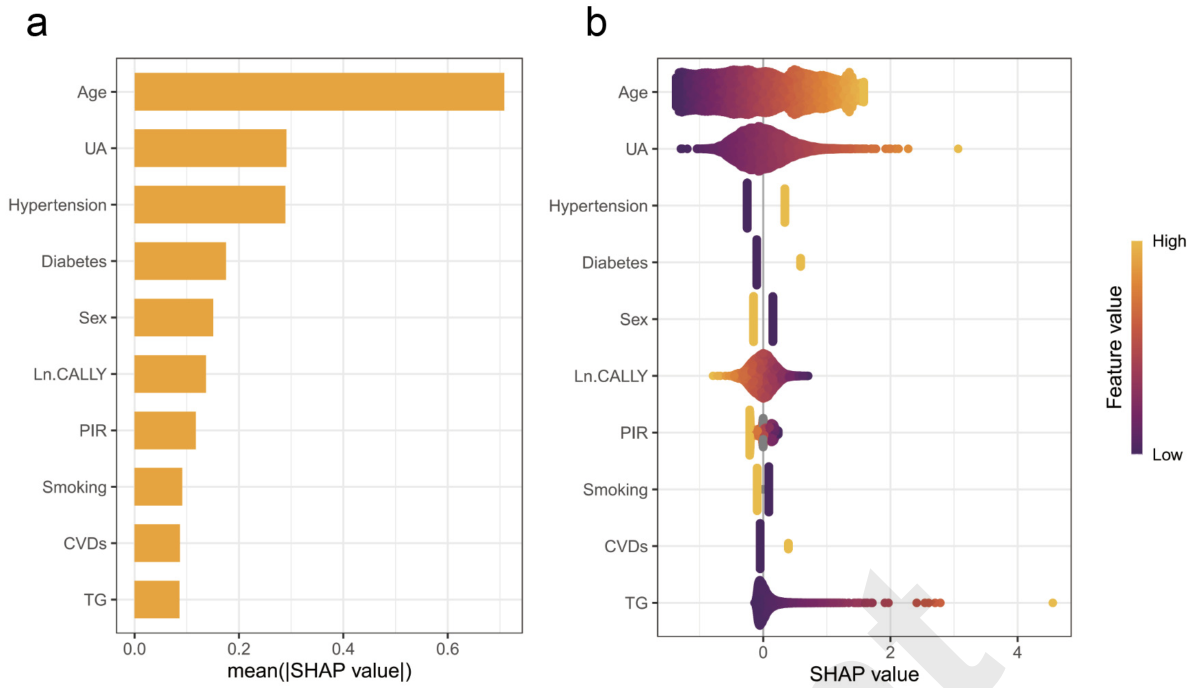

Figure 1 SHAP Value Analysis of Predictive Features. (a) Mean Absolute SHAP Value Ranking of Top 10 Features (b) SHAP Value Distribution Swarm Plot Showing Top 10 Features Impact and Value Relationships.

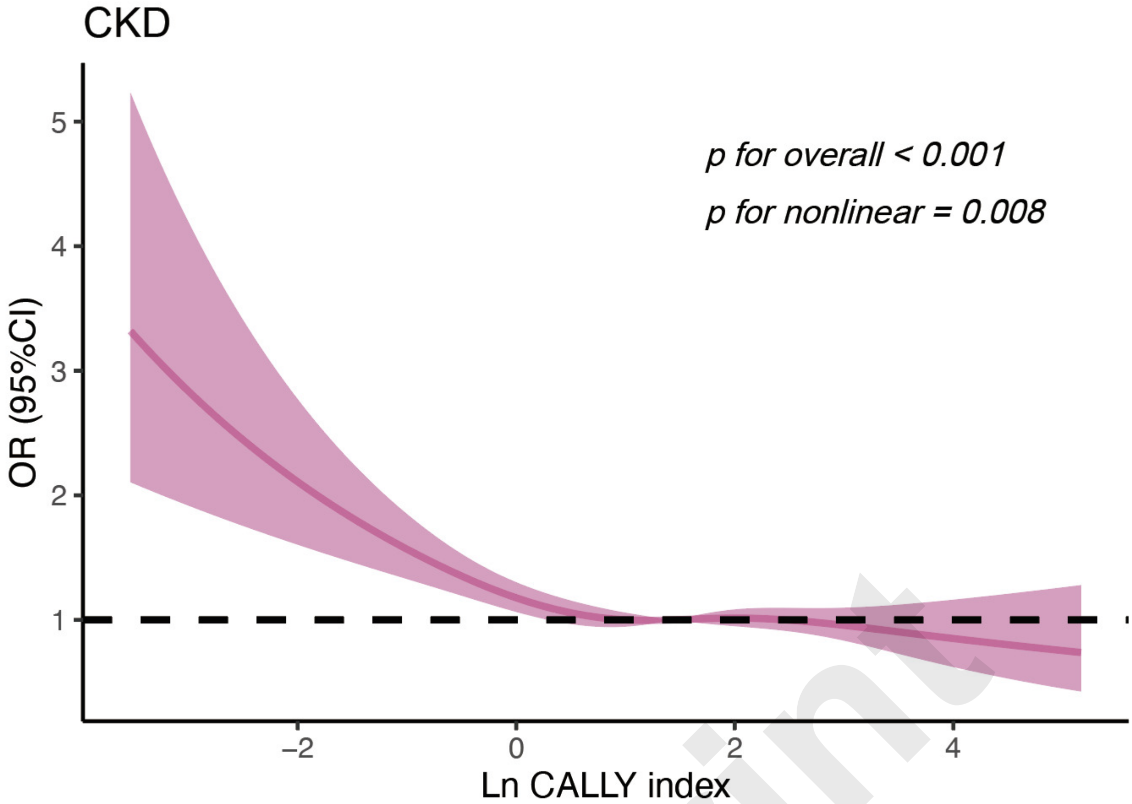

Figure 2 Restricted Cubic Spline Curve Demonstrating the Relationship Between Ln CALLY Index and CKD Risk.

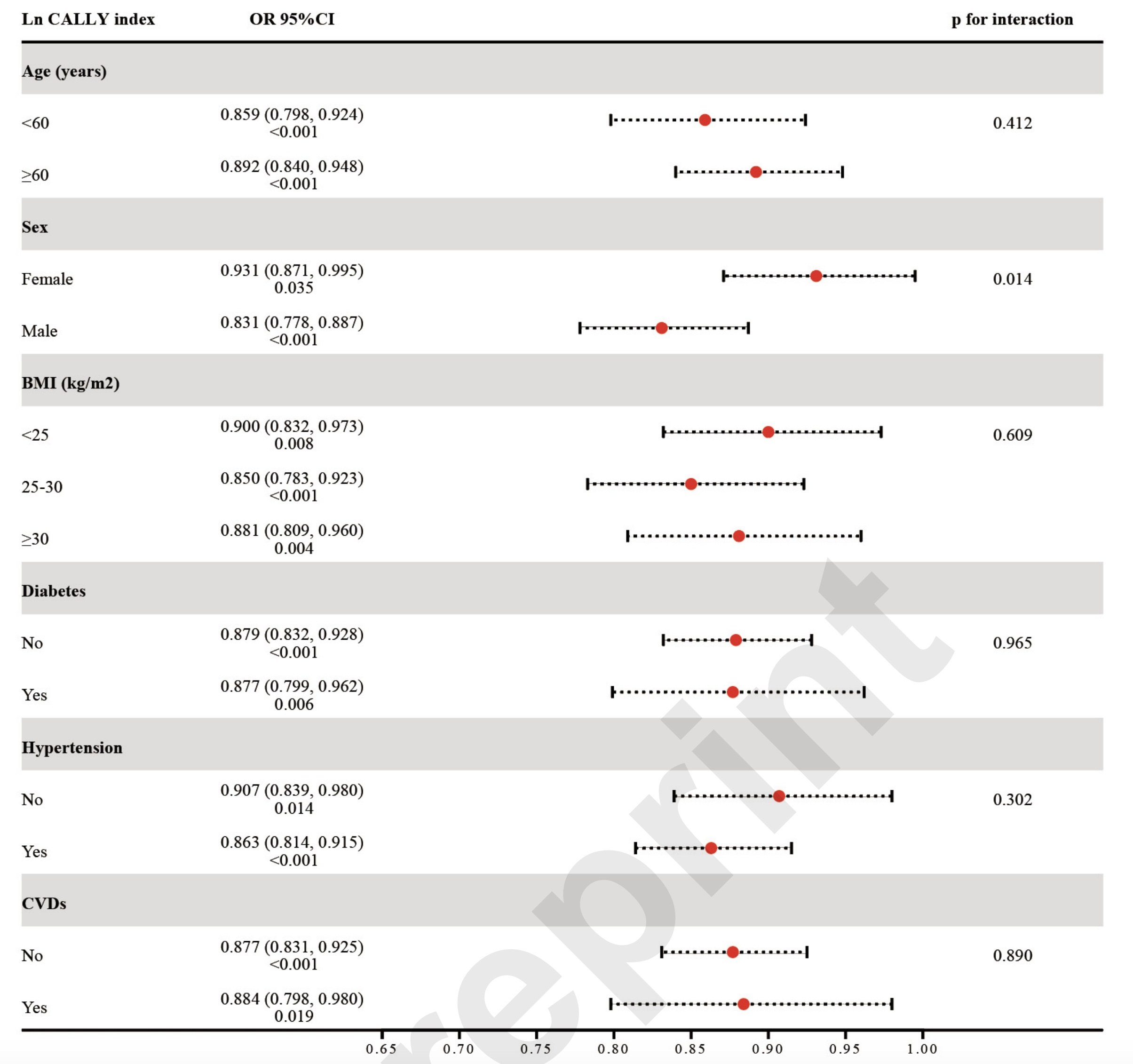

Figure 3 Subgroup-Specific Associations Between Ln CALLY Index and CKD Risk.

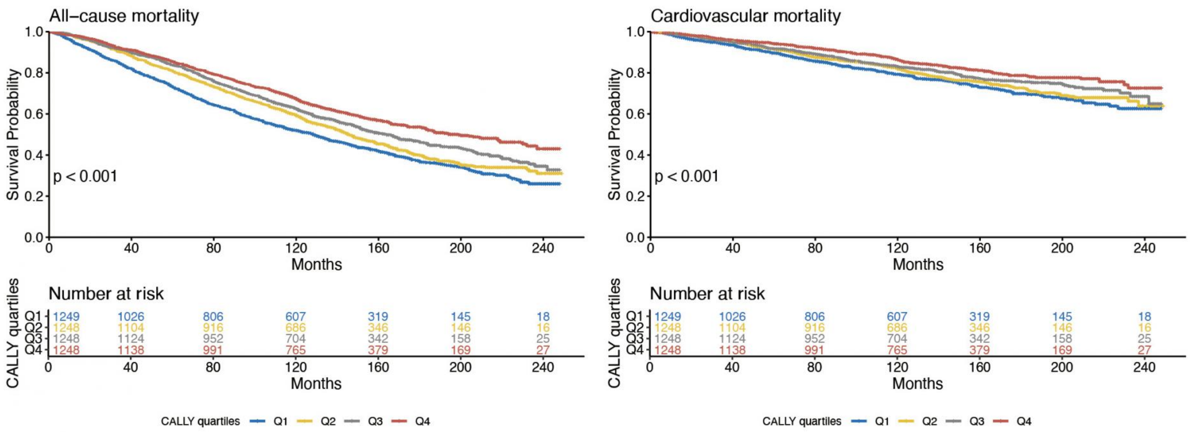

Figure 4 Kaplan-Meier Survival Curves for All-Cause and Cardiovascular Mortality According to CALLY Index Quartiles.